REVIEWERS

ESPGHAN would like to thank the following people for their services as Abstract Reviewers:

Nadeem Afzal
Carlo Agostoni
Assa Amit
Andras Arato
Henrik Arnell
Renata Auricchio
Irene Axelsson
Ulrich Baumann
Mark Beattie
Marc Benninga
Staffan Berglund
Patrick Bontems
Osvaldo Borrelli
Christian Braegger
Efrat Broide
Jiri Bronsky
Pierre Broue
Elaine Buchanan
Stephan Buderus
Yoram Bujanover
Sany Cadanel
Jaquim Calvo
Lerma
Angelo Campanozzi
Cristina Campoy
Foloso
Gemma Castillejo
Carlo Catassi
Christophe Chassard
Ania Chmielewska
Sonny Chong
Paula Crespo
Escobar
Nick Croft
Salvatore Cucchiara
Fugen Cullu
Çokuğraş
Lorenzo D’Antiga
Gerard Damen
Ruth De Bruyne
Elisabeth De Greef
Barbara de Koning
Lissy De Ridder
Thierry De Vreker
Dominique Debray
Tamas Decsi
Antal Dezsofi
Tietje Dijkstra
Jernej Dolinsek
Magnus Domellöf
Christoph Dupont
Ozlem Durmaz
Nick Embleton
Johanna Escher
Jackie Falconer
Mary Fewtrell
Natasa Fidler Mis
Yigael Finkel
Bjorn Fischer
Kim Fleischer
Michaelsen
Maria Fotoulaki
Esteban Frauca
Elvira George
Konstantinos
Gerasimidis
Isabel Goncalves
Costa
Emmanuel Gonzales
Frederic Gotttrand
Enke Grabhorn
Alfredo Guarino
Girish Gupte
Nedim Hadzic
Jane Hartley
Corina Hartman
Almuthe Christine
Hauer
Bruno Hauser
Loreto Hierro
Isa Hoffman
Iva Hojsak
Roderick Houwen
Jean-Pierre Hugot
Jessie Hulst
Seamus Hussey
Koen Huysentruyt
Flavia Indrio
Oleg Jadresin
Joerg Jehnel
Paloma Jara
Norman Junge
Panayota Kafritsa
Nicolas Kalach
Ino Kanavaki
Thomai
Karagiozoglou
Savvas V. Karkelis
Pia Karlslund-Akeson
Stavroula Karyda
Alemla Jaklin Kekez
Deirdre Kelly
Kathy Kennedy
Frank Kneepkens
Brigitte Kochavi
Henrik Köhler
Sanja Kolacek
Berthold Koletzko
Sibylle Koletzko
Bart Koot
Ilma Korponay-Szabo
Florence Lacaille
Alain Lachaux
Thierry Lamireau
Alexandre Lapillonne
Dariusz Lebenschstejn
Aron Lerner
Torbjörn Lind
Keith Lindley
Elena Lionetti
Andrea Lo Vecchio
Analou Louw
Thomas MacDonald
Sarah Macdonald
Giuseppe Maggiore
Markku Maki
Patrick McKiernan
Valerie McLin
Luisa Mearin
Dusanka Mitec-Turk
Erasm Miele
Giorgina Mieli-Vergani
Walter Mihatsch
Zrinja Mišak
Christian Molgaard
Yael Mozer-Glassberg
Thomas Müller
Simon Murch
Antal Nemeth
Jiri Nevoral
Edward Nieuwenhuis
Tena Nisetec
Valerio Nobili
Andreas Nydegger
Giuseppina Oderda
Joanne Olieman
Rok Orel
Anders Paerregaard
Ioanna Panayotou
Alexandra
Papadopoulu
Joanna Pawlowska
Licia Pensabene
Noel Peretti
Eva Pfister
Isabel Polanco
Irit Poraz
Hildegard Przyrembel
John Puntil
Shimon Reif
Carmen Ribes
Jacques Rigo
Firas Rinawi
Edmond Rings
Irena Rogelj
Eleftheria Roma
Claudio Romano
Kathleen Ross
Frank Ruemmele
Richard Russell
Silvia Salvatore
Camilla Salvestrini
Rene Scheenstra
Joachim Schweizer
Marco Sciveres
Neil Shah
Raanan Shamir
Eyal Shneyer
Marco Silano
Francoise Smets
Piotr Socha
Johannes Spalinger
Annamaria Staiano
Birgitta Strandvik
Hania Szajewska
Laszlo Szonyi
Merit Tabbers
Nikhil Thapar
Rut Anne
Thomassen
Mike Thomson
Sarah Tizzard
Patrick Tounian
Riccardo Troncone
Dominique Turck
Dan Turner
Christos Tzivinikos
Vaidotas Urbonas
Pietro Vajro
Saskia Van de Velde
Els Van de Vijver
Anemone van den Berg
Hans Van Goudeover
Indra Van Mourik
Patrick Van Rheezen
Myriam Van Winckel
Yvan Vandenplas
Gigi Veereman
Gabor Veres
Henk-Jan Verkade
Batia Weiss
Zvi Weizman
Jonathan Wells
Tobias Wenzl
Michael Wilschanski
David Wilson
Harland Winter
Philip Wintermeyer
Heiko Witt
Ioannis Xinas
Aglaias Zellos
Noam Zevt
Matthias Zilbauer
Clinical presentation and antibiotic susceptibility: results of the European pediatric helicobacter pylori registry

Michal Kori1, Katharina Werkstetter2, Andrea Sustmann3, Ana Isabel Lopez4, José Cabral5, Barbara Iwanczak6, Zrinjka Mišak7, Nicolas Kalach8, Ender Pehlivanoglu9, Meltem Ugras10, Matjaz Homan11, Maria José Martinez12, Pedro Urruzuno13, Mª Luz Cilleruelo Pascual14, Thomas Casswall15, Maria Rogalidou16, Sonny Chong17, Vaidotas Urbanas18, Eleftheria Roma19, Alexandra Papadopoulou20, Jernej Dolinšek21, Erasmo Miele22, Angelika Kindermann23, Francesca Rea24, Áron Cseh25, Sibylle Koletzko26

1Kaplan Medical Center, Rehovot, Israel  
2Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany  
3Dr. von Hauner Children's Hospital, Klinikum der Universität Munich, Munich, Germany  
4National Institute of Health, Lisbon; University Hospital Santa Maria, Lisbon, Portugal  
5Hospital Centre of Central Lisbon, Portugal  
6Medical University of Wroclaw, Wroclaw, Poland  
7Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia  
8St Vincent de Paul Hospital, Lille, France  
9Marmara University Faculty of Medicine, Istanbul, Turkey  
10Yeditepe University Medical Faculty, Pediatrics, Istanbul, Turkey  
11University Children's Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia  
12Hospital Niño Jesús, Madrid, Spain  
13Hospital Universitario Doce de Octubre, Madrid, Spain  
14Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain  
15Karolinska University Hospital, Stockholm, Sweden  
16University of Ioannina School of Medicine, Department of Pediatrics, Ioannina, Greece  
17Queen Mary’s Hospital for Children, St. Helier Hospital, Paediatrics, Carshalton, Surrey, United Kingdom  
18University Hospital Santariskiu Klinikos/ (Vilnius University Children's Hospital), Vilnius, Lithuania  
19National and Kapodistrian University of Athens, First Department of Paediatrics, Athens, Greece  
20Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece  
21University Medical Center (Umc) Maribor, Maribor, Slovenia  
22Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy  
23Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands  
24Bambino Gesu Children Hospital, Roma, Italy  
25Semmelweis University, Ist Department of Pediatrics, Budapest, Hungary

Objectives and study: Antibiotic resistance is one of the main causes for the low eradication rates of H. pylori infection. We aimed to describe the clinical presentation, endoscopic findings and antibiotic resistance of Helicobacter pylori (HP) strains in European pediatric patients.

Methods: Between 1/2013 and 9/2016 pediatric gastroenterologists from 21 centers in 16 European countries reported anonymously the clinical details of H. pylori infected patients to the EuroPedHP registry. Data included age, sex, height, weight and country of birth of child/parents, previous treatment for H. pylori, indication for endoscopy, endoscopic findings, antibiotic susceptibility results, and treatment prescribed. Antimicrobial susceptibility was measured with E-Test in 705 (75.4%), disk diffusion in 228 (24.4%) and real-time PCR in 1 (0.1%). Treatment success was evaluated using non-invasive tests (13C-urea breath test or stool antigen test).

Results: Of 934 included patients, 518 (55.5%) were female, mean age 12.0 yrs SD 4.0 range (1.4 – 21.0). There were 748 (80.1%) therapy naïve patients, 95 (10.1%) had received one, and 38 (4.1%) ≥ 2 treatment courses, previous treatment was unknown for 53 (5.7%). Indications for endoscopy
included abdominal pain in 580 (62.1%), dyspepsia in 102 (10.9%), anemia in 35 (3.8%), bleeding in 17 (1.8%), and other causes in 200 (21.4%) patients. Endoscopic findings revealed erosive or ulcerative esophagitis in 52 (5.5%) of patients. The macroscopic findings in the stomach revealed, nodularity, erosions and ulcers in 723 (77.4%), 94 (10.1%), and 12 (1.3%), respectively, and in the duodenum in 94 (10.1%), 42 (4.5%) and 41 (4.4%) respectively. Overall, antibiotic susceptibility results were not available in all patients, and were available for selected antibiotics only. The resistance rates were, clarithromycin (Cla) 28.8% (216/751), metronidazole (Met) 28.6% (214/748), amoxicillin 1.4% (9/628), tetracycline 0.2% (1/462), levofloxacin 4.8% (21/436) and rifampicin 12.9% (24/188). In 600 treatment naïve patients with results for both Cla and Met resistance, 354 (59.0%) were fully susceptible, 117 (19.5%) were resistant to Cla only, 96 (16.0%) resistant to Met only, and 33 (5.5%) were resistance to both antibiotics. Among 119 patients with known susceptibility who had failed at least one eradication treatment 28 (23.5%) were susceptible to both Met and Cla, 22 (18.5%) were resistant to Cla only, 34 (28.6%) resistant to Met, and 35 (29.4%) showed double resistance.

Conclusion: Our data from the European Pediatric Registry with biopsy-proven H. pylori infection confirms that gastric or duodenal, peptic ulcer disease (PUD) is rare in H. pylori infected symptomatic pediatric patients undergoing endoscopy (5.7%), while erosions without PUD are found more frequently but still uncommon (14.6%). Antibiotic resistance rates to Cla or Met prior to first treatment are high, 19.3% and 16% respectively. After treatment failure resistance to both Cla and Met raises from 5.5% to 29%. Our results support the recent recommendations from ESPGHAN/NASPGHAN that anti-H. pylori therapy including Cla or Met in pediatric patients should be tailored to antibiotic susceptibility in order to reach the goal of a primary eradication rate of at least 90%.
Intracellular localization of microbial transglutaminase and its influence on the transport of gliadin within human duodenal epithelium

Sebastian Stricker¹, Jan de Laffolie¹, Silvia Rudloff², Klaus-Peter Zimmer³

¹University Giessen, General Pediatrics and Neonatology, Giessen, Germany
²University Giessen, Institute of Nutritional Science, Giessen, Germany
³Zentrum für Kinderheilkunde und Jugendmedizin, Universitätsklinikum Gießen und M, General Pediatrics and Neonatology, Gießen, Germany

Objectives and study: Celiac disease (CD) is a complex inflammatory disorder triggered by the ingestion of gliadin and related prolamines. Its rising incidence over the past decades indicates that environmental factors play a major role in the pathogenesis. One of these factors might be microbial transglutaminase (mTG), an enzyme which is frequently used in the food industry to improve texture and nutritional characteristics of various food products and which could also originate from the intestinal microbiome. This protein, though showing a quite different amino acid sequence and ultrastructure, shares enzymatic and antigenic properties with the human tissue transglutaminase (TG2), the autoantigen in CD. In this study we aimed to examine the uptake and transport of the mTG in human duodenal biopsies of CD patients and controls and to further investigate the effect of this enzyme on the intracellular transport of gliadin.

Methods: Two biopsies were obtained from each of 7 CD and 11 control patients. One biopsy was incubated with mTG alone and one with mTG and simultaneously with Frazer's Fraction (FF), a pepsin/trypsin digest of gliadin. To ensure strict apical uptake of these proteins the biopsies were placed in one layer between two Ussing sliders. Three test series were performed: colocalization of mTG with the endoplasmic reticulum (ER) marker PDI as well as colocalization of gliadin with PDI or the late endosome (LE) marker LAMP2 in the presence of mTG. The evaluation of these experiments was performed on an electron microscopical level using immunogold for quantitation.

Results: In these two groups of CD patients and controls there was no significant difference in the distribution of mTG within enterocytes. MTG showed a strong labeling within the lamina propria, where gliadin was observed to a lesser extent. We found a significant amount of mTG within the ER of so-called RACE cells, which are characterized by an increased cytosolic antigen uptake (Am J Pathol 165: 425, 2004). In the presence of mTG, enterocytes in biopsies from CD patients showed more gliadin in the cytosol (31% in CD patients vs. 24% in controls, p = 0.024) and the basolateral membrane (9% in CD patients vs. 7% in controls, p = 0.011). However, controls contained more gliadin at the apical membrane than CD patients (13% vs. 9%, p = 0.008). In both groups the proportion of gliadin in the ER (8% in CD patients and 6% in controls) and LE (3% in CD patients and 2% in controls) of enterocytes exceeded the background label.

Conclusion: This study was the first to investigate the intraepithelial transport of mTG. Our findings reveal that mTG may influence the intracellular localization of gliadin in the intestinal mucosa of CD patients. We demonstrated that mTG reaches the lamina propria, indicating an antigenic interaction with cells of the immune system. Since mTG may not only been taken up with food stuffs, but could also be produced by bacteria from the intestinal microbiota, further investigations are needed with regard to the safety of mTG for CD patients and its role in pathogenesis.
Objectives and study: Hematopoietic stem transplant is considered the only curative therapy for monogenetic very early onset inflammatory bowel disease (VEOIBD) patients with specific immune defects such as Interleukin-10 Receptor-A/B (IL10RA/B) deficiency. We examined a reduced intensity conditioning regime and umbilical cord blood transplant in VEOIBD patients with IL10RA-deficiency. Our study enrolled a total of 7 VEOIBD patients (5 female, 2 male) with typical manifestations (recurrent and severe diarrhea within the first month of life, perianal complications), and 6 of them had malnutrition, 2 underwent gut-fistulation operations, 3 had family history.


<table>
<thead>
<tr>
<th>P1</th>
<th>P2</th>
<th>P3</th>
<th>P4</th>
<th>P5</th>
<th>P6</th>
<th>P7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Transplantation age</td>
<td>6mo</td>
<td>33mo</td>
<td>15mo</td>
<td>20mo</td>
<td>7mo</td>
<td>10mo</td>
</tr>
<tr>
<td>Transplantation BW</td>
<td>3.0kg</td>
<td>8.5kg</td>
<td>10.0kg</td>
<td>6.6kg</td>
<td>8.0kg</td>
<td>5.9kg</td>
</tr>
<tr>
<td>Chemotherapy strategy</td>
<td>RIC</td>
<td>RIC</td>
<td>RIC</td>
<td>MAC</td>
<td>RIC</td>
<td>RIC</td>
</tr>
<tr>
<td>Allele-matched HLA</td>
<td>8/10</td>
<td>9/10</td>
<td>10/10</td>
<td>8/10</td>
<td>8/10</td>
<td>8/10</td>
</tr>
<tr>
<td>Chimerism</td>
<td>98.6%(4wk)</td>
<td>99.3%(4wk)</td>
<td>99.30%(4wk)</td>
<td>99.97%(8wk)</td>
<td>98.26%(3wk)</td>
<td>99.89%(2wk)</td>
</tr>
<tr>
<td>Engraftment of neutrophils</td>
<td>Day +22</td>
<td>Day +33</td>
<td>Day +30</td>
<td>Day +22</td>
<td>Day +21</td>
<td>-</td>
</tr>
<tr>
<td>Engraftment of platelets</td>
<td>Day +26</td>
<td>Day +31</td>
<td>Day +27</td>
<td>Day +25</td>
<td>Day +28</td>
<td>-</td>
</tr>
<tr>
<td>GVHD and infections</td>
<td>II skin &amp; gut &amp; I gut liver CMV infection</td>
<td>II skin &amp; I liver Idiopathic pneumonia syndrome</td>
<td>II skin &amp; I &amp; liver Sepsis CMV infection</td>
<td>II skin &amp; liver</td>
<td>II skin CMV infection</td>
<td></td>
</tr>
<tr>
<td>Clinical status</td>
<td>CR</td>
<td>CR</td>
<td>CR</td>
<td>Dead</td>
<td>CR</td>
<td>Dead</td>
</tr>
</tbody>
</table>
Methods: We diagnosed seven VEOIBD infants with IL10RA gene deficiency by the Whole Exome Sequencing and Sanger Sequencing, and confirmed the impaired function of IL10 signaling axis. Umbilical cord blood transplant were performed in seven patients, and six received reduced intensity conditioning regimen and one received myeloablative-conditioning regimen.

Results: All seven IL10RA-deficiency patients received transplants at aged from 6 months to 33 months (average 14.8 months) with body weight ranged from 3 to 10 kg (average 6.8 kg). All of them had complete chimerism at 2-8 weeks after transplant, and six had successful engraftment of neutrophils and platelets. As a result, depending on our follow-up, five had complete remission without evidence of graft-versus-host disease or infections, while one died of multiple organ dysfunction syndrome (MODS) due to lung rejection at 6 months after transplant and another one died of MODS due to sepsis at 1 month after transplant (Table 1). Severe malnutrition and growth failure associated with IL10RA-deficiency were significantly improved post-transplant.

Conclusion: Based on our experience with these seven IL10RA-deficiency patients, we recommend umbilical cord blood transplant as a potential treatment for VEOIBD with a defined monogenetic immunodeficiency, and we suggest that reduced intensity conditioning chemotherapy is more suitable for the patient with severe malnutrition and bowel disease. To our knowledge, we took the lead in performing reduced intensity conditioning regimen and umbilical cord blood transplant to the IL10RA-deficiency patient with the youngest age (6 months) and lowest body weight (3 kg). So far, we are the single center that had the most successful cases.
The ability of the Rome III criteria and alarm symptoms to distinguish between pain-predominant functional gastrointestinal disorders and organic disorders in children

Agneta Uusijärvi¹, Ola Olen², Martina Eriksson³, Petter Malmborg⁴, Henrik Arnell¹

¹Karolinska University Hospital, Alb Children's Hospital, Paediatric Gastroenterology, Hepatology and Nutrition, Se-141 86 Stockholm, Sweden
²Karolinska Institutet, Department of Medicine Solna, Clinical Epidemiology Unit, Stockholm, Sweden
³Karolinska Institutet, Diagnostic Radiology, Stockholm, Sweden
⁴Sachsska Children's Hospital, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden

Objectives and study: The main objective of this study was to explore the ability of questionnaire-based Rome III criteria, alone and in combination with alarm symptoms, to discriminate between organic and functional diagnoses in children with gastrointestinal symptoms. A second aim was to describe all investigations that this group of patients underwent in clinical practice.

Methods: Consecutive patients aged 4-17 years (median age 10.8 years) seeking health care due to gastrointestinal symptoms in non-primary care in Stockholm 2013-2014 were offered participation. At inclusion, patients (or parents if the child was aged <10 years) answered a translated and adapted questionnaire, based on the Questionnaire on Paediatric Gastrointestinal Symptoms Rome III (QPGS-RIII) and alarm symptoms. The treating physician was blinded to the questionnaire response. A minimum of 6 months after the inclusion visit, the patients’ medical charts, including the medical charts prior to inclusion, were reviewed. Two experienced paediatric gastroenterologists set the most likely clinical diagnosis, independently from each other. In case of differing diagnosis these patients were discussed by the two experts until consensus was reached (‘gold standard’). Descriptive statistical analyses were performed.

Results: Of 258 children seeking health care for gastrointestinal symptoms, 16% had organic causes, 54% were diagnosed with pain-predominant functional gastrointestinal disorders (pFGID) and 30% were diagnosed with other functional causes (e.g. functional constipation). Most patients (59%) had made two or more previous visits for gastrointestinal complaints. A majority of the patients were tested for IgA transglutaminase antibodies (93%) and faecal calprotectin (59%). A minority (19%) of the patients underwent endoscopy. Abdominal x-ray or ultrasound was performed in 43% of the patients. Alarm symptoms were equally common in patients with organic diseases and functional disorders (83% and 80% respectively, p=0.66). The accuracy of a diagnosis set according to the Rome III criteria +/- alarm symptoms, extracted from patient responded questionnaires is presented in the table.
Conclusion: A symptom profile questionnaire based on the Rome III criteria was poor at discriminating between pFGID and organic causes of gastrointestinal symptoms and does not seem to have the potential to be a helpful decision tool for clinicians. Alarm symptoms according to a questionnaire were equally common among children with organic or functional disorders.

Table: Test characteristics of a patient responded questionnaire (Rome III criteria +/- alarm symptoms), children with non-pain-predominant functional disorders excluded.

<table>
<thead>
<tr>
<th>pFGID Questionnaire</th>
<th>Gold standard</th>
<th>pFGID Questionnaire + negative alarm symptoms</th>
<th>Gold standard</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>pFGID¹</td>
<td>OGIS²</td>
<td>Total</td>
</tr>
<tr>
<td>pFGID¹</td>
<td>104</td>
<td>27</td>
<td>131</td>
</tr>
<tr>
<td>no pFGID¹</td>
<td>30</td>
<td>13</td>
<td>43</td>
</tr>
<tr>
<td>Total</td>
<td>134</td>
<td>40</td>
<td>174</td>
</tr>
</tbody>
</table>

Sensitivity: 104/134=0.78
Specificity: 13/40=0.32
Positive predictive value: 104/131=0.79
Negative predictive value: 13/43=0.30

Sensitivity: 20/134=0.15
Specificity: 36/40=0.90
Positive predictive value: 20/24=0.83
Negative predictive value: 36/150=0.24

¹Pain-predominant functional gastrointestinal disorder according to the paediatric Rome III criteria
²Clinical diagnosis according to review of patient charts
³Organic gastrointestinal disorder
Screening for type 1 diabetes-, thyroid-, gastric- and adrenal-specific humoral autoimmunity in 529 celiac children and adolescents at diagnosis identifies as positive 1 every 9 patients

Chiara Maria Trovato¹, Claudio Tiberti², Francesca Panimolle², Francesco Valitutti¹, Caterina Anania¹, Susanna Morano², Salvatore Cucchiara³, Monica Montuori¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
²Sapienza University of Rome, Dept. of Experimental Medicine, Rome, Italy
³Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy

Objectives and study: Organ-specific autoimmune disorders are often associated with coeliac disease (CD). The coexistence of CD and organ-specific autoimmune disorders appears at least partly due to a common genetic predisposition localized in the HLA region of chromosome 6 (HLA DR3-DQ2 and DR4-DQ8 haplotypes). The aim of this study was to evaluate retrospectively, in a large cohort of 529 CD patients at disease diagnosis, the specific humoral immunoreactivity for four organ-specific autoimmune disorders known to be correlated to CD, namely type 1 diabetes, autoimmune thyroid disease, Addison’s disease and autoimmune atrophic gastritis.

Methods: A total of 529 coeliac patient sera at disease diagnosis (332 females; age range 3.0-17.7 years, mean age 8.8 ± 3.5 years) consecutively collected between 2005 and 2015. At the moment of the blood collection all the CD patients recruited in the study were on a gluten-containing diet and all of them underwent intestinal biopsies. The control group consists of 264 healthy subjects (CTRL) (104 females; age range 3.0-18.0 years, median age 11.8 ± 3.0 years) collected between 2010 and 2015. The immune response directed against insulin, glutamic-acid decarboxylase, tyrosine-phosphatase 2 (a.a.605-979), zinc cation efflux transporter, enzyme steroid 21-hydroxylase and parietal cells was analysed by a fluid-phase radioimmunoprecipitation method whereas thyroid peroxidase autoantibodies (TPOAb) were measured by using a commercially available RIA kit. The study was approved by the Ethical Committee of “Sapienza” University of Rome.

Results: Of 529 CD patients, 11.7% were positive for at least one of the organ-specific antibodies investigated, more frequently than CTRL subjects (6.4%, p=0.023), with type 1 diabetes-specific immune response significantly higher compared to thyroid and adrenal (p=0.006 and p<0.0001, respectively) but not gastric immunoreactivities. All of type 1 diabetes, atrophic-gastritis and Addison’s autoantibody-positive CD patients were not affected by the relative disease. Only 4.8% of autoantibody-positive CD patients had more than one disease-specific immunoreactivity.

Conclusion: 1 every 9 CD patients is positive for at least one among diabetes-, thyroid-, atrophic-gastritis- and adrenal-specific humoral autoantibodies. Despite our findings downside previous epidemiological data available in literature, this might still suggest to evaluate the prevalence of organ-specific autoimmunity at CD diagnosis.
The natural history of pediatric diagnosed coeliac disease: a 30 years follow-up study

Lorenzo Norsa¹, Marianna Bravo², Francesca Ferretti², Federica Branchi², Maria Teresa Bardella², Luca Elli²

¹Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
²Fondazione Ircss Ca' Granda Ospedale Maggiore Policlinico, Center for Prevention and Diagnosis of Celiac Disease, Milano, Italy

Objectives and study: Studies on patients with coeliac disease (CD) on very long follow-up are limited. We aim to evaluate clinical history, dietary adhesion, compliance to regular clinical follow up and accuracy of the gluten free diet (GFD) in patients with CD, diagnosed more than 30 years ago.

Methods: We collected data regarding clinical history of 196 patients. A questionnaire about GFD and gluten free products was returned by 90 of them. Patients were divided into 3 groups according to their adherence to GFD: 133 patients on a lifelong strict GFD, 29 patients on GFD but with at least 5 years of gluten containing diet (GCD), and 35 patients who reported to be on a GCD.

Results: No significant differences were found between groups regarding symptom and histology diagnosis, onset of associated autoimmune disorders, family history of CD and compliance to follow up. Follow-up histology was performed in 63 of them, with a significantly higher normal histology (p<0.0324) in patients on GFD. We recorded patients 20 patients with normal histology on GCD. No significant differences were found between groups in scores in GFD questionnaire.

Conclusion: We couldn’t highline any predictive factor to poor GFD adherence in adulthood. Poor adherence to the GFD is the major predictor of persistence of mucosal lesions but it does not necessarily imply the development of mucosal damage. A strict GFD does not necessarily lead to complete mucosal healing. A GCD does not necessarily cause relapse of villous atrophy. All patients shown a good knowledge of dietary rules and food gluten content, with high scores regardless their actual compliance to the GFD.
Genetic and serological profile as markers of disease susceptibility in siblings of children with inflammatory bowel disease

Marina Aloi1, Giulia D'Arcangelo2, Matteo Bramuzzo3, Giulia Catassi4, Claudio Romano5, Erasmo Miele6, Giuliana Morabito7, Salvatore Pellegrini8, Chiara Cuzzupà9, Caterina Strisciuglio10, Stefano Martelossi11, Salvatore Cucchiara1

1Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
2Sapienza University of Rome, Italy
3Gastroenterology and Nutrition Unit Institute for Maternal and Child Health, Irccs “burlo Garofalo”, Trieste, Italy
4Sapienza University, Rome, Italy
5University of Messina, Pediatrics Department, Messina, Italy
6Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
7University of Messina, Italy
8Policlinico Universitario G Martino, Messina, Italy
9Gastroenterology and Nutrition Unit Institute for Maternal and Child Health, Irccs “burlo Garofalo”, Trieste, Italy
10Second University of Naples, Department of Woman, Child and General and Specialistic Surgery, Naples, Italy
11Institute for Maternal and Child Health - Irccs “Burlo Garofolo”, Paediatric Department, Trieste, Italy

Objectives and study: Having a family history for inflammatory bowel disease (IBD) is the only known risk factor for disease development. Indeed, up to 30% of IBD patients report at least 1 first-degree relative with IBD, and siblings carry the highest risk. Recent data have shown that genetic and serological markers may predict IBD development. However, there are only few studies evaluating a genetically well-characterized population and at high risk for disease, such as siblings and twins. Therefore, aim of this study was to evaluate genetic and serological findings as markers of disease susceptibility in healthy siblings and twins of children with IBD.

Methods: This is the first phase of a prospective, longitudinal, multicenter, case-control study. Serum was collected from 80 siblings and twins of children with IBD and 77 healthy controls with no family history for IBD. Genotyping (Taqman) for variants of ATG16L1 (SNP rs2241880), STAT3 (SNP rs744166), ECM1 (SNP rs3737240), NKX2-3 (SNP rs10883365), was performed. Serological titers of anti-Saccharomyces cerevisiae (ASCA IgG and ASCA IgA), anti-neutrophil Cytoplasmic Antibodies (ANCA), anti-outer membrane porin C antibody (anti-OmpC), and antibacterial flagellin antibody (anti-CBir1), anti-A4-Fla2 (Fla2) and anti-FlaX (FlaX) were determined by specific enzyme-linked immunosorbent assay (ELISA). Perinuclear anti-neutrophil cytoplasmic antibodies (pANCA) was also performed using indirect immunofluorescence.

Results: Fifty-nine out of 80 cases (74%) and 50/77 controls (65%) were positive for at least 1 of the serum autoantibodies (p=0.29); a combination of any 4 of them was found in 3 cases (4%) and no controls (p=0.28). No significant difference was shown for any of the studied autoantibodies between cases and controls. Homozigosity for any susceptibility gene variant was found in 60 out of 80 cases (75%) and in 52/77 controls (67.5%) (p=0.37), with no significant association between family history and genotype status. No combination of gene variants significantly differed between cases and controls.

Conclusion: Our preliminary results argue against a role of commonly recognized genetic polymorphisms and microbial antibodies as markers of disease susceptibility in siblings of children with IBD. However, data from larger and prospective studies, possibly including microbial characterization, are warranted before drawing definite conclusions.
Practice differences in the diagnosis and management of adult and paediatric eosinophilic oesophagitis

Eyal Zifman1, Hagar Banai2, Raanan Shamir3, Yehuda Ringel4, Noam Zevit3

1Pediatric Gastroenterology Clinic, Meir Medical Center, Kfar Saba, Israel
2Department of Gastroenterology, Rabin Medical Center, Petach Tikva, Israel
3Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Petach-Tikva, Israel
4Department of Medicine, University of North Carolina School of Medicine, Chapelhill, United States

Objectives and study: Guidelines for the diagnosis and treatment of eosinophilic oesophagitis (EoE) do not differ significantly between adult and paediatric patients. However, it is not known if gastroenterologists treating adult or paediatric patients differ in their practice outside of research settings. We aimed to characterize the diagnostic and management practices of gastroenterologists who treat either adult (AG) or paediatric (PG) patients suspected of or diagnosed with EoE.

Methods: A 19 question multiple choice questionnaire was given to AG and PG during a scientific conference held in February 2016. Questions explored four areas of interest including: physician demographics, diagnosis and tissue sampling practices, management, and the need for societal publications on EoE.

Results: Filled questionnaires were returned by 85/180 AG and 30/40 PG. Special interest in EoE was reported more frequently by PG (53%) vs. AG (23%) (p=0.007). Compared to PG, AG had fewer EoE patients under their care (14% vs. 63% for ≥4 patients; p<0.001) and took oesophageal biopsies significantly less frequently in several scenarios: routine endoscopy without macroscopic findings (10% vs. 57%; p<0.001), dysphagia without macroscopic findings (83% vs. 100%; p=0.019), and gastro-oesophageal reflux symptoms with distal oesophageal erythema (44% vs. 100%; p<0.001). Fewer AG reported taking gastric and duodenal biopsies when EoE was suspected compared to PG (29% vs. 90%; p<0.001). Both groups reported that they perform proton pump inhibitor tests routinely (77% vs. 83%, p=0.47). However, in contrast to recommendations, AG more often follow patients clinically rather than endoscopically (30% vs. 0%, p<0.001). They were also far less inclined to implement elimination diets compared to PG (23% vs. 68%; p<0.001). Reading a guideline on EoE was reported by 44% of AG compared to 93% of PG (p<0.001). Only 53% of AG felt comfortable transitioning a paediatric patient to their adult practice while on an elimination diet, and 10% responded that they would not feel comfortable treating a stable EoE patient even after a completed work up.

Conclusion: Significant diagnostic and treatment disparities exist between gastroenterologists treating adult or paediatric patients with EoE. Differences spanned almost all diagnostic and management choices evaluated. These findings may impact rates of diagnosis, appropriate treatments and monitoring, and long term outcomes. They may also impact the success of transition from paediatric to adult care.
**GASTROENTEROLOGY: Coeliac disease**

G-O-009

**Prospective evaluation of transglutaminase antibody cut-off levels to predict screen-detected coeliac disease in the PreventCD cohort**

Ilma Rita Korponay-Szabo 1, Judit Gyimesi 2, Katharina Werkstetter 3, Sabine Vriezinga 4, Peter Szillat 5, Eckart Mummert 5, Gemma Castillejo 6, Paula Crespo Escobar 7, Corina Hartman 8, Renata Auricchio 9, Ania Chmielewska 10, Eva Martinez-Ojinaga Nodal 11, Isabel Polanco 12, Hania Szajewska 12, Sanja Kolacek 13, Raanan Shamir 14, Carmen Ribes Koninckx 15, Sibylle Koletzko 16, Riccardo Troncone 17, Luisa Mearin 18

1 University of Debrecen and Heim Pál Children's Hospital, Debrecen and Budapest, Hungary
2 Heim Pál Children's Hospital, Coeliac Disease Center, Budapest, Hungary
3 Dr. von Hauner Children's Hospital, LMU Munich, Division of Pediatric Gastroenterology and Hepatology, Munich, Germany
4 Leiden University Medical Center, Pediatrics, Leiden, Netherlands
5 Phadia GmbH Thermo Fisher Scientific, Freiburg, Germany
6 Hospital Universitario Sant Joan de Reus, Pediatric Gastroenterology Unit, Reus, Spain
7 Hospital Universitari I Politecnic La Fe, Valencia, Spain
8 Schneider Children's Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel
9 University “Federico II”, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy
10 Umeå University, Department of Clinical Science, Umeå, Sweden
11 La Paz University Hospital, Dept. of Pediatric Gastroenterology and Nutrition, Madrid, Spain
12 The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
13 Zagreb University Medical School, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
14 Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
15 La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
16 Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
17 University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy
18 Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands

**Objective and study:** Current ESPGHAN guidelines allow the non-invasive diagnosis of paediatric coeliac disease (CD) in clinical patients with relevant symptoms, serum transglutaminase 2 antibody levels above 10 times of the upper limit of normal (ULN), endomysial antibody positivity (EMA) and an HLA-DQ2 or DQ8 background. In this study we evaluated whether high serum antibody concentrations also predict CD in prospectively followed, regularly screened family members.

**Methods:** The PREVENTCD multicenter FP6 study (www.preventcd.com) enrolled in 8 European countries 977 DQ2 and/or DQ8 positive newborns with at least one family member diagnosed with CD and 944 were randomized for a prospective dietary intervention consisting of 100 mg of gluten per day or placebo between 4-6 months of age. After this, both groups consumed gradually increasing gluten amounts. Serum samples were collected at the age of 4, 6, 9, 12, 18 and 24 months, and then annually. I gA antibodies against transglutaminase 2 (TGA) and gliadin (AGA) were determined at Phadia’s laboratory. TGA was measured in years 2007-2014 by the Celikey Varelisa test, in years 2015-2016 by the Celikey ELIA method, which both utilize the same antigen but have 5 U/ml and 7 U/ml positivity cut-offs (as declared by the manufacturer), respectively. EMA tests were performed locally as needed. A small bowel biopsy was offered to asymptomatic children with persistent seropositivity (at least two TGA+ or three AGA+ results) or when symptoms appeared. CD was diagnosed in children with Marsh III histology lesions according to central evaluation by a reference pathologist blinded to the clinical and antibody results. In case of decreasing or increasing TGA
concentrations, the highest value before biopsy was taken into account. IgA deficient subjects were excluded from the present analysis.

**Results:** During follow-up, small bowel biopsy was performed in altogether 144 children and 124 children were diagnosed with CD by histology of whom 67 (54%) were asymptomatic. Of the 149 TGA+ children, 71 (48%) had values >100U/ml, 36 (24%) had values between 30-100U/ml and 42 had values <30 U/ml of which 14/42 had transient seropositivity. The table shows predictive values of TGA+ results. There was no statistical difference for disease prediction between symptomatic and asymptomatic children with TGA+ levels >4.0xULN.

**Table:**

<table>
<thead>
<tr>
<th>TGA-IgA xULN</th>
<th>Number of children</th>
<th>Number biopsied</th>
<th>Diagnosed with CD</th>
<th>Sensitivity for CD</th>
<th>Positive predictive value for CD (95% confidence interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt;1.0</td>
<td>149</td>
<td>127</td>
<td>122</td>
<td>99.2</td>
<td>96.1 (90.6-98.5)</td>
</tr>
<tr>
<td>&gt;2.0</td>
<td>135</td>
<td>120</td>
<td>115</td>
<td>93.5</td>
<td>95.8 (90.1-98.5)</td>
</tr>
<tr>
<td>&gt;4.0</td>
<td>119</td>
<td>110</td>
<td>109</td>
<td>88.6</td>
<td>99.1 (94.3-99.9)</td>
</tr>
<tr>
<td>&gt;6.0</td>
<td>105</td>
<td>100</td>
<td>100</td>
<td>81.3</td>
<td>100 (95.4-100)</td>
</tr>
<tr>
<td>&gt;10.0</td>
<td>93</td>
<td>88</td>
<td>88</td>
<td>71.5</td>
<td>100 (94.8-100)</td>
</tr>
</tbody>
</table>

**Conclusion:** TGA+ levels >6xULN measured by the utilized kits in one centralized laboratory safely predicted CD both in symptomatic and asymptomatic children and antibodies above this level were unlikely to disappear during follow up. Predictive cut-off levels of other TGA measuring kits may substantially differ and such differences, as well as inter-laboratory variations should be carefully considered when applying ESPGHAN guidance for omitting biopsy. Test-specific predictive values are to be systematically established in prospective studies on larger cohorts.

**Disclosure of interest:** E. Mummert and P. Szillat are employees of Phadia GmbH. The other authors have no conflict of interest.
Mass screening for coeliac disease among Saudi school-aged children: toward exploring the coeliac iceberg in Saudi Arabia

Abdulrahman Al-Hussaini1, Musa Khormi2, Moath Al-Turaiki3, Mosa Fagih4, Waheed Alkhamis5, Mona Al-Rajhi6, Thana Halal5, Sahar Alharbi6, Salman Bashir7, Aziz Alami Chentoufi8, Riccardo Troncone9

1King Fahad Medical City, Children’s Specialized Hospital, Riyadh, Saudi Arabia
2King Saud Medical City, Riyadh, Saudi Arabia
3King Salman Hospital, Riyadh, Saudi Arabia
4King Fahad Medical City, Pathology, Riyadh, Saudi Arabia
5Ministry of Education, Riyadh, Saudi Arabia
6King Fahad Medical City, Immunology Laboratory, Riyadh, Saudi Arabia
7King Fahad Medical City, Riyadh, Saudi Arabia
8King Fahad Medical City, Immunology, Riyadh, Saudi Arabia
9University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy

Background and objectives: Several reports from Europe suggested a prevalence rate of celiac disease (CD) of 1:100. In contrast, there are no comparable epidemiological studies in Saudi Arabia where CD is widely perceived as being uncommon. The objectives of the study were to determine the prevalence of CD and characterize the celiac iceberg among Saudi pediatric population in Riyadh, the capital city of Saudi Arabia.

Methods: Over the study period (January 2014 to June 2016), we have conducted a cross-sectional and prospective mass screening study that involved blood collection from a randomly selected 7931 Saudi students from primary and intermediate schools of both sexes in different regions of Riyadh. The blood specimens were tested for IgA-tissue transglutaminase (IgA-TTG). Students with positive IgA-TTG (> 20 U/L) were called in hospital to undergo a repeat of IgA-TTG and IgA-endomyseal antibody (IgA-EMA) test for borderline positive IgA-TTG (TTG = 20 – 60 U/L). Children with IgA-TTG > 60 U/L and children with borderline positive IgA-TTG and positive IgA-EMA were advised to undergo upper endoscopy and intestinal biopsies to confirm the diagnosis of CD. The diagnosis of CD was based on presence of ≥ Marsh grade 2 on biopsies or IgA-TTG > 200 U/L and positive IgA-EMA. In addition, we tested a random sample of 192 Saudi children for presence of CD-predisposing HLA-DQ2 and HLA-DQ8 alleles.

Results: We identified 222 students with positive IgA-TTG (2.8%). Celiac disease was diagnosed in 120 cases (1.5%, 1.67 Saudi children) [Mean age 11.5 ± 2.62 years; females 81 (78.6%)]. Another 51 children had persistently borderline positive IgA-TTG but negative EMA (0.64%) and the remaining 51 had transiently positive IgA-TTG. We have identified 3 patterns of clinical presentation in the 120 celiac cases: First is a clinically silent pattern which constituted 37% of the cases, second was a mild symptomatic form characterized by low grade intensity GI symptoms in presence of normal growth or overweight/obesity (48%), and a third form (15%) was characterized by GI symptoms and impaired growth. Children with CD had abdominal pains and growth impairment significantly more than the non-celiac group. The level of IgA-TTG titer correlated positively with the grade of villous atrophy on intestinal biopsies. ROC-curve analysis for the best cut-off value of IgA-TTG level for diagnosis of CD was 40 U/L (sensitivity 91.3% and specificity 75%). Fifty seven percent of the Saudi population carries HLA-DQ2 or DQ8 alleles.

Conclusion: Our study provides evidence of a high prevalence of CD among Saudi children (1.5%); a rate that is at least 2 times the average prevalence rate in Europe and North America. The high genetic susceptibility of the Saudi population could partially explain the high prevalence of CD in Saudi Arabia.
Dietary intake of milk powder before 2 years of age is not associated with coeliac disease in genetically at risk children: a prospective Swedish case-control study

Elin Malmberg Hård af Segerstad, Hye-Seung Lee, Carin Andrén Aronsson, Kalle Kurppa, Sibylle Koletzko, Ulla Uusitalo, Jimin Yang, Suvi M. Virtanen, Jill Norris, Daniel Agardh

1Skåne University Hospital, Department of Paediatrics, Malmö, Sweden
2Health Informatics Institute, Morsani College of Medicine, Department of Pediatrics, Tampa, Florida, United States
3Lund University, Department of Clinical Sciences, Malmö, Sweden
4University of Tampere and Tampere University Hospital, Tampere Centre for Child Health Research, Tampere, Finland
5Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
6University of South Florida College of Medicine, Tampa, United States
7Health Informatics Institute, Morsani College of Medicine, University of South Florida, Tampa, United States
8National Institute for Health and We, Haemeenlinna, Finland
9Colorado School of Public Health, Dept. of Epidemiology, Aurora, Co, United States

Objectives and study: Infant feeding practices has been postulated to explain country differences in prevalence of early childhood coeliac disease (CD). An intake of >5.0 g gluten per day imposed an almost 3-fold increased risk for CD in Swedish children compared to children consuming <5.0 g gluten per day before 2 years of age. Commercial porridges and gruels based on milk powder and gluten-containing cereals are common in the Swedish infant diet. During the production of milk powder, the milk is heated and evaporated whereby carbohydrates (lactose) react with proteins forming glycated proteins, so called Maillard products. Maillard products are capable of causing an inflammatory response. The aim of this study was to investigate, if high intake of milk powder triggers CD in genetically susceptible children.

Methods: Swedish children (n=2077) carrying the coeliac HLA risk-genotypes DQ2 and/or DQ8 were prospectively screened for CD from 2 years of age in The Environmental Determinants of Diabetes in the Young (TEDDY) study. From this cohort, a 1 to 3 nested case-control study was designed for 207 children with biopsy-proven CD who seroconverted to tissue transglutaminase autoantibody (tTGA) positivity at mean 37 (+SD 22) months of age. Controls were randomly selected among tTGA negative children matched for gender, HLA risk alleles and birth year of each case (621 pairs). Repeated 3-day food records were completed at 6, 9, 12, 18 and 24 months of age. Food intake data was categorized into food groups by type of food and food composition of main ingredients from which intake of milk powder and gluten could be estimated. Milk powder intake prior to seroconversion of tTGA for each case were compared between cases and controls using conditional logistic regression models; unadjusted, adjusted for having a first-degree relative with celiac disease (FDR-CD) and for gluten intake. A statistical significance was determined when two sided p-value<0.05.

Results: Reported intake of milk powder at 9 months showed a crude association with increasing risk of CD (OR=1.01; 95% CI=1.00-1.02, p=0.037). However, when adjusted for having a FDR-CD and/or gluten intake, the association lost significance. In contrast, the amount of gluten intake prior to seroconversion of tTGA was associated with CD between cases and controls (OR=1.09; 95% CI=1.03-1.16, p=0.004), i.e., for every increase in intake of gram gluten per day, the risk of CD increased by 9%. This was also true for total gluten intake (sum of all visits) prior to seroconversion of tTGA (OR=1.03; 95% CI=1.00-1.06, p=0.022). After adjusting for having a FDR-CD, the association remained significant.

Conclusion: Intake of milk powder during the first 2 years of life is not associated with CD in Swedish genetically susceptible children. Instead, these findings indicate that a high intake of gluten increase the risk of CD in early childhood.
**GASTROENTEROLOGY: Coeliac disease**

G-O-012

IgA anti-epidermal transglutaminase antibodies are synthesised in the small bowel mucosa of coeliac patients with dermatitis herpetiformis

Fabiana Ziberna¹, Daniele Sblattero², Luigina De Leo¹, Serena Vatta¹, Stefano Martelossi¹, Tarcisio Not¹, Irene Berti¹, Alessandro Ventura¹

¹Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Paediatric Department, Trieste, Italy
²University of Trieste, Department of Life Sciences, Trieste, Italy

Objectives and study: Dermatitis Herpetiformis (DH), an itchy papulovesicular cutaneous eruption, is a gluten-dependent extra-intestinal manifestation of coeliac disease (CD). The immunopathological hallmark of DH is the granular deposition of IgA in the dermal papillae. These antibodies colocalize with the epidermal transglutaminase (TG3), the main auto-antigen in DH disease. DH subjects show serum anti-tissue transglutaminase (TG2) and anti-TG3 autoantibodies. Commercial ELISA for testing reactivity against TG3 shows high specificity, but variable sensitivity (52-92%).

The aims of our study were:
- to develop an ELISA assay based on the activated form of TG3 to identify patients with DH;
- to verify the intestinal origin of IgA anti-TG3 antibodies by means of the phage-display antibody method;
- to produce isolated monoclonal anti-TG3 antibodies in IgG mini-body (with Fc) format to test them in immunopathological studies.

Methods: 255 serum samples were assayed: 13 coeliac patients with DH; 100 coeliac patients; 23 coeliac patients with no-DH dermatitis; 19 subjects suffering from other gastro-intestinal disorders (inflammatory bowel diseases, eosinophilic esophagitis, ingestion of different materials) with no-DH dermatitis (sick control group) and 100 children who had made a spontaneous recovery from food allergy and with no personal or family history of CD. All coeliac patients were biopsy-proven and were positive for anti-TG2 and EMA antibodies. Sera of 5 coeliac patients with DH were retested on gluten-free diet (GFD).

We analysed, for the IgA reactivity to the activated form of TG3, the intestinal and peripheral phage-display antibody libraries of 4 subjects: one CD patient, one sick control subject and 2 CD patients with DH, whom one tested negative for the ELISA assay against TG3.

Results: Autoantibodies against TG3 were detected in: 10/13 (76.9%) CD patients with DH, 3/100 (3%) CD patients, 1/23 (4.3%) CD patients with no-DH dermatitis, 1/19 (5.3%) sick controls and 2/100 (2%) subjects with food allergy. ELISA test showed a sensitivity of 76.9% and a specificity 97.1%. All CD patients with DH on a GFD were negative for anti-TG3 reactivity.

We isolated an anti-TG3 antibody only from the intestinal phage-display library of the CD patient with DH and with serum anti-TG3 antibodies. The monoclonal antibody, characterised by VH gene family 3, recognises TG3 but not TG2.

Conclusion: For the first time we demonstrated, by phage-display technique, the intestinal origin of IgA anti-TG3 antibodies. This can explain the gluten-dependency of DH disease that improves with GFD. The gluten-dependent autoimmune response to TG3 will be further verified by screening an intestinal phage-display antibody library of a CD patient with DH on a GFD.

Using the activated form of TG3 we produced a high specific and sensitive ELISA test.

The production of a monoclonal anti-TG3 mini-body will allow us to try identifying the role of these antibodies in DH disease.
OBJECTIVES AND STUDY: Coeliac disease is an immune-mediated condition that affects the lining of the intestine when exposed to gluten. The British Society of Paediatric Gastroenterology, Hepatology and Nutrition guideline on Coeliac Disease (2013) recommends that patients with Tissue Transglutaminase antibodies (TTG) less than 10 times normal should undergo duodenal biopsy to confirm a diagnosis of Coeliac Disease. However, there is a paucity of data on how often this correlates with a final diagnosis of Coeliac disease. This study is to measure the sensitivity of borderline Tissue Transglutaminase Antibody (TTG) levels (greater than normal but less than 10 times of normal values) in diagnosing Coeliac disease.

METHODS: The Study Population was children aged 1-16 years with TTG levels less than 10 times of normal seen at The Shrewsbury & Telford Hospitals NHS Trust. The study period was from January 2010 to September 2016.

Patients were identified from the biochemistry database. Relevant data including the clinical symptoms, TTG levels, IgA levels, HLA status and histology results were collected using the hospital data base. The histology results were classified according to the Modified Marsh Criteria.

RESULTS: A total of 52 patients had TTG levels between 2 – 19.9 U/ml which is less than ten times of the normal range used by our biochemistry laboratory. The median age of presentation was 10 years while the median TTG value was 4.2U/ml. 10 patients with Type 1 Diabetes Mellitus were detected to have border-line positive coeliac serology on routine testing.

Thirty-nine patients underwent endoscopy with duodenal biopsies. Ten patients had neither endoscopy nor HLA testing performed because of various reasons including parental choice, symptom resolution prior to endoscopy while still on a normal diet, or repeat TTG levels within the normal range.

29 children (56%) out of the cohort of 52 had histological changes consistent with coeliac disease and were diagnosed as such. Seven of these (24%) had Grade 1 Marsh criteria, 3 children (10%) had Grade 2 Marsh criteria and 19 (66%) had Grade 3 Marsh criteria.

There was no significant difference in symptomatology between the children who were diagnosed with coeliac disease and those with normal biopsies, apart from recurrent abdominal pain which was commoner in coeliac disease.

CONCLUSION: 56% of children with borderline TTG levels were diagnosed with coeliac disease based on biopsy changes. Symptomatology was of poor discriminatory value apart from recurrent abdominal pain which was commoner in coeliac disease. Children with border-line positive coeliac serology should have duodenal biopsies to confirm a diagnosis of coeliac disease.
Children with untreated coeliac disease have sub-clinical cardiac dysfunction: an observational analysis from India

Rishi Bolia¹, Anshu Srivastava¹, Surender Yachha¹, Aditya Kapoor², Ujjal Poddar¹

¹Sanjay Gandhi Post Graduate Institute of Medical Sciences, Pediatric Gastroenterology, Lucknow, India
²Sanjay Gandhi Post Graduate Institute of Medical Sciences, Cardiology, Lucknow, India

Objectives and study: Coeliac disease (CD) has now been recognized as a multi-system disorder and in addition to the better known clinical manifestations suggesting gluten intolerance, associations with cardiovascular diseases have also been reported. The present study was undertaken to assess cardiac function in patients with celiac disease and to assess the effect of a gluten-free diet on cardiac function.

Methods: We prospectively evaluated the cardiac function using echocardiography in 50 patients with CD (mean age 4.2 ± 1.1 yrs., 30 boys) at diagnosis and after a year of being on a gluten-free diet. Control group consisted of 25 healthy children free of any disease.

We also evaluated 100 children with CD on follow-up; 47 who were compliant to the dietary regime and 53 non-compliant patients.

Results: Children with newly diagnosed CD had significantly larger left ventricle end diastolic dimension (LVEDD) (35.33 ± .87 vs. 32.90 ± .91, p = 0.04), left ventricular ejection fraction (LVEF) < 0.55 (20% vs. 0% p = 0.01,) and a higher myocardial performance index (MPI) > 0.6 (66% vs. 36%, p = < 0.01) as compared to controls. Treatment with GFD for one year led to significant changes in isovolumic relaxation time (IVRT) (72.5 ± 4.2 vs. 50.62 ± 2.69, p = 0.0001) and deceleration time (dt) (121.05 ± 10.1 vs. 99.87± 8.5, p = 0.02), reflecting improvement in cardiac diastolic function. There was a decrease in the mean LVEDD (35.33 ± .87 vs. 34.12± 1.8, p = 0.63) and proportion of patients with an MPI of > 0.6. (66% vs. 47.5%, p = 0.5) even though it did not reach statistical significance.

Patients compliant with GFD had a significantly lower MPI than the non-compliant patients (.60 ± .03 vs. 0.66 ± .08, p = 0.04), reflecting improvement in, load-independent echocardiographic parameters

Conclusion: In this observational study of CD patients from India, we observed that subclinical cardiac dysfunction in children with CD at diagnosis is not uncommon. Improvement in echocardiographic parameters occurs with gluten-free diet and children who are non-compliant may continue to have persistent cardiac dysfunction.
Co-morbidities in adolescents with celiac disease: findings from a population-based cohort

Assa Amit1, Yael Frenkel-Nir2, Dorit Tzur2, Lior Katz2, Raanan Shamir3

1Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel
2Medical Corps, Israel Defence Forces, Ramat-Gan, Israel
3Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel

Objectives and study: Celiac disease (CD) is a systemic disorder associated with various autoimmune disorders and higher prevalence of other diagnoses and complications. The prevalence of associated diseases and complications varies in different reports. Thus, we aimed to investigate the association of CD with various medical conditions at late adolescence in a large cross-sectional population based study.

Methods: A total of 2,001,353 Jewish Israeli adolescents who underwent a general health examination at median age of 17.1 (16.9-17.4) years from 1988 to 2015 were included. Of these, comprehensive data regarding medical status was available for 1,588,041 (79%) subjects. A definite diagnosis of CD was based on accepted criteria. Covariate data included demographic measures, and data on associated medical conditions.

Results: Overall, data of 7145 subjects with CD and 1,580,896 controls were analyzed. Multivariate analyses showed that autoimmune diseases were significantly more common in subjects with CD including insulin dependent diabetes (RR=5.5), inflammatory bowel diseases (RR=3.8), arthritis (RR=2.4), thyroid diseases (RR=1.8), psoriatic skin disorders (RR=1.6) and asthma (RR=1.5). Further associations included bile stones (RR=3.6), migraine (RR=2.3), anemia (RR=1.7), and menstrual abnormalities in females (RR=1.5). Neither long bones fractures nor axial fractures were more common in adolescents with CD compared with controls.

Conclusion: Already at adolescence, CD is associated with multiple comorbidities, not limited to autoimmune disorders.
Diet adherence and daily life participation: Insights from children and adolescents with coeliac disease via a standardised scale

Sonya Meyerⁱ, Sara Rosenblumⁱ

¹University of Haifa, Department of Occupational Therapy, Haifa, Israel

Objectives and study: Coeliac disease (CD) is a chronic health condition precipitated by exposure to gluten and managing a restrictive gluten free diet is the only available treatment. However, adherence among children and adolescents in particular involves unique challenges and is often inadequate. The need to adhere to the diet increases challenges to their involvement in daily activities. However, there is paucity in profound understanding of their participation characteristics in food-related activities in everyday life and a void in the knowledge concerning how to assist them. Considering children's and adolescents' own perspectives of their life with CD is of importance. Therefore, the aim of this study was: 1. To develop and validate the Coeliac Disease-Children’s Activity Report (CD-Chart), a standardised measure that can map out these characteristics. 2. To create a database of effective organizational strategies that the children and adolescents with CD that use to manage their health condition while participating in daily activities.

Methods: This study included 126 children and adolescents between the ages of 8-18 years diagnosed with CD for over six months. The CD-Children activity report (CD-Chart) incorporates nine food-related activities, based on focus group outcomes and theoretical knowledge. The nine activities are measured by six core dimensions: frequency, preference, preparation, involvement, help, and self-determination. The CD-Chart was administered via face-to-face interviews. Participants were divided into two age groups of 8-11 years and 12-18 years in order to capture age and developmental related differences. A matched control group included 30 children and adolescents without CD. Following, the participants with CD were asked to describe what they do on their own when preparing themselves to participate in the various food-related activities.

Results: The CD-Chart items showed adequate internal reliability as measured by the preference dimension (α= .80). An independent-samples t-test indicated that the preparation scores were significantly higher for the group with CD (M=.899, SD=.060) than the control group (M=.004, SD=.023); t(38)=76.25, p <.001. Significant differences between the younger and older participants with CD in specific characteristics of the various CD-Chart dimensions will be presented. Children and adolescents descriptions generated a database of strategies that they defined as effective and useful. For example, I remind people, I prepared a lecture about CD for my class, I use the internet a lot. The strategies were classified into categories including strategies used at home, with the family, with friends and at school and general strategies.

Conclusion: The CD-Chart is a reliable and valid tool that contributes to characterizing the participation in food-related activities while managing the gluten-free diet among children and adolescents with CD. Incorporation of intervention tools, based on self-reported perceptions of the health condition, can be valuable in understanding the unique and individual needs of children and adolescents with CD. A database of effective strategies produced by children and adolescents with CD can assist health professionals in promoting effective self-management, dietary treatment adherence, and quality of life of children and adolescents with CD.
**GASTROENTEROLOGY: Coeliac disease**

**G-O-017**

The type of gluten consumed during the first 3 years has no effect on the risk of coeliac disease


1 Hospital Universitari I Politecnic La Fe, Valencia, Spain
2 Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
3 Instituto de Investigación Sanitaria La Fe, U. Bioestadística, Valencia, Spain
4 University “federico ii”, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Effid), University of Naples Federico II, Italy, Naples, Italy
5 Hospital Universitari Sant Joan de Reus, Urv, lipv, Dept. of Pediatric Gastroenterology Unit, Reus, Spain
6 Heim Pál Children's Hospital, Coeliac Disease Center, Budapest, Hungary
7 La Paz University Hospital, Dept. of Pediatric Gastroenterology and Nutrition, Madrid, Spain
8 Leiden University Medical Center, Pediatrics, Leiden, Netherlands
9 Dr. von Hauner Children's Hospital, LMU Munich, Division of Pediatric Gastroenterology and Hepatology, Munich, Germany
10 Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
11 University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Effid), University of Naples Federico II, Italy, Naples, Italy
12 La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

**Objectives and study:** Wheat varieties selected to elaborate pasta contain larger amount of gluten and more immunogenic sequences than wheat varieties used for baking. We investigated whether the type of gluten consumed during the first years of life influences the risk for CD in a European paediatric risk population.

**Methods:** Subjects from the randomized placebo controlled trial on timing of gluten introduction PreventCD (www.preventcd.com), (200mg gluten versus placebo between week 16-24), received increasing amounts of gluten from month 7 (500mg/day) to 9 months (1500mg/day) with unrestricted gluten intake thereafter. The mean daily gluten intake (MDGI) was assessed by specific developed food records (FRs) from 11 to 36 months of age at 12 different time points. Products were grouped in pasta, bread, infants’ cereals, biscuits, pastries and “others”. The percentage of each food group contributing to total MDGI was calculated. The Cox proportional hazards regression model was adjusted to assess the hazard risk of each independent variable assessed on the probability of developing CD: country, gender, intervention group (gluten or placebo), HLA risk group, gradual increase of pasta intake per unit (gram) and gradual consumption of other products (bread, infants’ cereals, biscuits, pastries and “others”) per unit (gram). CD diagnosis was confirmed according to the ESPGHAN criteria.

**Results:** At the time of analysis, 84 of 615 participants with available food records had developed CD (24/225 from Spain, 18/127 from The Netherlands, 24/135 from Hungary, and 18/128 from Italy). Gluten consumption assessed from a total of 6132 FRs revealed marked differences between countries. Bread intake was highest in The Netherlands at any age, ranging from 56% to 70% of the total MDGI. In contrast, pasta intake was significantly higher at any age in Italy contributing about 50% of total MDGI compared to 2% and 18% in Spain at 11 and 36 months, respectively; and 2% and 11% at any age in The Netherlands and in Hungary respectively. The consumption of infants’ cereals, as opposed to bread and pasta, decreased with age in all countries. The intake of biscuits, pastries and “others” was similar in all countries at any age. The Cox proportional hazards regression model showed that the HLA genotypes DQ2.5/DQ2.5 and DQ2.5/DQ2.2 and gender were statistically associated with CD development, hazard ratio (HR) 4.11; 95% CI, 1.43 to 11.81, p=0.008; and HR of
male gender was 0.16; 95% CI, 0.05 to 0.54, p=0.003, respectively. This association was independent of the type of gluten consumed, including the increase of pasta consumption (HR 0.99; 95% CI, 0.88 to 1.12, p=0.97). Also the other controlling variables, such as country intervention group and consumption of other products (no pasta), did not showed statistical significant association with CD development (p=0.40; 0.59 and 0.94 respectively).

**Conclusion:** Significant differences in the gluten intake (MDGI) from different types of products by young children in different European countries were observed. However, these differences, both from pasta and gluten from other sources, was not associated the risk of CD development at early age.
The effect of gluten free diet on clinical symptoms and on the intestinal mucosa of patients with potential coeliac disease

Roberta Mandile¹, Maria Rosaria Del Vecchio¹, Serena Scapaticci¹, Valentina Discepolo¹, Maria Antonia Maglio², Riccardo Troncone², Luigi Greco², Renata Auricchio²

¹University Federico II, Department of Translational Medical Sciences, Section of Paediatrics, Naples, Italy
²University Federico II, Department of Translational Medical Sciences, Section of Paediatrics & European Laboratory for the Investigation of Food-Induced Diseases (Elfid), Naples, Italy

Objectives and study: Benefits from gluten free diet (GFD) in patients with potential coeliac disease (PCD) remain debated. In the present study, we evaluate the effect of GFD on both clinical symptoms and the intestinal mucosa of PCD patients.

Methods: 44/330 (13.3%) paediatric patients with PCD were considered for this study (mean age 7.2 years) as they received a GFD from the moment of the diagnosis because of the presence of symptoms. Patients were prospectively followed up (mean time 42.3 months) with clinical and serological evaluation every 6 months. Moreover in 9 patients an intestinal biopsy, with a histological and immunohistochemical analysis, was performed after at least one year of GFD.

Results: Symptomatic PCD patients showed at diagnosis low grade of failure to thrive (38.6%), recurrent abdominal pain (34.0%), diarrhea (20.4%), short stature (6.8%), osteoporosis (6.8%), vomiting (4.5%), hypertransaminasemia (4.5%), low blood ferritin (4.5%), pervasive developmental disorder (2.4%), dermatitis (2.4%). We excluded from the analysis all those subjects who dropped out during follow-up (5/44) and those who received other therapies in addition to GFD (5/44). Of the remaining 34 patients followed-up on GFD, 53% positively responded to diet in the first 12 months (71% of patients with abdominal pain, 55.6% of patients with diarrhea and 50% of patients with vomiting), 41% did not respond to GFD or in them symptoms did not reappear when patients were challenged with gluten; 6% responded only partially. As expected, in all the patients GFD induced a fall of anti-TG2 blood levels in the first 6 months. Analyzing those (9/44) who received a second biopsy while on a GFD (mean GFD duration 34.7 months), no significant differences were observed in terms of Marsh grade, lamina propria CD25+ cells, CD3+ and γδ+ intraepithelial lymphocytes density; intestinal anti-TG2 deposits disappeared in only 2 patients.

Conclusion: In PCD, even though anti-TG2 serum level was reduced in all patients after the elimination of gluten from the diet, the expected disappearance of symptoms was noted only in half of patients. Also the inflammatory signs in the mucosa did not significantly respond to GFD. This suggests that caution is necessary in PCD before attributing all abnormalities to gluten. Randomised trials on the effect of GFD in PDC are necessary.
Development of a paediatric endoscopy global rating scale: results of a national pilot

Priya Narula¹, Raphael Broughton², Ronald Bremner³, Anna Pigott⁴, David Rawat⁵, Mick Cullen⁶, Nadeem Afzal⁶, Lucy Howarth⁷, Peter Gillett⁸, Paul Henderson⁹, K Venkatesh¹⁰, Christos Tzivinikos¹⁰, Janis Maginnis¹¹, Sharon McKenna¹, David Devadason¹², Sabari Loganathan¹³, Michael Stanton⁶, John Green⁷, Debbie Johnston²

¹Sheffield Children's Hospital, Sheffield, United Kingdom
²Jag, London, United Kingdom
³Birmingham Children's Hospital, Birmingham, United Kingdom
⁴Royal Stoke Children's Service, Stoke on Trent, United Kingdom
⁵The Royal London, Paediatric Gastroenterology, London, United Kingdom
⁶Southampton Children's Hospital, Southampton, United Kingdom
⁷John Radcliffe Children's Hospital, Oxford, United Kingdom
⁸Royal Hospital for Sick Children, Edinburgh, United Kingdom
⁹Royal Hospital for Sick Children, Paediatric Gastroenterology, Edinburgh, United Kingdom
¹⁰Alder Hey Hospital, Liverpool, United Kingdom
¹¹Royal Stoke Children's Hospital, Stoke on Trent, United Kingdom
¹²Nottingham Children's Hospital, Nottingham, United Kingdom
¹³Nottingham Children's Hospital, Paediatric Gastroenterology, Nottingham, United Kingdom

Background: The Endoscopy Global Rating Scale (GRS) provides a clear framework for service improvement and underpins the accreditation of endoscopy services. The GRS was originally developed as a patient centred quality improvement tool in 2005 for the adult services to drive up standards. The adult experience suggests demonstrable improvement in quality and safety with embedding of standards through the accreditation process. Services are required to score a Level B in all standards in order to apply for and, once achieved, to maintain accreditation from the Joint Advisory Group in GI endoscopy (JAG) in the UK.

Objectives and study: To develop a paediatric endoscopy GRS (P-GRS) as a quality improvement tool which would also define standards for accreditation of paediatric endoscopy services

Methods: A P-GRS working group was established in May 2015 and the membership of this group evolved to include representatives from the BSPGHAN endoscopy working group, district general hospital, paediatric surgery, allied health professional, and specialist input from the JAG. Feedback was actively sought from the patients and parents partnership group. A draft P-GRS was developed following extensive discussion and communication between the P-GRS working group and the JAG. This went through a process of consultation with the regional endoscopy leads BSPGHAN council and subsequently individual endoscopy leads. The draft version was revised based on feedback received. Nine sites nationally agreed to pilot the P-GRS and all pilot sites underwent a training day organised by JAG in May 2016. The first assessment against the P-GRS was completed in June 2016. A second assessment is to be completed in December 2016 and the results of this will be available before the meeting to share with the membership.

Results: Eight of the nine pilot sites completed a GRS assessment in June 2016, testing the standards in their service and identifying an action plan for their unit. The first results showed significant variation across the standards, which is in keeping with the first adult GRS submissions.

In the clinical quality domain, 12% of units achieved a level B or above in the leadership and organisation standard, 25% in safety, 63% in comfort, 25% in quality, 38% in appropriateness and 50% in results.

In the quality of patient experience domain, 38% of the units achieved a level B or above in the respect and dignity standard, 24% in the consent process including patient information, 38% in the patient environment and equipment, 12% in access and booking, none in productivity and planning, 38% in aftercare and none in patient involvement
In the workforce domain, 12% of the units achieved a level B or above in the teamwork standards, 26% in workforce delivery, 38% in professional development.

In the training domain, none of the units achieved a level B or above in the environment, training opportunity and resources standard, trainer allocation and skills standard or assessment and appraisal standard.

**Conclusion:** These results highlight a need for improvement in all paediatric endoscopy services. Overall, all units agreed this was a positive experience and this enabled the units to develop an action plan to improve their endoscopy services and share good practice. All pilot sites reflected on the measures in the P-GRS to ensure they were relevant to paediatric endoscopy services and fit for purpose.
Anxiety and salivary cortisol levels in children undergoing gastroscopy under sedation

Duygu Kara1, Burcu Volkan2, Nevzat Aykut Bayrak3, Cahit Ucar4, Mehmet Nuri Cevizci5, Sedat Yıldız4

1Erzurum Regional Training and Research Hospital, Anesthesiology and Reanimation, Erzurum, Turkey
2Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
3Diyarbakir Children's Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
4Inönü University School of Medicine, Department of Physiology, Malatya, Turkey
5Erzurum Regional Training and Research Hospital, Department of Pediatric Surgery, Erzurum, Turkey

Objectives and study: Gastrointestinal endoscopy can cause severe anxiety, fear, pain and stress in children. Anxiety experienced before the procedure can increase its duration, the drug dosage used and potential complications. Cortisol, the most important glucocorticoid hormone in humans, can increase under physiological stress. The purpose of this study was to determine anxiety levels of patients prior to endoscopy and their relation with blood and salivary cortisol level (SCL) and to examine the effect of these on the procedure.

Methods: 119 children undergoing gastroscopy under sedoanalgesia for various reasons were included in the study. In order to determine anxiety levels, saliva specimens were taken at any time on the day before the procedure to examine cortisol levels before and after endoscopy. Anthropometric measurements were performed, and history of additional chronic disease was investigated. Anxiety scores before endoscopy were calculated (Yale Preoperative Anxiety Scale Modified). Patients were monitored throughout sedoanalgesia, and duration of endoscopy, sedation and recovery and total propofol dosage were recorded. A control group was also established by taking saliva samples from healthy age- and sex-matched children.

Results: 119 children undergoing gastroscopy (age 10.9±3.2 years; 43.7% male) and 85 healthy children (age 11.8±2.8 years; 45.1% male) participated in the study. Patient group data are shown in Table 1. No difference was determined between the control and patient groups in terms of basal SCL (16.9±0.7 ng/ml vs 19.7±1.8 ng/ml, p>0.05). SCL before endoscopy in the patient group was significantly higher compared to basal and post-endoscopy values (p=0.001 and p=0.035). Anxiety level was positively correlated with propofol dose, duration of recovery ($r^2=0.34$, p<0.05) and negatively correlated with age ($r^2=-0.36$, p<0.05). Pre-endoscopy SCLs was positively correlated with anxiety level, duration of procedure, propofol dose and duration of recovery ($r^2=0.36$, p<0.05).
## Table: Patient group data

<table>
<thead>
<tr>
<th></th>
<th>Patient group (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety score</td>
<td>10.1±2.7</td>
</tr>
<tr>
<td>Length of procedure</td>
<td>9.1±1.9 min</td>
</tr>
<tr>
<td>Propofol dosage</td>
<td>3.9±1.6 mg/kg</td>
</tr>
<tr>
<td>Duration of recovery</td>
<td>11.2±4.3 min</td>
</tr>
<tr>
<td>Basal SCL</td>
<td>16.1±19.7 ng/ml</td>
</tr>
<tr>
<td>SCL before endoscopy</td>
<td>36.4±32.5 ng/ml</td>
</tr>
<tr>
<td>SCL after endoscopy</td>
<td>20.2±19.4 ng/ml</td>
</tr>
</tbody>
</table>

**Conclusion:** Childhood gastroscopy was a significant stress factor in this study, and this was reflected in SCL values. Considering that anxiety increases the drug dose used for sedoanalgesia and complications, we think that potential complications in the intra- and postoperative periods, need to be predicted by evaluating patients’ pre-procedure anxiety scores and that appropriate precautions should be taken.
Premature neonates and asymptomatic Clostridium difficile carriage: frequency, kinetics and isolates characterization

Laurent Ferraris¹, Catherine Eckert², Johanne Delannoy³, Jeanne Couturier¹, Frédéric Barbut², Marie-José Butel¹, Julio Aires³

¹University Paris Descartes, Paris, France
²Pierre and Marie Curie University and National Reference Laboratory for C. Difficile, Saint Antoine Hospital, Paris, France
³University Paris Descartes, Ea4065, Paris, France

Objectives and study: C. difficile is a major enteropathogen involved in adult nosocomial diarrhea. Its role in children is less well defined, but cases of C. difficile infection appear to be increasingly prevalent in pediatric patients. If it is accepted that C difficile is present frequently at high rates in neonates, there is little data available on premature neonates (PN), whose period of hospitalization is often prolonged. Our goals were to analyze the frequency and kinetics of asymptomatic C. difficile carriage by healthy PN and to characterize the isolates.

Methods: This study is a longitudinal and monocentric prospective study (Saint Vincent de Paul, Paris) including 124 healthy PN (inclusions 12 months, 2008-2009). Stool samples were taken at different times during hospitalization (1W: 1 week (≤ 8 days) (number of children, n = 85); 1M: 1 month (20d-40d) (n = 64); HD: hospital discharge (4d-149d) (n = 65)) and during post-hospitalization periods (1-3 months, n = 38; 3-6 months, n = 23; 6-9 months, n = 27; 9-12 months, n = 23; > 12 months, n = 34). C. difficile was isolated on the selective medium CLO-M (Biomérieux). The detection of toxins in the feces was carried out by the enzyme immunoassay Ridascreen®. The strains were characterized by PCR-ribotyping and PCR-multiplex for tcdA, tcdB, tcdC, cdtA, cdtB and tpi genes.

Results: Of the 379 samples analyzed, 199 (52.5%) were positive for C difficile in culture. The average level of C. difficile in stool samples was 6 log₁₀ colony-forming units (CFU)/g at 1S and decreased regularly to reach 5 log₁₀ CFU/g for samples ≥ 12 months. Among the 199 positive samples, only 10 toxigenic strains (5%) belonging to ribotypes 014/020/077, 017, 106, 126, or 430 were isolated, all from stools obtained after hospital discharge.

During hospitalization, the frequency of C difficile colonization was 20%, 61%, and 60% at 1S, 1M and HD, respectively. Ninety four percent of the strains were non toxigenic belonging to PCR-ribotypes FR082 and (CE)032. On selected samples, we were able to co-isolate different ribotypes from the same sample of one individual.

After hospital discharge, the proportion of colonized PN increased up to 74% (mainly ribotypes FR082 and (CE) 032). After 12 months, the frequency decreased to 53% and a higher diversity of the ribotypes was observed.

Investigation by MLVA of the clonal relationship among isolates is currently in progress.

Conclusion: During hospitalization, PN are colonized with NT strains of C. difficile at a high level. After hospital discharge, the frequency of colonization decreases but a diversification of the ribotypes and the appearance of toxigenic strains were observed. Together these results are of interest when considering the hypothesis that newborns may constitute a C. difficile community reservoir for infections.
Exclusive enteral nutrition mediates gut metabolic changes in children with Crohn's disease

Kay Diederen1, Jia Li2, Angelika Kindermann3, Marc Benninga4, Tim de Meij5, Evelien de Groot5, Wouter de Jonge6, James Kinross2, Jurgen Seppen6

1Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Imperial College London, Section of Biomolecular Medicine, London, United Kingdom
3Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
4Vu University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
5Vu University Medical Centre, Gastroenterology and Hepatology, Amsterdam, Netherlands
6Academic Medical Center, Tytgat Institute for Liver and Intestinal Research, Amsterdam, Netherlands

Objectives and study: The mechanism of action by which exclusive enteral nutrition (EEN) induces remission in active pediatric Crohn’s disease (CD) remains unknown. Profound modification of fecal metabolic profile in active CD has been described. Therefore, we aimed to (I) characterize the fecal metabolic profile associated with active CD, EEN treatment or EEN response, and (II) identify specific metabolites that provide evidence for EEN’s mechanisms of action.

Methods: We included 43 children (<18 years) with therapy naïve CD starting EEN (6 weeks; polymeric formula). Fecal samples were collected: [T0] prior to EEN, [T1] during EEN (±3 weeks); [T2] end treatment (±6 weeks), [T3] habitual diet (±4 months). Response to EEN was defined as >50% decline in fecal calprotectin level. Matched healthy controls (HC) fecal samples were collected. Metabolic profile was determined using 1H Nuclear Magnetic Resonance Spectroscopy (Bruker, Rheinstetten, Germany). Orthogonal partial least-squares discriminant analysis (OPLS-DA) were performed, cross-validation parameters were presented as R2 and Q2, and p value was generated from permutation tests. Metabolite(s) X associated with CD, EEN treatment or EEN response were extracted from OPLS-DA models (Benjamini-Hochberg correction).

Results: At baseline [T0], there was a clear separation of the fecal metabolic profile in CD from HC (R2=57.5%, Q2=0.53 , P<0.001). The fecal metabolic profile prior to EEN [T0] differed from that during EEN [T1] (R2=45.3%, Q2=0.06 , P=0.004). The fecal metabolic profile did not differ between baseline [T0] and time points after EEN cessation [T2 & T3]. However, when patients were stratified based on response to EEN therapy, there was a separation of the fecal metabolic profile of responders from non-responders at baseline [T0] (R2=52.2%, Q2=0.15 , P=0.030) and habitual diet [T3] (R2=69.2%, Q2=0.47 , P=0.01).

Valine, Leucine, Isoleucine, Propionate, cadaverine, Alanine, Lactate, Trimethylamine, Tyrosine, phenylalanine were found in higher concentrations in CD compared to HC. No metabolites differentiated time points or response to EEN.

Conclusion: Pediatric CD patients have a distinct fecal metabolic profile, that changes during the course of EEN. Furthermore, responders vs. non responders have a different fecal metabolic profile prior to therapy, indicating that gut metabolic environment might predict response to EEN.
Reliability assessment of endoscopic scoring tools using central video review of colonoscopies in paediatric patients with ulcerative colitis: data from the Canadian Children IBD Network.

Nicholas Carman1, Hien Huynh2, Catharine Walsh3, Amanda Ricciuto1, Marialena Mouzaki3, Eileen Crowley1, Peter Church1, Thomas Walters1

1The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
2The University of Alberta, Ped Gi Nutrition, Edmonton, Canada
3Hospital for Sick Children, Department of Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: Reliable and consistent endoscopic assessment of mucosal disease severity is important in the evaluation of patients with Ulcerative Colitis (UC). Of the commonly used assessment tools, the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) is likely more responsive than the Mayo Endoscopic Score (Mayo-ES). Neither however, have been formally evaluated in paediatric patients. Using videos of colonoscopies performed in patients from the Canadian Children IBD Network, we undertook to assess inter-rater reliability (IRR) for the UCEIS and Mayo-ES amongst Pediatric IBD physicians familiar with the tools, as well as non-IBD pediatric gastroenterologists.

Methods: Video recordings of ileo-colonoscopies of paediatric patients with UC undergoing endoscopic assessment at Network sites were utilised for the analysis. 8 physicians (4 IBD experts) reviewed the videos, blinded to clinical information, collecting data encompassing the UCEIS and Mayo-ES. A global assessment of endoscopic lesion severity (GELS) was also recorded using a visual analogue scale. IRR was measured using Intraclass correlation coefficients (ICCs). Correlation between scoring tools was measured using Spearman’s test of correlation (r).

Results: There was a broad range of endoscopic severity within the endoscopic assessments (median UCEIS 6 (Range: 3 to 8). The IRR for both Mayo-ES and UCEIS was excellent amongst IBD physicians. However, whilst the IRR for Mayo-ES was very good amongst non-IBD Gastroenterologists, for UCEIS it was only moderate (see table). Amongst IBD physicians, there was good correlation between the UCEIS score and Mayo-ES (r = 0.75, p <0.001), as well as between each score and the GELS (Mayo ES: r = 0.78, p<0.001; UCEIS: r = 0.72, p <0.001). Within the 3 items of the UCEIS, the most common sources of disagreement between readers were estimation of the degree of bleeding by all physicians, and evaluation of erosions/ulcers by non-IBD Gastroenterologists (see table).
### Table: Inter-rater reliability using ICC of UCEIS and Mayo Endoscopic Score for IBD physicians and non-IBD Gastroenterologists

<table>
<thead>
<tr>
<th></th>
<th>IBD Gastroenterologists</th>
<th>Non-IBD Gastroenterologists</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median UCEIS Score (min – max)</strong></td>
<td>6 (3 – 8)</td>
<td>7 (3 – 8)</td>
</tr>
<tr>
<td><strong>ICC – Total UCEIS Score (95% CI)</strong></td>
<td>0.87 (0.74 – 0.94)</td>
<td>0.55 (0.25 – 0.84)</td>
</tr>
<tr>
<td></td>
<td><em>p</em> = &lt;0.001</td>
<td><em>p</em> = 0.01</td>
</tr>
<tr>
<td><strong>ICC – Vascular Pattern (95% CI)</strong></td>
<td>0.80 (0.60 – 0.91)</td>
<td>0.81 (0.52 – 0.93)</td>
</tr>
<tr>
<td></td>
<td><em>p</em> = &lt;0.001</td>
<td><em>p</em> = &lt;0.001</td>
</tr>
<tr>
<td><strong>ICC – Bleeding (95% CI)</strong></td>
<td>0.50 (0.11 – 0.77)</td>
<td>0.51 (0.39 – 0.83)</td>
</tr>
<tr>
<td></td>
<td><em>p</em> = 0.01</td>
<td><em>p</em> = 0.03</td>
</tr>
<tr>
<td><strong>ICC – Erosions and Ulcers (95% CI)</strong></td>
<td>0.88 (0.76 – 0.95)</td>
<td>0.15 (-0.35 – 0.55)</td>
</tr>
<tr>
<td></td>
<td><em>p</em> = &lt;0.001</td>
<td><em>p</em> = 0.20</td>
</tr>
<tr>
<td><strong>ICC – Mayo Endoscopic Score (95% CI)</strong></td>
<td>0.88 (0.77 – 0.94)</td>
<td>0.72 (0.27 – 0.89)</td>
</tr>
<tr>
<td></td>
<td><em>p</em> = &lt;0.001</td>
<td><em>p</em> = 0.01</td>
</tr>
</tbody>
</table>

**Conclusion:** Centralised video review of colonoscopy is feasible for assessing endoscopic severity in paediatric UC. Assessment of the scoring tools (UCEIS and Mayo-ES) using video recordings showed excellent IRR in the hands of IBD physicians familiar with the tools. In non-IBD Gastroenterologists, IRR of the Mayo-ES was good, however reliability with the UCEIS score was poorer, perhaps reflective of the unfamiliarity with the tool. Repeat assessments following training in the application of the tool are planned.
Multiple operator small bowel ultrasound (SBUS) without oral fluid contrast correlates well with magnetic resonance enterography (MRE) and high accuracy in identifying small bowel inflammation in the diagnostic work-up for paediatric inflammatory bowel disease.

Sharon Probert1, James Slack1, Elizabeth Renji1, Maureen Lawson1, Christine Maville1, Clare Smith1, Leigh McDonald2, Susan Bunn1

1Great North Children's Hospital, Department of Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom
2Great North Children's Hospital, Department of Paediatric Radiology, Newcastle Upon Tyne, United Kingdom

Background: The ESPGHAN revised Porto criteria for the diagnosis of paediatric inflammatory bowel disease (IBD) 2014 considers MRE the small bowel imaging of choice. However, in many centres MRI is a limited resource and MRE involves cannulation, oral fluid load and is not possible in younger children. Wireless capsule endoscopy (WCE) proposed as an alternative, requires patency capsule first, both capsules may need to be placed endoscopically and is not available to all centres. SBUS is non-invasive, low-cost, and has widespread availability but is considered too operator dependant for wide application.

Aim: To review the correlation between 1) SBUS and MRE and 2) SBUS with ileal histology in children newly diagnosed with IBD in one centre where all radiologists undertake SBUS without oral contrast.

Methods: Retrospective electronic record and case note review of all children newly diagnosed with IBD in one tertiary unit between January 2015 and November 2016 (22 months).

Results: Of 118 children (69 male, median age 14; range 3 – 17 years) diagnosed over the study period with ulcerative colitis, (n=22); Crohn's disease (n=82) and IBDU ((n=15). 118 (100%) had upper GI endoscopy; 116 (98%) full colonoscopy to caecum and 96 (81%) ileoscopy with ileal biopsies. 107 (91%) had a SBUS at a median of 1 day (range -9 to 43 days) from endoscopy; 59 (50%) had a MRE a median of ; 54/118 (46%) had both SBUS and MRE at a median of 42 days apart. The SBUS examinations were carried out by 6 consultant radiologists. SBUS and MRE agreed in their findings in 46/54 (85%) cases – 21/54 (39%) with no small bowel disease and 33/54 (61%) in identifying small bowel disease including three with extensive / multifocal small bowel disease. The median time from SBUS to MRE in the non-concordant examinations was 32 days and the children had been started on therapy between examinations. In 4/8 non-concordance examinations ileal histology supported SBUS findings rather than MRE suggesting changes may have resolved by time of MRE examination.

Table: Comparing SBUS findings to ileal histology in all children undergoing SBUS (n=107):

<table>
<thead>
<tr>
<th></th>
<th>Value</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>85%</td>
<td>68% to 95%</td>
</tr>
<tr>
<td>Specificity</td>
<td>86%</td>
<td>74% to 94%</td>
</tr>
<tr>
<td>Positive Predictive Value</td>
<td>78%</td>
<td>65% to 87%</td>
</tr>
<tr>
<td>Negative Predictive Value</td>
<td>91%</td>
<td>81% to 96%</td>
</tr>
</tbody>
</table>

Summary: SBUS performed by any consultant radiologist without oral fluid contrast correlated well with MRE and has a high sensitivity and specificity in identifying terminal ileal inflammation when compared to ileal histology, though mild superficial inflammation was not identified by SBUS.

Conclusion: MRE is a limited resource in many centres and critical for detecting complications of IBD and assessing extensive or multifocal small bowel disease. WCE is not available in all centres, is cumbersome to perform and report with high rate of false positive detection of small bowel lesions. In most children newly presenting with IBD accuracy in identifying the underlying condition (CD, UC or
IBDU) is the main clinical concern and SBUS performs very well in identifying small bowel disease. We propose that SBUS performed within 24 hours of endoscopy should be the initial investigation of choice to prevent additional invasive testing, delay in diagnosis / initiation of therapy. Initial MRE can be safely limited to those children stratified at presentation or after SBUS to be at high risk of complications or complex / extensive disease.
GASTROENTEROLOGY: Inflammatory bowel disease

G-O-025

Fecal calprotectin accurately predicts symptomatic relapse in children and adolescent with inflammatory bowel disease in clinical remission

Kay Diederen¹, Daniel Hoekman¹, arjen Leek², Victorien Wolters³, Thalia Hummel⁴, Tim de Meij⁵, Bart Koot², Merit Tabbers⁶, Marc Benninga², Angelika Kindermann²

¹Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²University Medical Center Utrecht / Wilhelmina Children’s Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
³University Medical Center/Wilhelmina Children’s Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
⁴Medisch Spectrum Twente, Department of Pediatrics, Enschede, Netherlands
⁵VU University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
⁶Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: In children and adolescents with inflammatory bowel disease (IBD) in clinical remission, it is difficult to predict when a relapse will occur. Reliable data on the value of biomarkers of inflammation for predicting relapse in these young patients are lacking. Therefore, we aimed to investigate the predictive value of fecal calprotectin (FC) and CRP for symptomatic relapse in pediatric IBD in clinical remission.

Methods: In this cross-sectional cohort study, patients aged <18 years with Crohn’s disease or ulcerative colitis in clinical remission ≥3 months were included. At baseline, clinical and biochemical disease activity were assessed using the abbreviated-Pediatric Crohn’s Disease Activity Index (aPCDAI) or Pediatric Ulcerative Colitis Activity Index (PUCAI), and FC and CRP, respectively. Clinical remission was defined as an aPCDAI or PUCAI <10. Disease course over the subsequent 12 months was retrospectively assessed. Symptomatic relapse was defined as an aPCDAI or PUCAI score ≥10, with the need for treatment intensification. Multivariate Cox regression analysis was performed to evaluate whether FC and CRP were independent predictors for symptomatic relapse.

Results: In total, 114 patients in clinical remission were included (56% males; median age 14.9 years). Baseline FC level was higher in patients that developed a relapse compared to patients without symptomatic relapse (median 367µg/g vs. 117µg/g, p=0.014). FC level was an independent predictor for symptomatic relapse within 6 months from baseline (HR per 100µg/g: 1.15 [95%CI: 1.06–1.24], p=0.001), corresponding to a 15% increase in the probability of relapse per 100 µg/g increment, with fair predictive accuracy (AUC: 0.77, p<0.001). The optimal FC cut-off was 350 µg/g, with a sensitivity and specificity of 76% and 78%, respectively.

Baseline CRP level did not differ between patients with or without symptomatic relapse. CRP level was an independent predictor for symptomatic relapse within 6 months from baseline (HR per 1mg/L: 1.10 [95%CI: 1.01–1.19], p=0.025), corresponding to a 10% increase in the probability of relapse per 1 mg/L increment, with poor predictive accuracy (AUC: 0.67, p=0.036). The optimal CRP cut-off was 0.6 mg/L, with a sensitivity and specificity of 88% and 38%, respectively.

Conclusion: Levels of FC and CRP were both independent predictors of symptomatic relapse in pediatric IBD in clinical remission, with superior predictive test characteristics of FC. High FC levels at routine measurement justify careful disease monitoring and evaluation of current treatment.
The association of mucosal healing (MH), transmural healing (TH) and calprotectin in paediatric Crohn’s disease: a report from the ImageKids study

Inbar Nakar¹, Gili Focht², Peter Church³, Thomas Walters³, Sudha Anupindi⁴, Laureline Berteloot⁵, Johanna Escher⁶, Frank Rümmele⁵, Ruth Cytter-Kuint⁷, Mary Louise Greer⁸, Anne Griffiths³, Dan Turner⁹

¹Shaare Zedek Medical Center, Jerusalem, Israel
²Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
³The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
⁴Chop, Philadelphia, United States
⁵Nekar Hospital, Paris, France
⁶Erasmus MC-Sophia Children’s Hospital, Pediatric Gastroenterology, Rotterdam, Netherlands
⁷Shaare Zedek Medical Center, Radiology, Jerusalem, Israel
⁸Sickkids, Toronto, Canada
⁹Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: It is indisputable that patients achieving mucosal healing (MH) have a better prognosis, including lower risk for future relapses and hospitalizations, compared to those with residual inflammation. However, it is not uncommon to achieve MH but still have evidence of inflammation deeper in the bowel wall. Adult studies suggest that achieving transmural healing (TH), as reflected by MRE, may also be associated with improved outcomes. Fecal calprotectin (FC) can reflect mucosal inflammation but it is unknown whether it can predict also TH. We aimed to explore whether FC and CRP can accurately reflect MH, TH or both.

Methods: We used prospectively recorded data of paediatric CD patients collected for the ImageKids study. Children at disease onset or thereafter underwent an ileocolonoscopy and an MRE, when FC and CRP were obtained. Each MRE was scored independently by two experienced radiologists for severity of inflammatory disease utilizing 100mm visual analogue scale (VAS). MH was defined as SES-CD<3, TH as MRE-VAS<20mm and DR as both TH and MH. Correlational and diagnostic utility statistics have been employed.

Results: A total of 182 children (age 11.5±3.3 years, with disease duration of 2.8±2.6 years) have been included from 21 paediatric IBD international centers. MH with deeper transmural inflammation was noted in 17 (9.3%) children, TH with mucosal inflammation in 38 (21%), DR in 25 (14%) children, and mucosal and transmural inflammation in 102 children (56%). The rate of MH with deeper transmural inflammation was higher in the subgroup of patients evaluated after commencing treatment (excluding those at disease onset). Median FC (Figure) was lowest in the DR group (22mg/g (IQR 10-170)), followed by the MH & no TH group (306mg/g (83-838); P<0.001), higher in the TH & no MH group (569mg/g (166-1149); p<0.001), and highest in the no MH & no TH group (812mg/g (484-1699); p=0.007).

Area under ROC for calprotectin and CRP to predict DR were 0.93 (95%CI 0.89-0.98), and 0.82 (0.73-0.9), respectively. The best FC cutoff predicting DR was 100mg/g (sensitivity 72%, specificity 92%), and to predict MH 300mg/g (74%, 80%).

Normal CRP did not preclude bowel inflammation but was more closely associated with transmural rather than mucosal inflammation; the correlation of CRP was higher with MRE-VAS than with SESCD (r=0.46 vs. r=0.35; both p<0.001). In contrast, FC increased linearly with increasing SESCD disease severity; r=0.57 (p<0.001).
Conclusion: CRP reflects transmural inflammation better than mucosal inflammation, but still was inferior to FC. FC best reflects mucosal inflammation and to a lesser degree also transmural inflammation. Nonetheless, while FC<300mg/g can predict MH, a lower cutoff of <100mg/g may be appropriate to predict DR.

Disclosure of interest: The ImageKids study has been funded by an educational grant from Abbvie. However, Abbvie has not been involved in the study design, conduct, analyses or manuscript preparation.
The use of lipase and alanine transaminase to predict acute gallstone pancreatitis in the paediatric population

Maisam Abu-El-Haija¹, Tom Lin², Soofia Khan², Lin Fei², Tyler Thompson², Jaimie Nathan³

¹Cincinnati Children's Hospital Medical Center, Division of Gastroenterology, Hepatology and Nutrition, Cincinnati, United States
²Cincinnati Children's Hospital Medical Center, Cincinnati, United States
³Cincinnati Children's Hospital Medical Center, Division of Surgery, Cincinnati, United States

Objectives and study: Gallstone Pancreatitis (GP) in children occurs at a lower incidence when compared with adult patients. Early markers for diagnosis of GP in paediatrics have not been well studied. The ability to adequately differentiate GP in children from other causes of acute pancreatitis (AP) poses significant implications including early diagnosis leading to prompt intervention when indicated. We sought to assess the laboratory findings and clinical variables for early GP diagnosis from a prospectively enrolled registry of paediatric patients presenting with their first occurrence of AP.

Methods: Children <21-years-old presenting with their first episode of confirmed AP were prospectively enrolled in an internal registry at a large, tertiary care children's hospital. A cross sectional analysis from this registry between March 2013 to October 2016 was performed. AP cases with an etiology other than a gallstone etiology were classified as non-GP (viral, systemic illness, drug induced, metabolic, trauma, or idiopathic). Fisher's exact test and Wilcoxon rank sum test were used to compare demographic and clinical variables between the two groups GP and non-GP. In order to optimize prediction of GP, a multivariable logistic regression model was derived based off significant p-values, the Receiver Operating Characteristics (ROC) curve using stepwise selection.

Results: Within the study period, there were 114 patients enrolled into the AP registry; 21 GP, 93 non-GP. A univariate comparison between GP and non-GP patients found no significant differences in gender, age distribution, initial amylase elevations X upper limit of normal (ULN), creatinine, or total bilirubin. Comparing GP to non-GP, the median (IQR 25%, 75%) was found to be statistically higher for GP patients in: lipase XULN on admission: 31 (8.37, 78.4) vs 7 (3.8, 17), weight percentile for age: 86 (9, 99.9) vs 46.8 (0, 99.7), alanine aminotransferase (ALT): 302 (168, 441) vs 26 (20, 59), aspartate aminotransferase (AST): 170 (118, 260) vs 33 (20, 58), gamma-glutamyl transferase (GGT): 411 (197, 650) vs 29 (13, 111). Two variables remained significant on multivariate analysis: logALT and logLipase. A model built using these two variables for prediction of GP identified an ROC of 0.85. At a predictive probability of 0.35, the model had a 80% sensitivity, 93% specificity, 76% positive predictive value, 95% negative predictive value.

Conclusion: From our paediatric prospective AP registry, we identified significantly higher elevations in lipase ULN, weight percentile, ALT, AST and GGT that appear to differentiate AP patients presenting with GP. We built a model for predicting GP in the paediatric population that could help clinical management of AP patients. Future studies are needed to validate the use of laboratory findings and clinical variables in the work up of gallstone etiologies in the AP patients.
Figure 1: Gallstone Pancreatitis prediction model. The is a logistic regression model with logALT and logLipase(xULN) as predictors. The final model with 97 patients included.
Inherited CD55 deficiency in patients with early onset protein-losing enteropathy and thrombosis

Ahmet Ozen1, William A Comrie2, Rico Chandra Ardy3, Cecilia Domínguez Conde3, Buket Dalğıcı4, Omer Faruk Beser3, Aaron R Morawski9, Elif Karakoc-Aydiner1, Engin Tutar1, Safa Baris1, Figen Özçay8, Nina Kathrin Serwas3, Yu Zhang9, Helen F Matthews2, Stefania Pittaluga10, Les R. Folio11, Aysel Ünlüsoy Aksu4, Joshua J McElwee12, Ana Krolo3, Ayca Kiykim13, Zeren Barış14, Ismail Ogulur1, Scott Snapper15, Roderick Houwen16, Helen Leavis17, Deniz Ertem18, Renate Kain18, Sinan San14, tulay erkan19, Helen C. Su20, Kaan Boztug3, Michael J. Lenardo2

1Division of Allergy and Immunology, Marmara University, Department of Pediatrics, Istanbul, Turkey
2National Institute of Allergy and Infectious Diseases, National Institutes of Health, Molecular Development of the Immune System Section, Laboratory of Immunology, Bethesda, United States
3Ludwig Boltzmann Institute for Rare and Undiagnosed Diseases; Cemm Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria
4Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
5İstanbul University Cerrahpaşa Faculty of Medicine, Department of Pediatrics, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
6National Institute of Allergy and Infectious Disease, National Institutes of Health, Molecular Development of the Immune System Section, Laboratory of Immunology, Bethesda, United States
7İstanbul University Cerrahpaşa Faculty of Medicine, Department of Pediatrics, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
8Başkent University School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
9National Institute of Allergy and Infectious Disease, National Institutes of Health, Molecular Development of the Immune System Section, Laboratory of Host Defense, Bethesda, United States
10National Cancer Institute, National Institutes of Health, Laboratory of Pathology, Bethesda, United States
11Clinical Center, National Institutes of Health, Radiology and Imaging Sciences, Bethesda, United States
12Merck & Co, Merck Research Laboratories, Boston, United States
13Baskent University Faculty of Medicine, Pediatric Gastroenterology and Hepatology, Ankara, Turkey
14Baskent University Faculty of Medicine, Pediatric Gastroenterology, Ankara, Turkey
15Boston Children's Hospital, Boston, United States
16University Medical Center/Wilhelmina Children’s Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
17University Medical Center Utrecht, Dept. Rheumatology and Clinical Immunology, Utrecht, Netherlands
18Medizinische Universität Wien, Clinical Institute of Pathology, Vienna, Austria
19İstanbul University Cerrahpaşa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, İstanbul, Turkey
20National Institute of Allergy and Infectious Diseases, National Institutes of Health, Human Immunological Diseases Section, Laboratory of Host Defenses, Bethesda, United States

Objectives and study Studies of monogenic gastrointestinal diseases have revealed molecular pathways crucial for gut homeostasis and enabled the development of targeted therapies. A disease caused by complement dysregulation primarily affecting the gastrointestinal tract is heretofore unknown.

Methods: We studied 11 patients with abdominal pain and diarrhea caused by early-onset protein-losing enteropathy with primary intestinal lymphangiectasia, edema due to hypoproteinemia, malabsorption, and, less frequently, bowel inflammation, recurrent infections, and angiopathic thromboembolic disease. DNA sequencing was performed to identify gene variants. CD55 regulatory function including complement deposition, costimulation, and anaphylatoxin responses were assessed by shRNA and CRISPR-mediated gene suppression and rescue of CD55 expression using lentiviruses.
Results: In all patients, autosomal recessive mutations were identified in the gene encoding CD55/Decay accelerating factor, leading to loss of protein expression. Patient T lymphocytes and CD55-deficient cell lines displayed uncontrolled complement activation including C3d deposition and generation of C5a. Genetic reconstitution of CD55 normalized complement activation. Stimulation of anaphylatoxin receptors on patient T lymphocytes produced increased tumor necrosis factor, causing a decreased ratio of the anti-coagulatory protein thrombomodulin to the pro-coagulatory protein tissue factor. CD55 costimulation by CD97 and contingent production of interleukin-10 were defective in patient T lymphocytes.

Conclusion: CD55 deficiency with hyperactivation of complement, angiopathic thrombosis, and PLE (CHAPLE) disease is caused by abnormal complement activation due to biallelic loss-of-function mutations in CD55. (Funded by the National Institutes of Health, the European Research Council, and others; ClinicalTrials.gov number NCT00246857.)

An intestinal transcriptome analysis in fetal pigs reveals genes involved in glucose and lipid metabolism and immunity as valuable clues of maturity at birth

Ying Yao¹, Valentin Voillet², Maeva Jegou³, Magali San-Cristobal², Samir Dou³, Véronique Romé¹, Yannick Lippi, Yvon Billon⁵, Marie-Christine Pera⁶, Gaëlle Boudry¹, Laure Gress², Nathalie Iannuccelli⁶, Pierre Mormede⁶, Hélène Quesnel⁶, Laurianne Canario³, Laurence Liaubet², Isabelle Le Huêrou-Luron¹

¹Inra, Nutrition & Digestive, Nervous and Behavioural Adaptations, Saint-Gilles, France
²Inra Inpt ENVT Toulouse University, Genphyse, Castanet Tolosan, France
³Inra Agrocampus Ouest, Pegase, Saint Gilles, France
⁴Inra ENVT Inp-Purpan Ups Toulouse University, Toxalim, Toulouse, France

Objectives and study: Delayed physiological maturity at birth as observed in preterms compromises adaptation to extraterine life, and accordingly impairs perinatal survival and child health. The intestine, as the major organ for nutrient absorption and the largest immune organ, fulfills its maturation during the first postnatal weeks in neonates. However, key pathways and regulators of intestinal maturity still remain poorly characterized when their identification may provide clues about adequate adaptation to enteral feeding. Our aim was to comprehensively clarify intestinal development with the objective of finding relevant regulators of intestinal maturity by using two porcine breeds, divergent in neonatal morbidity and mortality, at two gestational ages during the late fetal developmental stage (PORCINET, ANR-09-GENM-005).

Methods: Chinese Meishan (MS) and Large White (LW) breeds have been chosen as two extreme breeds for piglet mortality at birth, a better survival rate being observed in MS piglets. Nine MS and nine LW sows were inseminated with mixed semen (LW and MS) to get litters composed of both purebred fetuses (LWLW or MSMS) and crossbred fetuses (LWMS from MS sows and MSLW from LW sows). At two key time points of fetal maturation (90 and 110 days of gestation; term gestation is 114 days in pigs), umbilical cord blood and jejunum samples were collected from 63 male fetuses distributed in eight groups (two ages and four genotypes). Twenty three phenotypic variables (plasma markers of metabolisms, hormones, intestinal morphometry and enzyme activities) were analyzed using standard methods. Hybridizations of 60K porcine microarrays (Agilent technology) with intestinal RNA were analyzed with a mixed linear model and a False Discovery Rate adjusted p-value < 1% to identify genes differentially expressed in the 4 fetal genotypes and at the 2 gestational ages.

Results: Two hundred and seventy four unique annotated genes combined differential expressions between 90 days and 110 days of gestation and between LW and MS genotypes. These differentially expressed genes (DEGs) were more particularly involved in the maturation process. In MS fetuses at day 110, functional enrichment analysis (GeneCoDis 3.0 software) disclosed overexpressed genes involved in glucose and lipid metabolisms, cell proliferation, vasculogenesis and hormone synthesis compared to MS fetuses at day 90. In LW fetuses, genes involved in immune pathways including phagocytosis, inflammation and defense processes were particularly changed in day 110 compared to day 90. The transcriptional regulator PPARGC1A was predicted to be an important regulator of DEGs in MS (Ingenuity® Pathway Analysis software). Fetal blood fructose level, intestinal lactase activity and villous height that were the best predicted phenotypic variables, showed correlated variances with 450 probes mostly involved in lipid metabolism, carbohydrate metabolism and cellular movement biological pathways (sparse Partial Least Square regression model, mixOmics).

Conclusion: Collectively, our findings indicate that the maturity of the intestine relies on maturation of both glucose and lipid metabolic pathways and immune phagocyte differentiation and inflammatory pathways in neonates. This process may partially be governed by PPARGC1A.
GASTROENTEROLOGY: Peptic disease and helicobacter pylori

G-O-030

Review of eradication therapy of Helicobacter pylori in children across Europe; is the dosing right? Results from EuroPedHp Registry

Vinod Kolimarala1, Katharina Werkstetter2, Sonny Chong3, Michal Kori4, Barbara Iwanczak5, Jernej Dolinšek6, Matjaz Homan7, Alexandra Papadopoulou8, Maria Rogalidou9, Eletheria Roma10, Maria José Martínez11, Pedro Urruzuno12, Mª Luz Cilleruelo Pascual13, Áron Cseh14, Andrea Sustmann15, Ender Pehlivanoglu16, Meltem Ugras17, Ana Isabel Lopez18, José Cabral19, Marta Tavares20, Nicolas Kalach21, Noam Zevi22, Thomas Casswall23, Julian Thomas24, Angelika Kindermann25, Zrinjka Mišak26, Erasmo Miele27, Francesca Rea28, Simona Faraci29, Vaidotas Urbonas30, Almuthe Christine Hauer31, Jacob Yahav32, Sibylle Koletzko32

1Epsom and St Heliers Hospital NHS Trust, Carshalton, United Kingdom
2Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
3Queen Mary's Hospital for Children, St. Helier Hospital, Paediatrics, Carshalton, Surrey, United Kingdom
4Kaplan Medical Center, Rehovot, Israel
5Medical University of Wroclaw, Wroclaw, Poland
6University Medical Center (Umc) Maribor, Maribor, Slovenia
7University Children's Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia
8Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece
9University of Ioannina School of Medicine, Department of Pediatrics, Ioannina, Greece
10National and Kapodistrian University of Athens, First Department of Paediatrics, Athens, Greece
11Hospital Niño Jesús, Madrid, Spain
12Hospital Universitario Doce de Octubre, Madrid, Spain
13Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
14Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary
15Dr. von Hauner Children's Hospital, Klinikum der Universität München, Munich, Germany
16Marmara University Faculty of Medicine, Istanbul, Turkey
17Yeditepe University Medical Faculty, Pediatrics, Istanbul, Turkey
18National Institute of Health, Lisbon; University Hospital Santa Maria, Lisbon, Portugal
19Hospital Centre of Central Lisbon, Lisbon, Portugal
20University Hospital Porto, Porto, Portugal
21St Vincent de Paul Hospital, Lille, France
22Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Petach-Tikva, Israel
23Karolinska University Hospital, Stockholm, Sweden
24Newcastle Hospital, Newcastle, United Kingdom
25Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
26Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
27Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
28Bambino Gesu Children Hospital, Roma, Italy
29Bambino Gesù Children Hospital, Digestive Endoscopy and Surgery Unit, Rome, Italy
30University Hospital Santariskiu Klinikos (Vilnius University Children's Hospital), Vilnius, Lithuania
31Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria
32Helicobacter Research Institute, Rehovot, Israel

Objectives and study: Successful eradication of H. pylori infections in pediatric patients remains a challenge. We used registry data to assess changes with recommended drug doses and treatment...
duration over time in a large cohort of symptomatic pediatric patients with biopsy proven H. pylori infection across Europe.

**Methods:** From 1/2013 until 9/2016 paediatric gastroenterologists from 21 centres in 16 European countries reported anonymously H. pylori infected patients, the type (triple, quadruple, sequential), dose, and duration of treatment to the EuroPedHP registry. In cases with available antibiotic susceptibility results treatment should be tailored accordingly. Treatment regimens applied were critically reviewed at the annual fall meetings of the ESPGHAN working group of H. pylori. Suggestions and recommendations for improvement and implementation were communicated in written to all working group members. For this analysis we used only data of treatment naïve patients to avoid a bias by having different proportions of patients after failed therapy over time. Recommendation regarding dose per day were given according to body weight groups: 15-<25, 25-<35, 35-<45 and >45 kg. For this analysis, patients with a body weight <15 kg and >55 kg or missing data for weight were excluded.

**Results:** Of 934 patients in the registry, 505 fulfilled the inclusion criteria for the present analysis. Thereof 472 patients (93%) received triple therapy, 21 quadruple therapy (4%) and 12 patients sequential therapy (2%). Duration of therapy was between 7-8 days in 34 patients (6.6%), 10-12 days in 192 patients (38%), 14-15 days in 277 patients (55%), and 21-28 days in 2 patients (0.4%). Medications with dosages and treatment duration during different time period is given in the table

**Table:**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Median (min-max) [all doses mg/kg body weight]</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PPI</td>
<td>1.05 (0.38-2.9)</td>
<td>1.1 (0.36-3.3)</td>
<td>1.3 (0.40-2.6)</td>
<td>1.4 (0.6-2.5)</td>
</tr>
<tr>
<td>Amoxicillin</td>
<td>46.5 (27.8-85.7)</td>
<td>47.6 (20.0-93.8)</td>
<td>55.6 (31.9-115.4)</td>
<td>60.0 (24.2-144.2)</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>20.0 (14.5-35.7)</td>
<td>20.7 (9.8-41.7.5)</td>
<td>23.2 (13.9-40.0)</td>
<td>22.7 (14.3-48.1)</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>19.7 (1.9-43.5)</td>
<td>20.6 (13.5-37.5)</td>
<td>21.7 (12.0-38.5)</td>
<td>21.7 (16.0-38.5)</td>
</tr>
<tr>
<td><strong>Frequency of patients treated for different durations (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7-9 days</td>
<td>17 (20.0%)</td>
<td>15 (8.3%)</td>
<td>4 (3.0%)</td>
<td>3 (2.8%)</td>
</tr>
<tr>
<td>10-13 days</td>
<td>30 (35.3%)</td>
<td>109 (60.6%)</td>
<td>36 (26.9%)</td>
<td>12 (11.3%)</td>
</tr>
<tr>
<td>14-15 days</td>
<td>38 (44.7%)</td>
<td>54 (30.0%)</td>
<td>94 (70.1%)</td>
<td>91 (85.9%)</td>
</tr>
<tr>
<td>&gt;15 days</td>
<td>0 (0%)</td>
<td>2 (1.1%)</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Conclusion:** Our descriptive analysis show that in spite of giving detailed recommendation for dosing there was a wide range for the different drugs given.
Over time, median doses for all drugs and the percentage of children receiving the recommended 2 weeks of therapy increased confirming that being part of the registry is able to improve patient care. Further analysis will show whether this will result in better eradication rates.
Anti-IL10 autoantibodies as a novel cause of very early onset inflammatory bowel disease (VEO IBD) with resolution of bowel inflammation on B-cell-directed immunomodulatory therapy

Sophie Hambleton¹, Andrew Cant¹, Andras Szabo², Sophie Davies³, Gabriela Barcenas-Morales⁴, Maureen Lawson⁵, Elizabeth Renji⁵, Rainer Doffinger³, Susan Bunn⁵

¹Great North Children's Hospital, Department of Paediatric Immunology, Newcastle Upon Tyne, United Kingdom
²Royal Belfast Hospital for Sick Children, Department of Paediatric Gastroenterology, Belfast, United Kingdom
³Addenbrooke's Hospital, Department of Clinical Biochemistry and Immunology, Cambridge, United Kingdom
⁴Fes-Cuautitlan, Laboratorio de Inmunologia, Cuautitlán Izcalli, Mexico
⁵Great North Children's Hospital, Department of Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom

Objectives and study: Anti-cytokine autoantibodies are increasingly recognised in disease pathogenesis. Homozygous loss of function mutations in interleukin-10 (IL10) and interleukin-10 receptors (IL10R) cause severe infantile (very early onset (VEO)) inflammatory bowel disease (IBD).

Aim: To present a novel cause of VEO IBD and its targeted immunological therapy.

Results: A female Caucasian infant, initially well, developed bloody diarrhoea and vomiting from age 3 months. Dietary restrictions initially induced mild improvement but sudden deterioration at 17 months required parenteral nutrition (PN) from aged 18 months. Referred to national service for evaluation at 19 months. Cytokine profiling identified high serum IL10. IL10R defects were excluded by functional testing. Anti-cytokine profiling revealed high titres of neutralising anti-IL10 autoantibody.

Clinical course, endoscopic findings and serial serum IL10 & IL10 autoantibodies:

<table>
<thead>
<tr>
<th>Age (months)</th>
<th>Therapy</th>
<th>Clinically</th>
<th>Endoscopic findings</th>
<th>IL-10 ▲ (pg/mL)</th>
<th>Anti IL10 autoantibodies</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>PN dependant with vomiting, pain and bloody diarrhoea.</td>
<td>Gastritis &amp; severe colitis with deep rolled edged ulcers</td>
<td>200.39</td>
<td>+ve 1/312500</td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>1,2,3</td>
<td>PN dependant with vomiting, pain and bloody diarrhoea.</td>
<td></td>
<td>90.37</td>
<td>+ve 1/312500</td>
</tr>
<tr>
<td>23</td>
<td>1,2,3</td>
<td>PN dependant with vomiting, pain and bloody diarrhoea.</td>
<td></td>
<td>18.93</td>
<td>+ve 1/162500</td>
</tr>
<tr>
<td>26</td>
<td>1,2,4, 5*</td>
<td>Improving vomiting, non-bloody diarrhoea, improving pain. PN stopped.</td>
<td>Gastritis &amp; colitis with improvement in size and depth of colonic ulcers</td>
<td>30.7</td>
<td>+ve 1/312500</td>
</tr>
<tr>
<td>27</td>
<td>1,2,4,5</td>
<td>Stable. Off PN. No vomiting. Ongoing diarrhoea &amp; abdominal pain</td>
<td>Gastritis &amp; colitis with improvement in size and depth of colonic ulcers</td>
<td></td>
<td></td>
</tr>
<tr>
<td>29</td>
<td>1,2,5</td>
<td>Well. No pain. One formed stool per day.</td>
<td></td>
<td>13</td>
<td>-ve 1/100</td>
</tr>
<tr>
<td>32</td>
<td>1,2,5</td>
<td>Well. No pain. One formed stool per day.</td>
<td>Normal stomach and colon except areas of mild colonic scarring.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Therapy: 1) IVIG 2g reducing to 0.5g/kg 2 weekly; 2) iv Rituximab 3 monthly; 3) iv methylprednisolone (MP) 2mg/kg/day then weaning; 4) oral prednisolone 1mg/kg/day then weaning; 5) Infliximab 10mg/kg 4-weekly, weaning to 5mg/kg 8-weekly. *Infliximab added due to clinical relapse on steroid taper. ▲ Normal Range 0-1 pg/mL.

Summary: The early onset severe colonic inflammation resembled that seen in IL10 pathway defects. We hypothesised functional deficiency of IL10 due to high titre of neutralising anti-IL10 antibodies. To target autoantibody production, we combined anti-B cell therapy with more conventional, gut-directed immunosuppression. The latter enabled rapid weaning from PN, but ultimate resolution of clinical symptoms and gastrointestinal pathology was not obtained until confirmed absence of anti-IL10 autoantibodies some 7 months after starting Rituximab. Infliximab is to be stopped and we plan to maintain the child on Rituximab and replacement scIG in the medium term.

Conclusion: Identification of an anti-cytokine antibody to IL10 as a novel pathogenic mechanism for VEO IBD has allowed a targeted immunological therapy with avoidance of long term immunosuppression and resolution, rather than control, of the inflammatory process.
Ankyrin repeat and zinc finger domain containing 1 mutations are associated with infantile-onset inflammatory bowel disease

Désirée van Haaften-Visser¹, Magdalena Harakalova¹, Enric Mocholi¹, Joris van Montfrans¹, Abdul Elkadri², Ester Rieter¹, Karoline Fiedler², Peter van Hasselt¹, Mieke van Haelst¹, Isaac Nijman¹, Wigard Kloosterman¹, Edward Nieuwenhuis¹, Aleixo Muise², Edwin Cuppen¹, Paul Coffer¹, Roderick Houwen³

¹University Medical Center Utrecht, Utrecht, Netherlands
²Hospital for Sick Children, Toronto, Canada
³University Medical Center/Wilhelmina Children’s Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands

Objectives and study: Infantile-onset inflammatory bowel disease (IO IBD) is an invalidating illness with an onset before two years of age and has a complex pathophysiology in which genetic factors are important. We aimed to further unravel the pathogenesis of IO IBD by using molecular genetic methods.

Methods: Homozygosity mapping and whole exome sequencing was performed in an IO IBD patient born to consanguineous parents, identifying a candidate gene, which was sequenced in twelve additional IO IBD patients. The function of the candidate gene and the effect of the mutations found were subsequently investigated.

Results: In the index IO IBD patient a homozygous p.R585Q mutation was identified in the Ankyrin Repeat and Zinc Finger Domain containing 1 (ANKZF1) gene. Sequencing of ANKZF1 in the additional IO IBD patients revealed one patient with compound heterozygous ANKZF1 p.V32_Q87del and p.E152K mutations and two patients with a single heterozygous ANKZF1 mutation: g.220094405C>T and p.Q638P respectively. While the function of ANKZF1 in mammals had not been previously evaluated, we now could show that ANKZF1 has an indispensible role in the mitochondrial response to cellular stress. ANKZF1 depletion was found to reduce mitochondrial integrity and mitochondrial respiration under these conditions. The ANKZF1 mutations identified in IO IBD patients with two mutated ANKZF1 alleles indeed resulted in dysfunctional ANKZF1, as shown by an increased level of apoptosis in patients’ lymphocytes, a decrease in mitochondrial respiration and an inability of ANKZF1 R585Q and E152K to rescue the phenotype of Vms1-deficient yeast, the yeast homologue of ANKZF1.

Conclusion: These data indicate that loss-of-function ANKZF1 mutations in IO IBD patients result in deregulation of mitochondrial integrity, which suggests a role of this pathway in the pathogenesis of IO IBD.
Mesalamine enemas for induction of remission in pediatric ulcerative colitis refractory to oral Mesalamine: a prospective cohort study

Arie Levine1, Baruch Yerushalmi2, Michal Kori3, Efrat Broide4, Yael Mozer-Glassberg5, Ron Shaoul6, Kajsa Leena Kolho7, Eyal Shteyer8, Hussein Shamali9, Oren Ledder9, Shlomi Cohen10, Sarit Peleg11, Chen Sarbagili-Shabat1, Gili Focht12, Ebby Shachmon9, Mona Boaz13, Avi On14, Dan Turner8

1Paediatric and Gastroenterology and Nutrition Unit, Wolfson Medical Center, Tel Aviv University, Holon, Israel
2Soroka University Medical Center and Faculty of Health Sciences, Ben-Gurion University of the Negev, Beer-Sheva, Israel
3Kaplan Medical Center, Rehovot, Israel
4The Kamila Gonczarowski Institute of Gastroenterology and Liver Diseases, Assaf Harofeh Medical Center, Tzrifin, Israel
5Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach-Tikva, Israel
6Rambam Medical Center, Haifa, Israel
7Helsinki University, Department of Pediatric Gastroenterology, Helsinki, Finland
8Juliet Keidan Institute of Paediatric Gastroenterology, Shaare Zedek Medical Center, The Hebrew University of Jerusalem, Jerusalem, Israel
9St Vincent Hospital, Nazareth, Israel
10“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
11Haemek, Afula, Israel
12Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
13Department of Nutrition Sciences, Ariel University, Epidemiology and Research Unit, E. Wolfson Medical Center, Holon, Israel
14Poria, Teverious, Israel

Objectives and study: Ulcerative colitis is a difficult to control disease in children. Oral mesalamine can induce remission in <40% of mild to moderate patients. The goal of the current study was to prospectively evaluate the ability of mesalamine enemas to induce remission in children with mild to moderate UC failing to achieve remission with high dose oral mesalamine.

Methods: This was a 3-week open label arm of a multicenter, single blinded randomized controlled trial for active UC (i.e. the MUPPIT trial). Children, aged 4-18 years of age, with a PUCAI score between 10-55 were enrolled after failing at least 3 weeks of full dose oral mesalamine. Patients treated with steroids or enemas in the previous month and those with isolated proctitis were excluded. Children received Pentasa enemas 25 mg/kg (max one gram) daily for three weeks in combination with the previous high dose oral mesalamine. The primary endpoint was clinical remission by week 3, defined as PUCAI<10.

Results: Thirty eight children were enrolled (mean age 14.6 ± 2.3 years; 17/38 (45%) with extensive colitis. Clinical remission was obtained in 42% (n=16) while response rate was 71% (n=27) at week 3. Remission rates were similar between left sided (43%) and extensive (41%) colitis, and did not differ between mild (44%) and moderate (41%) disease (P>0.05 for both). Eight children deteriorated and required steroids. There were no differences in baseline parameters between those who entered or failed to enter remission.

Conclusion: This is the first paediatric evidence that addition of mesalamine enemas to existing oral mesalamine can induce clinical remission in children with ulcerative colitis who are refractory to high dose oral mesalamine.
Gastroenterology: Inflammatory bowel disease

G-O-034

Vedolizumab in pediatric inflammatory bowel disease: a retrospective multi-center experience from the Paediatric IBD Porto group of ESPGHAN

Oren Ledder1, Tim de Meij2, Javier Martin de Carpi3, Lisa Richmond4, Shlomi Cohen5, Jiri Bronsky6, Ron Shaoul1, Arie Levine8, Johanna Escher9, Lissy De Ridder10, Frank Ruemmele12, Neil Shah13, Victorien Wolters14, Astor Rodrigues15, Holm Uhlig16, Darja Urlep17, Carsten Posovszky18, Kaija Leena Kolho19, Dan Turner20

1Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
2Vu University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
3Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain
4Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
5"Dana-Dwek" Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
6Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic
7Ron Shaoul Medical Center, Haifa, Israel
8Wolfson Medical Center, Department of Pediatric Gastroenterology, Holon, Israel
9Erasmus MC-Sophia Children's Hospital, Pediatric Gastroenterology, Rotterdam, Netherlands
10Erasmus MC-Sophia Children's Hospital, Department of Pediatric Gastroenterology, Rotterdam, Netherlands
11Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel
12Hôpital Necker Enfants Malades, Department of Pediatric Gastroenterology, Université Paris Descartes, Sorbonne Paris Cité, Aphp, Paris, France
13Great Ormond Street Hospital for Children Foundation Trust, Dept of Gastroenterology, London, United Kingdom
14University Medical Center/Wilhelmina Children's Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
15Oxford University Hospital, Department of Paediatric Gastroenterology, Oxford, United Kingdom
16Oxford University Hospital, Oxford, United Kingdom
17Ljubljana University Medical Center, Ljubljana, Slovenia
18Klinik für Kinder- und Jugendmedizin Universitätsklinikum Ulm, Ulm, Germany
19Helsinki University, Department of Pediatric Gastroenterology, Helsinki, Finland
20Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: Vedolizumab (VDZ) has proven as an effective medication in adult Inflammatory Bowel Disease (IBD). There has been increased off-label use of VDZ also in children but with very limited published experience. Therefore we aimed to describe the short-term effectiveness and safety of VDZ in children with IBD in the largest pediatric cohort to date.

Methods: Retrospective review of children (2-18 years) treated with VDZ from 17 centers affiliated with the Paediatric IBD Porto group of ESPGHAN. Baseline characteristics and explicit prior and current clinical data were recorded on a standardized REDcap case-report forms. Primary outcome was treatment success at week 14 and last follow-up, defined as steroid-free remission (i.e. wPCDAI≤12.5 or PUCAI≤ 10) without the need for new medications or surgical intervention. Safety data were also explicitly recorded.

Results: Of the 55 included children, 33 (60%) had UC/IBDU, and 22 (40%) had Crohn’s Disease (CD); [28 (51%) male, mean age at first VDZ dose 14.5±2.8 years, and median disease duration 3.5 years (IQR 1.8-5.1)]. All were previously treated with anti-TNF (27% primary failure, 49% secondary failure, 15% adverse reaction and 9% for other reasons) and 8 (15%) had prior surgical intervention.
Success rates at week 14 were 21% in UC, and only 9% in CD (p=0.24). Median follow-up period was 22 weeks (IQR 14-22) from VDZ initiation (range 6-76). Success rates by last follow-up were 39% in UC and 27% in CD (p=0.36). By the last follow-up 8 (15%) new children required surgery, of whom 6 had colectomy for UC (18% of the entire UC cohort). There were three mild adverse events to VDZ, including pruritis, transient dyspnea and mild periorbital oedema; there were no serious drug-related adverse events. Median fecal calprotectin decreased from 1168mcg/gm (IQR 609-1409) prior to treatment to 412mcg/gm (IQR 54-745) following treatment when available (p=0.013).

**Conclusion:** In this largest real-life cohort of VDZ use in pediatric refractory IBD to date, VDZ was safe and effective in 21% and 39% of UC at 14 weeks and last follow-up whereas in CD the rates were 9% and 27%. These data thus support previous findings of slow induction rate of VDZ, particularly in CD.

**Disclosure of interest:** A Rodrigues, Conflict with Abbvie
J Bronsky, Conflict with Abbvie, MSD
F Ruemmele, Conflict with Takeda
D Turner, Conflict with Abbvie, Janssen, Takeda
All other authors have no conflict of interest
Efficacy, safety and immunogenicity of CT-P13 following transition from reference infliximab (Remicade) in children with established inflammatory bowel disease: a multi-centre prospective, observational study

Malgorzata Sladek¹, Alessandra Vultaggio², Silvia Ghione³, Francesca Nencini⁴, Andrea Matucci⁴, Sara Pratesi⁵, Francesca Zanieri⁶, Monica di Paola⁷, Monica Paci⁸, Agata Wasilewska⁹, Katarzyna Ponanta-Gawron¹⁰, Enrico Maggi², Paolo Lionetti¹¹

¹Jagiellonian University Medical College, Department of Pediatrics, Gastroenterology and Nutrition, Cracow, Poland
²University of Florence, Centre of Research Denothe and Department of Experimental and Clinical Medicine, Florence, Italy
³Meyer Children’s Hospital, Gastroenterology and Nutrition, Florence, Italy
⁴University of Florence, Immunoallergology Unit Aou Careggi, Florence, Italy
⁵University of Florence, Centre of Research Denothe and Department of Experimental and Clinical Medicine, Florence, Italy
⁶University of Florence, Immunoallergology Unit, Aou Careggi, Florence, Italy
⁷University of Florence, Department of Neuroscience, Psychology, Drug Research and Child Health, Florence, Italy
⁸University of Florence, Pediatric Gastroenterology and Nutrition Unit, Aou Careggi, Florence, Italy
⁹University Children’s Hospital, Jagiellonian University Medical College, Department of Paediatrics, Gastroenterology and Nutrition, Krakow, Poland
¹⁰Jagiellonian University Medical College, Department of Paediatrics, Gastroenterology and Nutrition, Krakow, Poland
¹¹University of Florence, Meyer Children’s Hospital, Neurofarba Department, Gastroenterology and Nutrition, Firenze, Italy

Objectives and study: CT-P13 is the first approved biosimilar infliximab (IFX) for all indications of the reference product (Remicade®). Similar-but-not-identical nature of CT-P13 compare to Remicade®, the concept of extrapolating data from one therapeutic indication to another, very limited clinical data on its use in inflammatory bowel disease (IBD) may be puzzling to physicians. In the present study we aimed to gain data on the efficacy, safety and immunogenicity of transition from Remicade to CT-P13 in a real-life IBD paediatric patients.

Methods: In this prospective, multi-centre study, all paediatric IBD patients treated with Remicade® at two academic centres in Italy and Poland were electively transitioned to CT-P13. Registration was performed with a start time 2 months before transition, and for the each patient data on the efficacy, safety and immunogenicity were evaluated at the transition to CT-P13, at the second and fourth CT-P13 infusion with the follow up lasted for up to week 24-36. The primary end-point was the change in clinical disease activity and adverse reaction following transition. The secondary end-points included changes in inflammatory markers such as C-reactive protein (CRP), erythrocyte sedimentation (ESR), faecal calprotectin (FCP), infliximab trough level (TL) and development of anti-drug antibodies (ADAs).

Results: In total, 45 IBD children, 38 Crohn’s disease (CD) and 7 ulcerative colitis (UC) were transitioned at the mean time elapsed between the beginning of Remicade therapy of 23.6 ±15.5 months for CD and 12.0±15.5 months for UC. At the time of the transition 33/38 CD and 4/7 UC patients presented with clinical remission. We did not observe any change in clinical disease activity, CRP, ESR, FCP, IFX-TL for both CD and UC. Of three patients having CT-P13 discontinued, only for one case the reason was an adverse reaction with high ADAs, presented even before the transition. One patients developed new detectable ADAs, and one patient with detectable ADAs before transition presented with undetectable level thereafter.

Conclusion: Our data indicate that clinical efficacy, safety and immunogenicity profile were highly comparable before and after the transition from Remicade® to CT-P13 in paediatric IBD patients.

Disclosure of interest: M Sladek - has served as a speaker, consultant and/or advisory board member for MSD, Abbvie, EGIS and Mundipharma
Comparison of immunogenicity of biosimilar infliximab and originator infliximab in children with inflammatory bowel disease in real life clinical setting

Amar Wahid¹, Wolfram Haller¹, Theo Wong¹, Susan Protheroe¹, Ronald Bremner¹, Lisa Whyte¹, Rafeeq Muhammed¹

¹Birmingham Children's Hospital, Department of Gastroenterology, Birmingham, United Kingdom

Objectives and study: Biosimilar Infliximab (CT-P13) has been used for the treatment of paediatric Crohn's Disease (CD) and Ulcerative Colitis (UC) since 2015 in the United Kingdom. There are no randomised controlled trials (RCT) in children with Inflammatory Bowel Disease (IBD) assessing the immunogenicity of biosimilar Infliximab. Aim of the study is To compare the immunogenicity of Biosimilar Infliximab and originator Infliximab in children with IBD.

Methods: We performed a single centre evaluation of 220 patients (185 patients with CD and 35 with UC) who had received Infliximab for IBD. We analysed the rate of anti-Infliximab antibody positivity, clinical remission and co-immunosuppression.

Results: 60 children with CD received treatment with Biosimilar Infliximab. 34/44 (77%) had anti-Infliximab antibodies. 125 children with CD received treatment with Originator Infliximab. 55/78 (71%) had anti-Infliximab antibody positivity. There was no difference between disease characteristics, rate of clinical remission at 6 months and co-immunosuppression between these two groups.

20 children with UC received treatment with Biosimilar Infliximab. 7/11 (64%) had anti-Infliximab antibodies. 15 children with UC received treatment with originator Infliximab. 3/6 (50%) had anti-Infliximab antibodies. There was no difference between disease characteristics, rate of clinical remission at 3 months and co-immunosuppression between these two groups.

Conclusion: The rate of anti-Infliximab antibody formation was not different with the use of biosimilar and originator Infliximab. Most patients with anti-Infliximab antibodies achieved clinical remission. These findings are reassuring when considering change in clinical practice to the use of biosimilar infliximab, which has the advantage of significant cost savings for the health care systems.

Disclosure of interest: RM • speaker’s fee- MSD Immunology, Abbvie, Dr Falk and Pfizer
• Research grants- MSD Immunology & Abbvie
• Travel & meeting support- MSD Immunology, Abbvie, Dr Falk, Tillotts Pharma, Nestle, Takeda and Pfizer.
• Educational grants- Abbvie
• Consultancy work- Abbvie & Pfizer

Other authors have no interests to declare
Hypoalbuminemia and ASCA but not CRP or calprotectin are predictors for early surgery in pediatric Crohn's disease; results of the prospective GROWTH CD study

Arie Levine1, Seamus Hussey2, Malgorzata Sladek3, Kaja Kolho4, Javier Martin de Carpi5, Dan Turner6, Richard Russell7, Noa Cohen_Dolev8, Johanna Escher9

1Wolfson Medical Center, Department of Pediatric Gastroenterology, Holon, Israel
2National Children's Research Centre, National Centre for Paediatric Gastroenterology, Dublin, Ireland
3Jagiellonian University Medical College, Department of Pediatrics, Gastroenterology and Nutrition, Cracow, Poland
4Children’s Hospital, University Central Hospital and University of Helsinki, Department of Pediatric Gastroenterology, Helsinki, Finland
5Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain
6Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel
7Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
8The E.Wolfson Medical Center, Pediatric Ibd Research Center, Holon, Israel
9Erasmus MC-Sophia Children's Hospital, Pediatric Gastroenterology, Rotterdam, Netherlands

Objectives and study: Children with Crohn's disease (CD) are at a high risk for complications from both disease and treatment. The ability to predict risk and adverse outcomes at or close to diagnosis would allow patients to be stratified by risk, in order to avoid under treatment or overtreatment while reducing adverse outcomes from drug and disease. The goal of the current prospective study was to identify factors that would predict early complicated disease behavior or surgery.

Methods: The GROWTH CD study (Growth, Relapses and Outcomes With TTherapy) is geared to identify factors that could predict early outcomes such as complications and surgery by 24 months. Newly diagnosed children underwent colonoscopy, gastroscopy and imaging. They were phenotyped by the Paris classification and followed at baseline, 8, 12, 26, 52, 78 and 104 weeks. Twenty dichotomous and continuous variables were assessed, including serum biomarkers (ASCA, CBIR1, OMPC), measures of inflammation (ESR, CRP, Calprotectin), disease activity (PCDAI and PGA) and serum albumin. Predictors at diagnosis and week 12 (post induction treatment) served as prediction time points. Complications and surgery were recorded at weeks 78 and 104. Logistic regression and risk modeling was performed for best fit models.

Results: 285 children, median age 13 years, 60% male, were followed prospectively for 2 years, of whom 78 (27.3%) developed complications and 28 (9.8%) required surgery. Use of immunomodulators was not associated with decreased risk, (complications and surgery both p=0.9). Five parameters predicted increased risk of surgery (very high ESR wk 0, stricturing disease at diagnosis, and ASCA, albumin or elevated PCDAI >10 at week 12). The first 4 remained in the best fit model. The combination of Paris B2 (OR 4.2, CI 1.3-12.7) p=0.01, ESR>50 (OR 2.9, CI1.0-8.642) p=0.049 at baseline ,and Alb<3.6 (OR 4.9 CI 1.2-19.6) , p=0.024. and ASCA IgA (OR 1.02, CI 1.007-1.03) p=0.001 after therapy week 12. had a sensitivity 10%, specificity 98.7%, PPV 50% and NPV 89.4%, the model is significant (p<0.0001) and correctly classifies 88.6% of the study population requiring early surgery.

Conclusion: Hypoalbuminemia and ASCA at week 12 and very elevated ESR and complicated disease at baseline were good predictors for patients at risk for early surgery. Fecal calprotectin and CRP were not predictive at any time point.

Supported by grants from ECCO and the Thrasher Research Fund
Pouchitis in paediatric UC: a multicentre longitudinal cohort study from the Porto IBD working group of ESPGHAN

Esther Orlanski-Meyer,1 Chani Topf-Olivestone,1 Oren Ledder1, Mira Friedman1, Iris Dotan2, Lars-Folmer Hansen3, Angelika Kindermann4, Assa Amit5, Kaija Leena Kolho6, Sanja Kolacek7, Eytan Wine8, Caterina Strisciuglio9, Marina Aloj10, Richard Hansen11, Harland Winter12, Victor Manuel Navas López13, Lissy De Ridder14, Françoise Smets15, Dan Turner16

1Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
2Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Department of Gastroenterology and Liver Diseases, Tel Aviv, Israel
3Hvidovre University Hospital, Department of Pediatrics, Copenhagen, Denmark
4Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
5Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel
6Helsinki University, Department of Pediatric Gastroenterology, Helsinki, Finland
7Zagreb University Medical School, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
8Division of Pediatric Gastroenterology, Pediatrics, Edmonton, Canada
9Second University of Naples, Department of Woman, Child and General and Specialistic Surgery, Naples, Italy
10Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
11Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
12Massachusetts General Hospital for Children, Boston, United States
13Hospital Materno Infantil, Málaga, Spain
14Erasmus MC-Sophia Children’s Hospital, Department of Pediatric Gastroenterology, Rotterdam, Netherlands
15UCL, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Pediatric Gastroenterology and Hepatology Unit, Brussels, Belgium
16Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: Risk factors associated with the development of pouchitis in adults after formation of an ileal pouch anal anastomosis (IPAA) include severe inflammation at diagnosis, upper gastrointestinal (UGI) involvement, backwash ileitis, pancolitis, and extra-intestinal manifestations (EIM), all of which are more common in paediatric-onset UC. We thus aimed to assess outcomes and explore risk factors for pouchitis in children who underwent IPAA before the age of 18 years.

Methods: Data were retrospectively collected from 17 paediatric IBD centres from the Porto group of ESPGHAN. Electronic REDcap system was used, including explicit baseline characteristics, management, surgical information and medical short and long term follow up.

Results: A total of 129 children who underwent IPAA were included (50% male; 93% UC and 7% IBDU, mean age at diagnosis 10.5±4.2 years, median disease duration to colectomy 17 months (IQR 8-35.5 months) and median follow-up after pouch formation 36 months (IQR 21-64 months). Eighty-six children (67%) developed pouchitis during follow-up. In 33 (26%) the pouchitis was chronic, 10 of whom (8%) had Crohn’s-like disease of the pouch. Median time from pouch formation to the first episode of pouchitis was 10.5 months (IQR 6-22); in 54% of cases the first episode occurred within one year.

The experience of the surgeon was strongly associated with development of chronic pouchitis (8/54 (15%) in surgeons with ≥10 surgeries/year vs 11/27 (41%) in surgeons with <10/year, p=0.013). There was no significant added benefit to surgeon experience greater than 10 surgeries/year.
Other variables that were associated with development of pouchitis included: younger age at diagnosis (mean 9.9±4.3 vs 11.7±3.7 years; p=0.014), longer disease duration prior to colectomy (median 22 (IQR 10-39) vs 13 (6-29) months; p=0.026), and Ashkenazi Jewish ethnicity (7/15 Ashkenazi patients with chronic pouchitis vs 21/103 patients of other ethnicity; p=0.046). The following variables did not predict pouchitis: UGI involvement, disease extent, backwash ileitis, EIM, pANCA positivity, IPAA type, and high PUCAI score at diagnosis/surgery). Multivariate logistic regression showed that chronic pouchitis was associated with male gender (HR=4.3, 95%CI 1.2-14.7) and surgeon experience (<10 surgeries per/year) (HR=5.2, 95%CI 1.5-18.6) while controlling for age and disease duration.

**Conclusion:** UC patients who underwent IPAA during childhood developed pouchitis at a higher rate than usually described in adults. Surgeon experience seems to be an important controllable predictor of chronic pouchitis and should be taken into consideration in paediatric patients.
Transfer of *Bifidobacterium lactis animalis* HNO 19 administered orally to pregnant and lactating mother into breastmilk

Naomi Dewanto1, Agus Firmansyah2, Saptawati Bardosono3, Ali Sungkar4, Nani Dharmasetiawani5, Sudigdo Sastroasmoro6

1Siloam Hospitals, Pediatric, Jakarta, Indonesia
2Gastrohepatology Division, Department of Child Health, Faculty of Medicine, Universitas Indonesia – Cipto Mangunkusumo Hospital, Jakarta, Indonesia
3Faculty of Medicine University of Indonesia, Department of Clinical Nutrition, Jakarta, Indonesia
4University of Indonesia, Obstetri and Gynecology, Jakarta, Indonesia
5Budi Kemuliaan Hospital, Pediatric, Jakarta, Indonesia
6Faculty of Medicine The University of Indonesia / Dr. Ciptomangunkusumo Hospital, Pediatrics, Jakarta, Indonesia

Objectives and study: Probiotics are known to help gut maturity. It remains unclear, however, whether probiotics pass through the breast milk or the positive culture is a result of contamination. The objective of this study was to trace *Bifidobacterium animalis lactis* HNO19 administered orally to pregnant and lactating mothers in the breast milk at birth and when the baby aged 3 months.

Methods: Two parallel groups with double-blinded randomized controlled trial study was done from December 2014 until December 2015. *Bifidobacterium animalis lactis* HNO19 (also known as DR10) was used since it is not resident bacteria.

Results: DR10 was detected in the colostrum in 5 of 35 subjects and in the breast milk in 7 of 35 subjects when the baby aged 3 months. In contrast, DR10 was not detected in placebo group and in the skin swab.

Table: Result of breastmilk and skin swab DR10

<table>
<thead>
<tr>
<th>GROUP</th>
<th>DR10</th>
<th>Probiotic n = 35</th>
<th>Placebo n= 35</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Breastmilk</td>
<td>n = 35</td>
<td>Placebo n= 35</td>
</tr>
<tr>
<td></td>
<td>n</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>V₀</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>V₃</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Copy number/mL</td>
<td>Median ( min – max)</td>
<td>Probiotic</td>
<td>Placebo</td>
</tr>
<tr>
<td>Breastmilk</td>
<td>V₀</td>
<td>53.6 (25.3–74.4)</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>V₃</td>
<td>60.4 (5.7–65.7)</td>
<td>0</td>
</tr>
<tr>
<td>Skin swab</td>
<td>V₀</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>V₃</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>


Conclusion: Probiotic DR10 administered to pregnant and lactating women was detected in the colostrum and in the breast milk at 3 months. DR10 found in the breast milk came from inside (internal) and was not a contamination.
Quantitative analysis of meconium microbiota in healthy term infants reveals delayed colonization of Lactobacillus after cesarean delivery

Ravinder Nagpal1, Yuichiro Yamashiro1, Hirokazu Tsuji2, Takuya Takahashi2, Kazunari Kawashima3, Satoru Nagata4, Koji Nomoto2

1Juntendo University Graduate School of Medicine, Probiotics Research Laboratory, Bunkyo-Ku, Japan
2Yakult Central Institute, Kunitachi, Japan
3Gonohashi Obstetrics and Gynecology Hospital, Koto-Ku, Japan
4Tokyo Women’s Medical University, Paediatrics Medicine, Shinjuku, Japan

Objectives and study: It had long been believed that babies’ intestines are sterile until birth and the microbial colonization of infant gut begins during birth and promptly thereafter. However, some recent studies have indicated that fetuses might already be exposed to bacteria in-utero, although the quantitative data on these bacteria is sparse. Herein, we aimed to detect and quantify such bacteria in the meconium of healthy full-term neonates born vaginally or by C-section.

Methods: First-pass meconium samples from 151 healthy term Japanese infants (vaginal-delivery: n=134; C-section: n=17) were obtained within 24-48 hours of birth; RNA contents were extracted and subjected to reverse-transcription-quantitative PCR analyses using specific primers for Clostridium coccoides group, Clostridium leptum subgroup, Bacteroides fragilis group, Atopobium cluster, Prevotella, Bifidobacterium, Lactobacillus, Enterococcus, Enterobacteriaceae, Staphylococcus, Enterococcus, and Clostridium perfringens. Stool samples were also collected at age 3 and 7 days, 1, 3 and 6 months, and 3 years for follow-up analyses. The study was approved by the Institutional ethical committee, and prior written informed consent was obtained from the parents.

Results: Interestingly, several bacterial groups were detected in the meconium of both vaginally- and cesarean-born infants. B. fragilis group, Enterobacteriaceae, Enterococcus and Staphylococcus were detected in more than 50% of infants, with counts ranging from 5-7 log_{10} cells/g sample. About 33-34% of samples harbored Bifidobacterium and Lactobacillus in the range of 4-5 log_{10} cells/g; whereas C. coccoides group, C. leptum subgroup and C. perfringens in the range of 3-5 log_{10} cells/g were detected in about 10-20% of infants. Compared to vaginally-born, the meconium of cesarean-born infants were significantly less often colonized with Lactobacillus genus (6% vs. 37%) and L. gasseri subgroup (6% vs. 31%). Overall, seven Lactobacillus subgroups/species i.e. L. gasseri subgroup, L. ruminis subgroup, L. casei subgroup, L. reuteri subgroup, L. sakei subgroup, L. plantarum subgroup and L. brevis were detected in the samples from vaginally-born group, whereas only two members i.e. L. gasseri subgroup and L. brevis were detected in the cesarean group. Follow-up analysis revealed that, compared to vaginally-born infants, cesarean-born babies had significantly or insignificantly lower prevalence of several members of the Lactobacillus community at different time-points during the first six months of life; though these differences tended to disappear by age 3 years.

Conclusion: These data manifest the quantitative profile of bacterial pool present in the newborn’s first meconium and corroborate the notion that the microbial colonization of the infant gut may begin already before birth. In addition, delayed/ lower colonization of lactobacilli and relatively different proportions of facultative vs. obligatory anaerobes in the meconium of cesarean-born babies hint that the elements of cesarean-associated gut dysbiosis may start building up as early as the first day of life. Given the importance of early-life microbiota development in newborn’s growth and development, our data underline the need for comprehensive studies to investigate the sources, routes and significance of these bacterial clades in the prenatal niches, as well as to inspect the effect of these microbial exposures on baby’s long-term health.
GASTROENTEROLOGY: GI motility, GERD and functional GI disorders

G-O-041

Functional gastrointestinal disorders in children and adolescents from the European-Mediterranean area: a prevalence study

Elena Scarpato1, Sanja Kolacek2, Vlatka Konjik3, Danijela Jojkic-Pavkov4, Enriqueta Román Riechmann5, Aco Kostovski6, Eyad Altamimi7, Alexandra Papadopoulou8, Panayota Kafritsa9, Thomas Karagiozoglou-Lampoudi10, Raanan Shamir11, Aziz Koleilat12, Sirin Mneimneh13, Annamaria Staiano1

1Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
2Zagreb University Medical School, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
3Clinical Hospital Osijek, Pediatric Clinic, Department of Pulmology, Allergology, Immunology and Gastroenterology, Osijek, Croatia
4Institute for Child and Youth Health Care of Vojvodina, Department of Gastroenterology, Hepatology and Nutrition, Novi Sad, Serbia
5Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
6University Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece
7University of Athens, Athens Children’s Hospital “agia Sophia, Department of Pediatrics, Athens, Greece
8Alexander Technological Educational Institute of Thessaloniki, Laboratory of Clinical Nutrition “Christos Mantzoros” Department of Nutrition - Dietetics, Thessaloniki, Greece
9Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
10Makassed University General Hospital, Beirut, Lebanon

Objectives and study: Data on the prevalence of functional gastrointestinal (GI) disorders (FGIDs) in European children are scarce. This multicenter study aimed at assessing the prevalence of FGIDs in a community sample of children and adolescents from the European-Mediterranean Area.

Methods: Prevalence of FGIDs has been assessed using the questionnaires on pediatric GI symptoms based on Rome III Criteria (QPGS-RIII). Subjects have been enrolled in schools.

Results: We have enrolled 6602 subjects aged between 4-10 years (Group A: mean age, 7.7±1.9 years; females 50.8%), and 7039 subjects aged between 11-18 years (Group B: mean age, 13.8±2.1 years; females, 50.6%) from 9 countries: Croatia (A: 809, and B: 907); Greece (A: 727, and B: 589); Israel (A: 399, and B: 823); Italy (A: 1070, and B: 1048); Jordan (A: 822, and B: 766); Lebanon (A: 537, and B: 470); Macedonia (A: 711, and B: 844); Serbia (A: 828, and B: 829); and Spain (A: 699, and B: 866). Regarding subjects aged between 4-10 years, overall prevalence of at least one FGID was 17.4% (females 52.2%). Specifically, 11.6% met criteria for functional constipation, 3.9% for irritable bowel syndrome, 3.5% for aerophagia, 3.1% for abdominal migraine, 0.5% for non-retentive fecal incontinence, 0.3% for functional dyspepsia, 0.3% for functional abdominal pain (lower abdominal location), 0.3% for cyclic vomiting syndrome, 0.2% for functional abdominal pain (upper abdominal location), 0.2% for functional abdominal pain syndrome (lower abdominal location), 0.1% for functional abdominal pain syndrome (upper abdominal location), and 0.03% for adolescent ruminant syndrome. In addition, in 2.8% of the cases, subjects met criteria for two disorders at the same time (females 57.9%). Considering subjects aged between 11-17 years, overall prevalence of FGIDs was 19.5% (females 57.3%). Particularly, 13.1% fulfilled criteria for functional constipation, 7.8% for abdominal migraine, 6.3% for aerophagia, 5.6% for irritable bowel syndrome, 0.5% for functional dyspepsia, 0.5% cyclic vomiting syndrome, 0.4% for functional abdominal pain syndrome (lower abdominal location), 0.4% for non-retentive fecal incontinence, 0.2% for functional abdominal pain (lower abdominal location), 0.2% for functional abdominal pain syndrome (upper abdominal location), 0.1% for adolescent ruminant syndrome, and 0.1% for functional abdominal pain (upper abdominal location). In 6% of the subjects from Group B, two disorders were present at the same time.
(females 58.6%). Moreover, we detected significant differences in the frequency of specific disorders among the participating countries.

**Conclusion:** Our data confirm that FGIDs are common disorders, that are more frequent in subjects older than 10 years of age. Functional constipation, aerophagia, abdominal migraine and irritable bowel syndrome are the most common disorders in both age groups. Finally, we found significant differences in FGIDs prevalence among the involved countries. The project is funded by a network grant from the European Society for Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN).
The prognostic value of manometry testing in children with constipation treated with sacral nerve stimulation

Ilan Koppen1, Peter Lu2, Katherine Deans3, Peter Minneci3, Karen Diefenbach3, Seth Alpert3, Marc Benninga4, Desalegn Yacob2, Carlo Di Lorenzo2

1Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands
2Nationwide Children's Hospital, Pediatric Gastroenterology, Columbus, United States
3Nationwide Children's Hospital, Columbus, United States
4Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Evidence exists that sacral nerve stimulation (SNS) modulates anorectal and colonic function in adults with defecatory dysfunction and can be effective in the treatment of children with intractable constipation. However, prognostic factors of treatment success have not been identified. The aim of this study was to evaluate the prognostic value of anorectal manometry (AM) and colonic manometry (CM) in children with constipation treated with SNS.

Methods: Using a prospective patient registry, we identified patients who underwent AM or CM prior to SNS initiation for treatment of intractable constipation. Encounters at baseline, prior to SNS, and at the most recent follow-up visit were reviewed. Successful response to SNS was defined as having ≥3 bowel movements and <1 episode of fecal incontinence per week. We also compared medication usage, antegrade continence enema (ACE) usage, and PedsQL GI Symptom Scale (GSS) at baseline and follow-up. AM and CM testing prior to SNS were reviewed. We used Fisher’s exact test to evaluate for an association between AM/CM findings and response to SNS. We used Wilcoxon signed-rank test to compare median scores (GSS) at baseline and after SNS.

Results: We included 21 patients (57% female, median age 13 years at SNS initiation). Three patients had a history of anorectal malformation, 2 had Hirschsprung's disease, 1 had a spinal cord abnormality, and the remaining 15 were diagnosed with functional constipation. Seventy-one percent had urinary symptoms and 67% had fecal incontinence at baseline. Twenty children had undergone AM prior to SNS initiation and 7 had undergone CM. Of the 21 patients, 10 (48%) were classified as responders. Of the 11 non-responders, 1 had undergone SNS removal due to lack of response, 1 had undergone subsequent segmental colonic resection, and 2 had undergone SNS removal due to infection. Four of 10 responders were successfully weaned from laxatives and/or ACE at follow-up compared to none of the non-responders. Baseline AM and CM results and association with SNS response are shown in Table 1. Overall, the median GSS score improved from 50.0 before SNS to 61.1 after SNS (p=0.047).
Table: Association between response to SNS and manometry results and patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Responders (n=10)</th>
<th>Non-responders (n=11)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anorectal manometry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal resting pressure (n=19)</td>
<td>9 (90%)</td>
<td>6 (67%)</td>
<td>0.30</td>
</tr>
<tr>
<td>Normal sensation (n=14)</td>
<td>6 (75%)</td>
<td>6 (100%)</td>
<td>0.47</td>
</tr>
<tr>
<td>RAIR present</td>
<td>10 (100%)</td>
<td>9 (90%)</td>
<td>1.00</td>
</tr>
<tr>
<td>RAIR complete</td>
<td>9 (90%)</td>
<td>7 (70%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Normal interpretation</td>
<td>6 (60%)</td>
<td>5 (50%)</td>
<td>1.00</td>
</tr>
<tr>
<td><strong>Colonic manometry</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Postprandial response</td>
<td>3 (100%)</td>
<td>4 (100%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Response to bisacodyl</td>
<td>2 (67%)</td>
<td>4 (100%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Urge after bisacodyl</td>
<td>2 (67%)</td>
<td>4 (100%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Stools after bisacodyl</td>
<td>2 (67%)</td>
<td>4 (100%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Normal interpretation</td>
<td>2 (67%)</td>
<td>4 (100%)</td>
<td>0.43</td>
</tr>
<tr>
<td>Postprandial response</td>
<td>3 (100%)</td>
<td>4 (100%)</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Patient characteristics</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Functional constipation</td>
<td>7 (70%)</td>
<td>8 (73%)</td>
<td>0.89</td>
</tr>
<tr>
<td>Fecal incontinence</td>
<td>6 (60%)</td>
<td>8 (73%)</td>
<td>0.66</td>
</tr>
<tr>
<td>Urinary symptoms</td>
<td>5 (50%)</td>
<td>10 (91%)</td>
<td>0.06</td>
</tr>
</tbody>
</table>

**Conclusion:** In this sample of children with intractable constipation treated with SNS, AM and CM findings were not associated with successful or unsuccessful response to SNS. Therefore, abnormal AM or CM should not preclude children with intractable constipation from consideration of SNS treatment. Further studies with larger sample sizes are needed to better understand the role of manometry in the evaluation of children with intractable constipation treated with SNS.
Internet-delivered cognitive behaviour therapy for children with pain-related functional gastrointestinal disorders - a feasibility study

Maria Lalouni1, Brjánn Ljótsson2, Marianne Bonnert2, Erik Hedman2, Jens Högström3, Eva Serlachius2, Ola Olen4

1Karolinska Institutet, Department of Medicine, Solna, Stockholm, Sweden
2Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden
3Karolinska Institutet, Department of Clinical Neuroscience, Division of Psychology, Stockholm, Sweden
4Karolinska Institutet, Department of Medicine Solna, Clinical Epidemiology Unit, Stockholm, Sweden

Objectives and study: Pain-related functional gastrointestinal disorders (P-FGIDs) are highly prevalent in children and associated with low quality of life, anxiety and school absence. Treatment options are scarce and there is a need for effective and accessible treatments. Internet-delivered cognitive behaviour therapy (Internet-CBT) is effective for adult and adolescent IBS, but has not been evaluated for younger children. This was a within-group design feasibility study. The objectives were to assess acceptability, feasibility and preliminary effect sizes of Internet-CBT for children with P-FGIDs.

Methods: We included 31 children, 8-12 years, diagnosed with P-FGID, according to the ROME III criteria. Mean duration of abdominal symptoms was 3.8 years (sd=2.6). The treatment consisted of ten weekly modules of exposure-based cognitive behaviour therapy, provided to the children and parents, via an Internet platform. The children were instructed to provoke abdominal symptoms in a gradual manner, and to engage in previously avoided activities. Parents’ protocol included redirecting parental attention from the children’s pain behaviours, to the work with the exposure exercises. Assessments included gastrointestinal symptoms, quality of life, gastrointestinal-specific anxiety and school absence. The assessments were conducted online at pre-treatment, post-treatment, and 6-month follow-up. Means and standard errors were estimated and Cohen’s d effect sizes were calculated using multi-level linear mixed models.

Results: Most children completed all chapters (mean = 8.6 of 10 chapters) and 90% (n=27) reported that the treatment had helped them to deal more effectively with their symptoms. On a subjective assessment of the effects of the treatment 26 of 30 children reported that their symptoms had improved during the treatment. No child reported that the symptoms had worsened. We observed a large effect size on the primary outcome measure, child-rated gastrointestinal symptoms, from pre-treatment to post-treatment (Cohen’s d = 1.14, p<.001), and this effect was maintained at 6-month follow-up (Cohen’s d = 1.40, p<.001). Figure 1 shows the scores at pre, post and 6-month follow up.
We also observed large effect sizes on the secondary measures, quality of life (Cohen’s $d=1.26$, $p<.001$), and gastrointestinal specific anxiety (Cohen’s $d=0.92$, $p<.001$), from pre-treatment to post-treatment. These effects were maintained at 6-month follow-up (Cohen’s $d=1.43$, $p<.001$ and $d=1.24$, $p<.001$, respectively). Before treatment, 25 (80.6%) of the children reported school absence related to abdominal symptoms. At post-treatment and 6-month follow-up assessments, 14 (46.7%) and 10 (35.7%) children, respectively, reported school absence. At post 7 (23%) children did not fulfill ROME III criteria according to self-assessments and at 6-month follow-up 19 (61%) no longer fulfilled criteria. Parents’ assessments supported the results from children’s assessment.

**Conclusion:** This study shows that children with longstanding P-FGIDs, and their parents, perceive exposure-based Internet-CBT as a helpful and feasible treatment. Within-group effect sizes were large and remained stable at 6-month follow-up. The results are promising and have provided valuable information for a randomized controlled trial, which is currently being conducted by the research group.
Screening of esophageal varices in children using esophageal capsule endoscopy: result of a multicenter prospective study

Jacques Cardey¹, Catherine Le Gall², Laurent Michaud³, alain dabadie⁴, Cecile Talbote⁵, Marc Bellaiche⁶, Thierry Lamireau⁷, Emmanuel Mas⁸, Laure Bridoux-Henno⁹, Jerome Viala⁶, Alain Lachaux¹⁰

¹Necker-Enfants Malades Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Paris, France
²Femme Mère Enfant Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Lyon, France
³Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
⁴Chu Rennes, Pediatric Gastroenterology, Rennes, France
⁵Chu Rennes, Pediatric Gastroenterology, Rennes, France
⁶Robert Debré Hospital, Pediatric Gastroenterology and Nutrition, Paris, France
⁷University Hospital, Paediatric Gastroenterology, Rennes, France
⁸Centre Hospitalier Universitaire de Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, and Genius Group, Toulouse, France
⁹Chu Hôpital Sud, Pediatric Gastroenterology, Rennes, France
¹⁰Hôpital Femme Mère Enfant du Chu de Lyon, Pediatric Gastroenterology, Hepatology Nutrition Unit Reference Centre for Wilson Disease, Lyon, France

Objectives and study: Esophagogastroduodenoscopy (EGD) is the standard method for accuracy diagnosis of esophago-gastric varices in children. The aim of this first prospective multicenter study was to evaluate the esophageal capsule endoscopy (ECE) for this indication in pediatrics with portal hypertension (PHT).

Methods: From November 2011 to July 2013, children referred to 7 academic centers, aged from 7 to 18 years presenting with PHT and/or cirrhosis underwent ECE (PillCam® ESO 2, Given Imaging) followed by EGD. Each child had to pass a "candy test" prior to the ECE. ECE was first performed, EGD was scheduled after the ECE, usually the same day or within 7 days. Capsule recordings were blindly read by two endoscopists. They recorded the presence or absence of varices and, if present, graded the varices using the de Francis classification; a second classification using a Schreibman modified score (SMS), was also used. At EGD, varices were classified with the 3 endoscopic grades based on the Japanese Research Society for Portal Hypertension. The primary end point was to assess in children the sensitivity (SE) of ECE for the presence of esophageal varices by using EGD with sedation as the reference standard. Secondary objectives were to determine specificity (SP), positive and negative predictive values (PPV, NPV) for the presence of EV and concordance according to EV classification, the presence of gastric varices (GV), red signs on EV(RS) and portal hypertensive gastropathy, tolerance and procedure feasibility.

Results: A total of 102 patients were enrolled, 81 (52 boys, 29 girls) were included in the analysis with a mean age of 13.96 +/- 0.25 years. Of the 21 excluded patients, 16 were excluded for a failure at the candy test. Sensitivity for the detection of EV was 92%, specificity 100%, PPV 100% and NPV 79%. Based on 57/81 patients who had small and large varices at both ECE and EGD and using de Franchis classification, the SN, SP, PPV and NPV were: 55, 92, 89 and respectively 63% for a total overall accuracy of 72%. When SMS was used to classify the esophageal varices, the SN, SP, PPV and NPV calculated values were respectively: 100, 93, 94 and 100% for a total overall accuracy of 97%. For PHT gastropathy (70 patients), the SE, SP, PPV and NPV were respectively: 98.2, 53.8, 90.3 and 87.5 %. For gastric varices (21 patients with possible analysis), the SE, SP, PPV and NPV were respectively: 58.3, 90.3, 70 and 84.4%. For the red signs (RS) the SE, SP, PPV and NPV were respectively: 90.3, 84, 77.7 and 93.3 %. As for control of eradication of EV after an endoscopic variceal ligation (EVL) before inclusion (24 patients), if only ECE had been done, only 2 children would have had an inadequate indication of a new secondary prophylaxis; besides, none of the children was deprived of indication of EVL. For the children without any known EV (21 patients), the SE and SP for
the ECE were both 100 %. All subjects have preferred the ECE instead of the EGD procedure. No capsule endoscopy retention has been reported during the study.

**Conclusion:** In this study ECE had good performance in terms of presence of EV, classification of EV and presence of RS and could therefore be proposed for EV screening as well as a diagnostic tool for detection of grade 2-3 EV during cirrhosis and PHT. We proposed a modified classification to better differentiate stage 1 and stage 2 varices since the de Franchis classification underestimates stage 2 varices. ECE appeared insufficient for VG diagnosis. A successful candy test is an essential prerequisite.
GASTROENTEROLOGY: Coeliac disease

G-O-045

Awareness of ESPGHAN guidelines on coeliac disease among general paediatricians in Southwest England

Siba Paul¹, Helen Adams², Dharam Basude³

¹Bristol Royal Hospital for Children, Paediatric Gastroenterology, Bristol, United Kingdom
²University of Bristol, Bristol, United Kingdom
³University Hospital Bristol, Paediatric Gastroenterology, Bristol, United Kingdom

Objectives and study: ESPGHAN 2012 guidelines on paediatric coeliac disease (CD) recommend that symptomatic children with anti-tissue transglutaminase titres (anti-tTG) > 10 x the upper limit of normal (ULN), positive anti-endomysial antibody and HLA DQ2/8, can be diagnosed without a biopsy. However, non-biopsy diagnosis is not appropriate for certain groups of patients who continue to require a biopsy. This includes asymptomatic individuals with conditions associated with CD and those with anti-tTG<10xULN. Adequate knowledge of the ESPGHAN guidelines is required by general paediatricians to ensure suspected CD patients undergo appropriate investigations for an accurate diagnosis. Aims of the study:

1) To gain an understanding of awareness and use of ESPGHAN guidelines for diagnosing CD in children amongst general paediatricians

2) Provide recommendations to increase awareness if required.

Methods: A telephone/email survey was conducted of general paediatric consultants (n=140) across Southwest England with 11 DGHs. Survey included 8 questions to assess awareness and use of ESPGHAN guidelines, incorporating 3 main themes: when non-biopsy diagnoses can be made, when HLA-DQ2/8 genotyping should be requested and whether asymptomatic children from high-risk groups with anti-tTG>10xULN can be diagnosed without a biopsy.

Results: 85/140 (61%) responses obtained. 99% paediatricians are aware of ESPGHAN guidelines and non-biopsy/biopsy pathways for diagnosing CD. 83% of paediatricians were unable to state all conditions required for non-biopsy diagnosis. None could describe all appropriate situations where HLA-DQ2/8 genotyping should be requested. 33% of paediatricians responded that asymptomatic children with anti-tTG>10xULN can be diagnosed with CD without a biopsy while 24% said they were unsure or would seek advice.

Conclusion: Survey highlighted need for greater in-depth awareness of non-biopsy pathway and situations where HLA-DQ2/8 genotyping is indicated. There is possible misinterpretation regarding the ESPGHAN guidelines as 1/3rd of paediatricians considered non-biopsy pathway is applicable for asymptomatic children with anti-tTG>10xULN. There is need for improved understanding of the ESPGHAN guidelines amongst DGH paediatricians. A user friendly Apps is planned to improve the diagnostic process.
Access and effectiveness of fecal microbiome transplantation for recurrent clostridium difficile infection in the United States pediatric population: a universal stool bank experience

Shrish Budree¹, Pratik Panchal², Emilee Tu¹, Stacy Kahn³, Zain Kassam¹, Majdi Osman¹

¹Openbiome, Clinical Research, Boston, United States
²University of the Witwatersrand, Johannesburg, South Africa
³Boston Children’s Hospital, Inflammatory Bowel Disease Center, Boston, United States

Objectives and study: Recurrent Clostridium difficile infection (CDI) is a growing public health threat in pediatrics. Fecal microbiota transplantation (FMT) has emerged as an effective treatment for recurrent CDI, however logistical barriers have prevented universal adoption. Within the United States (US), the availability of FMT material from universal stool banks has expanded access for providers and patients. In contrast to adult data, there is a paucity of evidence regarding safety, effectiveness and access to FMT within the pediatric population. We present a geospatial analysis of FMT adoption among the pediatric population in combination with data on safety and effectiveness from a large universal stool bank (OpenBiome).

Methods: Data on pediatric centers that performed FMT using material from a universal stool bank were available by US ZIP Codes. Using standard Geographic Information System (GIS) methods, geocoded drive-time polygons were generated using network analysis for each FMT provider (TIGER/Line 2014, ArcMap 10.4, ESRI Business Analyst 2015).

US census data (National Laboratory LandScan 2015) with a 1 km² resolution were used to estimate population associated drive-times. Zonal statistics were used to estimate percentage of the US population within a 1-hour, 2-hour and 4-hour drive time from an FMT provider using simulated traffic for a Wednesday at noon for all facilities.

Quality assurance data on CDI classification, FMT delivery modality and clinical effectiveness were consecutively collected from a sub-group of 9 participating US pediatric healthcare facilities. The physician reported clinical cure rate at standard follow-up was recorded for each treatment.

Results: We identified 21 pediatric facilities that provided FMT from a universal stool bank: 10 were academic centers, 7 community hospitals, 3 private practices and 1 government affiliated facility. Most sites were in the Southern (8) and Northeast (5) United States, with fewer in the Midwest (3), Pacific (3), and Western (2) regions. Among pediatric centers partnered with a universal stool bank, 63.7% of the US population live within a 4-hour drive, 42.8% of the population within a 2-hour drive and only 27.8% of the population within a 1-hour drive of a pediatric FMT provider (Figure 1).
Complete safety and effectiveness data from the 9 participating pediatric facilities treating 69 patients was evaluated. Overall, the clinical cure rate from physician-reported data across all delivery modalities and CDI classifications was 85.5%. Clinical cure rates were 80.9% for patients treated by lower gastrointestinal (GI) delivery (n=48; 69.6%; colonoscopy = 46; enema =2) and 87.5% in those treated by upper GI delivery (n=21; 30.4%; nasogastric = 11; nasojejunal =3; EGD =7). There was no statistically significant difference in clinical cure between lower and upper GI delivery (p=0.47). No serious adverse events were reported.

**Conclusion:** To our knowledge this is the largest pediatric cohort reporting on safety, effectiveness and access to FMT. Our findings suggest that FMT in pediatric CDI has similarly high safety and effectiveness profiles to the adult populations, but pediatric access to FMT for recurrent CDI is still limited and has not been universally adopted within the US. Greater effort should be made to expand FMT access for pediatric patients and facilities such as large universal stool banks may be vital to achieving this goal.
Evaluation of Adalimumab effectiveness in anti-tumor necrosis factor - Naïve pediatric patients with Crohn's disease in clinical practice

Steven Steiner1, Eileen C. King2, KT Park3, Dinesh Pashankar4, Harohalli Shashidhar5, Boris Sudef6, Samantha Eichner7, Shiran Chen8, Jesse Pratt9, Richard Colletti10, Network ImproveCareNow11

1Riley Hospital for Children, Indiana University School of Medicine, Indianapolis, United States
2Cincinnati Children's Hospital Medical Center, Division of Biostatistics and Epidemiology, Cincinnati, United States
3Lucile Salter Packard Children's Hospital, Stanford University, Palo Alto, United States
4Yale-New Haven Children's Hospital, New Haven, United States
5New Hampshire's Hospital for Children, Manchester, United States
6University of Minnesota Masonic Children's Hospital, Minneapolis, United States
7Abbvie Inc., North Chicago, United States
8Cincinnati Children's Hospital Medical Center, Cincinnati, United States
9Cincinnati Children's Hospital Medical Center, Division of Biostatistics and Epidemiology, Cincinnati, United States
10University of Vermont Children's Hospital, Burlington, United States
11Improvecarenow, Burlington, United States

Objectives and study: Adalimumab is an anti-tumor necrosis factor (ATNF) agent approved for the treatment of Crohn's disease in children in the USA since September 2014. We assessed the duration and effectiveness of adalimumab treatment in pediatric Crohn's disease patients in clinical practice without prior ATNF therapy.

Methods: In a retrospective cohort study using registry data from clinical care visits at 43 centers in the USA in the ImproveCareNow Network, ATNF-naïve patients induced with adalimumab prior to 18 years old with at least one post-induction visit were identified. We assessed the duration of treatment and the clinical effectiveness of adalimumab based on steroid-free clinical remission using Physician Global Assessment (PGA, inactive) and Short Pediatric Crohn’s Disease Activity Index (sPCDAI, ≤10), as well as steroid-free clinical response using PGA (inactive or mild) and sPCDAI (≤25). Clinical care and frequency of visits were decided by the patient, parent and clinician. Data from clinical care visits were assessed every 3 +/- 1.5 months for 1 year, then every 6 +/- 3 months through 3 years. Descriptive statistics, Fisher’s Exact Test and multivariable logistic regression analyses were performed.

Results: There were 174 patients (57% male, 25% <13 years old at induction) treated with adalimumab from August 2008 – December 2015. The number of patients followed post-induction for 3, 6, 12, 24 and 36 months was: 174, 174, 154, 71 and 39; the percentage of followed patients remaining on adalimumab was: 100%, 95%, 94%, 97% and 80% (Table 1). Of patients on adalimumab at 3, 6, 12, 24 and 36 months: 69%, 75%, 79%, 94% and 81% were in steroid-free clinical remission by PGA; and 71%, 77%, 80%, 91% and 86% by sPCDAI. Of patients on adalimumab at 3, 6, 12, 24 and 36 months: 88%, 91%, 93%, 99% and 94% had a steroid-free clinical response by PGA; and 83%, 85%, 91%, 98% and 100% by sPCDAI. Concomitant immunomodulator therapy did not appear to improve outcomes.

Conclusion: In the largest series with the longest follow-up, adalimumab was durable and effective as initial ATNF therapy for pediatric Crohn’s disease in clinical practice. Of patients followed for 24 months, 97% remained on adalimumab. Steroid-free clinical remission was achieved in 91% - 94%, and steroid-free clinical response in 98% - 99%, of patients who remained on adalimumab for 24 months. The effect of dosage on outcomes is being investigated. These findings are important for patients, parents and clinicians considering ATNF therapy.
### Table 1

**Durability and Clinical Effectiveness of Adalimumab in anti-TNF Naïve Pediatric Crohn’s Disease**

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>3 Months</th>
<th>6 Months</th>
<th>12 Months</th>
<th>24 Months</th>
<th>36 Months</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients being followed for this duration post-induction</td>
<td>174</td>
<td>174</td>
<td>174</td>
<td>154</td>
<td>71</td>
<td>39</td>
</tr>
<tr>
<td>Patients remaining on adalimumab [n, (%)]</td>
<td>174 (100%)</td>
<td>174 (100%)</td>
<td>166 (95%)</td>
<td>145 (94%)</td>
<td>69 (97%)</td>
<td>31 (80%)</td>
</tr>
<tr>
<td>Steroid free remission-PGA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>25 (15%)</td>
<td>110 (69%)</td>
<td>120 (75%)</td>
<td>112 (79%)</td>
<td>64 (94%)</td>
<td>25 (81%)</td>
</tr>
<tr>
<td>No</td>
<td>145 (85%)</td>
<td>49 (31%)</td>
<td>40 (25%)</td>
<td>30 (21%)</td>
<td>4 (6%)</td>
<td>6 (19%)</td>
</tr>
<tr>
<td>Steroid free remission-sPCDAI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>39 (32%)</td>
<td>97 (71%)</td>
<td>106 (77%)</td>
<td>91 (80%)</td>
<td>42 (91%)</td>
<td>19 (86%)</td>
</tr>
<tr>
<td>No</td>
<td>85 (68%)</td>
<td>39 (29%)</td>
<td>32 (23%)</td>
<td>23 (20%)</td>
<td>4 (9%)</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>Steroid free response-PGA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>82 (48%)</td>
<td>140 (88%)</td>
<td>146 (91%)</td>
<td>132 (93%)</td>
<td>67 (99%)</td>
<td>29 (94%)</td>
</tr>
<tr>
<td>No</td>
<td>88 (52%)</td>
<td>19 (12%)</td>
<td>14 (9%)</td>
<td>10 (7%)</td>
<td>1 (1%)</td>
<td>2 (6%)</td>
</tr>
<tr>
<td>Steroid free response-sPCDAI</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>55 (44%)</td>
<td>113 (83%)</td>
<td>117 (85%)</td>
<td>104 (91%)</td>
<td>45 (98%)</td>
<td>22 (100%)</td>
</tr>
<tr>
<td>No</td>
<td>69 (56%)</td>
<td>23 (17%)</td>
<td>21 (15%)</td>
<td>10 (9%)</td>
<td>1 (2%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

**Disclosure of interest:**

Steiner, S. Financial support for research: Study funded by AbbVie

Eichner, S. Employee of AbbVie

Colletti, R. Consultancy: Consultant for AbbVie / other: University of Vermont receives research support for registry from AbbVie
Malignancy and mortality in paediatric patients with inflammatory bowel disease: a prospective international study supported by ESPGHAN and ECCO

Maria Joosse1, Martine Aardoom2, Dan Turner3, David Wilson4, Sibylle Koletzko5, Ulrika Fagerberg6, Christine Spray7, Malgorzata Sladek8, Ron Shaoul9, Eleftheria Roma10, Jiri Bronsky11, Daniela E. Serban12, Salvatore Cucchiara13, Gábor Veres14, Frank Ruemmele15, Helene Lengline16, Iva Hojsak17, Kajsa Leena Kolho18, Ieuan Davies19, Marina Alo13, Paolo Lionetti20, Genevieve Veereman21, Christian Braegger22, Eunice Trindade23, Anne Wewer24, Almuthe Christine Hauer25, Jorge Amil Dias26, Seamus Hussey27, Andrew S. Day28, Peter Lewindon29, Arie Levine30, Lissy De Ridder31

1Erasmus Medical Center, Department of Pediatric Gastroenterology, Rotterdam, Netherlands
2The Erasmus MC Sophia Children's Hospital, Department of Pediatric Gastroenterology, Rotterdam, Netherlands
3Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel
4University of Edinburgh, Department of Pediatric Gastroenterology, Child Life and Health, Edinburgh, United Kingdom
5Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
6Centre for Clinical Research, Västmanland Hospital, Department of Pediatric Gastroenterology, Västerås, Sweden
7Bristol Royal Hospital for Children, Department of Pediatric Gastroenterology, Bristol, United Kingdom
8Jagiellonian University Medical College, Department of Pediatrics, Gastroenterology and Nutrition, Krakow, Poland
9Rambam Hospital, Pediatric Gastroenterology Institute, Haifa, Israel
10University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
11Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic
12iuliu Hatieganu University of Medicine and Pharmacy, Department of Pediatric Gastroenterology, Cluj-Napoca, Romania
13Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
14Semmelweis University, First Department of Pediatrics, Budapest, Hungary
15Hôpital Necker Enfants Malades, Department of Pediatric Gastroenterology, Université Paris Descartes, Sorbonne Paris Cité, Aphp.Paris, France
16Université Paris Descartes, Sorbonne Paris Cité, Aphp, Hôpital Necker Enfants Malades, Department of Pediatric Gastroenterology, Paris, France
17Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
18Helsinki University, Department of Pediatric Gastroenterology, Helsinki, Finland
19University Hospital of Wales, Department of Pediatric Gastroenterology, Cardiff, United Kingdom
20Meyerchildren’s Hospital, Pediatric Gastroenterology, Meyerchildren’s Hospital, Florence, Italy
21Free University Brussels, 22department of Pediatric Gastroenterology and Nutrition, Brussels, Belgium
22Children's Research Centre, University Children's Hospital, Division of Gastroenterology and Nutrition, Zurich, Switzerland
23Hospital São João, Pediatric Gastroenterology Unit, Porto, Portugal
24University Hospital Hvidovre, Department of Paediatrics, Hvidovre, Denmark
25Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria
26Centro Hospitalar São João, Pediatric Gastroenterology Unit, Porto, Portugal
27National Children's Research Centre, National Centre for Paediatric Gastroenterology, Dublin, Ireland
28University of Otago Christchurch and Christchurch Hospital, 28department of Paediatrics, Christchurch, New Zealand
29University Of Queensland, Department of Paediatrics & Child Health, Brisbane, Australia
30Wolfson Medical Center, Department of Pediatric Gastroenterology, Holon, Israel
Objectives and study: The trend to use intensive immunosuppressive medications early in the course of paediatric-onset inflammatory bowel disease (PIBD) may increase the risk of treatment-associated malignancy and mortality. With a multinational collaboration in 24 countries, we aimed to evaluate the incidence and cause of malignancy and mortality in PIBD to better define the risk/benefit ratio of our new therapeutic strategies.

Methods: A prospective study was designed to identify all cases of malignancy and mortality in patients in whom PIBD was diagnosed < 19 years of age over a period of three years (Jan 2014 - Jan 2017). This study is being conducted in Europe (20 countries), Israel, Canada, Australia and New Zealand. National representatives requested paediatric and adult gastroenterologists to report cases every 6 months. Patients were eligible if malignancy and/or mortality occurred after the IBD diagnosis and < 26 years of age. The primary endpoint was cause of mortality in PIBD <19 years; secondary endpoints were malignancy and mortality rate in PIBD < 26 years and identification of risk factors for malignancy and mortality.

Results: In a preliminary analysis over a period of 30 months, 31 cases of cancer and 21 deaths in 46 children (23 males) who were diagnosed with IBD (ulcerative colitis (UC), n= 14, Crohn’s disease (CD), n=27, IBD unclassified, n=5) at a median age of 12.4 years (IQR 10.3-14.8) were identified. The median age at diagnosis of malignancy and mortality was 16.7 years (IQR 15.0-22.0) and 16.0 (IQR 14.0-20.8) respectively. Causes of mortality were infection (n=7), malignancy (n=6), PSC-related liver failure (n=1), unknown (n=2) and other causes not related to IBD (n=5, i.e. trauma (n=2), multi-organ failure, cardiac asthma and mitochondrial disease). Of the seven patients with a fatal infection, three patients used thiopurine monotherapy within three months prior to death. The remaining four patients had been exposed to a combination of an immunomodulator and biological therapy, of which only one was exposed during the three months prior to fatal infection. Hematopoietic malignancies were most frequently reported in this cohort (n=15 of which 6 males), consisting of Hodgkin lymphoma (n=6), non-Hodgkin lymphoma (n=8) and leukaemia (n=1). Other reported malignancies were colorectal carcinoma (n=8), biliary carcinoma (n=3), melanoma (n=1) and other non-IBD related causes (n=4). Of the patients with a hematopoietic malignancy, 14 patients were previously treated with thiopurine as either monotherapy (n=11) or in combination with a biological drug (n=3). Primary sclerosing cholangitis (PSC) was present in seven cases (15%) of whom four died; three of those had developed biliary cancer.

Conclusion: Contrary to our previous retrospective study, the current data do not confirm a predominance of fatalities in UC compared to patients with CD. In this cohort infections and cancer are the most frequent causes of mortality. Intriguingly, 93% of patients with a hematopoietic malignancy had been exposed to thiopurines. PSC is the most prominent identifiable risk factor for malignancy and fatal outcome. By identifying malignancy and mortality cases in 24 countries we have increased the data available on the worst outcomes in PIBD, enabling us to better understand the scale of the problem and to evaluate how many cancers in PIBD cause mortality. Our future aim is to calculate malignancy and mortality incidence by accessing national cancer and IBD registries.
Involvement of Parkinson's disease 7 in inflammatory bowel diseases: relation to interleukin-17 and tumor necrosis factor-alpha

Rita Lippai¹, Erna Sziksz², Domonkos Pap¹, Réka Rokonay¹, Apor Veres-Székely¹, Nóra Judit Béres¹, Katalin Eszter Müller¹, Áron Cseh¹, Gábor Veres¹, Attila Szabo¹, Ádám Vannay¹

¹Semmelweiss University, Ist Department of Pediatrics, Budapest, Hungary
²Mta-Se, Pediatrics and Nephrology Research Group, Budapest, Hungary

Objectives and Study: The therapy of inflammatory bowel diseases (IBD) is still unresolved, however, recent studies suggested the importance of interleukin (IL)-17. Parkinson's disease 7 (PARK7) is an antioxidant, immunoregulatory molecule, but its relation to IL-17 and the core TNF-α related pathway of IBD is completely unknown. Thus we aimed to investigate its involvement in the pathogenesis of IBD.

Methods: The mRNA expression, protein level and localization of PARK7 were determined in colon biopsies of children with IBD, in colon of wild type and IL-17 KO mice with dextran sodium sulphate (DSS)-induced colitis and in IL-17-treated HT-29 colonic epithelial cells by real-time PCR, western blot, flow cytometry, and immunofluorescence staining, respectively. The effect of PARK7 on TNF-α was measured in PARK7 specific silencing RNA treated HT-29 cells.

Results: Expression of PARK7 and IL-17 was increased in the colonic mucosa of children with IBD and also in the colon of wild type mice with DSS-induced colitis compared to controls. Lack of IL-17 in IL-17 KO mice prevented the DSS-induced elevation of colonic PARK7 level in vivo. Similarly, IL-17 treatment induced the production of PARK7 and TNF-α of HT-29 colon epithelial cells in vitro. TNF-α production were even more pronounced in the PARK7 siRNA treated HT-29 cells.

Conclusion: Increased expression of PARK7 in IBD suggest its involvement in the disease pathogenesis. Moreover, we demonstrated that PARK-7 is an endogenous regulator of the IL-17 induced production of TNF-α. Taken together our data suggest that PARK7 may be a therapeutic target in the future.

Keywords: PARK7, IL-17, IBD, TNF-α, DSS

Support: OTKA PD105361, -K108688, -K116928, LP2011-008
Mutations in Munc18-2 cause variant MVID in FHL5

Georg-Friedrich Vogel¹, Iris Krainer¹, Andreas Janecke², Thomas Müller¹, Carsten Posovszky³, Ernest Cutz⁴, Sabine Middendorp⁵, Michael Hess⁶, Lukas Alfons Huber⁶

¹Medical University Innsbruck, Paediatrics I, Innsbruck, Austria
²Medical University of Innsbruck, Innsbruck, Austria
³Klinik für Kinder- und Jugendmedizin Universitätshospital Ulm, Ulm, Germany
⁴The Hospital for Sick Children, Toronto, Canada
⁵Wilhelmina Children’s Hospital, Utrecht, Netherlands
⁶Medical University Innsbruck, Innsbruck, Austria

Objectives and study: FHL5 is an autosomal recessive disease caused by mutations in STXBP2/Munc18-2 which required for SNARE mediated membrane fusion. FHL5 causes haematologic and gastrointestinal symptoms. The latter are marked by congenital, intractable watery diarrhoea which is reminiscent of microvillus inclusion disease (MVID). So-far, the molecular pathophysiology remained poorly understood.

Methods: Four FHL5 patients, including three novel patients, are included in this study. Morphology of duodenal sections was analysed by electron and fluorescence microscopy. A Munc18-2 CaCo2 knock-out model cell line by CRISPR/Cas9 technology for the analysis of Munc18-2 dependent SNARE protein interaction was generated. Cargo trafficking was investigated in both patient material and the model cell line.

Results: Duodenal enterocytes display morphological characteristics of MVID: loss of apical microvilli, subapical accumulation of vesicles and tubules and partly microvillus inclusions. Furthermore, apical and subapical marker proteins mislocalise. Knock-out of Munc18-2 in CaCo2 cells yields a disease model cell line that shows Munc18-2 to be required for vesicular- and target-SNARE interaction in fusion of cargo vesicles with the apical plasma-membrane. As in MVID, loss of Munc18-2 selectively disrupts trafficking of apical brush-border proteins.

Conclusion: Munc18-2 is required in the same apical trafficking pathway of brush-border enzymes which causes MVID when disrupted. Our findings indicate STXBP2 to be the third gene, next to MYO5B and STX3, to cause MVID.
Cytomegalovirus infection in pediatric acute severe ulcerative colitis - a multicenter case-controlled study from the Pediatric IBD Porto group of ESPGHAN

Shlomi Cohen¹, Christine Martinez-Vinson², Marina Alo³, Dan Turner⁴, Assa Amit⁵, Lissy De Ridder⁶, Victorien Wolters⁷, Tim de Meij⁸, Patrizia Alvisi⁹, Jiri Bronsky¹⁰, Uri Kopylov¹¹

¹"Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
²Robert-Debré Hospital, Assistance Publique-Hôpitaux de Paris, Pediatric Gastroenterology Department, Paris, France
³Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
⁴Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel
⁵Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Hospital, Petach Tikva, Israel
⁶Erasmus MC-Sophia Children's Hospital, Department of Pediatric Gastroenterology, Rotterdam, Netherlands
⁷University Medical Center/Wilhelmina Children's Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
⁸VU University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
⁹Ospedale Maggiore, Paediatric Department, Bologna, Italy
¹⁰Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic
¹¹Sheba Medical Center, Department of Gastroenterology, Tel Aviv, Israel

Objectives and study: Data on the clinical course and outcomes of pediatric patients with cytomegalovirus (CMV) infection complicating acute severe ulcerative colitis (ASC) are very limited. The aim of our study was to compare the outcome of CMV-positive and negative pediatric ASC.

Methods: This was a multicenter retrospective case-controlled study, from centers in Europe and Israel. We included CMV-positive pediatric patients hospitalized for acute severe colitis and compared their outcomes (rate of colectomy during hospitalization and up to 1 year from the hospitalization) to matched CMV-negative controls.

Results: A total of 56 children from 10 centers were included. The patient cohort included 23 (41.1%) males/33 (58.9%) females, with a median age of 11.5 (interquartile range (IQR) 7-14) years. Fifty-two (92.9%) of the patients had extensive/pan-colitis colitis and the rest left sided colitis, with severe disease in 52 (92.9%) of the patients and moderate in 4 (7.1%). Fifteen patients were CMV-positive and 41 - CMV-negative. Significantly higher proportion of CMV positive patients were resistant to intravenous corticosteroids (p=0.009). After diagnosis of CMV infection, 14/15 patients were started on gancyclovir (5 mg/kg - 5/14 (35.7%) or 10 mg/kg – 9/14 (64.3%). During hospitalization, 3 (20%) CMV positive and 3 (7.8%) CMV-negative patients required colectomy (p=0.17). By 12 months of follow-up, 5 (33.3%) and 5 (12.5%) CMV positive and negative patients required colectomy, respectively (p=0.049). Previous anti-TNF exposure and Pediatric Ulcerative Colitis Activity Index score on index date were significantly associated with the risk of colectomy during hospitalization and by 12 months (p=0.037 and p=0.01 for previous anti-TNF exposure and p=0.021 for PUCAI) on univariate analysis, however none of the factors including CMV positivity retained significance on multivariate analysis.

Conclusions: A higher prevalence of CMV positivity was found in pediatric UC patients who required colectomy within 12 months of index hospitalisation, however the difference was not statistically significant on multivariate analysis. Further studies are merited to clarify the impact of CMV infection on the outcome of acute severe colitis in pediatric patients.
**GASTROENTEROLOGY: Inflammatory bowel disease**

**G-O-052**

**Crohn's Disease exclusion diet and partial enteral nutrition (CDED + PEN) vs exclusive enteral nutrition (EEN) - microbiome changes of a randomized clinical trial (RCT) in pediatric CD: remission is associated with similar structural and functional profiles**

Katherine Dunn¹, Rotem Sigall Boneh², Joseph Bielawski³, Dan Turner⁴, Johan van Limbergen⁵, Arie Levine⁶

¹Dalhousie University, Biology, Halifax, Canada  
²Wolfson Medical Center, Pediatric Gastroenterology and Nutrition Unit, Tel Aviv, Israel  
³Dalhousie University, Mathematics & Statistics, Halifax, Canada  
⁴Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel  
⁵Iwk Health Centre / Dalhousie University, Pediatrics, Halifax, Canada  
⁶Wolfson Medical Center, Department of Pediatric Gastroenterology, Holon, Israel

**Objectives and study:** EEN is able to induce remission in CD patients, but can be difficult to maintain. A novel dietary intervention that combines partial enteral nutrition with an exclusion diet, that excludes foods proposed to trigger dysbiosis and inflammation (CDED+PEN) has been shown effective. We aim to compare the gut microbiome of CD participants in a prospective RCT comparing these diets, and to assess whether microbiome profiles can identify subgroups that are able to sustain remission.

**Methods:** 24 paediatric patients received either CDED + 50% Modulen for 6 weeks, then CDED+25% Modulen for 6 weeks (**Group 1**) or EEN with Modulen for 6 weeks followed by free diet plus 25% Modulen (**Group 2**). Remission was present in 11/14 (78.5%) in Group 1, and 8/10 (80%) in Group 2. One patient from Group 1 relapsed by week 12. DNA from fecal samples collected at three time points (baseline, w6 and w12) was sequenced for 16S and whole metagenome. Taxonomic composition was inferred from 16S (QIIME) and from metagenomes (Metaphlan) and inferred for function (Diamond/HUMAnN).

**Results:** Both interventions induced an increase in alpha diversity by w12. EEN patients experienced a transient reduction in diversity at w6, whereas CDED+PEN did not. Taxonomic and functional profiles were similar by w12. Pooling the results for both diets, the taxonomic composition of the 18 patients who sustained remission differed significantly from the 6 patients who did not. Twenty-two 16S-derived operational taxonomic units had different relative abundance \((p \leq 0.05)\), with a subgroup of eleven identified according to a false discovery threshold \((q\text{-value})\) of 0.15. Similar taxonomic results were inferred from the metagenome. Analysis of the functional repertoire yielded a similar pattern; 1811 genes differed between patients who sustained remission and those who did not, with 711 identified according to \(q\text{-value} < 0.05\). To confirm that these results (taxonomic and functional) were not being driven by the signal associated with a single diet, we separately compared the remission patients for each diet to the pooled set of patients who did not maintain remission. Results were consistent for both diets, but with slightly smaller subgroups of genes. Supervised modeling is currently underway to investigate if functional and taxonomic profiles can be exploited to predict patient outcomes.

**Conclusion:** Microbiome changes induced by CDED+PEN 50% are comparable with EEN in a paediatric RCT with active CD. Remission achieved with either dietary intervention is associated with similar structural and functional profiles.
Pediatric Gastroesophageal Reflux Disease (GERD): Systematic review on prognosis

Maartje Singendonk¹, Merit Tabbers², Marc Benninga¹, Miranda Langendam³

¹Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
³Academic Medical Centre, Department of Clinical Epidemiology, Bioinformatics and Biostatistics, Amsterdam, Netherlands

Objectives and study: Knowledge regarding prognosis and factors influencing the clinical course of pediatric gastro-esophageal reflux disease (GERD) enables health care professionals to provide accurate information, patient-tailored treatment and identify risk factors for unfavorable outcomes. Aim of this study was to summarize the evidence on prognosis and prognostic factors of pediatric GERD.

Methods: We conducted a literature search in Embase and MEDLINE/PubMed to identify prospective follow-up studies on the prognosis or prognostic factors of pediatric GERD. Methodological quality was assessed by the Quality in Prognostic Studies (QUIPS) tool. Due to large heterogeneity between studies with regard to study populations and outcome measures, no meta-analysis was performed. Data were tabulated and presented descriptively.

Results: The search yielded a total of 5365 references; four publications met our inclusion criteria (risk of bias moderate-high). The percentage of children with a diagnosis of GERD with esophagitis that had persisting symptoms requiring anti-reflux medication at follow-up (12 months to >5 years) ranged from 38% - 68%. In children with a diagnosis of GERD without esophagitis, 1.4% developed esophagitis at follow-up (>5 years); none developed Barrett’s esophagus. Age of onset of GERD symptoms <5 years, presence of esophagitis and the use of acid-suppressants at time of initial diagnosis were associated with less favorable outcome.

Conclusion: There are only few studies published on prognosis and predictive factors of pediatric GERD, showing large heterogeneity and poor methodological quality. Based on the present literature, we are unable to identify those children at risk for poor prognosis.
Mind the gap: discrepant costs between actual and recommended treatments of infant functional gastrointestinal disorders

Carlos Lifschitz1, Thomas Ludwig2, James Mahon3, Nikhil Thapar4, Julie Glanville3, Mohammad Miqdady5, Miguel Saps6, Seng Hock Quak7, Irene Lenoir-Wijnkoop8, Mary Edwards3, Hannah Wood9, Hania Szajewska9

1Hospital Italiano, Buenos Aires, Argentina
2Nutricia Research, Singapore, Singapore
3University of York, York Health Economics Consortium, York, United Kingdom
4Great Ormond Street Hospital, London, United Kingdom
5Sheikh Khalifa Medical City, Pediatric Gastroenterology, Hepatology & Nutrition Division, Abu Dhabi, United Arab Emirates
6Nationwide Childrens Hospital, Columbus, United States
7National University Health System, Paediatrics, Singapore, Singapore
8University of Utrecht, Utrecht, Netherlands
9The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland

Objectives and study: Recent reviews and studies have indicated that functional gastrointestinal disorders (FGIDs) and related signs and symptoms may have a substantial impact on the budgets of third party payers and/or parents. The objective of this study is to estimate the cost of illness (COI) of FGIDs and related signs and symptoms in infants to the third party payer and to parents for a developed country.

Methods: England was chosen as an exemplar country due to the availability and quality of data on healthcare resource use, both publicly and privately, and the availability of these data in the English language. The population of interest were healthy term infants (under 12 months of age) with colic, regurgitation, and/or functional constipation, and their related signs and symptoms. In constructing the calculation, estimates and assumptions (where necessary) were chosen to provide a lower bound (minimum) of the potential overall cost. The true COI can thus be no lower than that estimated.

Results: The de novo calculation estimated that the total COI of treating FGIDs in infants in England were at least £72.3 million per year in 2014/15 of which £50.0 million was National Health Service expenditure on prescriptions, community care, and hospital treatment. Parents incurred £23.2 million in costs through purchase of over the counter remedies. In brief, this estimated total COI of at least £72.3 million is constituted by prescriptions for medications (£5.8 million) and formulas (£0.9 million), health visitor appointments (£3.5 million), general practitioner appointments (£26.0 million), admitted patient care (£9.3 million), accident and emergency department visits (£3.6 million), over the counter colic medicines (£13.6 million), and over the counter anti-regurgitation formulas (£9.6 million). It is likely that the total COI estimate is still a significant underestimate of the true costs. The costs of alternative therapies, treatments or diagnostic tests received by infants as inpatients, medications without clear age categorization (i.e. proton pump inhibitors, prescriptions for constipation remedies), costs associated with side effects from inappropriate interventions, and time off work by parents could not be adequately estimated and omitted from the calculation.

Conclusion: Infant FGIDs incur significant costs to both parents and to the third party payer for health care. The number and kind of prescribed products and products sold over the counter to treat FGIDs suggest that there are gaps between treatment guidelines, which emphasize parental reassurance and nutritional advice, and their implementation.

Disclosure of interest: T. Ludwig is an employee of Nutricia Research.
Diagnosis of celiac disease according to ESPGHAN guidelines - results from the Prospective Celiac Disease Diagnostic Evaluation study (ProCeDE)

Katharina Werkstetter1, Ilma Korponay-Szabo2, Alina Popp3, Vincenzo Villanacci4, Marianna Salemme8, Gabriele Heilig1, Søren Lillevang5, Luisa Mearin6, Carmen Ribes Koninckx7, Adrian Thomas8, Riccardo Troncone9, Birgit Filipiak-Pittroff1, Markku Mäki10, Steffen Husby11, Sibylle Koletzko1

1Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
2Heim Pál Children's Hospital, Celiac Disease Center, Budapest, Hungary
3Tampere Center for Child Health Research, University of Tampere and Tampere University Hospital, Tampere, Finland, University of Medicine and Pharmacy “carol Davila”, Bucharest, Romania, Bucharest, Romania
4Spedali Civili Brescia, Institute of Pathology, Brescia, Italy
5Odense University Hospital, Dept. of Clinical Immunology, Odense, Denmark
6Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
7La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
8Royal Manchester Childrens Hospital, Manchester, United Kingdom
9University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy
10University of Tampere and Tampere University Hospital, Tampere Centre for Child Health Research, Tampere, Finland
11Odense University Hospital, Hans Christian Andersen Children's Hospital, Odense, Denmark

Objectives and study: The current ESPGHAN guidelines allow pediatric gastroenterologists to diagnose celiac disease (CD) without biopsies in symptomatic children with serum antibodies against transglutaminase-type2 (TGA-IgA) ≥10-times upper limit of normal (≥10xULN), positive endomysium antibodies (EMA) in a second sample, and HLA-DQ2/DQ8 positivity. The Prospective Celiac Disease Diagnostic Evaluation study (ProCeDE) aimed to evaluate in a clinical multi-center setting whether this approach reaches a positive predictive value (PPV) ≥99%.

Methods: From Nov 2011 to May 2014, 33 pediatric centers in 21 countries prospectively recruited consecutive patients who underwent duodenal biopsies for suspected CD. Inclusion criteria were positive TGA-IgA (or CD-specific IgG-based antibodies) at any titer, symptoms or risk for CD, gluten-containing diet and no previous CD diagnosis. Data comprised medical and family history, symptoms, physical examination, basic lab tests, local results of TGA, EMA and histopathology. Central analysis included serology (EMA, eight TGA-IgA and one TGA-IgG kits), and two HLA-haplotyping tests. Histology slides were blindly reviewed by reference-pathologists. Based on all information, diagnosis was made for each patient, stratified in 1) proven CD, 2) no CD and 3) unsolved cases without final diagnosis comprising potential CD (confirmed seropositivity but negative histology) or contradicting results. Patients were excluded from analysis in case of incomplete sample sets, poor quality of biopsies making histology non-evaluable, or IgA deficiency. PPVs and positive likelihood ratios for the criteria to omit biopsies were calculated with 95% confidence intervals (CI).

Results: Of 803 recruited patients, 60 were excluded (incomplete data, low IgA), further 36 had non-evaluable biopsies, leaving 707 for final analysis (65.1% girls, median age 6.2 years). Thereof 57.3% had at least one symptom of malabsorption (diarrhea, weight loss, growth retardation, anemia), 31.4% reported other symptoms, and 11.3% were asymptomatic. Final diagnosis was proven CD in 645 (91.2%), no CD in 46 (6.5%), and 16 patients (2.3%) remained unsolved. PPVs of high TGA-IgA (≥10xULN) and in combination with other criteria are shown in the table. For PPV analyses, unsolved cases are either allocated to “no CD” or were excluded in a sensitivity analysis.
Table:

<table>
<thead>
<tr>
<th>Criteria to omit biopsies considering local TGA- and EMA-IgA and central HLA results</th>
<th>PPV [95% CI]</th>
<th>Final cohort (N=707) (unsolved cases were considered as “no CD”)</th>
<th>Sensitivity analysis (cohort excluding 16 unsolved cases, N=691)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TGA-IgA ≥10xULN</td>
<td>99.13 [97.80;99.76]</td>
<td>99.78 [98.80;99.99]</td>
<td></td>
</tr>
<tr>
<td>+ EMA-IgA positivity</td>
<td>99.56 [98.40;99.95]</td>
<td>100.0 [99.18;100.0]</td>
<td></td>
</tr>
<tr>
<td>+ EMA-IgA + HLA positivity</td>
<td>99.56 [98.40;99.95]</td>
<td>100.0 [99.18;100.0]</td>
<td></td>
</tr>
<tr>
<td>+ EMA, HLA + any symptom</td>
<td>99.75 [98.61;99.99]</td>
<td>100.0 [99.08;100.0]</td>
<td></td>
</tr>
<tr>
<td>+ EMA, HLA + symptom(s) of malabsorption</td>
<td>100.0 [98.68;100.0]</td>
<td>100.0 [98.68;100.0]</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** If ESPGHAN criteria are correctly followed the diagnosis of CD can be made without biopsies with a PPV of >99%. HLA testing does not add any diagnostic value in this setting of high TGA-IgA and EMA-positivity but may help to disclose CD. Symptoms of malabsorption further slightly increase the likelihood of CD. As insufficient quality of biopsies is frequent but often not reported by the local pathologist, histopathology by itself cannot serve as reference for validation of laboratory based tests.

**Disclosure of interest:** Sibylle Koletzko received fundings for this study from Euroimmun, Eurospital, INOVA diagnostics, Phadia-ThermoFisher, R-Biopharm/Zedira, and Schär. The study was further supported by the following non-profit organisations: ESPGHAN, AOK Bayern and the Celiac Disease societies of Denmark, Finland, Germany, Hungary, Italy, The Netherlands and the United Kingdom.
Patient-derived pancreatic ductal organoids and intestinal organoids to study CFTR function

KYU SHIK MUN1, Kavisha Arora1, Maisam Abu-El-Haija2, Jaimie Nathan3, John Clancy1, Joseph Palermo2, Anjaparavanda Naren1

1Cincinnati Children's Hospital Medical Center, Division of Pulmonary Medicine, Cincinnati, United States
2Cincinnati Children's Hospital Medical Center, Division of Gastroenterology, Hepatology and Nutrition, Cincinnati, United States
3Cincinnati Children's Hospital Medical Center, Division of Surgery, Cincinnati, United States

Objectives and study: Cystic Fibrosis (CF) is an inherited genetic disorder caused by mutations in the Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) which lead to a shortened lifespan. CFTR protein is a cAMP-regulated chloride and bicarbonate transport channel that helps regulate fluid and electrolyte transport through the apical membrane of epithelial cells. CF affects multiple organs including lung, liver, pancreas, kidneys, and intestine. Over 2000 mutations in the CFTR genes have been described that can be classified into six classes based on synthesis, location, and dysfunction of the CFTR protein. In this study, our aims were twofold: (1) to generate patient-derived pancreatic ductal epithelial cell cultures to test CFTR function in response to a cAMP-activating agonist (Forskolin/FSK), and (2) to compare CFTR function of intestinal enteroids and pancreatic ductal organoids from the same patient.

Methods: Isolation and culture of human pancreatic ductal organoids and intestinal enteroids

Pediatric patients undergoing total pancreatectomy with islet autotransplantation (TPIAT) for chronic pancreatitis were studied. Discarded explant tissue was obtained, including duodenum, pancreatic duct and the remnant pancreas cell pellet following islet isolation. Tissue was collected according to standard research protocols approved by the Department of Pathology at Cincinnati Children's Hospital (IRB2011-2616).

Pancreatic ductal tissues and intestinal crypts from discarded human pancreas and duodenum, respectively, were isolated surgically. Single cell pellets were obtained from the tissues and cultured in 3-D Matrigel matrix.

Measurement of fluid secretion in real-time

Fluid secretion was measured by increase in organoid volume as previously described by our group (J Biol Chem 290:11246-11257; Biochemistry 53:4169-4179). At least 20 organoid images were obtained for comparison of fluid secretion.

Results: Isolated human pancreatic ductal tissues were used to generate organoids, as shown in

These stem cells clustered into a small sphere after isolation and grew into a larger sphere over time. The mutation of this patient was serine protease inhibitor Kazal-type1 (SPINK1). Unstimulated pancreatic ductal organoids showed a high rate of basal fluid secretion (over 60%), while treatment with the epithelial sodium channel (ENaC) inhibitor, amiloride, reduced the secretory process to below 30%. Treatment with 10 μM FSK, a stimulator of cAMP-dependent CFTR-mediated fluid secretion, increased secretion to almost 65% within two hours of treatment. The basal secretion of ductal organoids was markedly higher than intestinal organoids, which is over 20%, from the same patient.
**Conclusion:** We have successfully cultured patient-derived human pancreatic ductal organoids and intestinal organoids in 3-D matrix and importantly, determined CFTR function. Interestingly, amiloride treatment followed by FSK treatment demonstrated very high CFTR-dependent fluid secretion in the pancreatic ductal organoids. We now have the ability to monitor real-time CFTR function of human pancreatic ductal and intestinal epithelium using the fluid secretion assay. The rate of fluid secretion from different organs, pancreatic ductal and intestinal, differed significantly. This model will provide the opportunity to further study both pathophysiology and therapeutic strategies in CF.
The ancient wheat species Triticum monococcum has a reduced in vivo immunogenicity: implication for celiac disease prevention

Stefania Picascia\textsuperscript{1}, Alessandra Camarca\textsuperscript{2}, Roberta Mandle\textsuperscript{3}, Renata Auricchio\textsuperscript{4}, Gianfranco Mamone\textsuperscript{2}, Riccardo Troncone\textsuperscript{4}, Salvatore Auricchio\textsuperscript{3}, Carmen Gianfrani\textsuperscript{5}

\textsuperscript{1}Institute of Protein Biochemistry (Ibp), Cnr, Naples, Italy
\textsuperscript{2}Institute of Food Sciences, Cnr, Avellino, Italy
\textsuperscript{3}University Federico II, Department of Translational Medical Sciences, Section of Paediatrics, Naples, Italy
\textsuperscript{4}University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Ital, Naples, Italy
\textsuperscript{5}Institute of Protein Biochemistry (Ibp), Cnr and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy; Naples, Italy

Objectives and study: In the recent time there is an increasing interest to find wheat varieties with null or low toxicity for treatment or prevention of Celiac Disease. T. monococcum, a diploid (AA genome) ancient wheat is among the most promising candidate species, for the low content of gluten stimulatory peptides and for the higher in vitro digestibility (1;2). However, very little is known on T. monococcum in vivo immunogenicity in celiac patients.

Methods: We used a short (3 days) wheat challenge (SGC) to assess the in vivo immunostimulatory properties of gluten from T. monococcum (ID331 cultivar) and hexaploid wheat T. aestivum (Sagittario cultivar). Seventeen celiacs (aged 6-14yrs) in disease remission participated to the study. Seven patients consumed for 3 days 3 sandwiches with common wheat, whereas 10 consumed ID331 wheat sandwiches, containing an equivalent amount of gluten, approximately 12 g/die. Immune reactivity to diploid and hexaploid gluten and to dominant α-gliadin peptide, DQ2.5-glia-α1/2, was analyzed on fresh peripheral blood mononuclear cells (PBMCs) by IFN-γ ELISPOT assay.

Results: The SGC with common wheat mobilized in peripheral blood a remarkable number of IFN-γ secreting cells in response to hexaploid gluten (median fold increase day6/day0: 2.9, range 0.1 - 7.5; p<0.05), and to the DQ2.5-glia-α1/2 (median fold increase day6/day0: 4.2, range 0.8 - 4.4, p<0.05). Conversely, diploid monococcum wheat elicited in the blood a reduced number of T cells releasing IFN-γ to gliadin (median fold increase day6/day0 1.2, range 0 - 4.7; p=ns) or dominant gluten peptide (median fold increase day6/day0 2.0, range 0.8 - 4.4, p=ns).

Conclusion: This study showed a reduced in vivo immunogenicity of diploid wheat compared to hexaploid common cereal in celiac patients, thus confirming our previous in vitro data. Although T. monococcum is a cereal not suitable for the diet of celiac disease patients, its reduced immunogenicity, in comparison to common wheat, strongly suggested that a diet based on this grain could be efficacious to prevent CD in at risk subjects.
Faecal microbiota profiles at diagnosis in paediatric inflammatory bowel disease. Prediction of disease severity and subsequent need of biologic therapy

Christine Olbjørn¹, Milada Cvancarova Småstuen², Espen Thii-Evensen³, Britt Nakstad⁴, Jon Rove⁵, Christina Casén⁶, Torbjørn Lindahl⁶, Morten Vatn⁷, Gøri Perminow⁸

¹University of Oslo, Institute of Clinical Medicine, Campus Akershus University Hospital, Oslo, Norway
²Oslo and Akershus University College of Applied Sciences, Faculty of Health Sciences, Oslo, Norway
³Rikshospitalet, Oslo University Hospital, Department of Gastroenterology, Oslo, Norway
⁴Institute of Clinical Medicine, University of Oslo, Campus Akershus University Hospital, Oslo, Norway
⁵Akershus University Hospital, Pediatric and Adolescent Medicine, Lørenskog, Norway
⁶Genetic Analysis As, Oslo, Norway
⁷University of Oslo, Institute of Clinical Medicine, Epigen Institute, Campus Akerhus University Hospital, Oslo, Norway
⁸Ullevål, Oslo University Hospital, Department of Pediatrics, Oslo, Norway

Objectives and study: Imbalances in the faecal microbiota with a reduction in biodiversity; dysbiosis, have been identified in inflammatory bowel disease (IBD). Our aim was to study and compare the faecal microbiota in paediatric patients with newly diagnosed untreated IBD with the microbiota of healthy children and paediatric patients with gastrointestinal symptoms but no IBD. We also related the microbiota profiles to IBD subgroups and later treatment.

Methods: Faecal samples were collected from 235 children and adolescents. Eighty had Crohn’s disease (CD), 27 ulcerative colitis (UC) and 3 IBD unclassified, 50 were non-IBD symptomatic patients and 75 were healthy children between age two and 18 years. The microbiota was analysed using a 16s rRNA DNA based test with the GA-map technology (Genetic Analysis AS, Oslo, Norway) measuring probe signal intensity (PSI) of 54 bacterial DNA probes covering 300 bacteria on different taxonomic levels. We compared the PSI values of the three groups; healthy children, IBD patients and non-IBD patients. Using non-parametric methods, we selected six probes where the PSI was lower in IBD compared to non-IBD patients. For each of these six probes, IBD patients were given 1 point if their PSI was lower than the median PSI value of non-IBD patients. The points were summarized as a Score ranging from 0-6 points. Logistic regression was used to model possible associations between this Score and risk of having IBD.

Results: Most bacterial PSIs were reduced in IBD and non-IBD patients (p< 0.001) compared to healthy controls. IBD patients had reduced abundance of Firmicutes (Eubacterium p=0.006, Holdemanella p=0.038, Streptococcus p=0.046), Tenericutes and Bacteroidetes (Parabacteroidetes p=0.02), p=0.002, and Bifidobacterium, p=0.02, compared to the non-IBD symptomatic patients. CD patients had an overall lower diversity compared to UC patients, but this did not reach statistical significance except for Mycoplasma, where CD patients had a lower abundance (p=0.045). IBD patients with extensive disease according to the Paris classification L3/E3 had more Clostridiales (Ruminococcus gnavus), p=0.02, and CD patients with L3 had more Proteobacteria, p=0.04, than patients with limited disease. Upper gastrointestinal manifestations in CD patients were associated with higher PSIs of the Firmicutes Bacilli, Clostridia and Veillonella (p=0.008) and the Proteobacteria Helicobacter, p=0.008, and lower PSIs of the Proteobacteria Shigella and Escherichia (p=0.05). IBD patients who later received biologic therapy with TNF blockers (64/110) had lower diversity at baseline for Firmicutes, Tenericutes (Mycoplasma p=0.009) and Bacteroidetes, p=0.015, compared to IBD patients who were treated with conventional (exclusive enteral nutrition, immunomodulators, corticosteroids, 5-Aminosalicylic acids) medications (46/110). Patients who reached 3 or more points using the Score were 2.2 times more likely to have IBD compared to non-IBD (OR=2.2, 95%CI 1.1-4.5, p=0.027).

Conclusion: Microbiota profiles may be used to stratify paediatric IBD into diagnostic and prognostic subgroups. A severe dysbiotic microbiota profile in newly diagnosed paediatric IBD is associated with a phenotype with more extensive disease and subsequent need of TNF blocker treatment.
GASTROENTEROLOGY: Coeliac disease

G-O-059

Cell phenotype and cytokine profile in the intestinal mucosa of children with over or potential coeliac disease

Serena Vitale1, Veronica Santarlasci2, Alessandra Camarca3, Stefania Picascia1, Renata Auricchio4, Lorenzo Cosmi2, Francesco Annunziato2, Riccardo Troncone5, Carmen Gianfrani6

1Institute of Protein Biochemistry (Ibp), Cnr, Naples, Italy
2University of Florence, Department of Experimental and Clinical Medicine and Denothe Center, Florence, Italy
3Institute of Food Science (Isa), Cnr, Avellino, Italy
4University “federico ii”, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy
5University “Federico II”, Department of Translational Medicine & European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
6Institute of Protein Biochemistry (Ibp), Cnr and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy

Objectives and study: Coeliac disease (CD) is characterized by a variable combination of gluten-dependent symptoms, genetic factors, specific antibodies and enteropathy. Most patients show a variable degree of enteropathy (overt CD), but a minority shows absence of villous atrophy despite the presence of CD-specific autoantibodies (potential CD). We investigated the cytokine profile and the phenotype of intestinal T-cells from children affected by overt versus potential CD.

Methods: Cell phenotype and cytokine production patterns were analysed by flow cytometry, in either gluten-raised T cell lines (TCLs) and freshly isolated mucosal cells. Jejunal biopsies were obtained from 19 overt CD (mean age 5.1 yr), 16 potential CD patients (8.5 yr) and 12 non-CD children (4.2 yr). Phenotypic analysis was carried out on unstimulated cells, whilst cytokines were detected by intracytoplasmic staining after PMA/Ionomycin stimulation.

Results: Increased number of CD3 TCRγδ+ cells, mainly CD4CD8 double negative cells, was found in TCLs from overt CD patients compared to potential CD (p<0.004) or non-CD healthy (p<0.03) subjects. A higher fraction of IL-4 producing cells, mainly CD4+ cells, was detected in TCLs from children with normal mucosa, either potential CD or non-CD control children, (p<0.0007 potential CD vs overt CD, and p<0.02 non-CD vs overt CD, respectively). Ex vivo analysis on freshly isolated intestinal cells confirmed the significant increased frequency of TCR γδ+ cells in gut mucosa of children with villous atrophy (p<0.02 overt CD vs potential CD, and p<0.001 overt CD vs non-CD). However, a higher percentage of TCR γδ+ cells was detected in potential CD compared to healthy mucosa (p<0.04 potential CD vs non-CD). An increased expansion of IL-4 producing T cells of CD4+ phenotype was found in biopsies from potential CD compared to overt CD patients (p<0.05).

Conclusion: Our study confirms in CD patients an expansion of TCRγδ+ T-cells, particularly in subjects with enteropathy (overt CD). The transition to villous atrophy seems to be characterized by a dramatic disappearance of IL4+ cells. These findings may offer biomarkers useful to characterize the different stages of CD.
Clinical symptoms underestimate endoscopic inflammation in paediatric PSC-IBD

Amanda Ricciuto¹, Nicholas Carman¹, Jennifer Fish², Eileen Crowley¹, Aleixo Muise¹, Peter Church¹, Thomas Walters¹, Binita M. Kamath³, Anne Griffiths²

¹The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
²Hospital for Sick Children, Division of Gastroenterology, Toronto, Canada
³The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: Inflammatory bowel disease with primary sclerosing cholangitis (PSC-IBD) has a distinct phenotype, characterized by pancolitis and frequent backwash ileitis, but a relative paucity of overt clinical symptoms. The well-known greater risk of colonic neoplasia (where chronic inflammatory activity is a risk factor) led us to hypothesize that symptoms might be an inaccurate reflection of endoscopic disease activity in children with PSC-IBD.

Methods: In this single-centre prospective study performed at the Hospital for Sick Children, Paediatric UC Activity Index (PUCAI), physician global assessment (PGA) and fecal calprotectin (FC) were measured in all paediatric PSC-IBD patients undergoing colonoscopy. Children with colonic IBD without PSC served as controls. Colonoscopies were scored by two blinded IBD physicians using the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) and endoscopic PGA. Spearman correlations were calculated between variables. PUCAI and FC were compared between patients with and without endoscopic remission (UCEIS 0-1) in both groups. UCEIS scores were compared between PSC-IBD patients and controls in clinical remission (PUCAI <10). Results are reported as medians with interquartile ranges.

Results: 24 PSC-IBD and 32 colonic IBD patients were enrolled. As hypothesized, in PSC-IBD patients, the correlations between symptom-based assessments of disease activity and endoscopy were poor (r=0.421 for PUCAI vs. UCEIS; r=0.196 for PGA vs. UCEIS). The correlation between FC and UCEIS was significantly better (r=0.782) in this group. FC correlated poorly with both PUCAI and clinical PGA. In contrast, in controls, PUCAI correlated well with UCEIS (r=0.824); this correlation was superior to that of FC vs. UCEIS (r=0.696). The correlation between PUCAI and FC was better in controls than in PSC-IBD patients (r=0.525 vs. 0.367). In controls, both FC and PUCAI differed significantly between patients with and without endoscopic remission (FC 87 [71-547] vs. 2310 [1896-6578] µg/g, p=0.0001; PUCAI 0 [0-0] vs. 35 [15-40], p<0.001). In PSC-IBD patients, however, only FC differed significantly (42 [37-92] vs. 2205 [348-7606] µg/g, p=0.02); PUCAI was similar between PSC-IBD patients with and without endoscopic remission (p=0.52). In addition, UCEIS scores were significantly higher in PSC-IBD patients in clinical remission than controls in clinical remission (2.5 [1-4] vs. 0 [0-2], p=0.046).
Table: Spearman correlations between symptom-based, biochemical and endoscopic markers of disease activity in paediatric PSC-IBD patients

<table>
<thead>
<tr>
<th></th>
<th>PUCAI</th>
<th>Clinical PGA</th>
<th>FC</th>
<th>CRP</th>
<th>UCEIS</th>
<th>Endoscopic PGA</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUCAI</td>
<td>1.0</td>
<td>0.73 p=0.002</td>
<td>0.37</td>
<td>0.64</td>
<td>0.42</td>
<td>0.40 p=0.08</td>
</tr>
<tr>
<td>Clinical PGA</td>
<td>0.73</td>
<td>1.0</td>
<td>-0.027</td>
<td>0.32</td>
<td>0.20</td>
<td>0.25 p=0.36</td>
</tr>
<tr>
<td>FC</td>
<td>0.37</td>
<td>-0.027 p=0.95</td>
<td>1.0</td>
<td>0.76</td>
<td>0.78</td>
<td>0.82 p=0.002</td>
</tr>
<tr>
<td>CRP</td>
<td>0.64</td>
<td>0.32 p=0.31</td>
<td>0.76</td>
<td>1.0</td>
<td>0.85</td>
<td>0.80 p&lt;0.001</td>
</tr>
<tr>
<td>UCEIS</td>
<td>0.42</td>
<td>0.20 p=0.50</td>
<td>0.78</td>
<td>0.85</td>
<td>1.0</td>
<td>0.98 p&lt;0.001</td>
</tr>
<tr>
<td>Endoscopic PGA</td>
<td>0.40</td>
<td>0.25 p=0.36</td>
<td>0.82</td>
<td>0.80</td>
<td>0.98</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Conclusion: Symptoms underestimate endoscopic activity in paediatric PSC-IBD. FC appears to be more accurate in this setting. Given the emerging importance of the gut-liver axis in PSC, increasing attention must be paid to achieving mucosal healing, particularly in children in early phases of PSC, where the possibility of altering biliary disease progression may be greatest.
Outcome of children with potential coeliac disease (PCD): a multicenter study

Silvia Ghione1, Patrizia Alvisi2, Benedetta Chianucci1, Cristiana Retetangos2, Monica Paci1, Anna Maria Gissi1, Sara Naldini1, Laura Lacitignola1, Paolo Lionetti3

1Meyer Children’s Hospital, Gastroenterology and Nutrition, Florence, Italy
2Ospedale Maggiore, Paediatric Department, Bologna, Italy
3University of Florence, Meyer Children’s Hospital, Neurofarba Department, Gastroenterology and Nutrition, Firenze, Italy

Objectives and study: Potential Coeliac Disease (PCD) is defined as the presence of coeliac disease-related antibodies (anti-transglutaminase, TG2; anti-endomysium, EMA) usually with a low level of positivity in genetically predisposed individual who have a normal duodenal mucosa. Management of patients with PCD is controversial. Usually symptomatic patients start a gluten-free diet (GFD), whereas those who are asymptomatic are kept on a free diet (FD). In a retrospective, multicentre study we evaluate the natural history of PCD in children for a period of time of at least 5 years.

Methods: Children with EMA and TG2 low level of positivity, CD HLA compatible (HLA DQ2 and/or DQ8), normal IgA and a normal intestinal mucosa villos architecture (Marsh type 0 or 1) were included. According to the presence or absence of symptoms and TG2 levels, patients, at first consultation, underwent an intestinal biopsy (Group 1) or the intestinal biopsy was postponed and clinical evaluation and serologic marker monitoring was planned (Group 2). In Group 1 symptomatic PCD patients started a GFD whereas asymptomatic continued a FD. Every 4-6 months all patients performed a clinical and serological control (TG2, EMA). Intestinal biopsy was repeated (or performed if not done) if symptoms worsened and/or TG2 levels increased. Serology negativization was defined when TG2 was negative in two subsequent controls (about 1 year).

Results: 207 children (120 F, 87 M; 4.9 ± 4.0 years) with suspected PCD were included and followed for 4.7 ± 3.1 years. Group 1 (129 pts) compared with Group 2 (78 pts) had a higher percentage of patients with TG2 >2 xN (34% vs 15%, p<0.005).

In Group 1: CD was diagnosed at first consultation in 10/129 patients (7.8%). Symptomatic PCD patients (16 pts) on a GFD reported relief of symptoms in 87.5% (14/16) and 81.3% (13/16) of them had serology negativity within in 12 months of GFD. Asymptomatic PCD patients (103 pts) kept on a FD showed serology negativization in 56.3%(58/103), antibody levels fluctuation in 26.2%(27/103) and developed CD in 17.5% (18/103). The median time of serology negativization was significantly shorter in younger (<2.5 years) compared to older children (487 vs 1125 days, p =0.02 Kaplan Meyer Log-Rank Test analysis).

In Group 2: no patient developed symptoms or showed increase of antibody levels. In these children intestinal biopsy was not performed and 62 out of 78 become antibody negative during follow-up, (80%) whereas 16/78 (20%) continued to show fluctuation of antibody titre. Also in this group, younger patients showed a shorter period of negativization time.

Conclusion: PCD is common in children with low levels of CD specific antibody titres and a minority of them on a FD develop CD. The majority shows fluctuation or even negativization of TG2 and EMA. In younger children this negativization occurs in a shorter period of time. In asymptomatic patients with low levels of antibodies is probably reasonable to postpone intestinal biopsy and continue follow-up.
Re-exploring the iceberg of celiac disease in children: preliminary results of a multicenter Italian screening project based on a rapid HLA DQ test

Simona Gatti¹, Tiziana Galeazzi¹, Anil Kumar Verma¹, Chiara Monachesi¹, Roberta Annibali¹, Alessandra Palpacelli¹, Giada Delbaldo¹, Elisa Franceschini¹, Anna Maria Colombari², Antonio Marchesini¹, Linda Balanzoni³, Novella Scattolo³, Mauro Cinquetti², Elena Lionetti⁴, Carlo Catassi¹

¹Università Politecnica Delle Marche, Department of Pediatrics, Ancona, Italy
²Ospedale Fracastoro, Pediatric and Neonatal Care Unit, Verona, Italy
³Ospedale Fracastoro, Chemo-Clinical Analysis Laboratory, Verona, Italy
⁴Marche Polytechnic University, Department of Paediatrics, Ancona, Italy

Objectives and study: This observational multicenter study aimed to assess the prevalence of celiac disease (CD) autoimmunity and overt CD in school age children by using HLA typing as the initial screening test, and to redefine the clinical spectrum of CD and the ratio between known and unknown subjects in Italian children.

Methods: children aged between 5-10 years, attending the primary school in Ancona and Verona, were invited to participate and enrolled after a written consent was obtained. No exclusion criteria were formulated and already diagnosed celiac patients were included in the final analysis. Celiac Gen Screen (Biodiagene) based on a rapid single PCR reaction HLA on a single blood drop (on filter paper or 10 µl into a specific tube) was used to identify HLA DQ2/DQ8 susceptible subjects. Serum anti-transglutaminase IgA antibodies (TTG) and total IgA were performed in HLA positive patients. Anti-endomysium antibodies (EMA) and anti-deamidated gliadin peptides IgG antibodies were searched in TTG positive and IgA deficient patients respectively. Biopsy was performed according to the ESPGHAN criteria.

Results: from May 2015 to November 2016, 4647 subjects have been HLA screened (81.7% of the eligible population). Results of the first 3411 subjects that have completed the screening are available. Out of the 1447 HLA positive subjects (43.2%, 95% CI 41.7-44.63), 1263 (87.2% of the screened population) underwent the serological evaluation. CD autoimmunity was found in 54 patients with 40 receiving a diagnosis of CD (1.2%, 95% CI 0.38-0.92). 36% of new diagnosed children were asymptomatic and 55% required biopsy for further confirmation. CD was already known in 18 children (0.39%, 95% CI 0.22-0.60) with a total prevalence of CD in the screened cohort of 1.56% (95% CI, 1.39-1.99).The ratio of known/undiagnosed CD 1:2.2.

Conclusion: Preliminary results indicate a CD prevalence of 1.56% in age-school children, confirming an increase in prevalence compared to Italian 90’ data. Due to increased awareness of the disease, the ratio between known and unknown cases has profoundly changed but there are still 70% of cases remaining undiagnosed. Final results will give the exact figure of the current prevalence of CD in school-age children. Considering its high sensitivity and feasibility, the rapid HLA test would be an appropriate tool to perform screening of CD in the general population.
Ultra-short coeliac disease: Prevalence and characteristics in children

Nevzat Aykut Bayrak¹, Burcu Volkan², Esra Polat³, Sevilay Özmen⁴

¹Diyarbakir Children's Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
²Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
³Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
⁴Erzurum Regional Training and Research Hospital, Pathology, Erzurum, Turkey

Objectives and study: The histologic findings in Coeliac disease (CD) might have a variable severity with patchy distribution. Latest guideline suggests obtaining at least one biopsy from the duodenal bulb and at least four from the second and third portion of duodenum to increase the detection rate of CD. Rarely, histologic changes may be limited only in the duodenal bulb, which is called as ultra-short CD (USCD). The prevalence of USCD is reported up to 12% of children with CD. The aim of the study is to evaluate the prevalence and clinical characteristics of USCD in children.

Methods: Biopsy proven CD cases diagnosed between August 2015 and November 2016 in three paediatric gastroenterology centres were included in the study. Histopathological specimens were re-evaluated and graded according to Marsh-Oberhuber classification. Demographic data, symptoms, biochemistry (haemoglobin, albumin, ferritin) and anti-tissue transglutaminase (TTG) IgA levels at the time of diagnosis were recorded. Patients with insufficient data, inadequate biopsy, selective IgA syndrome and other accompanying systemic disease were excluded. The data of USCD patients was compared with the CD patients with duodenal involvement.

Results: From a total of 394 CD patients, 368 were eligible (mean age:8.67±4.26 years, 61.4% girls, mean BMI z-score: -1.27±1.8, mean TTG IgA: 240.8±141.7 U/mL). USCD was found in 14 patients (3.8%). USCD patients had better BMI z-scores (0.2±3.71 vs -1.4±1.5, p<0.01) and lower TTG IgA levels (111.1±68.7 vs 252.1±132.9, p<0.01) compared with other CD patients. Demographic, symptomatic and biochemical data was similar between the groups.

Conclusion: Our cohort suggests that, USCD is a rare entity, characterized by better nutritional status and lower TTG IgA levels in children with CD. On the other hand, if adequate duodenal bulb biopsies were not obtained from USCD patients in this cohort, 3.5% of patients would be misdiagnosed.
Gluten free diet in children: a comparison of compliance rates and growth parameters between biopsy and non-biopsy diagnosed children

Nabil El-Lababidi¹, Jaromír Běláček², Peter Szitanyi¹, Jiří Zeman¹, Pavel Frühaufl¹

¹First Faculty of Medicine, Charles University and the General University Hospital in Prague, Department of Paediatrics and Adolescent Medicine, Prague, Czech Republic
²First Faculty of Medicine, Charles University, Institute of Biophysics and Informatics, Prague, Czech Republic

Objectives and study: Coeliac disease (CD) is an immune mediated systemic disorder elicited by gluten and related prolamines in genetically susceptible individuals. The only known and effective treatment for CD is a strict, life-long gluten free diet (GFD). Up to 2012, the only acceptable method for diagnosing CD was histological findings of changes corresponding with this illness in tissue biopsies obtained from the thin intestine. In 2012, the term non-biopsy diagnosis was introduced by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN). When fulfilling certain strict criteria, the diagnosis of CD can be established without histological verification of the disease. The aims of this study are firstly, the evaluation of the compliance rate with GFD in newly diagnosed children with CD; secondly, a comparison of this rate in children diagnosed with histological verification of this disease and in those diagnosed using the non-biopsy approach, and finally, the evaluation of possible growth parameter differences between these two groups.

Methods: Newly diagnosed children with CD were followed up. Their growth parameters and tissue transglutaminase antibody (tTGA) levels were evaluated at regular intervals. Normalization of tTGA by 9 months since the commencement of a GFD was regarded as a compliance criterion. Due to the assumed non-normal distribution of the acquired data, a Mann-Whitney test was elected for statistical evaluation. All children were diagnosed in adherence with the ESPGHAN guidelines.

Results: 105 newly diagnosed children with CD (average age 7.7 years) between 01/2013 and 12/2014 were enrolled into the study. Compliance by 9 months since the start of a GFD was achieved in 67 of them (63.8%). 38 out of 50 biopsy diagnosed children (76%) were found to be compliant at that time. Only 29 of the 55 non-biopsy diagnosed children (57%) were found to be compliant at the same time. A statistically significant difference between these two groups in favour of the biopsy approach one with a \( p \) value of 0.014 was calculated. A statistically significant difference in growth parameters between the two groups in favour of the biopsy approach one was also found (height gain difference with a \( p \) value of 0.02, weight gain difference with a \( p \) value of 0.004 and height-to-weight ratio improvement difference with a \( p \) value of 0.022).
Conclusion: A 63.8% overall GFD compliance rate was found. A statistically significantly higher compliance rate and growth parameters improvement in children with histologically verified CD in comparison with those diagnosed using the non-biopsy approach was found. This documented difference warrants further research on larger patient cohorts. Should this difference be verified, re-evaluation of the diagnostic approach of CD in children might be required.

This research was supported by the Ministry of Public Health of the Czech Republic, grant RVO VFN 64165/2012.
Circulating microRNAs as potential non-invasive diagnostic biomarkers of coeliac disease in children

Cristina Felli¹, Francesca Ferretti¹, Paolo Uva², Anna Alisi³, Valerio Nobili⁴, Andrea Masotti¹

¹Bambino Gesù Children’s Hospital-Irccs, Rome, Italy
²Crs4 Bioinformatics Laboratory, Parco Scientifico e Tecnologico Polaris, Pula, Italy
³Bambino Gesù Children’s Hospital an, Rome, Italy
⁴Bambino Gesù Children’s Hospital-Irccs, Hepato-Metabolic Disease Unit and Liver Research Unit, Rome, Italy

Objectives and study: The gold standard for the diagnosis of coeliac disease (CD) is a combination of serological screening assays and biopsy collection of intestinal mucosa. However, according to ESPGHAN guidelines the diagnosis of CD in the paediatric setting could be made by highly sensitive and specific mini-invasive serological tests avoiding duodenal biopsy. Unfortunately, current serologic tests take into account the adaptive immune response in CD but are not adequate to completely assess the severity of intestinal inflammation or to monitor the disease progression.

MicroRNAs (miRNAs) circulating in plasma/serum are highly stable and their expression profile can be successfully used to monitor the disease state and/or its progression. Thus, circulating miRNAs represent a powerful mini-invasive tool for diagnostic and therapeutic management. The aim of this study was to identify by next-generation sequencing, for the first time, the profiles of circulating miRNAs in the serum of children affected by CD to find potential biomarkers of the disease and to monitor how a gluten-free diet (GFD) can affect their expression levels.

Methods: We enrolled two independent sets of subjects comprising 120 individuals overall. Each set (n=60) is composed by twenty children with active CD, twenty on GFD and twenty healthy individuals (controls). The first set was used as a training set, the second as the validation set. We compared the extraction efficiency of several commercial RNA isolation kits to choose the method that offered the best recovery and reproducibility efficiency for downstream analyses. We assessed the expression of circulating miRNAs from serum by small RNA-Seq (HiSeq 2000, Illumina). The expression levels of statistically significant deregulated miRNAs have been confirmed by real time qPCR (QuantStudio™ 12K Flex RT-qPCR System) on the same set and validated on the second independent set.

Results: Among the dysregulated miRNAs detected by small RNA sequencing, eight of them showed a significant (FDR<0.05) differential expression in at least one group of samples. In particular, two miRNAs were upregulated specifically only in active CD compared to healthy donors, whereas three miRNAs were downregulated only on GFD compared to healthy donors. Other miRNAs showed a marked downregulation in GFD compared to both CD and controls. The majority of these miRNAs have been further validated by qPCR.

Conclusion: This study identified, for the first time, the expression profiles of CD-associated circulating miRNAs with an important diagnostic potential. Circulating miRNAs specifically associated with a GFD regimen may increase further the diagnostic usefulness (clinical monitoring and follow-up).
Gene expression analysis after a short oral challenge with ancient monococcum wheat in celiac disease patients

Martina Galatola¹, Donatella Cielo¹, Daniela Furlan¹, Carmen Gianfrani², Riccardo Troncone¹, Luigi Greco¹, Renata Auricchio¹

¹University "Federico II", Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy
²Institute of Protein Biochemistry (Ibp), Cnr and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy; , Naples, Italy

Objectives and study: In the Celiac Disease (CD) community there is a strong interest to find wheat species with a reduced, or null, toxicity suitable for celiac patients. Among the candidate wheat grains, the ancestral diploid species *Triticum monococcum* is the most investigated. We aimed to analyze the changes in the expression profile of several genes involved in inflammatory pathways in peripheral blood of CD patients upon a brief consumption of *Triticum monococcum* (ID331 cultivar).

Methods: Nineteen pediatric patients (age 6-14yrs) with CD and compliant to a gluten free diet were recruited. The subjects were randomly divided into two groups; 11 patients consumed for three days sandwiches made with *T. monococcum* ID331 flour, whilst the remaining 8 patients ears sandwiches made with soft wheat flour (*T. aestivum* Sagittario cultivar). The amount of sandwiches was standardized to contain an equivalent amount of gluten, approximately 12 g/die. Peripheral blood cells were obtained at day0 and after 6 days from the start of gluten challenge. The RNA was obtained using the PAXgene™ Blood RNA Systems (PreAnalytiX). The expression of the inflammatory genes (IL-12A, IL-18, NFkB1), and of genes candidate for risk prediction (TNFAIP3, SH2B3, TNFSF14, TAGAP, cREL, RGS1, LPP) was estimated by Taqman real-time quantitative PCR.

Results: The patients who ingested *T. monococcum* showed a different gene expression compared to the patients who ingested *T. aestivum*. These expression differences concerned the interleukin and candidate genes that are involved in the inflammatory pathways. In particular, IL12A is significantly down-regulated in patients treated with ID331 compared to Sagittario, with a fold change of 0.5 *(p<0.05)*. IL-18 and candidate genes RGS1, NFkB1, TNFAIP3 and c-REL were down-regulated and clustered in ID331 compared to Sagittario where the expression is more variable.

Conclusion: A brief oral exposure to diploid *T. monococcum* gluten activated in CD patients PBMC, likely of intestinal origin, the expression of genes involved in inflammatory pathways, but of much lower intensity compared to gene expression in patients orally exposed to hexaploid *T. aestivum*. These findings, even if preliminary, confirm that ancient wheats are not recommendable for CD patients, but open the way for future research on the possible applications of alternative grains to prevent CD in predisposed subjects.
Faecal short chain fatty acids in untreated and treated children with coeliac disease

Konstantinos Gerasimidis¹, Konstantina Zafeiropoulou¹, Mary Mackinder¹, Antonia Karanikolou¹, Olga Biskou¹, Elaine Buchanan², Tracey Cardigan³, Hazel Duncan⁴, Richard Russell⁵, Richard Hansen³, Cristine Edwards¹, Paraic McGrogan³

¹University of Glasgow, Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, Glasgow Royal Infirmary, Glasgow, United Kingdom
²Royal Hospital for Children, Nutrition and Dietetics, Glasgow, United Kingdom
³Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom

Objectives and study: Recent literature indicates that the gut microbiota and its metabolic activity might be altered in children with coeliac disease (CD). However, the role of the gut microbiota in CD is unclear and the results among studies remain inconclusive. SCFAs are produced from bacterial fermentation of the fibre. They are important for the whole body metabolism and mediate immune response. The aim of this study was to measure the faecal concentration of SCFA in treated and untreated children with CD and compared them with healthy controls.

Methods: Faecal samples were collected from CD children on GFD for more than a year (Long Standing patients - LS); from newly diagnosed untreated CD children (ND), and following treatment with GFD for 6 and 12 months and from healthy controls (HC). SCFAs were measured using Gas Chromatography (GC). The data were analyzed using Mann – Whitney and Kruskal - Wallis tests and expressed as medians (Q1–Q3).

Results: Faecal samples were collected from 45 LS, 27 ND and 57 HC children. Among the 27 ND children, 13 adhered on GFD and gave us samples 6 and 12 months later. The relative abundance of acetate, isobutyrate, butyrate, isovaleric and valeric acids was significantly different between the LS, ND and HC (p<0.05). Regarding the absolute concentrations per wet matter it was found that only isovaleric and valeric acids were significantly different between the LS, ND and HC (p=0.041 and p=0.036, respectively). Specifically, isovaleric acid (µmol/gr wet sample) was significantly decreased in the group of LS (2.70 (1.75 – 3.65)) compared to ND (3.74 (2.60 – 4.68)) and HC (3.42 (2.57 – 4.56)), (p=0.040 and p=0.024, respectively), whereas valeric acid (µmol/gr wet sample) was significantly decreased in the LS (2.22 (1.55 – 3.05)) only opposed to the HC (2.85 (2.13 – 3.86)), (p=0.010). The relative abundance of acetate, isobutyrate, butyrate and isovaleric acid was significantly different during the 12 months period of treatment with GFD (p<0.05). Only acetate acid (%) was significantly increased 6 months after the adherence on GFD (74.01 (67.82-76.95)) compared to the ND on Gluten Containing Diet (GCD) (65.09 (61.27-68.65), (p=0.007), while isobutyrate, butyrate and isovaleric were significantly decreased 6 months after the adherence on GFD compared to ND on GCD (p=0.046, p=0.028 and p=0.046 respectively). The relative abundance of isobutyrate and isovaleric acid was still significantly decreased 12 months after the treatment with GFD (p=0.039 and p=0.033, respectively).

Conclusion: In this study differences concerning the relative abundance and absolute concentration of SCFAs between the HC and the ND were not observed However, differences among the LS and the ND or the LS and the HC were found. Furthermore, differences on the relative abundance of certain SCFAs were obvious 6 and 12 months after the adherence on GFD. Thus, it may be the GFD responsible for the altered composition of the produced SCFAs from the gut microbiota of children with CD and not the factor of the CD itself. Although these differences were significant in our results, further research is needed to conclude to such a conclusion, since the first part of our study is cross – sectional designed and we cannot assume causality based on that.
Selected genomic variants may account for overlapping susceptibility between non-Hodgkin lymphoma and paediatric celiac disease patients of Hellenic origin

Angeliki Panagiotara¹, Maro Krini², Kleopatra Spanou³, Maria Kanariou³, Nikki Constantinidou³, George Chrousos⁴, Eleftheria Roma², George P. Patrinos¹, Theodora Katsila¹

¹University of Patras, Pharmacy, Patras, Greece
²National and Kapodistrian University of Athens, First Department of Pediatrics, Athens, Greece
³“aghia Sophia” Children’s Hospital, Immunology and Histocompatibility, Athens, Greece
⁴University of Athens School of Medicine, First Department of Pediatrics, Aghia Sophia Children’s Hospital, Athens, Greece

Objectives and study: The mechanisms underlying interindividual variability in immune response are complex, comprised of both inherited genetic variation and cumulative antigenic exposure to infectious and other environmental challenges that shape immunological memory. Even though common variations in genes of the immune system have evolved through selective pressure to ensure host-pathogen symbiosis, such genomic variants may predispose to chronic inflammatory disease and malignant diseases of the lymphoid system. Evidence that genetic susceptibility plays a part in lymphomagenesis is provided by strong and consistent findings from registry and population-based epidemiological studies.

Herein, we explore single nucleotide polymorphisms in selected genes for overlapping susceptibility between non-Hodgkin lymphoma and paediatric celiac disease. This is not the first time a hypothesis is set on the incidence of lymphoproliferative disorders in patients with autoimmune disease. Notwithstanding, it is still unclear how to identify celiac disease patients with an increased risk of developing a lymphoproliferative disorder.

Methods: Extensive data mining, pathway analysis and literature review resulted in the selection of genomic variants in \(\text{TNF-alpha, IL10, LTA and IRF4}^{\text{genes}}\). For data validation, celiac paediatric patients of Hellenic origin (n=109) and their ethnically matched counterparts (n=111) were genotyped by allele-specific PCR, PCR-RFLP and Sanger sequencing. Amplification was carried out according to the KAPA2G Fast HotStart protocol (KAPABIOSYSTEMS, MA, USA). Hardy-Weinberg equilibrium was determined using the Cochran-Armitage trend test and the exact test. Genotype and allele frequencies were evaluated using the Fisher Exact test. A two-tailed p-value of <0.05 was considered statistically significant. The R project for statistical computing (R i386 3.2.1) was used.

Results: Selected genomic variants in \(\text{TNF-alpha, IL10, LTA and IRF4}^{\text{genes}}\) are possible candidates for overlapping susceptibility between non-Hodgkin lymphoma and paediatric celiac disease patients of Hellenic origin.

Conclusion: Selected genomic variants in \(\text{TNF-alpha, IL10, LTA and IRF4}^{\text{genes}}\) may account for overlapping susceptibility between non-Hodgkin lymphoma and paediatric celiac disease patients of Hellenic origin empowering patient stratification via the identification of celiac disease patients with an increased risk of developing a lymphoproliferative disorder.
New markers for coeliac disease: anti-neo-epitope human and microbial transglutaminases

Torsten Matthias1, Daniel Agardh2, Patricia Jeremias1, Sandra Neidhöfer3, Aaron Lerner4

1Aesku.Kipp Institute, Research, Wendelsheim, Germany
2Lund University, Department of Clinical Sciences, Lund, Sweden
3Aesku. Kipp Institute, Wendelsheim, Germany
4B. Rappaport School Medicine, R&D, Haifa, Israel

Objectives and study: Microbial transglutaminase (mTg) and human tissue Tg (tTg) form complexes with gliadin peptides and present neo-epitopes. The aim was to test the diagnostic performance of antibodies against both non-complexed and complexed forms of both transglutaminases in children with celiac disease (CD) and compared with disease controls.

Methods: Serum samples at day of intestinal biopsy were collected from 350 CD children (mean age 7.4 years) and 215 disease controls (mean age 10.2 years) and tested using the following ELISAs detecting IgA, IgG or both IgA+IgG combined: tTg (for in house research use only), AESKULISA®s tTg New Generation (tTg neo-epitope (tTg-neo)) & mTg neo-epitope (mTg-neo, RUO). Results were correlated to the degree of intestinal injury, using the revised Marsh criteria.

Results: The diagnostic performances against the different antigens were compared (table), mTg-neo Check had the highest sensitivity and tTg IgA the highest specificity. Comparing the different correlations between antibodies’ isotypes, the tTg Check (r=0.7889, p<0.0001) and tTg-neo check (r=0.7544, p<0.0001) as well as tTg and tTg-neo IgA (r= 0.7571 and r= 0.7279, p<0.0001 respectively) were the best indicators of intestinal damage in CD.

Table:

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>AUC</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>tTg-neo Check</td>
<td>82.06</td>
<td>97.67</td>
<td>0.964</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>mTg-neo Check</td>
<td>93.82</td>
<td>51.63</td>
<td>0.890</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tTg Check</td>
<td>89.38</td>
<td>95.73</td>
<td>0.973</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tTg-neo IgA</td>
<td>72.65</td>
<td>98.60</td>
<td>0.943</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>mTg-neo IgA</td>
<td>45.29</td>
<td>98.60</td>
<td>0.813</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tTg IgA</td>
<td>86.18</td>
<td>99.53</td>
<td>0.969</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tTg-neo IgG</td>
<td>82.35</td>
<td>86.05</td>
<td>0.921</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>mTg-neo IgG</td>
<td>89.41</td>
<td>67.44</td>
<td>0.886</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>tTg IgG</td>
<td>41.76</td>
<td>99.07</td>
<td>0.941</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: It is suggested that the combination of tTg-neo IgA/IgG antibodies should be used preferably to reflect intestinal damage during screening and diagnosing childhood CD. The tTg & tTg-neo assays show similar diagnostic performance and recommended as good screening tests for CD in children. mTg-neo IgG presents a new serological biomarker for CD.

Disclosure of interest: Author Name: Dr. Torsten Matthias conflict because CEO of AESKU Diagnostics GmbH & Co. KG
Prospective validation of antibody-based diagnostic procedures for paediatric coeliac disease-the ABCD Study

Johannes Wolf,1 David Petroff,2 Thomas Richter,3 Marcus Auth,4 Holm Uhlig,5 Martin Laaß,6 Peter Lauenstein,1 Andreas Krahl,9 Norman Händel,9 Jan de Laffolie,10 Almuthe Christine Hauer,11 Thomas Kehler,12 Gunter Flemming,13 Astor Rodrigues,14 Frank Schmidt,15 Wolf-Dietrich Huber,6 Dirk Hasenclever,17 Thomas Mothes

1Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Medical Faculty of the University and University Hospital Leipzig, Leipzig, Germany
2Clinical Trial Centre, University of Leipzig, Leipzig, Germany
3Children’s Hospital of the Clinical Centre “sankt Georg” Leipzig, Leipzig, Germany
4Alder Hey Children’s NHS Foundation Trust, Department of Paediatric Gastroenterology, Hepatology and Nutrition (GHN), Liverpool, United Kingdom
5Oxford University Hospital, Oxford, United Kingdom
6Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Children’s University Hospital, Dresden, Germany
7German Center for Diagnostics, Department of Pediatrics, Wiesbaden, Germany
8Children’s Hospital „prinzessin Margarete“, Darmstadt, Darmstadt, Germany
9Univ.-Kinderklinik Leipzig, Leipzig, Germany
10University Giessen, General Pediatrics and Neonatology, Giessen, Germany
11Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria
12Helios Hospital, Department of Paediatrics, Plauen, Plauen, Germany
13University Children’s Hospital Leipzig, Leipzig, Germany
14Hospital Oxford, Department of Paediatrics, University of Oxford, United Kingdom
15University Children’s Hospital Halle, Halle, Germany
16University Children’s Hospital Vienna, Paediatric Nephrology and Gastroenterology, Vienna, Austria
17Institute for Medical Informatics, Statistics & Epidemiology (Imise), University of Leipzig, Leipzig, Germany

Objectives and study: Diagnosis of coeliac disease (CD) uses clinical, genetic, serological and duodenal morphological findings. Recent guidelines of the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), based largely on retrospective data, suggest omitting biopsies if the concentration of IgA-antibodies to tissue transglutaminase (IgA-aTTG) exceeds 10-times the upper limit of normal (10×ULN) and if further criteria are met. The ESPGHAN proposed that the performance of these guidelines be evaluated prospectively. In a recent retrospective study, we proposed two diagnostic procedures based on (a) IgA-aTTG and total IgA and (b) IgA-aTTG and IgG-antibodies to deamidated gliadin. They use both one- and tenfold ULN, resulting in the classification “CD”, “non-CD” or “biopsy required”. The prospective multicentre AbCD study was performed to validate positive/negative predictive values (PPV/NPV) of these procedures.

Methods: Thirteen centres from Germany, United Kingdom and Austria enrolled paediatric patients scheduled for duodenal biopsy to confirm or rule out CD. Antibodies were measured by a blinded laboratory and tissue sections underwent reference pathology. After follow-up, the paediatricians made a diagnosis largely following routine clinical procedures. The trial was registered on the Internet Portal of the German Clinical Trials Register (https://drks-neu.uniklinik-freiburg.de/drks_web/setLocale_EN.do; DRKS00003854).

Results: For 898 of 949 participants, serum, biopsy, and follow-up data were available (592 CD, 345 non-CD, 24 no final diagnosis). The PPV/NPV of the two diagnostic procedures were 0.988/0.934 and 0.988/0.958. Model-based extrapolation shows that PPV/NPV remain above 0.95 with LCB >0.9 even at a prevalence as low as 4%. Endomysium antibodies and HLA-typing did not improve PPV in samples with IgA-aTTG ≥10×ULN. Notably, the discrepancy rate between pathologists is 4.2% and comparable to the error rate in the serological procedures.

Conclusion: The two procedures allow diagnosis or exclusion of CD without biopsy in three quarters of patients presenting at the paediatric gastroenterologist with the test kits examined. Our results have major personal and health care implications in clinical practice (avoiding many biopsies, reducing
costs, endoscopy waiting times, patient risks, and delay of treatment). We have shown that HLA-typing as well as EmA tests are not required in unequivocal cases and that endoscopic procedures to assess duodenal biopsies are not required in three quarters of paediatric patients with suspected CD.

**Disclosure of interest:** TM reports a grant from the European Regional Development Fund (ERDF) and from EUROIMMUN Medizinische Labordiagnostika AG (Dassow, Germany) for performing this trial. TM and HHU were two of the inventors of the patent "Peptides and their use in a procedure for diagnostics of coeliac disease and dermatitis herpetiformis," (German patent DE10005932) with inventors' boni paid by Leipzig University until 2014. HHU reports project collaboration with Eli Lilly and UCB Pharma, consultancy for Boehringer Ingelheim irrelated to the manuscript. JW received a grant from the German Coeliac Society and of EUROIMMUN (Lübeck, Germany) for a coeliac screening project in "LIFE Child" of the Research Centre of Civilization Diseases (Leipzig, Germany), outside the submitted work. TR reports a grant from EUROIMMUN (Lübeck, Germany) for coeliac screening in the Childrens' Hospital St Georg Leipzig, Germany, outside the submitted work. MKHA reports non-financial support from British Society for Paediatric Gastroenterology (BSPGHAN) during the conduct of the study and non-financial support from Nutricia plus Advance Medical Nutrition outside the submitted work. All other authors have no conflicts of interest to disclose.
GASTROENTEROLOGY: Coeliac disease

G-eP-009

Probiotic prevent gliadin induced activation of mTOR pathway and NFK beta in CaCo2 cells

Merlin Nanayakkara¹, Giuliana Lania², Valentina Discepolo³, Cristiana De Musis³, Alessandra Poerio³, Riccardo Troncone², Maria Vittoria Barone⁴

¹University of Naples, Department of Translational Medical Science, Elfid, Napoli, Italy
²University Federico II, Department of Translational Medical Sciences, Section of Paediatrics & European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
³University Federico II, Department of Translational Medical Sciences, Section of Paediatrics, Naples, Italy
⁴University of Naples, Department of Translational Medical Science, Elfid, Naples, Italy

Objectives and study: Undigested gliadin peptides are able to stimulate both innate and adaptive immune response and to cause damage to the intestinal mucosa of CD patients. GFD exposes celiac patients to nutritional deficiency. In fact, the consumption of some nutrients, particularly fibers, iron, calcium and folate, is lower than normal in patients who adhere to GFD. Alternative therapies for CD have been proposed, in particular one of this is focused on the destruction of gliadin peptides present in the food, while another approach has the goal of blocking the entry of peptides in the intestinal epithelium, preventing the activation of the immune response. Probiotics have characteristics that could be useful in both these areas.

Cells and organisms need to integrate information from the environment to ensure that they only grow when conditions are favorable. The highly conserved Ser/Thr protein kinase target of rapamycin (TOR) is a key integrator of environmental cues, including nutrient and growth factor availability as well as stress. Under nutrient-rich conditions, TOR promotes cell growth by stimulating biosynthetic pathways, including protein synthesis, and by inhibiting cellular catabolism such as through repression of the autophagy pathway. The opposite happens in conditions or caloric restriction.

This study describes a novel effect of probiotics in the prevention of undigested gliadin peptides effects on mTOR pathway and we have studied the effect of undigested gliadin peptide P31-43 on the mTOR pathway and the ability of probiotics to prevent them.

Methods: We treated Caco-2 cells an intestinal cell line, for 30 minutes with crude gliadin peptic-tryptic peptides (PTG), or P31-43 alone, and after pretreatment for 30’ with LP CBA L74 (LP CBA L74) or Lactobacillus rhamnosus GG (ATCC 53103) (1x10⁸) valuating the level of phosphorylation of mTOR, p70S6k/ p4EBP-1 and marker of inflammation pNFK-β by western blot. We analyzed marker of autophagy LC3 by immunofluorescence.

Results: Levels of phosphorylation of mTOR, p70S6k/ p4EBP-1 were increased after treatment of PTG and P31-43 indicating that intestinal epithelia cells responded to the gliadin peptides activating the mTOR pathway. Moreover we observed an increase of phosphorylation of NFK-β. Pretreatment with probiotic LP CBA L74 and Lactobacillus rhamnosus GG (ATCC 53103) prevented both the mTOR pathway activation and the NFK-β phosphorylation. P31-43 reduced LC3 staining and probiotic treatment was able to prevent also this reduction.

Conclusion: In an intestinal epithelial cell line we showed that PTG and P31-43 were able to induce the mTOR pathway and reduce the autophagy marker LC3. Probiotics could prevent both these effects.
The value of plasma I-FABP in non-invasive diagnosis of coeliac disease in patients with moderately elevated IgA tTG titers

Irene Oldenburger¹, Victorien Wolters¹, Tineke Kardol-Hoefnagel², Roderick Houwen¹, Henny Otten²

¹University Medical Center/Wilhelmina Children’s Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
²University Medical Center Utrecht, Laboratory of Translational Immunology, Utrecht, Netherlands

Objectives and study: Current diagnostic guidelines for Coeliac Disease (CD) still require a small intestinal biopsy in patients with IgA tTG levels <10x the upper limit of normal (ULN). The search is on for markers that may enable a non-invasive diagnosis of CD in this specific group. Serum intestinal-fatty acid binding protein (I-FABP), a sensitive marker for intestinal epithelial damage, may provide this.

Methods: From May 2008-April 2016 a total of 99 children with a clinical suspicion of CD and IgA tTG <10x ULN were included in the study. All patients underwent a small intestinal biopsy within 3 months after their blood sample was taken and had no dietary changes in between. I-FABP levels were determined retrospectively in these children using a commercially available ELISA that selectively detects human I-FABP (provided by HBT, Uden, the Netherlands). As a control group served 161 children diagnosed with familial short stature or constitutional growth delay, all with normal IgA tTG titers.

Results: I-FABP concentrations (median 668 pg/ml, SD 668 pg/ml) in the 99 patients with a clinical suspicion of CD were significantly (P < 0.0001) elevated compared to controls (median 263 pg/ml, SD 292 pg/ml). Also serum I-FABP levels in the 75 patients with histologically proven CD (median 729 pg/ml, SD 702 pg/ml) were significantly different (P<0.0001) from controls (median 263 pg/ml SD 292 pg/ml), but did not differ significantly (P=0.12) from the I-FABP levels in the 24 patients with a clinical suspicion of CD but a normal small intestinal histology (median 497 pg/ml, SD 535 pg/ml).

However when further analysing only the 27 patients with a tTG 5-10x ULN, an ROC curve analysis resulted in a 100% specificity for detecting CD patients when using a cut-off level of ≥880 pg/ml. Indeed out of 27 patients with a tTG between 5-10x ULN all 13 patients who also had an I-FABP ≥880 pg/ml had histologically proven CD. I-FABP levels in CD patients with tTG <5x ULN (median 726 pg/ml, SD 637 pg/ml) and I-FABP levels in non-CD patients with tTG <5x ULN (median 463 pg/ml, SD 558 pg/ml) did not differ significantly (P=0.27), nor did an ROC curve analysis provide any relevant cut-offs.

Conclusion: Based on these data, addition of I-FABP to the diagnostic procedure of CD may provide a biopsy free diagnosis of CD in the subgroup of patients with an IgA tTG 5-10x ULN.
Does gluten trigger many ophthalmological problems in celiac children?

Eyel Sevinç¹, Arzu Karatepe², Nergiz Sevinç³

¹Kayseri Training and Education Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Kayseri, Turkey
²Kayseri Training and Education Hospital, Ophthalmology, Kayseri, Turkey
³Erciyes University Public Health, Kayseri, Turkey

Objectives and study: Ophthalmic symptoms are rare in celiac disease (CD). Although some studies have found that celiac disease is negative effect on the eye, it was not investigated in children with CD. The aim of this study was to determine any possible eye involvement in children with CD.

Methods: Thirty-one with classic CD (aged 5-18) were compared to 34 healthy age and sex matched normal children as control. In addition to a complete ophthalmologic examination, all children were scanned by Pentacam Scheimpflug camera and Spectral domain Optical Coherence Tomography, and Schirmer and break-up time (BUT) tests were performed.

Results: The mean age of the 31 celiac children (12 male, 39%; 19 female, 61%) and 34 controls (14 male, 41%; 20 female, 59%) in the sample was 11.0 ± 4.4 (4-18) and 10.4 ± 2.6 (5-15) years, respectively (p=0.473). For celiac children, the mean follow-up period was 5.4 ± 1.7 (3-7.2) years. Serum endomysial antibody (EMA) levels were negative in eight (26%) of the celiac children and was positive in twenty-three of them (74%) while it was negative in all (100%) control children. Serum EMA was significantly higher in the celiac children than the controls. The eyes of children with CD did show decreased anterior chamber depth (3.5 ± 0.2, 3.7 ± 0.2; p<.001), decreased anterior chamber volume (170.8 ± 25.5, 190.7 ± 27.4; p<.001), lower Schirmer (17.9 ± 9.1, 21.6 ± 4.1; p=.038), and lower BUT (10.8 ± 3.8, 12.1 ± 1.7; p=.046), as well as lower retinal nerve fiber layer (general 102.8 ± 8.2; 108.9 ± 10.1; p<.001). We could not find any statistically significance between EMA-negative celiac children and controls for anterior chamber volume, Schirmer and BUT.

Conclusion: Our study indicated retinal nerve fiber, anterior chamber shallowing, and qualitative and quantitative reduction in tears were significantly lower in the celiac children than the controls. We recommend performing routine ocular examination even in asymptomatic celiac children, who should be periodically monitored.
ESPGHAN guidelines for the diagnosis and management of celiac disease and their implementation - how big is the gap between ideal and reality? A quality-of-care survey in Europe

Katharina Werkstetter1, Ania Chmielewska2, Jernej Dolinšek3, Frederiek Estourgie-van Burk4, Ilma Korponay-Szabo5, Kalle Kurppa6, Zrinjka Mišak7, Alexandra Papadopoulou8, Alina Popp9, Carmen Ribes Koninckx10, Boglárka Szentes1, Peter Szitanyi11, Anna Theisen1, Riccardo Troncone12, Gábor Veres13, Christina West14, Sibylle Koletzko1

1Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
2Umeå University, Department of Clinical Science, Umeå, Sweden
3University Medical Center (Umc) Maribor, Maribor, Slovenia
4Academic Medical Center Amsterdam, Department of Pediatrics, Amsterdam, Netherlands
5Heim Pál Children's Hospital, Celiac Disease Center, Budapest, Hungary
6University of Tampere and Tampere University Hospital, Tampere Centre for Child Health Research, Tampere, Finland
7Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
8Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece
9Tampere Center for Child Health Research, University of Tampere and Tampere University Hospital, Tampere, Finland, University of Medicine and Pharmacy "Carol Davila", Bucharest, Romania, Bucharest, Romania
10La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
11First Faculty of Medicine, Charles University and the General University Hospital in Prague, Department of Paediatrics and Adolescent Medicine, Prague, Czech Republic
12University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Naples, Italy
13Semmelweis University, First Department of Pediatrics, Budapest, Hungary
14Umeå University Hospital, Department of Clinical Sciences, Pediatrics, Umeå, Sweden

Objectives: In 2012 the ESPGHAN published evidence-based guidelines for the diagnosis and management of Celiac Disease (CD) in children. To evaluate how well these guidelines are actually implemented and accepted in primary care practice we conducted a quality-of-care survey in several European countries.

Methods: From February 2015 to December 2016, an anonymous online-survey was performed in 13 European countries (Croatia, Czech Republic, Finland, Germany, Greece, Hungary, Italy, Poland, Romania, Slovenia, Spain, Sweden, The Netherlands). The target group comprised pediatricians and/or general practitioners since they are usually the first contact for pediatric patients with symptoms indicative for CD. Participants were invited via email by their respective medical association. The back-to-back translated survey included demographic questions and five medical case-examples with multiple-choice answers regarding CD management.

Results: In total 2489 physicians completed the survey (71.5% female, 64.5% ≥45 years of age, 86.8% pediatricians). The response to question 1) which test(s) are reliable to exclude CD in a boy with short stature was given correctly (anti-tissue transglutaminase IgA (TGA-IgA) and/or EMA-IgA plus total IgA) by 59.0%, but less specific tests as antibodies against native gliadin IgA and IgG were also included in the responses of 22.4% and 17.6% of physicians respectively. The responses to the question 2) which symptoms or conditions are an indication for CD testing, 89.9% would screen in first degree relatives of CD patients, 71.4% in type 1 diabetes, 66.5% in irritable bowel syndrome, 62.2% in refractory constipation, 47.1% in unexplained elevated transaminases, 45.6% in trisomy 21, and 21.3% in Turner’s syndrome. The responses to the question 3) in which situations TGA-IgA results are not reliable, 74.9% answered if total IgA was not detectable, 69.4% in case of gluten-free diet for 6 weeks, 59.0% in case of gluten-free diet for 6 weeks, and 45.6% in unexplained elevated transaminases, 45.6% in trisomy 21, and 21.3% in Turner’s syndrome. The responses to the question 4) in which situations TGA-IgA results are not reliable, 74.9% answered if total IgA was not detectable, 69.4% in case of gluten-free diet for 6 weeks, 21.3% in Turner’s syndrome. The responses to the question 4) in which situations TGA-IgA results are not reliable, 74.9% answered if total IgA was not detectable, 69.4% in case of gluten-free diet for 6 weeks, 21.3% in Turner’s syndrome. The responses to the question 4) in which situations TGA-IgA results are not reliable, 74.9% answered if total IgA was not detectable, 69.4% in case of gluten-free diet for 6 weeks, 21.3% in Turner’s syndrome. The responses to the question 4) in which situations TGA-IgA results are not reliable, 74.9% answered if total IgA was not detectable, 69.4% in case of gluten-free diet for 6 weeks, 21.3% in Turner’s syndrome.
62.6% would refer the girl to a pediatric gastroenterologist, but 17.3% would initiate a gluten-free diet, and 20.1% would repeat serology either to exclude transient antibodies or if symptoms deteriorate. Responses to the question 5) how to proceed in a brother of a CD patient with repeatedly negative TGA-IgA, positive HLA-DQ2, abdominal pain and diarrhea, only 48.0% would investigate other causes than CD, while 30.4% would choose endoscopy to prove serological negative CD, 16.0% would perform tentative gluten-free diet, and 3.7% consider proven CD.

Conclusions: Our results show that there are still major deficits in the implementation of the ESPGHAN guidelines for CD. The incorrect use and interpretation of antibody tests and the unfounded initiation of gluten-free diet are alarming. Appropriate dissemination and training activities in primary health care settings need to be urgently implemented.

Disclosure of interest: Sibylle Koletzko received for this study funding from Nestec LtD, Switzerland
**Are coeliac disease and type 1 diabetes linked**

**Fabiana Ziberna**, Luigina De Leo, Serena Vatta, Stefano Martelossi, Tarcisio Not, Alessandro Ventura

1Institute for Maternal and Child Health - Ircs "Burlo Garofolo", Paediatric Department, Trieste, Italy

**Objectives and study:** An association between coeliac disease (CD) and type 1 diabetes mellitus (T1DM) has been reported and it seems to be related to the duration of exposure to gluten in lately diagnosed CD patients.

In the effort to define the relationship between these two diseases, we investigated a 2 year old child with CD-related HLA DQ2 haplotype, suffering from IgA deficiency (3 mg/dl) and with a T1DM onset (antibodies: anti-insulin 0.5 U/ml, anti-IA-2 20 U/ml, anti-GAD 77.63 U/I/ml). She tested negative for serum IgG anti-TG2 antibodies (1.1 U/ml; positive value >10 U/ml) but tested positive for IgG anti-deamidated gliadin antibodies (14 U/ml, positive value >10 U/ml). The patient underwent to gastrointestinal endoscopy that did not show intestinal histological alterations and the intestinal specific IgM-TG2 deposits were negative. She remained on a gluten containing diet. After 1 year, she developed classical CD-related gastrointestinal symptoms (enteritis, vomit and diarrhoea) and seroconverted for IgG anti-TG2 antibodies (529 U/ml). The second gastro-duodenal biopsy showed intestinal mucosa atrophy and the presence of intestinal IgM-TG2 deposits.

Our aims were:

- to verify if CD was already present at the onset of T1DM by using the more sensitive phage-display antibody assay;
- to investigate a possible intestinal origin of two T1DM-related markers: auto-antibodies against glutamic acid decarboxylase 65 kDa isoform (GAD65) and protein tyrosine phosphatase-like protein (IA-2).

**Methods:** We constructed by phage-display technique a total IgM intestinal B-lymphocytes (IBL) antibody library from the first and second biopsy to select against TG2. Moreover, we produced a total IgG IBL phage-display antibody library from the first biopsy to investigate the mucosal immune response against the two T1DM-related autoimmune antibodies.

**Results:** We did not isolate specific IgM anti-TG2 clones from the first biopsy but we found IgM anti-TG2 positive clones from the second biopsy. By sequence analysis, the IgM anti-TG2 clones were comprised of VH1,3,4,5 family genes. Moreover, we isolated IgG anti-GAD65 clones from the first biopsy specimen library. The clones were comprised of VH1 and VA3 gene family. Whereas we did not isolate any intestinal IgG anti-IA-2 antibodies.

**Conclusion:** Our data show that undiagnosed CD was not already present at T1DM onset. In this case CD did not trigger T1DM, showing an apparent independent origin of these two diseases. For the first time we demonstrated the intestinal mucosa production of IgG antibodies against GAD65 by phage-display libraries, supporting the pivotal role of the gut immune system in the T1DM pathogenesis.

We are investigating the patient’s peripheral B-lymphocytes phage-antibody library for the anti-GAD response to verify its intestinal specificity and compare the results with the intestinal anti-GAD immune response from an IgG IBL library of a control subject.
Impact of intravenous antibiotics on the gut microbiota in children with cystic fibrosis

Raphael Enaud, Thomas Bazin, Aurélien Barré, Thomas Barnetche, Christophe Hubert, Haude Clouzeau, Stephanie Bui, Macha Nikolski, Cecile Bebear, Laurence Delhaes, Thierry Lamireau, Thierry Schaeverbeke

1Chu de Bordeaux, Bordeaux, France
2Bordeaux Bioinformatics Center Cbib, Bordeaux, France
3Plateforme Génome Transcriptome, Centre de Génomique Fonctionnelle de Bordeaux, Bordeaux University, Bordeaux, France
4Crcm, Chu de Bordeaux, Bordeaux, France
5University of Bordeaux, Usc Ea 3671, Bordeaux, France
6University Hospital, Paediatric Gastroenterology, Bordeaux, France

Objectives and study: Gut microbiota is now considered as an organ in its own right. A disturbance of its equilibrium - called dysbiosis - is implicated in the pathophysiology of various diseases, in particular in the evolution of cystic fibrosis, the first paediatric genetic disease. Among the affected organs in this disease, there is a chronic low grade intestinal inflammation and microbiota disturbances. The study of the intestinal flora in the cystic fibrosis shows a dysbiosis characterized in particular by a decrease in diversity and an increase of bacterial abundance. The impact of this dysbiosis in cystic fibrosis appears to be both digestive (intestinal inflammation, nutritional status) and systemic (pulmonary exacerbations, quality of life, liver damage). It has been shown that abnormalities of the intestinal microbiota occur gradually during the first months of life in children with cystic fibrosis. These disturbances may be influenced by various environmental factors, including the use of repeated antibiotic therapy prescribed for pulmonary exacerbations.

The main objective of this work was to study the evolution of the intestinal microbiota after an intravenous antibiotic treatment in children with cystic fibrosis.

Methods: Twenty-one children with cystic fibrosis were included and followed during 3 months. Seven of them received an ATB IV cure for 15 days and 14 patients were in the control group. A study of the intestinal microbiota by high-throughput sequencing and digestive inflammation by faecal calprotectin was performed and repeated during follow-up of participants.

Results: The impact of ATB IV cures on the intestinal microbiota appeared to be moderate. Its composition varied after a course of an intravenous antibiotic: 60.7% of the bacteria present initially were found 3 months after the cure in the same patient. However, we have not been able to demonstrate a taxonomic node under or over-represented in post-antibiotic therapy. Intestinal inflammation was present in 71% of patients and appeared to be correlated with an overrepresentation of Streptococcus (ratio: 2.50, p-value = 0.042) in patients with faecal calprotectin greater than 250 µg/g. These results may encourage the development of an interventional study evaluating the efficacy of short course oral antibiotics to treat intestinal inflammation. Finally, the presence of diarrhoea appeared to be inversely correlated with the presence of intestinal inflammation, suggesting that this symptom could be a mechanism regulating bacterial multiplication in order to prevent intestinal inflammation.

Conclusion: This preliminary study finds a limited impact of intravenous antibiotic therapy on the intestinal microbiota but seems to reinforce the link between dysbiosis and intestinal inflammation. This study shows for the first time an over representation of Streptococcus in cystic fibrosis with patient with inflammation intestinal.
A multicentre registered clinical trial on diagnostic practice in pediatric pancreatitis (PINEAPPLE - Pain in early phase of pediatric pancreatitis)

Dóra Mosztbacher1, Andrea Párniczky2, Anna Tóth3, Alexandra Demcsák3, Ila Veronika4, István Tokodi5, Maisam Abu-El-Hajja6, Flora Szabo7, Orsolya Kadenczki8, Boglárka Fehér8, Gábor Veres1, Kinga Kaán1, Félix Juhász1, Enikő Horváth1, Natália Lásztity2, Zsolt Bognár2, Csaba Bereczki3, Tamás Decsi9, Ildikó Guthy10, Andrea Szentesi11, Péter Hegyi12

1Semmelweis University, First Department of Pediatrics, Budapest, Hungary
2Heim Pál Children's Hospital, Budapest, Hungary
3University of Szeged, Faculty of Medicine, Department of Pediatrics and Pediatric Health Center, Szeged, Hungary
4Dr. Kenessey Albert Hospital, Department of Pediatrics, Balassagyarmat, Hungary
5Szent György Teaching Hospital of County Fejér, Department of Pediatrics, Székesfehérvár, Hungary
6Cincinnati Children's Hospital Medical Center, Division of Gastroenterology, Hepatology and Nutrition, Cincinnati, United States
7Children's Hospital of Richmond at Vcu, Richmond, United States
8University of Debrecen, Faculty of Medicine, Department of Pediatrics, Debrecen, Hungary
9University of Pécs, Faculty of Medicine, Department of Pediatrics, Pécs, Hungary
10Szabolcs-Szatmár-Bereg County Hospital, Jósa András University Teaching Hospital, Nyíregyháza, Hungary
11University of Pécs, Institute for Translational Medicine, Pécs, Hungary
12University of Pécs, Mta-Szte Tgrr & University of Szeged, Pécs, Szeged, Hungary

Objectives and study: There is a rising incidence in the field of pediatric pancreatitis (PP), however the documented incidence of PP is very low, less than 1/100,000 in almost all European countries, whereas it is around 3.6-13.2/100,000 in the USA and Australia. The aim of the PINEAPPLE study is to estimate a current incidence worldwide and understand the practice of the diagnosis of PP. Furthermore we would like to develop EBM guidelines which would help to evaluate the necessity of PEM (pancreas enzyme measurement) and abdominal ultrasonography when a child has abdominal pain.

Methods: PINEAPPLE is a registered (ISRCTN35618458), observational, multinational clinical trial and the prestudy protocol is already published (http://www.ncbi.nlm.nih.gov/pubmed/26641250). The PINEAPPLE-R subtrial is a retrospective review on children and adult records appearing at ER units, whereas, the PINEAPPLE-P subtrial is a prospective part of the study where detailed patients data are collected, PEM and abdominal imaging are performed in all cases when abdominal pain occurs. Until now we enrolled 26846 patient records into the PINEAPPLE-R and 225 patients into the PINEAPPLE-P subtrial from eleven pediatric and one adult centres.

Results: PINEAPPLE-R: 8.3% (1970/23644) of the pediatric and 19% (603/3202) of the adult patients appeared at ER unit with abdominal pain. In case of abdominal pain 9.7% of pediatric and 86% of the adult patients had PEM, 30% of the pediatric and 86% of the adult patients had transabdominal ultrasonography. The rate of the diagnosed pancreatitis in adults was twelve times higher than the PP. Further in the children population where 21.6% (157/728) PEM were performed, the incidence of pancreatitis was six times higher, than in case where just 2.8 % (35/1242) PEM were performed. PINEAPPLE-P: 5 pancreatitis of 225 patients with abdominal pain were diagnosed.

Conclusion: The PINEAPPLE-R clearly shows that the number of PEM performed at ER units are unacceptably low in children, which correlates with the incidence of the disease. More patients are crucially needed for PINEAPPLE-P to develop EBM guidelines.
Soluble P-selectin, VCAM-1, and asymmetric dimethylarginine levels are not predicted by clinical characteristics of cystic fibrosis

Jan Nowak1, Irena Wojsyk-Banaszak2, Edyta Madry3, Andrzej Wykretowicz4, Patrycja Krzyzanowska1, Slawomira Drzymala-Czyz1, Agata Nowicka5, Andrzej Pogorzelski6, Ewa Sapiełka1, Wojciech Skorupa8, Mariusz Szczepanik1, Aleksandra Lisowska1, Jarosław Walkowiak1

1Poznan University of Medical Sciences, Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland
2Poznan University of Medical Sciences, Department of Pediatric Pneumonology, Allergology and Clinical Immunology, Poznan, Poland
3Poznan University of Medical Sciences, Department of Physiology, Poznan, Poland
4Poznan University of Medical Sciences, Department of Cardiology-Intensive Therapy, Poznan, Poland
5Poznan University of Medical Sciences, Department of Pulmonology, Allergology and Respiratory Oncology, Poznan, Poland
6Institute of Tuberculosis and Lung Diseases, Department of Pneumology and Cystic Fibrosis, Rabka, Poland
7Out-Patient Clinic for Cf Patients, Gdansk, Poland
8National Institute for Tuberculosis and Lung Diseases, I Department of Lung Diseases, Warsaw, Poland

Objectives and study: Increasing survival of cystic fibrosis (CF) patients draws attention to their cardiovascular health. Soluble P-selectin, vascular cell adhesion molecule 1 (sVCAM-1), and asymmetric dimethylarginine (ADMA) are all linked to endothelial function. We aimed to assess the correlates of concentrations of these three molecules in CF.

Methods: A cross-sectional study was performed. Soluble P-selectin, sVCAM-1, and ADMA levels were determined using ELISA. The following data were also obtained: forced expiratory volume in 1 second (FEV1, percentage), exocrine pancreatic status (fecal elastase-1, ELISA), CF-related liver disease status, Pseudomonas aeruginosa colonization, high-sensitivity C-reactive protein concentration (hsCRP, immunoturbidimetry), and body mass index (BMI). Genotypes of the CFTR gene (cystic fibrosis transmembrane conductance regulator) were classified as severe (classes I and II) or other. Multivariable regression models for prediction of sP-selectin, sVCAM-1, and ADMA were built, which included all the above clinical and laboratory parameters as well as patient’s age and sex (all effects regression).

Results: 108 patients with CF (median age [IQR]: 22.0 years [19.1-31.0]; 61 female, 47 male) and 51 healthy subjects (HS; 24.1 years [21.7-28.1]; 31 female, 20 male) volunteered for the study. BMI was lower in the CF group (20.5 kg/m2 [18.4-22.2] vs. 21.6 kg/m2 [19.9-23.4], p = 0.02, Mann-Whitney U test) and hsCRP levels were higher (0.36 mg/dL [0.11-0.71] vs. 0.05 mg/dL [0.03-0.10], <10-10). The concentrations of sP-selectin and ADMA did not differ between the two groups (sP-selectin 155 ng/mL [129-188] vs. 156 ng/mL [144-177], p = 0.48; ADMA 1.33 nmol/L [0.50-3.11] vs. 2.38 nmol/L [0.54-4.06], p = 0.06). sVCAM-1 was higher in CF patients (1018 ng/mL [851-1279] vs. 861 ng/mL [806-979], p <10-4). It was also greater in CF patients with exocrine pancreatic insufficiency compared with those who were pancreatic-sufficient (1043 ng/mL [897-1306] vs. 895 ng/mL [781-1007], p = 0.003). None of the multivariable regression models for the prediction of the three investigated biomarkers’ concentrations in CF patients was valid; the same was true after limiting predictors to FEV1%, exocrine pancreatic insufficiency, BMI, severe CFTR mutation, age, and sex.

Conclusion: sP-selectin and ADMA levels in patients with CF and HS did not differ significantly. Although the concentration of sVCAM-1 was higher in CF patients compared with HS, none of the main clinical characteristics of CF was found to be its independent correlate.
Cystic fibrosis linked functional impairment and gut microbiota signatures: from omics data to clinical cue

Pamela Vernocchi, Federica Del Chierico, Alessandra Russo, Fabio Majo, Maria Cristina Valerio, Luca Casadei, Antonella La Storia, Francesca De Filippis, Cristiano Rizzo, Cesare Manetti, Paola Paci, Enza Montemitro, Danilo Ercolini, Federico Marini, Ersilia Fiscarelli, Bruno Dallapiccola, Alfredo Miccheli, Vincenzina Lucidi, Lorenza Putignani

Objectives and study: Cystic fibrosis (CF), is a disorder affecting the exocrine glands of the respiratory, digestive and reproductive systems and there appear to be a link with the gut microbiota, including a possible association of pulmonary evolution with its dysbiosis. High-throughput metagenomics-based approaches may actually assist in unveiling this complex network of symbiosis modifications. The aim of this work was to provide a functional picture of the gut microbiota of CF patients by omic approach. Since there is a high variability due to antimicrobial therapy and genetic causes we conduct a study of the gut microbiota in the first period of life of patients and preschool children.

Methods: Thirty-one faecal samples from either CF patients and healthy children (HC) (age range 1-6 years) were collected at Bambino Gesù Children's Hospital. The metabolomics (MB) analyses were performed by GC-MS/SPME and 1H-NMR, while metagenomics (MG) analysis was carried out by 454 pyrosequencing platform. To characterize the differences between CF and HC subjects from a multi-omic platforms, chemometric classification methods were adopted as partial least squares discriminant analysis (PLS-DA) and were performed using bioinformatic MATLAB toolbox, in order to attempt the translational clinical results.

Results: About 200 volatile organic compounds, 150 shared between HC and CF children and 50 belonged only to CF patients were detected and quantified by GC-MS/SPME and about 20 molecules characterized with 1H-NMR. The inter-individual variability of molecules levels resulted high. The CF fecal microbiota profile were associated to high levels of 4-aminobutyrate (GABA), choline, ethanol, propylbutyrate and pyridine, and low levels of sarcosine, 4-methylphenol (p-cresol), uracil, glucose, acetate, phenol, benzaldehyde and methylacetate. The microbiota composition was characterized by a high abundance of Propionibacterium and Clostridiales, and low abundance of Egerthella, Eubacterium, Ruminococcus, Dorea, Lachnospiraceae and Others at genus level. The CF-induced changes in gut bacteria community and in fecal metabolome depict a picture of dysbiosis.

Conclusion: The present study evidenced a first fused metagenomic and metabolomic fecal profile characterizing the CF children compared to controls. Moreover, the identification of endogenous and bacterial CF biomarkers, can directly reflect alterations at the intestinal level due to CFTR function defects. Moreover, by this integrated approach it’s possible to generate personalized “omics” charts that can be used to support the child nutritional state and for the evaluation of gut absorption in CF patients, hence provide a translational medicine tool.
**Probiotic and postbiotic effects of L. rhamnosus GG against RV-induce diarrhea**

Vittoria Buccigrossi¹, Maiara Brusco de Freitas², Eugenia Bruzzese³, Noemi Iannuzzi¹, Antonella Marano¹, Alfredo Guarino¹

¹University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
²Federal University of Santa Catarina, Brazil, Department of Nutrition, Graduate Program in Nutrition, Florianopolis, Brazil
³University of Naples Federico II, Naples, Italy

**Objectives and study:** Rotavirus (RV) causes diarrhea through combined cytotoxic and enterotoxic effects induced by the virus and its enterotoxin NSP4, respectively. *L. rhamnosus GG* (LGG) is included in the ESPGHAN guidelines as active treatment for acute gastroenteritis. Aim of this study was to evaluate the mechanisms of efficacy in an *in-vitro* model of RV diarrhea.

**Methods:** Living LGG microorganisms or LGG conditioned medium (LGGm) were used to stimulate Caco-2 cell monolayers. The enterotoxic effect was evaluated by NSP4-induced ion secretion whereas the cytotoxic effect by the RV epithelial damage. The short circuit current (Isc) and transepithelial resistance (TER) were measured in the Ussing chamber system as parameters of ion secretion and epithelial integrity, respectively.

**Results:**

Inhibition of RV-induced epithelial damage:
RV induced a 68% of decrease in tissue resistance, that was reduced to 21,2% in the presence of LGG compared to initial value (p<0,05). LGGm did not protect Caco-2 cell monolayers by RV cytotoxic damage (LGGm+RV -51,7% vs RV -66,5% of TER decrease compared with initial value of transepithelial resistance; p=0,446).

Inhibition of NSP4-induced fluid secretion: LGG significantly reduced NSP4-induced ion secretion in Ussing chamber both in its living form (LGG+NSP4=0,9±0,9 vs NSP4=7,3±0,9 µA/cm²; p<0,05) and in form of conditioned medium (LGGm+NSP4=-0,5±0,63 vs NSP4=9,24±0,73 µA/cm²; p<0,05).

**Conclusion:** LGG counteracts RV-induced diarrhea by inhibiting both cytotoxic and enterotoxic mechanisms of RV diarrhea. First, LGG inhibits chloride secretion by the action of specific moiety secreted in the medium with a direct pharmacologic-like action. This is considered a postbiotic effect. Subsequently, live bacteria exert a long-lasting effect restituting the barrier and protecting epithelial integrity with a probiotic effect.

Conflict of interest: The study was supported by Dicofarm SpA.

Disclosure of interest: The research was supported by Dicofarm SpA
The diagnostic accuracy of clinical dehydration scales used in children with acute gastroenteritis

Anna Falszewska¹, Piotr Dziechciarz¹, Hania Szajewska¹

¹The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland

Objectives and study: The accurate clinical assessment of the degree of dehydration in the course of gastroenteritis is essential for further management. However, assessment of dehydration remains difficult. We evaluated the diagnostic accuracy of the three scales commonly used for the evaluation of dehydration in children. The scales included the Clinical Dehydration Scale (CDS), the World Health Organisation (WHO) scale, and the Gorelick scale.

Methods: A prospective, observational study involving a convenience sample of children admitted to the Department of Paediatrics of a university-affiliated children’s hospital was carried out between October 2014 and December 2016. Eligible participants were children aged 1 month to 5 years with acute diarrhoea, defined as a decrease in the consistency of stools (loose or liquid) and/or an increase in the frequency of evacuations (≥3 in 24 hours), with or without fever or vomiting. The symptoms could not last longer than 5 days. Promptly after hospital admission, prior to rehydration therapy, the degree of dehydration and patient’s weight were recorded on a pre-specified data sheet. The final body weight evaluation took place upon the patient’s discharge. The clinical reference standard was the percentage weight change between the discharge and admission weights. On the basis of a two-by-two table, the sensitivity, specificity, positive likelihood ratio (LR), and negative LR were calculated for every dehydration cut-off point of each scale.

Results: Of 129 children enrolled in the study, 119 patients had complete data for analysis. Only 9.2% of the children presented with moderate to severe dehydration (≥5%). The table presents the sensitivity, specificity, positive LR, and negative LR for every dehydration cut-off point of each scale. Only the CDS showed limited value in confirming a diagnosis of dehydration ≥6% [LR (+) 3.92, 95% CI 1.15 to 9.07], with no value in ruling dehydration out [LR (-) 0.57, 95% CI 0.17 to 0.99].

Table:

<table>
<thead>
<tr>
<th></th>
<th>CDS scale</th>
<th>WHO scale</th>
<th>Gorelick scale</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>&lt;3%</td>
<td>3-6%</td>
<td>≥6%</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>0.31</td>
<td>0.63</td>
<td>0.5</td>
</tr>
<tr>
<td></td>
<td>(0.2-0.4)</td>
<td>(0.4-0.8)</td>
<td>(0.07-0.9)</td>
</tr>
<tr>
<td>Specificity</td>
<td>0.82</td>
<td>0.43</td>
<td>0.87</td>
</tr>
<tr>
<td></td>
<td>(0.6 – 0.9)</td>
<td>(0.3 – 0.55)</td>
<td>(0.8 – 0.9)</td>
</tr>
<tr>
<td>LR (+)</td>
<td>1.76</td>
<td>1.1</td>
<td>3.92</td>
</tr>
<tr>
<td></td>
<td>(0.8 – 4.2)</td>
<td>(0.7 – 1.5)</td>
<td>(1.1 – 9.1)</td>
</tr>
<tr>
<td>LR (-)</td>
<td>0.83</td>
<td>0.87</td>
<td>0.57</td>
</tr>
<tr>
<td></td>
<td>(0.67 – 0.87)</td>
<td>(0.2 – 0.2)</td>
<td>(0.45 – 0.5)</td>
</tr>
</tbody>
</table>

Vol. 64, Supplement 1, April 2017 112
1.1) 1.5) 0.99) 1.1) 1.3) 1.4) * (95% CI)

**Conclusion:** In our cohort, the CDS had limited diagnostic value in ruling in severe dehydration in children with acute gastroenteritis. Neither the WHO scale nor the Gorelick scale were a helpful tool in dehydration assessment.
The effect of gelatin tannate in acute diarrhea in children

Soner Sertan Kara¹, Burcu Volkan², Ibrahim Erten³

¹Erzurum Regional Training and Research Hospital, Department of Pediatric Infectious Diseases, Erzurum, Turkey
²Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
³Erzurum Regional Training and Research Hospital, Department of Pediatrics, Erzurum, Turkey

Objectives and study: Acute gastroenteritis (AGE) is a common cause of morbidity and mortality worldwide. The management of children and infants with viral AGE mainly depends on oral or intravenous hydration, breastfeeding, and early refeeding. Probiotics are also beneficial. Gelatin tannate (GT) is a nonabsorbable antidiarrheal agent investigated in few clinical studies. The aim of this study was to investigate the effects of GT on children with viral AGE.

Methods: This randomized, placebo-controlled, prospective study involved children aged from six months to 10 years with acute diarrhea. After assessment all patients including anthropometric measurements, physical examination, and Modified Vesikari and CDS scores, children not complying with the study protocol or with diarrhea with a known non-viral etiology were excluded. Patients were randomized on the basis of order of presentation. The patient and his/her parents were blinded to the treatment drug. The study group received GT (250 mg sachet) four times a day plus oral rehydration solution (ORS) plus peroral zinc (15 mg/day) for five days. The control group received identical appearing maltodextrin containing placebo sachets four times a day plus ORS plus peroral zinc for five days. Stool frequency and numbers of patients with diarrhea in each group were compared at 12, 24, 48, 72, 96, and 120 hours. Duration of diarrhea and weight changes after 120 hours was recorded.

Results: Seventy one children were included in the study group, while 73 children were included in the control group. The groups were not different in terms of age, anthropometric measurements, admission Vesikari and CDS scores, numbers of diarrhea and vomiting episodes during the previous 24 hours, or duration of diarrhea until admission. Mean stool frequency was lower in the study group at 0-12 hours (3±1.8 vs. 3.6±1.9, p=0.04). The study group exhibited more weight gain after 120 hours of treatment and shorter total duration of diarrhea, although the difference was not statistically significant. Fewer patients in the study group had diarrhea at the end of 12, 24, 96, and 120 hours. Patients treated with GT with Bristol scores of 7 at admission exhibited more weight gain than patients with Bristol scores of 6 (296±38 vs. 137±39, p=0.04). Rotavirus was the mostly determined etiological agent in the study, and like other etiologies, GT improves diarrhea better, but not statistically significant, than placebo in children with rotavirus. No adverse events were recorded in any patients.

Conclusion: GT resulted in a decreased stool frequency at 12 hours in children with viral gastroenteritis. It shortened total duration of diarrhea and resulted in more weight gain compared to placebo in children with AGE.
Evaluation of gut microbiota and fecal butyrate concentration in children affected by non-IgE mediated cow’s milk allergy

Roberto Berni Canani¹, Rita Nocerino², Lorella Paparo², Antonio Amoroso², Antonio Calignano³, Carmen De Caro⁴, Cathryn Nagler⁴, Mario Laiola⁵, Francesca De Filippis⁵, Danilo Ercolini⁵

¹University of Naples “Federico II”, Translational Medical Science-Elfid-Geinge Advanced Biotechnologies, Naples, Italy
²University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
³University of Naples “Federico II”, Department of Pharmacy, Naples, Italy
⁴University of Chicago, Department of Pathology, Illinois, United States
⁵University of Naples “Federico II”, Agricultural Sciences, Division of Microbiology, Portici (Naples), Italy

Objectives and study: Gut microbiota is involved in cow’s milk allergy (CMA) pathogenesis. It has been demonstrated that gut microbiota of subjects with IgE-mediated CMA exhibits significant differences if compared with healthy controls, and that treatment with extensively hydrolysed casein formula (EHCF) containing the probiotic *L. rhamnosus* GG (LGG) increases the relative abundance of butyrate-producing bacteria and fecal butyrate levels. We aimed to evaluate gut microbiota composition and butyrate production in children affected by non IgE-mediated CMA and compare them with healthy controls

Methods: Infants with non-IgE-mediated CMA and healthy children, with negative clinical history for any allergic condition and not at risk for atopic disorders were enrolled in the study. We evaluated 46 non IgE-mediated CMA children (age range 11-18 months): patients with recent evidence of non-IgE-mediated CMA at diagnosis (group 1); patients with diagnosis of non IgE-mediated CMA treated for at least 6 months with EHCF (group 2); patients with diagnosis of non IgE-mediated CMA treated for at least 6 months with EHCF+LGG (group 3); patients with a previous diagnosis of non IgE-mediated CMA, but with evidence of oral tolerance acquisition, treated with EHCF+ LGG (group 4). During the same study period, 20 healthy age matched controls (group 5) were also enrolled. Microbiota composition was studied by 16S rRNA gene amplicon sequencing (V3-V4 region) on Illumina MiSeq platform. Fecal butyrate concentration was evaluated by gas chromatography interfaced to a mass spectrometer.

Results: Non IgE-mediated CMA subjects exhibited significant changes in gut microbiota composition if compared with healthy controls, while microbial diversity was not affected by the health status. Hierarchical clustering based on fecal microbiota composition highlighted a separation of CMA subjects, while treated (EHCF and EHCF + LGG) clustered together with healthy controls. When considering the phylum level composition, only Bacteroidetes was significantly increased in CMA. Specific signatures characterized the microbiota of CMA infants. Genus-level analysis revealed that *Streptococcus* was decreased, while *Bacteroides*, *Alistipes* and *Haemophilus* were increased in CMA compared to healthy controls (*p*<0.05). Their abundance decreased following both the treatments (*p*<0.05). In particular, EHCF + LGG treated children showed a significantly lower level of *Bacteroides* compared to EHCF. On the contrary, higher abundance of *Lactobacillus* was found in EHCF + LGG (*p*<0.05). Health status (healthy controls vs CMA subjects) was the largest contributor to *Bacteroides* differential abundance (*p*<0.00396), suggesting that CMA was the most important variable explaining the levels of *Bacteroides* in gut microbiota. Both the treatments affected sub-genus diversity of *Bacteroides*. Remarkably, the treatment with EHCF + LGG appeared to restore the *Bacteroides* sub-genus pattern, bringing such diversity much similar to that shown by the healthy controls. Finally, the fecal concentration of butyrate was significantly higher in non IgE-mediated CMA infants treated with EHCF + LGG when compared with those treated with EHCF alone.

Conclusion: Non IgE-mediated CMA is associated to gut microbiota dysbiosis. Sub-genus *Bacteroides* diversity differentiates healthy and CMA infants and it is restored in EHCF + LGG treated subjects. This dietary strategy is also able to increase butyrate production.
Dipotassium glycyrrhizate modulates genes with a key role in mucosal healing in mice with a DSS-induced colitis and improves in vitro epithelial barrier functions

Roberta Vitali¹, Francesca Palone¹, Maria Pierdomenico¹, Eleonora Colantoni¹, Manuela Costanzo¹, Marina Aloi², Paolo Rossi², Salvatore Cucchiara², Laura Stronati⁴

¹Enea, Radiobiology and Human Health, Rome, Italy
²Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
⁴Sapienza University of Rome, Cellular Biotechnology and Hematology, Rome, Italy

Objectives and study: Background: Dipotassium glycyrrhizate (DPG) is a salt of glycyrrhizin, a compound produced by the licorice plant, Glycyrrhiza glabra, with well-known anti-inflammatory properties. We previously showed that DPG significantly reduces the DSS-induced colitis in mice and improves mucosal healing (MH).

The aims of the present study are: 1) to identify in vivo genes involved in MH pathways that are modulated by DPG during inflammation; 2) to investigate in vitro the effects of DPG on epithelial barrier functions.

Methods:

In vivo: C57BL/6 mice were divided into 3 experimental groups: DSS 3%-treated mice, DSS 3% + DPG 8mg/Kg-treated mice and control mice. After 7 days, mice were sacrificed and the colon removed. Samples were analyzed by a PCR array (QIAGEN) to evaluate the expression levels of a panel of 84 genes central to MH response. A threshold of 3.5 times was chosen.

In vivo/In vitro: Results were validated by RT-PCR and Western Blot.

In vitro: HT29 and Caco2 cell lines were used to evaluate DPG effect on epithelial functional markers (F-actin and Zonulin-1 expression, Wound Healing Assay (scratch test), Trans Epithelial Electric Resistance (TEER) measurements) during inflammation induced by cytomix (TNFalfa+INFgamma).

Results:

In vivo: DSS treatment significantly up-regulated 19 MH genes, as showed by comparing DSS-treated vs control mice. These genes were significantly down-regulated to control values by DPG treatment, as showed by comparing DSS+DPG mice vs DSS mice. Genes were classified into 6 different functional groups: cytokines (IL-10, IL-1β, IL-6), chemokines (CCL12, CCL7, CXCL1, CXCL3, CXCL5), extracellular matrix components/collagen proteins (Col3a1, Vtn), growth factors (Csf3, Fgf2, Fgf7), remodelling enzymes (Mmp9, Timp1, Plat, Plaur, Serpine1), others (Plgs2). Expression analysis was confirmed by RT-PCR. Moreover, selected genes (MMP9, VTN, Col3a1, TIMP-1 and Plaur), chosen among those more representative for each functional group, were confirmed also by western blot.

In vitro: DPG+cytomix exposure down-regulated F-actin stress fibers and induced a recovery of Zonulin-1 expression as compared to cells treated with cytomix alone. Furthermore, DPG significantly increased TEER and wound closure rates, as evidenced by scratch test. Finally, DPG reduced protein levels of VTN, TIMP-1 and Plaur.

Conclusion: Conclusions: DPG down-regulates genes, central in MH response, previously altered by DSS-mediated colitis in mice, restoring a proper tissue recovery. Moreover, DPG strongly improves epithelial barrier function and morphology.

These data suggest that, due to the total lack of side effects, DPG may represent an innovative tool for the management of human intestinal inflammation.
Colon organoids characterization and early mechanisms of carcinogenesis in FAP patients

Nolwenn Laborde¹, Muriel Quaranta², Delphine Bonnet³, Barange Karl³, Nathalie Vergnolle², Claire Racaud-Sultan⁵, Emmanuel Mas⁴

¹Centre Hospitalier Universitaire de Toulouse, Pédiatrie- Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, Toulouse, France
²Institut de Recherche En Santé Digestive, Toulouse, France
³Chu Toulouse, Pôle Digestif, Toulouse, France
⁴Centre Hospitalier Universitaire de Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie and Genius Group, Toulouse, France

Objectives and study: Familial Adenomatous Polyposis (FAP) is mainly caused by germline mutations in Adenomatous polyposis coli (APC) gene, which down regulates Wnt signaling pathway. FAP is associated with a 100% lifetime risk of developing colorectal cancer. Carcinogenesis in the colonic mucosa is complex and mechanisms of adenoma development and carcinoma transformation in FAP remain unclear.

As animal models of FAP do not accurately reflect the multistep process occurring in human disease, we developed a 3D culture model, i.e. human colon organoids established from FAP patients, to perform research on adenoma development.

Methods: Colon organoids were established from adenomatous and non-adenomatous crypts of FAP patients and from healthy controls (HC). We modulated the culture conditions by selectively depleting Wnt3a, R-spondin and EGF to study human adenoma formation.

Results: As expected, FAP organoids (n=8) grew without addition of Wnt3a but HC organoids (n=6) did not. However, FAP organoids remained dependent on both R-spondin and EGF. Compared to HC organoids, they were hyperproliferative and immature, as shown by a significant increase in the number of Ki67- and CD24/CD44-positive cells respectively. Adenomatous organoids were larger and displayed more budding than non-adenomatous ones, mimicking aberrant crypts formation in adenomas. They were also more dependent on EGF for both survival and budding development. Preliminary results of gene expression suggested different stemness phenotypes between adenomatous and non-adenomatous areas.

Conclusion: The organoid model of FAP presents characteristics of the human disease and thus will allow the investigation of carcinogenesis. EGF is a key factor for budding crypt development and survival of adenomatous organoids. This model may be useful for development of new chemopreventive drugs for FAP patients.
RIP3, a regulator of necroptosis, promotes inflammation by increasing cytokine and inflammasome molecule levels as well as altering membrane permeability in intestinal epithelial cells.

Eleonora Colantoni¹, Anna Negroni¹, Vincenzo Cesi¹, Francesca Palone¹, Manuela Costanzo¹, Salvatore Oliva², Saverio Mallardo², Laura Stronati³, Salvatore Cucchiara³

¹Enea, Radiobiology and Human Health, Rome, Italy
²Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
³Sapienza University of Rome, Cellular Biotechnology and Hematology, Rome, Italy

Objectives and study: Background: RIP3 kinase and its target MLKL are the main players of necroptosis, a newly discovered pathway of regulated cell death, that is induced by cytokines, toll-like receptors and intracellular RNA and DNA sensor. Distinct from apoptosis, necroptosis is thought to be a form of protease-independent cell death. Owing to the release of immunostimulatory intracellular components after cell-membrane rupture, necroptosis is considered a proinflammatory death and is involved in several diseases, including inflammatory bowel disease (IBD).

In a previous work, our group demonstrated that RIP3 and MLKL are highly expressed in intestinal mucosa of children with IBD.

The aim of the present study is to investigate in vitro the role of RIP3 in promoting intestinal inflammation.

Methods: A RIP3 overexpressing intestinal cell line, HCT116RIP3, was produced in our laboratory and compared to a parental cell line, HCT116, that did not express RIP3. TNFa was used to induce necroptosis and necrostatin-1 to inhibit it, as assessed by MTT viability assay. The active form of MLKL, p-MLKL was analyzed by immunofluorescence. IL-8 and IL1beta as well as E-cadherin mRNA expression were evaluated by real-time PCR. Inflammasome proteins NLRP3 and caspase-1 were analysed by western blot.

Results: Exposure to TNFa induced necroptosis in HCT116RIP3, but not in HCT116 cells, as confirmed by the translocation of p-MLKL to the plasmatic membrane. A significant increase (p<0.05) of mRNA levels of IL-8 and IL1beta as well as a decrease of the adhesion molecule E-cadherin (p<0.05), which is involved in epithelial permeability, was showed in HCT116RIP3 cells as compared to HCT116 cells. Furthermore, HCT116RIP3 cells displayed increased level (p<0.05) of the inflammasome proteins NLRP3 and caspase-1. All results were reverted by exposing cells to necrostatin-1.

Conclusion: Collectively, these results show that over-expression of RIP3, a regulator of the programmed necrosis called necroptosis, significantly increase intestinal inflammation and epithelial permeability. These data suggest that therapeutic strategies targeting the cell death machinery may represent a promising new option for the treatment of inflammatory enteropathies.
A 12 week maintenance therapy with a new Prepared Viscous Budesonide (PVB) in paediatric eosinophilic esophagitis

Salvatore Oliva, Danilo Rossetti, Saverio Mallardo, Paolo Rossi, Sara Isoldi, Paola Papoff, Sandra Lucarelli, Salvatore Cucchiara

1Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
2Sapienza University of Rome, Picu, Department of Paediatrics, Rome, Italy

Objectives and study: A new pre-prepared oral viscous budesonide (PVB) has been effective in inducing clinical and histological remission in pediatric Eosinophilic Esophagitis (EoE). This study aims to evaluate the efficacy of a 12-week maintenance therapy with PVB on clinical, endoscopic and histological remission.

Methods: We prospectively enrolled pediatric patients with active EoE (diagnosed according to the ESPGHAN criteria, J Pediatr Gastroenterol Nutr 2014;58:107-18). After 12 weeks of induction therapy with PVB (< 150 cm: 2 mg bid; >150cm: 4 mg bid), patients achieving a complete histological remission (a peak eosinophil count of <6/HPF in all esophageal levels) underwent a maintenance remission phase with half dose of PVB (1mg or 2mg) for other 12 weeks. Endoscopy was performed at 0,12,24 and 36 weeks. Clinical symptom score (CSS) (Gupta SK, Clin Gastroenterol Hepatol 2015;13:66-76), endoscopy (EoE Endoscopic Reference Score, EREFS, modified) (Gut 2013;62:489-95) and histology (count of eosinophils/hpf at all esophageal levels) were evaluated. Serum cortisol was evaluated at baseline, 12, 24 and 36 weeks.

Results: We enrolled 20 children (15 male, 5 female; median age 10 years, range 4-10). After 12 weeks of induction therapy (week 12), 18 patients (90%) were in remission, exhibiting a striking reduction in clinical, endoscopic and histologic scores (p<0.01). At the end of maintenance therapy (week 24), remission was still observed in 17 patients (85%), while only in 9 (45%) at week 36 (12 weeks after the end of treatment). No significant difference in cortisol levels was observed during the study period as compared to baseline pre-trial values.

Conclusion: In the great majority of patients with EoE, initially responding to PVB, a dose reduction of the latter was effective in maintaining remission at week 24. However, this effect did not continue at a 12 week follow up after the end of the treatment. According to these results, in EoE pediatric patients PVB might be proposed for a long-term therapeutic strategy to maintain remission of the disease.

Disclosure of interest: Salvatore Oliva served as consultant for Medtronic
Diagnosis of non-coeliac gluten sensitivity: definitive data of the first double blind placebo controlled trial in paediatric

Antonia Gentile¹, Fernanda Cristofori², Lucia Verzillo¹, Francesca Arezzo¹, Carlo Polloni³, Valentina Giorgio⁴, Silvia Marcanio⁴, Elvira Verduci⁵, Elisa D'Angelo⁵, Stefania Dell'atte⁸, Ruggiero Francavilla⁸

¹University of Bari Aldo Moro/Department of Interdisciplinary Medicine, Bari, Italy
²Ss. Annunziata Hospital/ Pediatric Department, Taranto, Italy
³Department of Paediatrics Santa Maria del Carmine Hospital, Rovereto, Italy
⁴Department of Paediatrics, Catholic University, Rome, Italy
⁵San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
⁶S. Maria Incoronata Dell’olmo Hospital/Pediatric Clinic, Cava Dei Tirreni (Sa), Italy
⁷Tandoi Group Factory, Corto (Bari), Italy
⁸University of Bari, Bari, Italy

Objectives and study: Aim of the study is to evaluate the real prevalence of non celiac gluten sensitivity (NCGS) trough a double blind placebo controlled (DBPC) re-challenge in children presenting with gluten related symptoms, after the exclusion of celiac disease (CD) and wheat allergy (WA).

Methods: The present study includes 36 patients. Eight patients were excluded because of spontaneous resolution of symptoms. Per protocol, patients who referred an improvement of symptoms of at least 30% after gluten free diet (GFD), underwent DBPC cross over trial. Cross over trial consisted in: during GFD, patients assumed both pure gluten (10 g/daily) and placebo for two weeks respectively, spaced out by a washout week.

We evaluated symptoms through several questionnaires: Daily Visual Analogue Scale, IBS-Severity Score (IBS-SS), State-Trait Anxiety Inventory for Children (STAIC), modified Bristol stool chart and extra-intestinal symptoms questionnaire.

NCGS diagnosis was performed only in those patients who presented both the following IBS-SS variations: (i) > 30% when assuming pure gluten and (ii) reduced or stable values when assuming placebo.

Results: 28 children completed the challenge (aged 4-18 years; mean age 12 years). 11 patients presented symptoms only when eating gluten. Therefore, the final diagnosis of NCGS was confirmed only in 39% of patients with self-reported gluten related symptoms. Abdominal pain was the most prevalent symptom (all patients), followed by diarrhea (3 patients) and dyspepsia (3 patients). The extra-intestinal symptoms were: asthenia (10 patients), headache (8 patients), arthromyalgia (6 patient), foggy mind (1 patient), mouth ulcers (2 patients).

The STAIC score showed the same trend during the re-challenge phase: only NCGS patients had a worse quality of life taking gluten (13.2±0.7 vs 10.3±1.7, p=0.007) whereas not-NCGS subject worsen only taking placebo(11.7±2.5 vs 10.7±1.8, p=0.55). It’s interesting to know that IBS-SS increased in not-NCGS patients when assuming placebo suggesting the importance of nocebo effect.

Conclusion: NCGS is a clinical condition that exists in children too, but the diagnosis requires a DBPC, as indicated by the recent Salerno experts’ criteria, to exclude the nocebo effect and avoid unnecessary GFD.
Onset of tolerance in IgE-mediated and non-IgE-mediated cow's milk protein allergy

MAHUET Julie, ANTON Michel, Piloquet Hugues

1Reunion University Hospital, South Reunion Hospital Group, Saint Pierre, Reunion
2Nantes University Hospital, Allergology, Nantes, France
3Nantes University Hospital, Nantes, France

Objectives and study: Cow's milk protein allergy (CMPA) is a common disease in childhood. It affects 1.9 to 4.9% of children, non-IgE-mediated CMPA representing 60% of cases. CMPA appears in the first year of life and disease duration varies depending on the immunological type. According to the studies, the cure rate of the non-IgE-mediated form is very different. The objective of this study was to assess the onset of tolerance in two-year-olds with non-IgE-mediated CMPA. Secondary objectives were to describe IgE and non-IgE-mediated CMPA characteristics, determine predictive IgE levels of tolerance and risk factors for cow's milk protein reintroduction failure.

Methods: Retrospective inclusion of children allergic to cow's milk protein, admitted between August 2006 and October 2013 to day hospital at Nantes University Hospital in France, for cow's milk protein reintroduction test. Patients with positive IgE (greater than 0.35 IU/L) and a positive prick test (≥ 3 mm) were defined as IgE-mediated CMPA. Patients defined as non-IgE-mediated CMPA had a clinical history compatible with delayed allergy, negative IgE levels and a positive or negative patch test.

Results: At 7 years of follow-up, 618 children had reintroduction of cow's milk proteins and 75% were non-IgE-mediated CMPA (461 patients). In non-IgE-mediated CMPA group, tolerance at the age of 2 years was 384/461, ie 83% +/- 3.4%, IC95 [79.6-86.4]. Then, acquisition of tolerance was 92% at the age of 3, 94% at the age of 4 and 95% at the age of 5. In IgE-mediated CMPA group, tolerance at the age of 2 years was 52/157, ie 33% +/- 7.4%, IC95 [25.6-40.4]. Thereafter, the acquisition of tolerance was 50% at age 3, 59% at age 4 and 68% at age 5. Tolerance was acquired significantly earlier in non-IgE-mediated CMPA group than in IgE-mediated CMPA group (p <0.0001). In multivariate analysis in non-IgE-mediated CMPA group, patients with asthma and with neurological symptoms at diagnosis were at greater risk of reintroduction failure. In IgE-mediated CMPA group, independent risk factors to reintroduction failure were asthma and type of milk used. Compared to non-IgE-mediated group, IgE-mediated CMPA group were significantly associated with allergy of peanut, nut, egg, wheat (p <0.0001), fish (p = 0.001), potato, soy, beef (p = 0.003) and calf (p = 0.015).

Conclusion: Our study demonstrated that asthma was an independent predictive factor of early reintroduction failure in IgE-mediated CMPA group, and also in non-IgE-mediated CMPA group. It has also shown that the age of tolerance acquisition was later than expected in the non-IgE-mediated CMPA group.
Utility of Endoscopic Reference Score (EREFS) and histological features to predict the histological response to proton pump inhibitor therapy in patients with eosinophilic esophagitis

Enrique La Orden Izquierdo¹, Mª Luz Cilleruelo Pascual², Carolina Gutierrez Junquera³, Beatriz Martínez Escribano³, Ana I. Rayo Fernández⁴, Enrique Salcedo Lobato⁵, Pedro Urruzuno Tellería⁶, Gloria Rodrigo García⁶, Alfonso Barrio Merino⁶, Iván Carabaño Aguado⁶, Encarna Lancho Monreal¹⁰, Ana I. Ruiz Díaz¹¹, Ignacio Mahillo Fernández¹², Enriqueta Román Riechmann²

¹Hospital Universitario Infanta Elena, Paediatric Gastroenterology Unit, Valdemoro, Madrid, Spain
²Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
³Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
⁴Hospital Universitario Severo Ochoa, Paediatric Gastroenterology Unit, Leganés, Madrid, Spain
⁵Hospital Universitario Doce de Octubre, Paediatric Gastroenterology, Madrid, Spain
⁶Hospital Universitario 12 de Octubre, Paediatric Gastroenterology, Madrid, Spain
⁷Hospital Universitario Infanta Cristina, Paediatric Gastroenterology Unit, Parla, Madrid, Spain
⁸Hospital Universitario Fundación Alcorcón, Paediatric Gastroenterology Unit, Alcorcón, Madrid, Spain
⁹Hospital Universitario Rey Juan Carlos, Pediatric Gastroenterology, Mostoles, Madrid, Spain
¹₀Hospital Universitario del Tajo, Pediatric Gastroenterology, Aranjuez, Madrid, Spain
¹¹Hospital El Escorial, Paediatric Gastroenterology Unit, El Escorial, Madrid, Spain
¹²Hospital Universitario Fundación Jiménez Díaz, Epidemiology and Biostatistics, Madrid, Spain

Objectives and study: Eosinophilic esophagitis (EoE) is an emerging disease that produces oesophageal dysfunction whose incidence is increasing. Its management includes the evaluation after treatment with proton pump inhibitor (PPI) therapy. EREFS endoscopic score is useful to graduate the endoscopy appearance. The objective of this study is to describe the clinical, endoscopic, and histologic features in patients with oesophageal eosinophilia, before and after proton pump inhibitor (PPI) treatment, and the utility of the EREFS score and histologic findings to predict histologic response.

Methods: We prospectively enrolled new patients under 15 years old with oesophageal eosinophilia diagnosed between September 2014 and August 2016 in thirteen Hospitals of the southwest area of Madrid. Clinical profile of the patients is reported and EREFS score and histologic findings were analyzed, before and after PPI treatment (omeprazole equivalent dose between 1-2 mg/kg/day) for 8 weeks at least. All statistical analyses were performed with SPSS v.15.0.1. This study was approved on July 2014 by the Ethics Committee of Fundación Jiménez Díaz.

Results: One hundred and thirty six patients (67.6% males, 0.6-14.89 years, mean 9.7 years, median 10.43 years) were included. The most frequent clinical symptoms were: 43.3% abdominal pain, 44.1% dysphagia, 41.1% food impaction, and 25% vomiting. The most frequent comorbidity was: *Helicobacter* gastritis (8%), coeliac disease (3.6%), Gastroesophageal reflux (4.4%) and infectious esophagitis (2.9%). About 41.2% of children reported clinical symptoms with specific foods, the most frequently involved were milk and rice. Histological response was observed in 71 children (52%). The EREFS score and peak eosinophil count (PEC) were evaluated pre and post PPI treatment (table). Pretreatment EREFS score was similar in responders and non responders to PPI. Pretreatment PEC in each oesophagus segment were significantly higher in non responders.
Table: Peak eosinophil count and EREFS score:

<table>
<thead>
<tr>
<th></th>
<th>PPI nonresponders (n=65)</th>
<th>PPI responders (n=71)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>EREFS</td>
<td>3.2±1.7</td>
<td>2.85±1.38</td>
<td>2.7±1.6</td>
</tr>
<tr>
<td>PEC distal</td>
<td>54±32</td>
<td>47±33</td>
<td>44±33</td>
</tr>
<tr>
<td>PEC médium</td>
<td>58±33</td>
<td>43±32</td>
<td>43±29</td>
</tr>
<tr>
<td>PEC proximal</td>
<td>41±30</td>
<td>44±37</td>
<td>27±34</td>
</tr>
</tbody>
</table>

Conclusion: 52% of children with oesophageal eosinophilia responded to PPI treatment. Pre EREFS score is not useful to predict the responsiveness to PPI treatment. Pretreatment mean peak eosinophil count was significantly higher in nonresponders to PPI, as observed in a previous publication in a smaller group of patients (Gutiérrez Junquera C et al. JPGN 2016; 62(5):704-710).
Similar presentation but heterogeneous clinical course, gastrointestinal (GI) pathology, immunological defects in 5 children presenting with subsequently confirmed tricho-hepato-enteric syndrome (THE)

Jemma Cleminson¹, Andrew Cant², Sophie Hambleton², Terry Flood², Mary Slatter², Andrew Gennery⁴, Marieke Emonts⁵, Wolfram Haller³, Maureen Lawson⁴, Elizabeth Renji⁴, Susan Bunn⁴

¹Great North Children's Hospital, Department of Paediatrics, Newcastle Upon Tyne, United Kingdom  
²Great North Children's Hospital, Department of Paediatric Immunology, Newcastle Upon Tyne, United Kingdom  
³Birmingham Children's Hospital, Department of Paediatric Gastroenterology, Birmingham, United Kingdom  
⁴Great North Children's Hospital, Department of Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom

Objectives and study: Background:

THE, also known as phenotypic diarrhoea, is a rare autosomal recessive condition affecting exosome-mediated RNA surveillance usually presenting in first months with diarrhoea and intestinal failure with variable associated features. The GI dysfunction is felt to be a disorder of enterocyte function rather than immune-mediated damage and no treatment modalities have been identified.

Aim: To compare clinical features, immunological defects, gastrointestinal histology and outcome in 5 children presenting with THE.

Subjects, Methods and Results: We present 5 children with THE (1 male) subsequently confirmed to have mutation TTC37. All examined had trichorrhexis nodosa and all presented with intractable diarrhoea in first 2 months of life. All required PN but were weaned at between 5 and 15 months.
<table>
<thead>
<tr>
<th>Liver disease</th>
<th>Immunology</th>
<th>Other features</th>
<th>Gastrointestinal histology</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 ♀</td>
<td>Increasing transaminitis and synthetic dysfunction</td>
<td>PCP and disseminated adenovirus, Hypogammaglobulinemia, Neutropaenia. Lymphopaenia</td>
<td>Neutrophilic oesophagitis. Normal duodenum. Colonic focal cryptitis and apoptosis</td>
<td>Died 8/12 acute liver failure + sepsis</td>
</tr>
<tr>
<td></td>
<td>Hepatosplenomegaly</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 ♀</td>
<td>Moderate transaminitis</td>
<td>Hypogammaglobulinemia Treated sclg</td>
<td>Hypopigmented skin patches</td>
<td>Normal duodenum Normal colon</td>
</tr>
<tr>
<td></td>
<td>Resolved aged 21/12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 ♀</td>
<td>Prolonged conjugated hyperbilirubinaemia as infant</td>
<td>Enterovirus encephalitis Pneumococcal septicaemia Specific antibody deficiency IgM increased Abnormal cytokine profile with no production of IL12</td>
<td>IUGR Dandy Walker malformation VSD and ASD</td>
<td>Normal duodenal mucosa Minimal focal active colitis</td>
</tr>
<tr>
<td></td>
<td>Mild transaminitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Resolved aged 27/12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 ♀</td>
<td>None until 10/12 when started immunosuppresson</td>
<td>DCT+ve. Weak anti-islet cell ab +ve Specific antibody deficiency Treated prednisolone, Tacrolimus and sclg from 10/12</td>
<td>Hypopigmented skin patches</td>
<td>Duodenal villous atrophy and focal erosion. Colonic apoptosis</td>
</tr>
<tr>
<td></td>
<td>when persistent transaminitis</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5 ♂</td>
<td>Icterus prolongatus - florid hepatitis with microgranulomas on liver biopsy aged 3/12</td>
<td>Normal</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hypergammaglobulinemia aged 12 years</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** The presentation of THE is consistent, but the clinical course, GI pathology, immunological defects and outcome are variable. The immunodeficiency may be corrected by HSCT but the intestinal features appear unchanged. Distinguishing from autoimmune enteropathy is critical and identifying trichorrhexis nodosa whilst genetic tests awaited may aid diagnosis and prevent potential harmful treatment choices.
GASTROENTEROLOGY: Endoscopy

G-eP-031

Treatment of esophageal stenosis with stenting: the French experience

Raphael ENAUD1, Adele ROBERT1, Laurent REBOUSSIÈRE1, Sophie Heissat2, Alain Lachaux3, Bruno RAUQUELAURE4, Emmanuel Mas5, Jerome Viala6, Thierry Lamireau7

1University Hospital, Paediatric Gastroenterology, Bordeaux, France
2Hopital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology, Lyon, France
3Hôpital Femme Mère Enfant du Chu de Lyon, Pediatric Gastroentgy, Hepatology Nutrition Unit; Reference Centre for Wilson Disease, Lyon, France
4Assistance Publique, Pédiatrie Multidisciplinaire, Marseille, France
5Centre Hospitalier Universitaire de Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, and Genius Group, Toulouse, France
6Robert-Debré Hospital, Assistance Publique-Hôpitaux de Paris, Departments of Pediatric Digestive and Respiratory Diseases, Paris, France
7University Hospital, Paediatric Gastroenterology, Bordeaux, France

Objectives and study: Esophageal stenosis often occur in children after surgical repair of esophageal atresia or after caustic burns. Their treatment is based on endoscopic dilations, which can be associated with the application of Mitomycine C or corticosteroids. Oesophageal stenting can be proposed in case of failure of these therapies. The aim of this study was to report on the French experience on technical difficulties and results of treatment of oesophageal stenosis with stent.

Methods: A survey on the use of esophageal stent in children has been conducted among French pediatric centers. Patient characteristics, cause of esophageal stenosis, treatments before stenting, endoscopic procedure of stenting and outcome were recorded via a questionnaire.

Results: Four French pediatric centers had experience of esophageal stenting in children. Between December 2009 and June 2016, 52 stents have been placed in 12 patients (8 boys/4 girls) aged of 2.7 years (0.4-14.25). The cause of stenosis was caustic burn (n=7), esophageal atresia (n=4) or peptic esophagitis (n=1). The number of previous endoscopic dilations was 6.7 (2-16) per patient, and 10 children had a previous oeso-coloplasty. Stenosis was multiple in 6 children, localized in the medium of the esophagus (n=9), the proximal esophagus (n=6) or the distal esophagus (n=4). Difficulties were encountered in 8 procedures, but stenting was feasible in all cases. Adverse events occurred in 16 procedures (31%): dysphagia (n=1), lung infection (n=2), retching (n=6) or thoracic pain (n=7). After a mean stay of 7.8 weeks (3 days-5 months), the stent was removed during a scheduled procedure in 34 cases (66%) and in emergency procedure in 18 cases (33%) because of stent migration (n=14), respiratory distress (n=2) or pain (n=1). Removal was difficult in 12 cases (23%), and was associated with a perforation in one case, which was successfully treated with the placement of another stent. After a mean follow-up of 73 weeks (1-127), the stent was still present in one child. The stent had been removed in the other 11 children but stenosis recurred afterwards in 10 of them.

Conclusion: Stenting is a feasible option in children with refractory esophageal stenosis. Nevertheless, it is not always well tolerated and stenosis often reoccurred after removal of the stent.
Schreibman modified classification enables to optimise the diagnosis of oesophageal varices (OV) through oesophageal capsule endoscopy (OCE) for children

Jacques Cardey¹, Catherine Le Gall², Laurent Michaud³, alain dabadie⁴, Cecile Talbotec⁵, Marc Bellaiche⁶, Thierry Lamireau⁷, Emmanuel Mas⁸, Alain Lachaux⁹

₁Necker-Enfants Malades Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Paris, France
²Femme Mère Enfant Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Lyon, France
³Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
⁴Chu Rennes, Pediatric Gastroenterology, Rennes, France
⁵Hôpital Necker-Enfants Malades, Pediatric Gastroenterology, Hepatology and Nutrition, Paris, France
⁶Robert Debré Hospital, Pediatric Gastroenterology and Nutrition, Paris, France
⁷University Hospital, Paediatric Gastroenterology, Bordeaux, France
⁸Centre Hospitalier Universitaire de Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, and Genius Group, Toulouse, France
⁹Hôpital Femme Mère Enfant du Chu de Lyon, Pediatric Gastroentgy, Hepatology Nutrition Unit, Reference Centre for Wilson Diseaseologie, Lyon, France

Objectives and study: OCE performances for OV diagnosis partly depend on OV classification and reading methods. We evaluated the relevance of the different classifications for children, in order to be able to grade OV during OCE procedure, and therefore to monitor treatments and supervision.

Methods: From November 2011 to July 2013, 102 children having a portal hypertension and/or cirrhosis, ranging from age 7 to 18, were selected. OCE (PillCam ESO 2®, Given Imaging) and oesophagogastroduodenoscopy (OGD) under general anaesthesia (reference procedure) were performed the same day or in a 1 week delay by different endoscopists and recorded on video. OCE reading was carried out blindly, reviewed and corrected by 2 experts. For OV endoscopic classification, we used one of the 3 grades conventional classifications; for the OCE we compared the de Franchis classification with a modified one of Schreibman with varice stage C1: <2/3 and varice stage C2: >2/3 of a quarter of the circumference of the thumbnail; OV stage C1= OV grade 1 and OV stage C2= OV grade 2 and 3). Apart from sensitivity (SE), specificity (SP), positive and negative predictive value (respectively PPV and NPV) were examined for both classifications.

Results: 81 children were enrolled, amongst them 63 had OV and 24 had already been treated by endoscopic variceal ligations. Analysis reveals that:
1) with the de Franchis classification, for OV measured as C1 with OCE: SE, SP, PPV and NPV were respectively 75, 71.4, 63.2 and 81.4 %; for OV measured as C2: SE, SP, PPV and NPV were respectively 54.8, 96, 89.5 and 77.4 %, with a Kappa index of concordance of 0.608 (p<0.001) between the classification obtained through OVC and the one undertaken during OGD.
2) with the Schreibman modified classification, for OV measured as C1 with OCE: SE, SP, PPV and NPV were respectively 75, 100, 100 and 86 %; for OV measured as C2: SE, SP, PPV and NPV were respectively 100, 96, 94 and 100 % with a Kappa index of concordance of 0.851 (p<0.001) and only 2 cases of overestimation of grade 1 OV.

Conclusion: This study reveals that OCE performances for OV classification and concordance with OGD depend on the type of classification used. A Schreibman modified classification enables to get an OV classification that is close to the one obtained during OGD, and therefore to detect grade 2 and 3 OV that would both justify prophylactic band ligation, especially since OCE is also an effective procedure for diagnosis of the red signs on OV. OCE, a non-invasive method to diagnose OV, may be offered for detection and monitoring of OV for children after a successful “candy test”. 
Performance of common disease activity markers in comparison to the mayo endoscopic sub-score and the UCEIS in a paediatric ulcerative colitis cohort

Amanda Ricciuto1, Nicholas Carman1, Jennifer Fish2, Eileen Crowley1, Aleixo Muise1, Thomas Walters1, Binita M. Kamath3, Anne Griffiths1, Peter Church1

1The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
2The Hospital for Sick Children, Division of Gastroenterology, Toronto, Canada
3The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: Clinical and biochemical markers are frequently used as surrogates of inflammatory burden in paediatric ulcerative colitis (UC), with endoscopy generally considered the gold standard. We aimed to compare commonly used markers (physician global assessment (PGA), Paediatric UC Activity Index (PUCAI), C-reactive protein (CRP) and fecal calprotectin (FC)) with endoscopic disease activity, reflected by the Mayo Endoscopic Sub-score (MES) and variations of the more recently developed UC Endoscopic Index of Severity (UCEIS), which includes 3 sub-scores pertaining to vasculature, ulceration and bleeding.

Methods: In this single-centre prospective study, PGA, PUCAI, CRP and FC were measured contemporaneously in children with UC undergoing colonoscopy. Colonoscopies were scored by an independent, blinded IBD physician. Spearman correlations were determined with the MES and variations of the UCEIS (rectosigmoid UCEIS, individual segment UCEIS scores for the rectum, left colon, transverse colon and right colon, UCEIS extent score (summed segment scores), worst segment UCEIS score, and UCEIS sub-scores for vasculature, ulcers and bleeding (both per segment and as sub-scores summed across the colon)).

Results: 35 treated UC patients were included (52% male, median age at diagnosis 12.7 years, median disease duration 2.2 years, 55% MES 0-1, 45% MES 2-3, 41% pancolitis). Overall, the different versions of the UCEIS and MES correlated similarly with PUCAI, PGA and FC (see Table). Correlations were best with PUCAI (r = 0.8) and good with PGA and FC (r = 0.6-0.7). Correlations were poorer and more dissimilar with CRP; the rectosigmoid UCEIS and MES, but not the UCEIS extent score, correlated significantly with CRP. In examining the UCEIS sub-scores, FC correlated most strongly with the ulcer item, both when considering the worst segment and when the ulcer subscore was summed across the colon (r = 0.75 and 0.64, respectively). All 4 clinical and biochemical markers displayed progressively poorer correlations with segment UCEIS scores from the rectum proximally to the right colon; all were significantly correlated with rectum and left colon UCEIS scores, but all correlations became non-significant by the transverse or right colon.
**Table:** Spearman Correlations Between Clinical, Biochemical and Endoscopic Disease Activity Markers

<table>
<thead>
<tr>
<th>Mayo Endoscop i c Sub-score</th>
<th>UCEIS extent score</th>
<th>Worst segment UCEIS</th>
<th>Rectosigmoid UCEIS</th>
<th>Rectum UCEIS</th>
<th>Left colon UCEIS</th>
<th>Transverse colon UCEIS</th>
<th>Right colon UCEIS</th>
</tr>
</thead>
<tbody>
<tr>
<td>PGA of clinical disease activity</td>
<td>0.72 &lt;0.0001</td>
<td>0.71 &lt;0.0001</td>
<td>0.67 0.0002</td>
<td>0.67 0.0002</td>
<td>0.68 0.0003</td>
<td>0.65 0.0046</td>
<td>0.54 0.12</td>
</tr>
<tr>
<td>PUCAI</td>
<td>0.83 &lt;0.0001</td>
<td>0.81 &lt;0.0001</td>
<td>0.82 &lt;0.0001</td>
<td>0.82 &lt;0.0001</td>
<td>0.85 &lt;0.0001</td>
<td>0.79 &lt;0.0001</td>
<td>0.48 0.008</td>
</tr>
<tr>
<td>Fecal calprotectin</td>
<td>0.66 0.003</td>
<td>0.62 0.006</td>
<td>0.68 0.002</td>
<td>0.66 0.003</td>
<td>0.62 0.006</td>
<td>0.70 0.0013</td>
<td>0.22 0.39</td>
</tr>
<tr>
<td>C-reactive protein</td>
<td>0.69 0.0008</td>
<td>0.37 0.11</td>
<td>0.29 0.22</td>
<td>0.51 0.02</td>
<td>0.60 0.005</td>
<td>0.51 0.02</td>
<td>0.28 0.24</td>
</tr>
</tbody>
</table>

1st row – Spearman correlations; 2nd row – p-values

**Conclusion:** Variations of the UCEIS and MES correlated similarly with clinical and biochemical markers of disease activity in this paediatric UC cohort. Correlations were strongest with PUCAI, good for FC, but poorer and more variable for CRP. FC appeared to be “driven” by the ulcer sub-score of the UCEIS. All 4 markers correlated best with UCEIS scores in the left colon and poorly with scores in the right colon, suggesting that PUCAI, PGA, FC and even CRP are primarily reflective of distal disease.
Safety and efficacy of a novel haemostatic agent Hemospray® in the emergent endoscopic management of acute upper gastrointestinal bleeding in children

Mike Thomson1, Prithviraj Rao1, Priya Narula1, Arun Urs2, David Campbell2, Dalia Belsha3

1Sheffield Childrens NHS Foundation Trust, Paediatric Gastroenterology, Sheffield, United Kingdom
2Sheffield Children's Hospital NHS Foundation Trust, Sheffield, United Kingdom
3Sheffield Children's Hospital Foundation Trust, Sheffield, United Kingdom

Objectives and study: Acute upper gastrointestinal bleeding (AUGIB) remains virtually the last paediatric emergency that is still managed badly in many centres. Attendant mortality is mainly contingent on the lack of recognition that emergency endoscopy, and the skill mix and experience of the endoscopist. A novel endo-haemostatic topically applied powder (Hemospray®) has the advantage of extreme ease of use and hence may lower the threshold of competency required by the endoscopist thereby potentially reducing mortality. A recent adult study reported technical success of 88% and re-bleeding risk of 16% with no reported adverse events. (1)

Aim is to prospectively evaluate the efficacy and the safety of Hemospray® in paediatric AUGIB.

Methods: Prospective enrolment of children fulfilling the Sheffield AUGIB score for likely need for endo-haemostatic intervention of >8/24. (2) Hemospray® was applied using the Cook application device and a follow up endoscopy at 72 hours, 7 days and 1 month was offered to the families and occurred in those deemed to have clinical need pre-discharge. Regional Ethics Committee approval was obtained.

Results: 14 applications of Hemospray® occurred in 12 patients (7 male), 7.1 (0.7-15.0) years, 25.1 (10.3-67.8) kg. Sheffield scoring system for likely requirement for endoscopic intervention due to ongoing active bleeding was applied with 8/12 having had blood transfusion and 8/12 with Hb drop of >20g/l. 10 patients had pre-existing conditions, one patient had excessive NSAID ingestion and one patient had no past history of note. Hemospray® application was easy, took 8 (5-15) minutes, was immediately successful in achieving haemostasis and no adverse events were observed. Repeat endoscopy in 6 patients at 72 hours revealed healing of the bleeding lesion, however 2 patients required a second application due to ongoing bleeding - one also required endoclip application and one required laparotomy which was temporarily successful but subsequent interventional radiographic embolization of the afferent vessel was needed.
**Table:**

<table>
<thead>
<tr>
<th>Pre-existing condition</th>
<th>Findings on endoscopy</th>
</tr>
</thead>
<tbody>
<tr>
<td>NSAID intake (4 hourly for 48 hours)</td>
<td>Gastric ulcer</td>
</tr>
<tr>
<td>TPN dependant, short gut</td>
<td>Gastric ulcer x2</td>
</tr>
<tr>
<td>Nil of note</td>
<td>Gastric ulcer</td>
</tr>
<tr>
<td>Portal hypertension</td>
<td>Erosive gastritis</td>
</tr>
<tr>
<td>Post-polypectomy of large gastroduodenal polyp</td>
<td>Post-EMR Gastric bleed</td>
</tr>
<tr>
<td>Small bowel diaphragm disease</td>
<td>Post-web division bleed</td>
</tr>
<tr>
<td>Duchene muscular dystrophy</td>
<td>Duodenal and gastric ulcer</td>
</tr>
<tr>
<td>Acute pancreatitis</td>
<td>Erosive gastritis and duodenitis</td>
</tr>
<tr>
<td>Glanzmann's thrombocythaenia</td>
<td>Actively bleeding angiodysplasia</td>
</tr>
<tr>
<td>GVHD, ileal stricture, ileostomy</td>
<td>Bleeding ileal ulcers</td>
</tr>
<tr>
<td>Hereditary spherocytosis, recent splenectomy</td>
<td>Gastric ulcer</td>
</tr>
<tr>
<td>Cerebral palsy, seizures</td>
<td>Haemorrhagic gastritis</td>
</tr>
</tbody>
</table>

**Conclusion:** Hemospray® appears effective in the majority of paediatric AUGIB in this preliminary prospective series, is easy and quick and is associated with no observable adverse events. It has the potential to transform the management of this emergency due to its ease of performance, thereby opening the door to relatively inexperienced paediatric endoscopists.

**References:**

Reducing avoidant behaviour improves gastrointestinal symptoms in adolescents with irritable bowel syndrome: a mediation analysis of exposure-based cognitive behaviour therapy

Marianne Bonnert¹, Johan Bjureberg², Maria Lalouni³, Erik Hedman¹, Eva Serlachius¹, Brjánn Ljótsson¹

¹Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden
²Karolinska Institutet, Clinical Neuroscience, Stockholm, Sweden
³Karolinska Institutet, Department of Medicine, Solna, Stockholm, Sweden

Objectives and study: Irritable bowel syndrome (IBS) is common among adolescents and has a large negative impact on quality of life. Stress has been proposed as an important target in treatment to reduce gastrointestinal symptoms, and consequently relaxation training is common in psychological IBS-treatments. However, a pattern of avoidant behaviour is commonly seen in the IBS-population, which is associated with more gastrointestinal (GI) symptoms. Exposure-based cognitive behaviour therapy (CBT) targets the avoidant behaviour in order to reduce symptoms. The aim was to investigate mechanisms of change in exposure-based CBT delivered over the Internet (Internet-CBT) for adolescents with IBS.

Methods: Using data from a randomized controlled trial (N=101; Bonnert et al, Am J Gastroenterol, 2016), we investigated if two proposed mediators, avoidant behaviour (assessed with IBS-BRQ) and perceived stress (assessed with PSS-10), mediated improvement in global GI symptoms in exposure-based internet-delivered CBT (Internet-CBT) compared to a waitlist for adolescents with IBS. The outcome was the Gastrointestinal symptoms rating scale for IBS (GSRS-IBS), and the independent variable was change over time as a function of group. Assessments were made weekly for both the outcome and the mediators during the whole treatment period. Mediation was estimated with mixed model regression analyses, estimating the paths connecting three variables, the X (independent variable), M (mediator variable), and Y (outcome variable). The X→M relationship is estimated by the a-path and the M→Y relationship, controlling for X, is estimated by the b-path, and the X→Y relationship is estimated by the c-path. The c' path, is the remaining effect of the independent variable X on the outcome Y when controlling for the mediator M. The total mediated effect, or indirect effect, is calculated as the product of the a and b estimates, denoted ab. The criterion for mediation is that the 95% confidence interval (CI) does not contain zero, in this study obtained by bootstrap replication. For illustration, see Figure.

![Diagram of mediation analysis](attachment://mediation_diagram.png)
Results: We found that change in avoidant behaviour but not perceived stress mediated the effect of exposure-based Internet-CBT on GI symptoms. The decrease in avoidant behaviour explained a large part (67%) of the total treatment effect. We also observed a unidirectional relationship over time between avoidant behaviour and GI symptoms. For details, see Table 1.

Table: Results mediation-analysis

<table>
<thead>
<tr>
<th></th>
<th>a (se), p</th>
<th>b (se), p</th>
<th>ab (95% CI)</th>
<th>c' (se), p</th>
<th>Pm</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS-BRQ</td>
<td>-1.08 (0.39), .006</td>
<td>0.34 (0.02), &lt;.001</td>
<td>-0.37 (-0.09,-0.62)</td>
<td>-0.17 (0.19), .373</td>
<td>67%</td>
</tr>
<tr>
<td>PSS-10</td>
<td>0.004 (0.11), .972</td>
<td>0.41 (0.06), &lt;.001</td>
<td>0.002 (-0.08, 0.09)</td>
<td>-0.55 (0.21), .009</td>
<td>0.3%</td>
</tr>
</tbody>
</table>

a=effect of treatment assignment on slope of mediator. b=effect of mediator on outcome. ab=mediated effect c’=remaining effect controlling for the mediated effect. Pm=Proportion mediated effect. IBS-BRQ=Irritable bowel syndrome-Behavioral Response Questionnaire. PSS-10=Perceived Stress Scale-10 items version.

Conclusion: Exposure-based Internet-CBT for adolescent IBS leads to reduced avoidance and thereby reduced GI symptoms. Our results suggest that stress reduction is not a necessary treatment target to relieve GI symptom, which is important to consider when designing new psychological treatments for IBS.
Internet-delivered exposure-based cognitive behaviour therapy for adolescents with functional abdominal pain or functional dyspepsia: a feasibility study.

Marianne Bonnert¹, Ola Olen², Maria Lalouni³, Erik Hedman¹, Josefin Särnholm¹, Eva Serlachius¹, Brjánn Ljótsson¹

¹Karolinska Institutet, Department of Clinical Neuroscience, Stockholm, Sweden
²Karolinska Institutet, Department of Medicine, Solna, Clinical Epidemiology Unit, Stockholm, Sweden
³Karolinska Institutet, Department of Medicine, Solna, Stockholm, Sweden

Objectives and study: Functional abdominal pain (FAP) and functional dyspepsia (FD) are common in adolescents and associated with low quality of life. Exposure-based cognitive therapy is efficient for adult and adolescent irritable bowel syndrome (IBS), but has not been evaluated for adolescent FAP/FD. The aim of this study was to evaluate the feasibility and potential efficacy of internet-delivered cognitive behaviour therapy (Internet-CBT) based on behavioural exposure for adolescents with FAP or FD.

Methods: This was an open pilot with a pretest-posttest design. Thirty-one adolescents with FAP or FD according to Rome III criteria, living in Sweden and aged 13-17 were included. All received Internet-CBT. The Internet-CBT consisted of 10 weekly online modules mainly focused on exposure to abdominal symptoms and reduced avoidance behaviours. Parents received a separate intervention that helped them support the adolescent’s work with the exposure exercises and reduce parental behaviours that could maintain the adolescent’s focus on abdominal symptoms. Feasibility criteria included acceptable adherence, treatment credibility, treatment satisfaction and potential efficacy. The primary outcome for potential efficacy was the adolescent-reported Faces Pain Rating scale, measuring pain intensity. Secondary outcomes included adolescent- and parent-reported gastrointestinal symptoms (Children’s Somatization Index, CSI, the gastro subscale) and quality of life (Paediatric Quality of Life Inventory, PedsQL). Assessment points were at pre-treatment, and at post-treatment.

Results: Post-treatment data attrition rates were low (6.5%), and adherence to treatment was acceptable with an average of 72% completed modules, including the six (19.4%) adolescents that dropped out from treatment. Participants reported the treatment to be credible and 82% reported overall satisfaction with treatment. Analyses with dependent t-test showed a significant and large effect on the primary outcome from pre-treatment to post-treatment (Standardized mean difference, Cohen’s $d = 0.96$, $p<.001$, 95% CI [0.37, 1.56]). Participants also made significant and large improvements on secondary outcomes of adolescent-reported gastrointestinal symptoms (Cohen’s $d=0.86$, $p<.001$) and quality of life (Cohen’s $d=0.91$, $p<.001$).

Table:
<table>
<thead>
<tr>
<th></th>
<th>Pretreatment, m(sd)</th>
<th>Posttreatment, m(sd)</th>
<th>Cohen’s d (CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Pain intensity</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(Faces)</td>
<td>7.07 (2.08)</td>
<td>4.55 (3.02)***</td>
<td>0.96 (0.37, 1.56)</td>
</tr>
<tr>
<td><strong>Secondary outcomes:</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Quality of life</strong></td>
<td>68.65 (14.54)</td>
<td>81.72 (14.11)***</td>
<td>0.91 (0.58, 1.24)</td>
</tr>
<tr>
<td>(PedsQL)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GI symptoms (CSI)</strong></td>
<td>9.06 (4.55)</td>
<td>5.32 (4.07)***</td>
<td>0.86 (0.36, 1.37)</td>
</tr>
</tbody>
</table>

**Conclusion:** Internet-CBT based on exposure exercises for adolescents with FAP or FD is a feasible treatment, that potentially improves pain intensity, gastrointestinal symptoms, and quality of life, with large effect sizes. These results need to be confirmed in a randomized controlled trial.
GASTROENTEROLOGY: GI motility, GERD and functional GI disorders

G-eP-037

Impaired postprandial colonic response in the presence of coordinated propagating colonic contractions suggests an extrinsic neuropathy in children with intractable functional constipation

Ilan Koppen1, Lukasz Wiklendt2, Desalegn Yacob3, Carlo Di Lorenzo3, Marc Benninga4, Phil Dinning5

1Emma Children’s Hospital/Academic Medical Center, Amsterdam, Netherlands
2Flinders University, Adelaide, Australia
3Nationwide Children’s Hospital, Pediatric Gastroenterology, Columbus, United States
4Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
5Flinders Medical Centre, Adelaide, Australia

Objectives and study: High-resolution colonic manometry (HR-CM) enables detailed description of colonic motor patterns. In a recent study using HR-CM, a novel motor pattern was described in healthy adults; pan-colonic pressurizations. This motor pattern consists of pressure events that occur simultaneously across all colonic sensors, are associated with anal sphincter relaxation and increase in number after a meal. In adults with intractable functional constipation (FC) this motor pattern was significantly less common. Our aim was to determine whether pan-colonic pressurizations could be identified in children with intractable FC.

Methods: We performed a retrospective analysis of children with FC who underwent HR-CM. A solid-state catheter with 36 sensors (spaced at 3 cm intervals) had been placed into a prepared colon. Colonic manometry recordings lasted 2 hours before and after a meal, followed by 1 hour of recording after bisacodyl was infused into the proximal colon. To describe the postprandial response, dominant frequencies of contractile activity were quantified for 1 hour before and after initiation of the meal. All recordings were examined for the presence of pan-colonic pressurizations (peak amplitude <50 mmHg, occurring simultaneously across all intracolonic sensors) and high amplitude propagating contractions (HAPCs; peak amplitude ≥75 mmHg, migrating aborally over ≥15 cm).

Results: We included 23 children (median age 11.6 years, 13 male). Overall, the normal post-prandial increase in 2–4 cycle per minute activity was diminished or absent. We were unable to find evidence of pan-colonic pressurizations. In most children (n=20, 87%; table 1) antegrade rapidly propagating pressure waves were observed. These motor patterns (previously labeled as a long single motor patterns) were recorded at a median of 2.9/hour (IQR 1.5–16.0) prior to the meal and their number did not increase after the meal: 4.4/hour (IQR 0.9–10.6). HAPCs were observed in 4 & 6 children before and after the meal respectively and in 18 children after bisacodyl (Table 1). In all 5 children without HAPCs, long single motor patterns were recorded and in all 3 children without long single motor patterns, HAPCs were observed.
**Table:**

<table>
<thead>
<tr>
<th></th>
<th>Amplitude (mmHg; median, IQR)</th>
<th>Velocity (mm/s; median, IQR)</th>
<th>Distance of propagation (cm; median, IQR)</th>
<th>Patients exhibiting this motor pattern (n, %)</th>
<th>Amount per manometry recording (median, IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Long single motor patterns</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Preprandial</td>
<td>6.0 (3.3-14.1)</td>
<td>20.0 (14.2-27.0)</td>
<td>81 (69-93)</td>
<td>20, 87%</td>
<td>13.5 (5.0-34.25)</td>
</tr>
<tr>
<td>- Postprandial</td>
<td>5.9 (3.3-13.9)</td>
<td>18.7 (11.7-25.5)</td>
<td>84 (69-99)</td>
<td>14, 61%</td>
<td>8 (4.25-32.25)</td>
</tr>
<tr>
<td>- Post-bisacodyl</td>
<td>5.8 (3.3-13.3)</td>
<td>20.7 (15.9-29.2)</td>
<td>81 (66-90)</td>
<td>19, 83%</td>
<td>9 (2-17)</td>
</tr>
<tr>
<td></td>
<td>5.5 (3.2-12.3)</td>
<td>18.0 (15.8-23.6)</td>
<td>87 (81-93)</td>
<td>11, 48%</td>
<td>2 (1.5-2)</td>
</tr>
<tr>
<td><strong>HAPCs</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Preprandial</td>
<td>103.4 (66.2-145.3)</td>
<td>2.5 (1.6-3.6)</td>
<td>30 (18-45)</td>
<td>18, 83%</td>
<td>9 (6-17.25)</td>
</tr>
<tr>
<td>- Postprandial</td>
<td>87.3 (58.2-130.8)</td>
<td>2.4 (1.6-3.6)</td>
<td>30 (18-45)</td>
<td>4, 17%</td>
<td>3 (2.5-3.5)</td>
</tr>
<tr>
<td>- Post-bisacodyl</td>
<td>92.9 (61.5-137.1)</td>
<td>2.5 (1.7-3.8)</td>
<td>28.5 (18-42)</td>
<td>6, 26%</td>
<td>3 (3-3)</td>
</tr>
<tr>
<td></td>
<td>103.4 (66.2-145.3)</td>
<td>2.5 (1.6-3.6)</td>
<td>30 (18-45)</td>
<td>18, 83%</td>
<td>6.5 (5-10.75)</td>
</tr>
</tbody>
</table>

**Conclusion:** Our data suggest that pan-colonic pressurizations are absent in children with intractable FC. However, we recorded coordinated propagating motor patterns (long single motor patterns, HAPCs or both) in all children, indicating a preservation of neural pathways within the enteric nervous system. The impaired colonic response to a meal supports the hypothesis that an extrinsic neuropathy may exist in children with intractable FC.
Chronic intestinal pseudo-obstruction in children: early experience of the National Diagnostic Service in United Kingdom

Anna Rybak\(^1\), Kelly Larmour\(^2\), Efstriatos Saliakellis\(^1\), joanne brind\(^3\), Keith Lindley\(^1\), Francesco Valitutti\(^1\), Osvaldo Borrelli\(^4\), Nikhil Thapar\(^1\)

\(^1\)Great Ormond Street Hospital, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom
\(^2\)Great Ormond Street Hospital, Department of Dietetics, London, United Kingdom
\(^3\)Gosh, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom
\(^4\)Great Ormond Street Hospital for Children NHS Foundation Trust, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom

Objectives and study: Chronic intestinal pseudo-obstruction in children (CIPO) is a rare, and disabling disorder. In April 2012, National Paediatric Pseudo-obstruction Diagnostic Service (PPOD) was set up at Great Ormond Street Hospital in United Kingdom (UK) to provide a service for the diagnosis and management of CIPO in children. This study presents a four-year experience of the PPOD service, including a clinical description of the paediatric CIPO population captured by it.

Methods: This is a retrospective analysis of patients admitted within the PPOD service, between April and December 2016, with suspected diagnosis of CIPO. The ultimate diagnosis of CIPO was confirmed on the presence of at least 2/4 of the following criteria: (1) antroduodenal manometry (ADM) evidence of small intestinal neuromuscular involvement; (2) radiological evidence of recurrent and/or persistently dilated loops of small intestine with air fluid levels; (3) presence of the conditions definitively associated with paediatric CIPO and (4) inability to maintain adequate nutrition and/or growth on oral feeding alone. Clinical data, including age of onset of symptoms, dominant symptoms, results of the ADM, surgical procedures, feeding history and histology results of small intestine full thickness biopsies, were analyzed.

Results: Out of 113 children referred to the PPOD Service, 50 were definitively diagnosed with CIPO (26 girls), with median age at symptoms' onset of 5 months (range: from birth to 168 months). 83.3% children presented with first symptoms <1 year of age life. Median age at assessment was 45 months in the first half-time of service (32/50) and 35.5 months in the second half (18/50). Based on the ADM results, majority of patients had patterns consistent with neuropathic involvement (33), 1 with myopathy and 6 were consistent with both, neuropathy and myopathy. In 10 patients diagnosis of CIPO was based on clinical criteria. 46% of children had dominant upper gastro-intestinal (GI) tract presentation (nausea, vomiting, gastro-oesophageal reflux, feeding intolerance), 40% presented with lower GI tract symptoms (abdominal pain, abdominal distension, constipation). 29 children (58%) underwent colonic manometry, and majority of them (55%) showed colonic neuropathy. Out of 50 children with CIPO, 34 patients (68%) had an ileostomy performed, 9 (18%) had partial or total colectomy and 1 patient ultimately underwent multi-visceral transplantation. 35/50 patients had full thickness biopsy of small bowel. In 20/35 cases (57%) no histological abnormalities could be identified. Total parenteral nutrition (TPN) was required by 48% of children (23/48), 10 patients were on full enteral feeds; 4 patients remained on oral feeding.

Conclusion: Over the first four years of the UK national PPOD Service, we diagnosed an average of 11 patients a year, 5-fold higher than before the national UK service was established, with a trend towards decreasing age at first assessment (3.3 vs 11.3 years pre-2012, data not shown). Making the definitive diagnosis earlier is especially important given the majority of patients presented with the onset of the first symptoms <1 year of age, progress quickly to dependence on TPN. The majority of our patients underwent ileostomy formation soon after diagnosis and also showed large bowel dysmotility. The development of national CIPO registries and services is likely to be of benefit to improving early diagnosis, expertise in management and ultimately outcomes of CIPO.
Crying, pain, acid and non acid reflux in infants: which correlation?

Silvia Salvatore¹, Federica Pagliarin², Koen Huysentruyt³, Kris Van de Maele⁴, Yvan Vandenplas⁴

¹University of Insubria, Varese, Italy
²University of Insubria, Pediatrics, Varese, Italy
³Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
⁴Uz Brussel, Paediatrics, Brussels, Belgium

Objectives and study: The role of gastroesophageal reflux (GER) in crying and pain in infants still needs clarification. Infant crying is frequently interpreted as a manifestation of painful GER and acid inhibitors are often used. Correct recognition of pain is recommended by the World Health Organisation to enable optimal treatment and alleviate suffering. The objective of this study was to evaluate the relation between pain assessed by the Face, Legs, Activity, Cry, Consolability (FLACC) validated scale and GER in infants.

Methods: We conducted a prospective study (from March 2015 to September 2016) consecutively enrolling infants submitted to esophageal multichannel intraluminal impedance (MII) (Sleuth®, Sandhill Highland Ranch, CO, USA) for suspected GER-disease. Respiratory abnormalities or persisting crying episodes occurring during the investigation were recorded in a diary and scored by parents previously instructed to use the FLACC score. Symptoms were considered as temporally associated with GER if occurred within a 2-minutes period of time. All pH-impedance tracings were automatically and manually analysed by one of the author blinded to the results of the FLACC score. Total acid reflux exposure rate (RI) was defined as abnormal, indeterminate or normal when >7%, between 3 and 7%, and <3% according to ESPGHAN guidelines. The relation between the FLACC score and the presence/absence, duration, kind and extension of GER events was calculated. Statistical analysis was performed using Kruskal-Wallis (test H) and t test when appropriate.

Results: We recruited 62 subjects (age 15 days -23 months, mean age 5.5, SD 5.1, median age 3.5 months; 36 males). During the investigation 452 episodes of crying were recorded and scored with FLACC. Among them, 217 (48%) were temporally associated with GER and 235 (52%) were not. The median value of FLACC in the two groups was exactly the same (FLACC =5) whilst it was significantly (P < 0.001) lower in infants with abnormal RI compared to the ones with indeterminate or normal RI (FLACC 7 and 5, respectively). GER occurred significantly more often before crying than simultaneously or after crying (p=0.001) but without a significant different median of FLACC. Proximal extension, young age and duration of GER did not show a significant different value of FLACC. Conversely, 128 episodes of crying were associated with weakly acidic reflux and presented a significant higher value of FLACC compared to 89 acid reflux events (FLACC 5.6 vs 4.7, test T, P=0.0076).

Conclusions: FLACC scale shows that painful crying is not significantly associated with GER in infants. Distal reflux can cause similar pain to proximal GER whilst weakly acidic reflux may be perceived even more painful than acid GER.
Intra- and interrater reliability of the Chicago Classification of achalasia subtypes in pediatric High Resolution Esophageal Manometry (HRM) recordings

Maartje Singendonk, Rachel Rosen, Jac Oors, Nathalie Rommel, Michiel van Wijk, Marc Benninga, Sam Nurko, Taher Omari

1Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Children’s Hospital Boston, Center for Motility and Functional Gastrointestinal Disorders, Boston, United States
3Academic Medical Center, Department of Gastroenterology and Hepatology, Amsterdam, Netherlands
4University of Leuven, Translational Research Center for Gastrointestinal Diseases, Leuven, Belgium
5Flinders University, School of Medicine, Bedford Park, Australia

Objectives and study: Subtyping achalasia by high resolution manometry (HRM) is clinically relevant as response to therapy and prognosis have shown to vary accordingly. The reliability of diagnosing achalasia and its subtypes in pediatric patients based on HRM remains undefined. The aim of this study was to assess inter- and intrarater agreement (reliability) of diagnosing achalasia and achalasia subtyping in children using the Chicago Classification (CC) V3.0.

Methods: Six experienced observers (experience from ≥500 HRM analyses) analysed 40 pediatric HRM recordings (22 achalasia and 18 non-achalasia cases) during two separate sessions at least one week apart by using dedicated analysis software (ManoView 3.0), requiring manual adjustment or removal of anatomical landmarks. CC metrics driving the achalasia diagnosis and achalasia subtyping (integrated relaxation pressure (IRP4s), distal contractile integral (DCI), intrabolus pressurization pattern (IBP) and distal latency (DL)) were extracted and analysed in a hierarchical order according to the CC algorithm. Cohen's kappa (2 raters; kappa further annotated as κ) and Fleiss' κ (≥2 raters) were used for categorical data and the intraclass correlation coefficient (ICC) was used for ordinal data.

Results: Based upon results of the dedicated analysis software only, intra- and interrater reliability were excellent and moderate (κ=0.89 and κ=0.52 respectively) for differentiating achalasia from non-achalasia cases. For subtyping achalasia, reliability decreased to substantial and fair (κ=0.72 and κ=0.28 respectively). When observers were allowed to change the software driven diagnosis according to their own interpretation of the manometric patterns, intra- and interrater reliability increased for diagnosing achalasia (κ=0.98 and κ=0.92 respectively) and for subtyping achalasia (κ=0.79 and κ=0.58 respectively). Substantial to excellent intra- and interrater reliability was found for parameters driving the achalasia diagnosis (IRP4s and DCI), whilst parameters involved in subtyping achalasia cases (IBP and DL to respectively determine panesophageal pressurization and spasm) showed more variability (Table 1).
**Conclusion:** Intra- and interrater agreement for differentiating achalasia from non-achalasia patients using HRM and the CC was very good to excellent when results of automated analysis software were interpreted by experienced observers. More variability was seen when purely relying on the software driven diagnosis and for subtyping achalasia patients.

### Table:

<table>
<thead>
<tr>
<th></th>
<th>Intrarater reliability, κ (Mean)</th>
<th>Interrater reliability, κ</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Diagnosing Achalasia (all cases; n = 40)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. Mean IRP4s &gt; 15mmHg</td>
<td>0.79</td>
<td>0.78</td>
</tr>
<tr>
<td>2. 100% of swallows failed peristalsis</td>
<td>0.77</td>
<td>0.81</td>
</tr>
<tr>
<td><strong>Subtyping Achalasia (achalasia cases only; n = 22)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Panesophageal pressurization ≥ 20% of swallows</td>
<td>0.93</td>
<td>0.58</td>
</tr>
<tr>
<td>4. Spasm ≥ 20% of swallows</td>
<td>0.35&lt;sup&gt;2&lt;/sup&gt;</td>
<td>–&lt;sup&gt;3&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

κ, Cohen's kappa estimate for intra-rater reliability and Fleiss' kappa estimate for inter-rater reliability; IRP4s, integrated relaxation pressure. <sup>1</sup>Mean kappa values calculated after applying Fisher's Z-transformation; <sup>2</sup>based on results of 3 observers as for the other 3 observers n = 22 studies were pairwise excluded (distal latency (DL) not uniformly obtained); <sup>3</sup>n = 22 studies pairwise excluded (DL not uniformly obtained), no studies to perform interrater reliability analysis.
Antroduodenal manometry assessment: variability amongst experts in a single center

Francesco Valitutti¹, Anna Rybak², Robert Dziubak³, Efstriatos Saliakellis², Nikhil Thapar⁴, Keith Lindley², Osvaldo Borrelli⁴

¹Sapienza- University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
²Great Ormond Street Hospital, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom
³Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom
⁴Great Ormond Street Hospital for Children NHS Foundation Trust, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom

Objectives and study: Antroduodenal manometry (ADM) is valuable clinical utility for the assessment of small intestine neuromuscular function in children with symptoms and signs of severe gastrointestinal motility disorders, such as chronic intestinal pseudo-obstruction. In the last decade, manometric techniques have dramatically improved with the development of high-resolution manometry (HRM) enabling more detailed definition of pressure profiles along segments of the gut. The pressure data obtained during the recording may be presented as conventional pressure line plots (CLP) and pseudo-three-dimensional pressure topographic plots (PTP). It has been suggested that the latter may improve the measurements of small intestine motility by removing some of the ambiguity detected during line plot analysis. Our study aimed to assess and calculate inter-observer agreement between experts in single centre for both CLP and PTP, as well as to assess reliability of both data display options.

Methods: We reviewed 14 ADM studies performed in our institution in the 2 years since November 2014. All studies were anonymised by a research fellow and independently presented to each of three experienced neurogastroenterologists (observers) for analysis. All ADMs had been performed using a low compliance water-perfused manometric system and a custom built water-perfused PVC manometric catheter with 20 recording ports at 2.5-cm intervals. For each observer, data from individual studies were displayed both as CLP and PTP and presented for analysis in different time slots on different days (minimum 6 week interval between CLP and PTP evaluation of the same study). Inter-observer reliability was assessed in both CLP and PTP. During ADM trace evaluation, individual observers considered categorical and quantitative data such as: final diagnosis (normal, neuropathy, myopathy, features of both neuro-myopathy), number of phase III over 18 hours, shape of phase III, presence of simultaneous bursts, recognizable conversion to postprandial pattern, sporadic increased baseline during bursts of contraction. The statistical analysis was based on Cohen’s and Fleiss’ kappa values, which indicate excellent agreement with kappa > 80%, and poor inter-observer agreement < 60% of kappa value.

Results: Analysis using CLP manometry in terms of final diagnosis revealed fair inter-observer agreement (Fleiss’ kappa: 64%, p<0.001, all three obs. combined; Cohen’s kappa: 73%, p<0.001, obs. 1 vs obs. 2; Cohen’s kappa: 60%, p<0.01, obs. 1 vs obs. 3; Cohen’s kappa: 60%, p<0.01, obs. 2 vs obs. 3). For PTP manometry analysis results suggested overall poor agreement (Fleiss’ kappa: 36%, p<0.01, all three obs. combined), except in one observer comparison (Cohen’s kappa: 70%, p<0.01, obs. 1 vs obs. 3). With regards to correlation between CLP and PTP in individual observers, there was a poor agreement in two (Cohen’s kappa: 36% and 45%, p:ns) and a good agreement in one (Cohen’s kappa: 85%, p<0.01, obs. 3 CLP vs obs. 3 PTP).

Conclusion: Albeit well-established for other motility investigations such as oesophageal and anorectal manometries, current PTP analysis is arguably not as reliable as CLP in the assessment of antroduodenal motility pattern. Since ADM is a very advanced study performed only in highly specialized centres, caution should be used when interpreting data, especially if only a single physician reports each study. A careful account of the clinical picture needs to be incorporated in decision making.
A synbiotic partial whey hydrolysate with reduced lactose decreases infantile colic and improves quality of life; a randomized open pilot study

Ioannis Xinias¹, A Analitis², Yvan Vandenplas³

¹Hippocration Hospital, 3rd Pediatric Department, Thessaloniki, Greece
²National and Kapodistrian University of Athens, Department of Hygiene, Epidemiology and Medical Statistics, Faculty of Medicine, Athens, Greece
³Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives and study: The aim was to evaluate the efficacy of a formula containing partially hydrolyzed whey protein, reduced lactose, Bifidobacterium lactis (B lactis) and galacto-oligosaccharides (GOS) in formula fed infants presenting with infantile colic (IC), defined as episodes of unsoothable crying for more than three hours per day during more than three days a week without organic cause.

Methods: The efficacy of the study formula was evaluated during one month in 40 term born infants (mean age: 1.0 ± 0.4 months; range 20 days-3 months) presenting with IC. Twenty full-term formula fed infants with IC which were not offered any dietary intervention served as control. All parents completed the parent form of a Quality of Life (QoL) questionnaire, assessing the burden of IC on family life. Parents were also asked to report stool frequency and composition, and to rate the benefit of the formula at the follow-up visit.

Results: The infants in the control group were slightly older than these in the intervention group. Crying time did not differ at inclusion. The test formula reduced crying time from 3.2 hours (P25-75 3.1 - 3.3) to 0.5 hours (0.3 - 0.8). Although the decrease in crying time was also significant in the control group (from 3.5 (3.2-4.5) to 2.0 (2.2-3.0), the difference in decreased crying time between the intervention and control group was statistically significant (2.7 versus 1.2 hours, or 1.5 hours/day less crying in the intervention group).

Stool composition became looser only in the intervention group. Defecation frequency showed no statistically significant change in either group.

Median scores of the QoL questionnaire obtained at inclusion, decreased after one month in both the intervention and the control group for the majority of the variables indicating improvement. More specifically, in the intervention group median scores improved significantly for all parameters. In the control group, all parameters improved as well except for the parent-child interaction and QoL related social interaction with friends and relatives. The median score changes for all the 7 QoL questionnaire variables between inclusion and after the intervention was significantly greater in the treatment group compared to the control group. The median score regarding the benefit of intervention versus no intervention was also statistically significant lower, i.e. better, in the intervention group.

Conclusion: The test-formula significantly reduced the duration of crying episodes as well as the burden of the overall QoL.
Esophageal eosinophilia in children: Has H. pylori infection a protective role?

Kleoniki Roka1, Aikaterini Roubani1, George Chouliaras1, Daphne Margoni1, Paraskevi Papadogeorgou1, Amalia Patereli2, Kalliopi Stefanaki2, Ioanna Panayotou3, Alexandra Papadopoulou4, Eleftheria Roma5

1University of Athens, First Department of Paediatrics, Athens, Greece
2Aghia Sophia Children’s Hospital, Pathology Department, Athens, Greece
3Iaso Children’s Hospital, Athens, Greece
4Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece
5University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece

Objectives and study: Helicobacter pylori (H. pylori) infection has been inversely associated with allergic diseases. We aimed to study the prevalence of esophageal eosinophilia (EE) in children who underwent first esophagogastroduodenal endoscopy (EGD) and it’s correlation with H. Pylori infection.

Methods: All children who underwent EGD at a single pediatric gastroenterology center from 2000 until 2016 were retrospectively included. Clinical, endoscopic and histological findings were studied. EE was defined the presence of at least 15 eosinophils per HPF in esophageal biopsy. H.pylori infection was defined by positive culture or by positive histology and CLO-test. Those children with negative or not available culture and only one positive biopsy based (histology or CLO) test were further evaluated by 13C urea breath test and the positives were also included in the H. Pylori infected group. Patients with inflammatory bowel disease, celiac disease and caustic ingestions were excluded from the study. We divided our patients into two groups: patients with H.Pylori (+) and patients with H.Pylori(-) gastritis.

Results: We studied 640 patients with H.Pylori(+) and 1415 patients with H.Pylori(-) gastritis. Statistical significant difference was observed only for age (9.7 vs 7.6 years, respectively, p<0.001). Absence of eosinophils in esophagus was observed in 93.5% of H.Pylori (+) patients vs 83.8% of H.Pylori(-) ones (p<0.01). Eosinophils above 15/HPF were identified in only 2 children (0.3%) with H.Pylori(+) gastritis, compared to 64 (4.5%) with H.Pylori(-) gastritis (p=0.0002). Patients with no EE were 2.7 times more likely to have H.Pylori (+) gastritis compared to those without (OR=2.7, 95%CI:1.96-3.89, p<0.0001). Furthermore, patients with EE were 15.11 times less likely to have H. Pylori (+) gastritis compared to those without (OR=15.11, 95%CI:3.69-61.93, p=0.0002)

Conclusion: Esophageal eosinophilia is significantly less common in children with H. Pylori infection. Further studies to clarify whether this observation is due to a protective role of H. Pylori are needed.
GASTROENTEROLOGY: Inflammatory bowel disease

G-eP-044

Phenotypic features and clinical outcomes of pediatric inflammatory bowel disease patients with arthritis

Osnat Nir\(^1\), Firas Rinawi\(^2\), Raanan Shamir\(^3\), Assa Amit\(^4\)

\(^1\)Tel Aviv University, The Sackler School of Medicine, Tel Aviv, Israel
\(^2\)Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach-Tikva, Israel
\(^3\)Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
\(^4\)Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel

Objectives and study: Inflammatory bowel diseases (IBD) are associated with extra-intestinal manifestations including arthritis. Peripheral arthritis occurs in approximately 10-20\% of CD and 5-10\% of UC patients, respectively whereas axial arthritis occurs in approximately 3-5\% of IBD patients. Despite the fact that arthritis is a known extra-intestinal manifestation of IBD, the natural history and clinical outcomes of this phenotype are not yet clearly described.

Methods: The medical records of 430 pediatric onset IBD patients diagnosed from 2002 to 2015 were reviewed retrospectively. Baseline characteristics included age at onset, gender, severity indices, laboratory data, extra-intestinal manifestations, endoscopic findings and anthropometric measurements. Main outcome measures included time to first flare, hospitalization, surgery and biologic therapy.

Results: Of the 301 crohn's patients [median age 14.1 years, (IQR 12.1-15.8); 126 (42\%) females], 37 (12.3\%) had peripheral or axial arthritis while 44 (14.6\%) had arthralgia, at diagnosis. Arthritis and arthralgia were more common in females (p=0.028). Patients with arthritis demonstrated higher rates of anemia (hemoglobin of 10.5 vs. 11.2 gr/dl; p=0.014), higher rated of family history of IBD (p=0.003), and significantly lower rates of perianal disease (2.7\% vs. 16.9\%; p=0.013). There were neither significant differences in other phenotypic features such as disease location/behavior nor in severity indices between groups. Patients with arthritis were more likely to be treated with biologic therapy (HR 2.1, 95\% CI 1.3-3.3; p=0.003) but there were no differences in time to surgery, first flare and hospitalization. During follow-up 22 patients developed arthritis (8.3\%) after a median time of 4.5 years. Arthralgia at diagnosis was a predictor for the development of arthritis (p=0.04).

Of 129 patients with ulcerative colitis [median age 13.7 years (IQR 11-15.8); 57 (44\%) females], 3 (2.3\%) had arthritis and 16 (12.4\%) had arthralgia. Patients with arthralgia had significantly lower albumin (3.7 vs. 4.2gr/dl; p=0.029) and higher CRP (0.86 vs. 0.28 mg/dl; p=0.006) and were more subjected for corticosteroids (p=0.03) and immunomodulators therapies (p=0.003) following diagnosis. Time to colectomy was significantly shorter in patients with arthralgia (HR 2.6, 95\% CI 1.0-7.1; p=0.04). During follow-up 18 patients developed arthritis (15.5\%) after a median time of 4 years. Arthralgia at diagnosis was a significant predictor for the development of arthritis (p<0.001).

Conclusion: Pediatric IBD patients with arthritis have distinct phenotypic features including lower rate of perianal crohn's disease. Although not defined as an extra-intestinal manifestation arthralgia at diagnosis appears as a predictor for colectomy in ulcerative colitis and as a significant risk factor for the development of arthritis during follow-up.
Characterisation and classification of paediatric inflammatory bowel disease through application of machine learning

James Ashton¹, Enrico Mossotto², Tracy Coelho³, RM Beattie¹, Ben MacArthur³, Sarah Ennis⁴

¹Southampton Children's Hospital, Paediatric Gastroenterology, Southampton, United Kingdom
²University of Southampton, Department of Human Genetics and Genomic Medicine, Southampton, United Kingdom
³University of Southampton, Institute for Life Sciences, Southampton, United Kingdom
⁴University of Southampton, Department of Human Genetics and Genomic Medicine, Southampton, United Kingdom

Objectives and study: Management of paediatric inflammatory bowel disease (PIBD) is influenced by disease type, severity and extent although this is not always straightforward to determine. This study aimed to develop and utilise a machine learning (ML) model to classify disease derived from PIBD endoscopic and histological data.

Design: Data underwent principal component analysis (PCA), multidimensional scaling (MS) and hierarchical clustering were applied as unsupervised algorithms. Support vector machines, recursive feature elimination and cross-validation as supervised algorithms.

Results: 239 patients (age <18 years) were included; 143 with Crohn’s disease (CD), 67 with ulcerative colitis (UC), 29 with inflammatory bowel disease unclassified (IBDU).

PCA and MS revealed overlap of CD/UC with broad clustering but no clear delineation into groups. IBDU was scattered throughout with no clustering. The lack of clusters signifies significant complexity in distinguishing CD, UC and IBDU phenotypes. Hierarchical clustering identified four novel patient subgroups characterised by differing colonic involvement, 1 of these groups was enriched for CD, 1 was enriched for UC.

Three supervised ML models of CD/UC classification were developed and assessed for accuracy utilising endoscopic, histological and combined endoscopic/histological data, see table 1. The combined model was validated on 48 additional independent PIBD patients with CD/UC classification accuracy of 83.3%.

Twenty-nine IBDU patients were analysed using the combined model. They were assigned a relative probability of CD/UC disease type; 17 patients had a probability greater than 80%.

Table:

Table 1 Performance of the three optimised supervised models, * indicates histological features.

<table>
<thead>
<tr>
<th>Input</th>
<th>Accuracy (Area under the curve)</th>
<th>(Number of) Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endoscopy</td>
<td>70.97% (0.78)</td>
<td>(5) Duodenum, Ileum, D-Colon, Rectum, Perianal</td>
</tr>
<tr>
<td>Histology</td>
<td>76.85% (0.82)</td>
<td>(1) Ileum</td>
</tr>
<tr>
<td>Combined (Endoscopy and histology)</td>
<td>82.65% (0.86)</td>
<td>(8) Duodenum, Ileum, D-Colon, Rectum, Perianal, Oesophagus.<em>, Ileum</em>, A-Colon*</td>
</tr>
</tbody>
</table>
**Conclusion:** This study employs a mathematical model of histological and endoscopic IBD data and provides a high classification accuracy. Unsupervised data modelling categorises patients into four novel subgroups, regardless of their CD/UC diagnosis. This study presents a blueprint for clinical data modelling in IBD to assist diagnosis and management.
Thalidomide-induced peripheral neuropathy in children with inflammatory bowel disease

Matteo Bramuzzo1, Gabriele Stocco2, Marcella Montico3, Serena Arrigo4, Angela Calvi5, Paola Lantieri6, Stefano Costa7, Salvatore Pellegrini8, Giuseppe Magazzù9, Jacopo Barp10, Silvia Ghione11, Paolo Lionetti12, Giovanna Zun13, Massimo Fontana13, Teresa Di Chio14, Giuseppe Maggiore15, Marzia Lazzerini16, Marianna Lucato17, Chiara Udina17, Maria Chiara Pellegrini17, Andrea Chicco6, Marco Carrozzi18, Giuliana Decorti17, Alessandro Ventura19, Stefano Martelossi19

1Gastroenterology and Nutrition Unit Institute for Maternal and Child Health, Ircss “burlo Garofalo,” Trieste, Italy
2University of Trieste, Department of Life Sciences, Trieste, Italy
3Institute for Maternal and Child Health Ircss “Burlo Garofalo”, Trieste, Italy
4Gaslini Children Hospital, Pediatric Gastroenterology and Endoscopy Unit, Genoa, Italy
5Institute “giannina Gaslini”, Paediatric Gastroenterology Unit, Genoa, Italy
6Institute “giannina Gaslini”, Neuropsychiatry Unit, Genoa, Italy
7University of Messina, Paediatric Gastroenterology and Cystic Fibrosis Unit, Messina, Italy
8Policlinico Universitario G Martino, Messina, Italy
9University of Messina, Celiac Regional Centre, Pediatric Gastroenterology and Cystic Fibrosis Unit, Messina, Italy
10University of Florence, Meyer Children Hospital, Department of Sciences for Woman and Child Health, Florence, Italy
11Meyer Children’s Hospital, Gastroenterology and Nutrition, Florence, Italy
12University of Florence, Meyer Children’s Hospital, Neurofarba Department, Gastroenterology and Nutrition, Firenze, Italy
13Children’s Hospital “v. Buzzi” Milan, Paediatric Department, Milan, Italy
14University of Pisa, Paediatric Gastroenterology and Hepatology, Pisa, Italy
15Department of Medical Science, University of Ferrara, Ferrara, Italy
16Institute for Maternal and Child Health, Ircs “burlo Garofolo”, Clinical Epidemiology and Public Health Research Unit, Trieste, Italy
17University of Trieste, Department of Medical, Surgical and Health Sciences, Trieste, Italy
18Institute for Maternal and Child Health, Ircs “Burlo Garofolo”, Paediatric Neurology, Trieste, Italy
19Institute for Maternal and Child Health, Ircs “Burlo Garofolo”, Paediatric Department, Trieste, Italy

Objectives and study: Thalidomide is effective in inducing and maintaining remission in children with inflammatory bowel disease (IBD) refractory to standard treatments. However long-term thalidomide use may be limited by the development of thalidomide-induced peripheral neuropathy (TPN). Our study aimed to investigate the risk factors and the outcome of TPN in children with IBD.

Methods: Within a retrospective multi-centre cohort study we evaluated prevalence and evolution of TPN in children treated with thalidomide 1.5-2.5 mg/Kg/day and regularly followed-up with clinical and electrophysiological neurological assessment. To detect predisposing factors to TPN, the clinical history of patients who developed TPN and of patients who didn’t was compared. Genotyping of variants in ABCA1 (rs363717), ICAM1 (rs1799969), PPARD (rs2076169), SERPINB2 (rs6103), and SLC12A6 (rs7164902) genes, previously associated with TPN, and in CYP2C19 (rs4244285), which may influence thalidomide conversion to an active metabolite, was performed by TaqMan assays (Thermoscientific).

Results: One hundred forty-two patients were identified: 64% had Crohn’s disease, 35% ulcerative colitis and 1% IBD-unclassified. Mean age at thalidomide start was 14 years. TPN was found in 72.5% of patients: 38.7% had clinical and electrophysiological alterations, 26.8% had exclusive electrophysiological anomalies, 7.0% had exclusive neurological symptoms. Median TPN-free period of treatment was 16.5 months; the percentage of TPN-free patients was 70.0% and 35.6% at 12 and 24 months of treatment respectively. TPN was a sensory neuropathy in 75% and a sensorimotor neuropathy in 17% of cases. Symptoms did not interfere with daily activities. TPN was the cause of drug suspension in 41.8% patients. Clinical symptoms resolved in 89.2% of cases while instrumental alteration persisted in more than half of the patients during a short follow-up. Baseline characteristics and previous medical history were not found to be associated with TPN. The risk of TPN increased
depending on the mean daily dose (50-99 mg/day adjusted-Hazard Ratio 2.62 95%CI 1.31-5.21; 100-149 mg/day adj-HR 6.16 95%CI 20.9-13.06; >150 mg/day adj-HR 9.57 95%CI 2.6-35.2). Single nucleotide polymorphisms in ICAM1 (rs1799969) and SERPINB2 (rs6103) genes were found to be protective against TPN (OR 0.15 95%CI 0.03-0.82 and 0.36 95%CI 0.14-0.88, respectively).

**Conclusion:** TPN developed in more than two thirds of children with IBD but was generally mild and reversible during the follow-up. Cumulative dose was the most relevant risk factor for TPN while variants in genes involved in neuronal inflammation were protective.
NUDT15 and ABCC4, genetic risk factors associated with thiopurine-induced leukopenia in children with Crohn’s disease: a single center study

Sujin Cho¹, Sunghee Lee², Insook Jeong², Seakhee Oh², Kyungmo Kim²

¹Asan Medical Center, Pediatrics, Seoul, Korea, Rep. of South
²Seoul Asan Medical Center, Seoul, Korea, Rep. of South

Objectives and study: Mutations in the TPMT gene are a well-known genetic factor of thiopurine-associated leukopenia in pediatric Crohn’s disease (CD). Recently, new genetic loci were identified to be associated with thiopurine metabolism. Herein, the aim of the study is to investigate the association between thiopurine-induced leukopenia and genetic polymorphisms of new loci in pediatric CD.

Methods: This report included 348 children with CD signed informed consent to genetic analysis in Asan medical center. For 348 subjects of enrolled patients, genotyping for TPMT p.Y240C (rs1142345) and NUDT15 p.R139C (rs116855232) was performed using the TaqMan® genotyping technology and also analyzed novel genotype of ABCC4 c.621+537T>A (rs943288) by GWAS. We retrospectively investigated the using dose (mg/weight) of thiopurines (azathioprine and 6-mercaptopurine) and the onset period of the leukopenia (WBC <4000/µl).

Results: The mean age of the 348 children (237 boys and 111 girls) with CD at the time of diagnosis was 14.86 ± 2.14 years. Among them, 40.6% (n=126) experienced thiopurine-associated leukopenia. The risk allele frequency of TPMT p.Y240C, NUDT15 p.R139C, and ABCC4 c.621+537T>A were 1.14% (n=8/696, 8 heterozygotes), 11.49% (n=80/696, 3 homozygotes and 74 heterozygotes), 35.37% (n=162/458, 24 homozygotes and 114 heterozygotes), respectively. Three children of four with TPMT c.Y240C (P=0.156), 52 of 64 with NUDT15 pR139C (P<0.05), and 68 of 136 with ABCC4 621+537T>A (P<0.05) showed leukopenia during the thiopurine therapy. In a multi-variant analysis, thiopurine-induced leukopenia was significantly associated with NUDT15 p.R139C (P < 0.05, odds ratio (OR)=8.112), ABCC4 c.621+537T>A (P<0.05, OR=3.003), and sex (male) (P < 0.05, OR=2.374).

Conclusion: The variants NUDT15 p.R139C and ABCC4 c.621+537T>A were associated with thiopurine-associated leukopenia rather than the well-known TPMT mutation in Korean children with CD. This report suggests that screening on thiopurine controlling genes may give clinicians a help to set a treatment guideline for pediatric CD patients.
**GASTROENTEROLOGY: Inflammatory bowel disease**

**G-eP-048**

**X-linked inhibitor of apoptosis protein (XIAP) genetic variants in paediatric-onset IBD**

Eileen Crowley¹, Abdul El Kadri², Neil Warner³, S Zhang⁴, J Horowitz⁴, J Staples⁴, J Overton⁴, F Dewey⁴, C Gonzaga-Jaureguí⁴, Anne Griffiths¹, Aleixo Muise¹

¹The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
²Medical College of Wisconsin, Paediatric Gastroenterology, Milwaukee, United States
³Cell Biology, Research Institute, Hospital for Sick Children, Toronto, Canada
⁴Regeneron Center, Regeneron Pharmaceuticals Inc., Tarrytown, Ny 10591, United States

**Objectives and study:** Inflammatory bowel disease (IBD) has a multifactorial aetiology, with complex interactions between genetic and environmental factors. Recent studies have suggested an increasing spectrum of human monogenic diseases that can present with IBD-like intestinal inflammation. Mutations in XIAP result in an X-linked recessive disorder whose phenotype is highly heterogeneous with respect to age of presentation and severity of disease and is poorly understood. Due to X chromosome inactivation heterozygous female carriers can also be symptomatic. Although a severe phenotype with infantile onset disease and predisposition to hemophagocytic lymphohistiocytosis (HLH) or X-linked lymphoproliferative syndrome (XLP) is recognized, one recent study has reported XIAP variants in 4% of male pediatric IBD patients. The aim of this study is to explore the phenotypic characteristics of the XIAP cohort and to establish the XIAP incidence rate within our sequenced cohort.

**Methods:** 1250 individual Hospital for Sick Children pediatric IBD patients have undergone whole exome sequencing in collaboration with the Regeneron Genetics Center. Within the cohort, 39 variants were called across the XIAP gene - 29 of which were high quality, rare (maf <0.01), protein coding variants predicted to be deleterious. 13 of these variants were present in 15 affected patients all of which have been Sanger validated. Case notes were retrospectively reviewed to ascertain phenotypic features of IBD in these 15.

**Results:** Of the 15 patients (80% males), 14 (93%) were diagnosed with IBD. 13 (92%) of these with Crohn’s disease and 1 (7%) with ulcerative colitis. At the time of diagnosis, CD involved small bowel and colon (L3) in 50% children, colon (L2) in 14% and ileum (L1) in 28%. 21% of the children had perianal disease, with a further 21% having extra intestinal manifestations of IBD (erythema nodosum, fevers, large joint arthritis). A further infant was diagnosed with primary HLH and received a bone marrow transplant. This infant did have some gastrointestinal involvement with diffuse damage noted in the colonic mucosa and frequent apoptotic cells. 14% of these children had a first degree relative with IBD. 21% underwent ileocaecal resection with 57% progressing to biologic therapy. As compared to our overall sequenced cohort of males < 15 years (n=357), 9 affected males had a diagnosis of Crohn’s disease (2.5%). Patient samples, monocytes, are now undergoing a functional test to determine tumour necrosis factor (TNF) production of monocytes in response to NOD2 stimulation by muramyl dipeptides (L18-MDP) for the functional diagnosis of XIAP deficiency.

**Conclusion:** Analysis of this large pediatric cohort confirms the highly varied phenotypic spectrum of IBD associated with XIAP mutations. Functional studies may more completely explain the observed variation. Our data quotes a lower incidence rate of XIAP variants of 2.5% compared to that quoted previously in the literature of 4% of male pediatric IBD patients.

**Disclosure of interest:** For all Regeneron Genetics Center authors - S. Zhang, Horowitz J, Staples J, Overton JD, Dewey F, Gonzaga-Jaureguí C

These are full time employees of the Regeneron Genetics Center, Regeneron Pharmaceuticals Inc. and receives stock options as part of compensation.
Early use of therapeutic drug monitoring to individualize infliximab therapy in paediatric IBD: a multicentre prospective cohort study

Eileen Crowley¹, Nicholas Carman⁴, Valerie Arpino¹, Karen Frostit, Amanda Ricciuto², Mary Sherlock³, Jeffrey Critch⁴, David Mack⁵, Eric Benchimol⁶, Kevan Jacobson⁷, Sally Lawrence⁸, Jennifer DeBruyn⁹, Wael El-Matary¹⁰, Anthony Otley¹¹, Hien Huynh¹², Aleixo Muise¹, Peter Church¹, Thomas Walters¹, Anne Griffiths¹

¹The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
²Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
³Mcmaster Children's Hospital, DIV GI, Hamilton, Canada
⁴Janeway Children's Health & Rehabilitation Centre, DIV GI, St John's, Canada
⁵Children's Hospital of Eastern Ontario, DIV GI, Ontario, Canada
⁶Children's Hospital of Eastern Ontario, Ottawa, Canada
⁷BC Children's Hospital, Pediatric Gastroenterology, Vancouver, Canada
⁸B.C. Children's Hospital, Division of Gastroenterology, Vancouver, Canada
⁹Alberta Children's Hospital, DIV GI, Calgary, Canada
¹⁰Children's Hospital Research Institute of Manitoba, DIV GI, Winnipeg, Canada
¹¹Iwk Health Centre / Dalhousie University, Pediatrics, Halifax, Canada
¹²The University of Alberta, Ped GI Nutrition, Edmonton, Canada

Objectives and study: Therapeutic drug monitoring (TDM) during infliximab (ifx) maintenance therapy is regularly used in Canadian IBD centres both to assess loss of response and allow dose optimization, with pre-infusion trough levels in the range of 5-10 ug/ml recommended as targets. Levels achieved at the start of maintenance among pediatric patients are highly variable, and often suboptimal even at week 12. Limited data exist in adults or children concerning the role of TDM and target levels during induction. Within the Canadian Children IBD Network (CIDsCANN), we measured ifx levels during induction, aiming to determine the optimal levels required to achieve target 5-10 ug/ml at the start of maintenance.

Methods: Beginning in May 2016, children initiating ifx at SickKids Hospital and at other centres within the CIDsCANN inception cohort study had trough levels measured by ELISA at the time of the final induction and first maintenance infusions (doses 3 and 4). Induction regimens were at the discretion of the treating physician, but often intensified among patients with severe UC. Influence of patient demographics and baseline clinical disease activity (physician global assessment and wPCDAI or PUCAI) on early trough levels were assessed.

Results: From May to December 2016 at 9 participating sites, 66 children (median age 11.8 years, 53% male, 52% CD, 48% UC/IBD-U) were included. Induction regimen was “standard” (0,2, 6 weeks) in 77% and intensified in 23% (O,1, 4 weeks; all steroid refractory colitis). Table 1 gives characteristics of those receiving standard vs intensified regimens. As shown in Table 1, IFX levels were highly variable in both groups prior to 3rd induction dose. Within the standard induction dosing cohort, the interval between dose 3 and 4 was shortened in 50%. Of those, 41% attained targeted 5-10 dose 4 levels. Despite higher dosing per kg during induction and shorter interval prior to dose 4 in the intensified regimen, IFX levels at start of maintenance were comparable to patients receiving standard induction.
### Table:

<table>
<thead>
<tr>
<th></th>
<th>Standard induction</th>
<th>Intensified induction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Population (n)</td>
<td>51</td>
<td>15</td>
</tr>
<tr>
<td>Gender (% male)</td>
<td>53%</td>
<td>23%</td>
</tr>
<tr>
<td>Age in yrs (median, IQR)</td>
<td>12.0 (7.9-14.3)</td>
<td>9.4 (6.5 – 13.8)</td>
</tr>
<tr>
<td>Type of IBD</td>
<td>60% CD; 40% UC/IBD-U</td>
<td>86% UC/IBD-U; 14% CD</td>
</tr>
<tr>
<td>PGA at first infusion</td>
<td>30% severe; 16% moderate; 38% mild; 16% quiescent</td>
<td>60% severe; 20% moderate; 20% mild</td>
</tr>
<tr>
<td>Mean dose (mg/kg)</td>
<td>6.04mg/kg</td>
<td>7.95 mg/kg</td>
</tr>
<tr>
<td>Induction duration (weeks)</td>
<td>6</td>
<td>4</td>
</tr>
<tr>
<td>Pre-dose 3 level (median, IQR)</td>
<td>16.4ug/mL (10.1-26.7)</td>
<td>16.2ug/mL (IQR 11.9-28.8)</td>
</tr>
<tr>
<td>Pre-dose 4 level (median, IQR)</td>
<td>9.68ug/mL (4.37-15.09)</td>
<td>9.56ug/mL (7.69-19.96)</td>
</tr>
</tbody>
</table>

**Conclusion:** Variability in infliximab exposure is evident during induction. Adjusting dose intervals based on pre 3rd dose induction levels, appears to increase the likelihood of entering maintenance dosing on target. An intensified regimen is necessary for patients with active colitis to achieve comparable post induction levels. The results suggest that the use of TDM during induction to individualize dosing more consistently ensures adequate drug exposure at start of maintenance.
Autoantibodies against glycoprotein 2 isoforms in children and adolescents with inflammatory bowel disease

Martin Laaß1, Nadja Robert2, Lydia Noß1, Gunter Flemming3, Jan de Laffolie4, Dirk Roggenbuck5, Karsten Conrad2

1Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Children’s University Hospital, Dresden, Germany
2Technische Universität Dresden, Institute of Immunology, Dresden, Germany
3University Children’s Hospital Leipzig, Leipzig, Germany
4University Giessen, General Pediatrics and Neonatology, Giessen, Germany
5Faculty Environment and Natural Science, Brandenburg University of Technology, Institute of Biotechnology, Senftenberg, Germany

Objectives and study: Autoantibodies against acinus cells of exocrine pancreas (PAB) are regarded specific for Crohn’s disease (CD) and can be detected by indirect immunofluorescence in one third of the patients with CD. More recently autoantibodies against Glycoprotein 2 (GP2) as the main target of PAB have been detected in CD patients. Anti-GP2 antibodies are associated with a more complicated course of CD in adults. Four different GP2 isoforms with different length and antibody binding sites have been identified so far, but not been explored in serological studies. We aimed to investigate the diagnostic utility of autoantibodies against all four isoforms of GP2 in an exclusively pediatric population for the first time.

Methods: We included 278 children and adolescents with inflammatory bowel disease (IBD) from three children’s university hospitals in Germany: 164 with CD, 114 with ulcerative colitis (UC), 83 disease controls (acute gastrointestinal infection, non-specific gastrointestinal functional disorders) and 219 healthy controls. IBD patients were grouped according to the Paris classification. Sera were tested with ELISA using four different isoforms of GP2 and for anti-\textit{Saccharomyces cervisiae} antibodies, antineutrophil-cytoplasmic antibodies and PAB.

Results: Anti-GP2 antibodies were significantly more prevalent in patients with CD than in UC and controls. We found a sensitivity of 38% (with a specificity of 95%) for anti-GP2 IgG against isoform 4 in CD. Only 5.3% of our children with UC and only 1.8 % of our 218 controls without gastrointestinal symptoms were positive for anti-GP2 isoform 4 IgG antibodies. Anti-GP2 IgA against isoform 1 and anti-GP2 IgG against isoform 4 possessed the best diagnostic values for identification of CD. For the differentiation of CD from UC anti-GP2 IgG against isoforms 3 and 4 were most accurate markers. Anti-GP2 antibodies were associated with a more complicated disease behavior and bowel surgery in CD. Antibodies against GP2 isoform 4 IgG were positive in 50.0% (32/64) of CD patients with stenosis, fistula or both (B2, B3, B2+B3) in contrast to 27.0% (27/100) of CD patients with B1 (p = 0.0047). Patients with perianal fistulae compared with patients without showed significantly higher titers for IgA antibodies against isoform 1 and 2 (p=0.0279 and p=0.0102 respectively).

In a group of 47 CD patients we calculated Paediatric Crohn’s Disease Activity and measured titers of anti-GP2 at ≥ two different time-points. In these patients anti-GP2 IgG against isoform 4 proved to be a stable marker over time independent of disease activity.

Conclusion: Anti-GP2 antibodies are specific markers for pediatric CD. This biomarker can potentially identify patients with risk for more complicated disease may help pediatric gastroenterologist in their decisions for an early and aggressive treatment. It would be advisable to include a distinct combination of serological markers in prospective interventional studies.
Objectives and study: Due to the underlying disease, malnutrition status, immunosuppressive and biological therapies, the prevention of vaccine preventable diseases (VPD) in children with inflammatory bowel disease (IBD) is an increasingly recognised issue. In order to give specific recommendations, an ESPGHAN commentary on the risk of infection and prevention in paediatric patients with IBD was published in June 2012 (1). The aims of this study were to describe the compliance with ESPGHAN recommendations for vaccination and immunization status in IBD children and to evaluate differences among patients diagnosed before and after June 2012.

Methods: This retrospective, multicentre study included 12 pediatric IBD referral centres. Each center was asked to retrospectively collect the following data from children with a diagnosis of IBD before and after June 2012: demographic details, diagnosis characteristics, therapies, vaccinations and immunization status at diagnosis and at the start of immunosuppressants (IM) and biologics, reasons for incomplete immunization and decision making on IM and biologics.

Results: Three-hundred-ninety-four IBD children [M/F: 224/170; Median age at enrolment: 15 years; Crohn’s Disease (CD): 218; Ulcerative Colitis (UC): 164; Inflammatory Bowel Disease Unclassified (IBD-U): 12] were enrolled between May and November 2016. Among these, 50.2% and 48.8% were respectively diagnosed before and after June 2012. At diagnosis, the percentages of completion for single vaccination were: Diphtheria (99%), Tetanus (99%), Poliomyelitis (99%), Hepatitis B (99%), Pertussis (89%), Haemophilus Influenzae (69.3%), Pneumococcus (17.3%) Meningococcus C (23.9%), Measles (86%), Mumps (79.4%), Rubella (79.4%), Chickenpox (18.4%), HPV (4.1%) and Rotavirus (2%). Complete immunisation, according to the ESPGHAN commentary, was reported in 36% of the children. Among children with incomplete immunisation, before starting IM therapy, were recommended in 54.7% patients. In the remaining children, the reasons for not vaccinating were: need for immediate IM therapies (31.3%), parental refuse (8.4%), vaccination costs (3.4%) and other (56.9%). Two-hundred-fifteen (54.4%) out of 394 children started IM [Azathioprine: 204 (94.8%), Methotrexate: 9 (4.1%), other: 0.9%]. Among the children who started
AZA, EBV status was only checked in 70 patients (34.3%), with 29 (41.4%) resulting EBV immunised and 41 EBV naive (58.6%). Biologics was started in 154 (39%) children [Infliximab: 79.8%, Adalimumab: 20.1%]. Tuberculosis screening before starting biologics was practised in 145/154 patients (94.1%) with different methods: Tuberculin Skin Test (38.6%), Quantiferon TB Gold (65.5%), T-SPOT TB (0.6%) and chest radiography (71%). Only 117/394 (29.6%) patients yearly practice influenza vaccination. No significant differences were identified between patients diagnosed before and after 2012 in all the analysed variables.

**Conclusion:** This study suggests a poor compliance with the ESPGHAN recommendations, highlighting the need of new strategies to deal with VPD in IBD children.

**Disclosure of interest:** Annamaria Staiano served as investigator and member of advisory board for the following companies: D.M.G, Valeas, Angelini, Miltè, Danone, Nestlé, Sucampo, Menarini. Erasmo Miele served as speaker, as investigator and member of advisory board for the following companies: Abbvie, Angelini, Bioprojet, Ferring, Menarini, Milte, Valeas. The remaining authors have no conflict of interest to declare.
GASTROENTEROLOGY: Inflammatory bowel disease

G-eP-052

Infliximab induced psoriasis in a cohort of children with inflammatory bowel disease: a 12 years follow up study

Christine Martinez-Vinson¹, Olivier Courbette², camille aupiais³, Jerome Viala⁴, Jean-Pierre Hugot¹

¹Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris., Pediatric Gastroenterology Department, Paris, France
²Hopital Robert Debré, Service des Maladies Respiratoires et Digestives de L'enfant, Paris, France
³Hopital Robert Debré, Service de Biostatistique, Paris, France
⁴Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris., Departments of Pediatric Digestive and Respiratory Diseases, Paris, France

Objectives and study: In adult Inflammatory bowel disease (IBD), skin adverse reactions have an estimated prevalence of 1.6 to 22%. This side effect occurs more frequently in patients treated with infliximab (IFX) for IBD. Datas in the pediatric population are lacking so far.

Methods: All patients aged 2 to 18 years, with Crohn’s disease (CD) or Ulcerative colitis (UC) and treated for the first time by IFX between January 2002 and March 2014, were considered for inclusion in this monocentric retrospective study.

Results:

Baseline Patients:

115 patients were treated with IFX for CD and 23 for UC. IFX treatment was initiated at the age of 14, about 2 years after diagnosis. The indication for treatment was in 61.6 % (n = 85) resistance to conventional therapy, in 26.8 % (n = 37) a perianal fistulizing disease and in 11.6 % (n = 16) a severe colitis. At the first injection, the median PCDAI was 35 (25; 45) for CD and the median PUCAI 35 (25; 45) for UC. The duration of treatment with IFX ranged from 45 days to 8 years and median was 23.9 months (11.6 ; 36.5).

Psoriasis:

20 patients (14% of the cohort) had an IFX-induced psoriasis. 70% of them (n = 14) of patients were in remission when the psoriasis was diagnosed. Psoriasis was diagnosed at the 8th injection (6; 15), though 355 (239; 532) days after the start of biotherapy. 20% of patients had a combo therapy: 50% of them were treated by 6-mercaptopurine, 25% by azathioprine and 25% by methotrexate. The median IFX trough levels (TRI) when psoriasis occured was 4.7 mcg / mL (1.8; 9.6) and 4.1 mcg / mL (2.1, 8.8) at the previous visit. Median Antibodies to IFX (ATI) rate was 0%. All were supported by local treatments. No patients discontinued biotherapy following the psoriasis. Personal or family history of psoriasis, and the smoking status have not been collected. We compared the population of patients with psoriasis (n = 20) and without psoriasis (n = 127) with an univariate model. All children in the psoriasis group were followed for a CD. There was more perineal location of CD in psoriasis group with a significant difference (p = 0.033).

Conclusion: 14% of our IBD patients treated with IFX developed psoriasis during follow-up. All were CD, more frequently it occurred for CD with perineal lesions, at the 8th injection in median, with no ATI.
Mortality in childhood-onset inflammatory bowel disease - a population-based cohort study spanning 50 years

Ola Olen¹, Johan Askling¹, Michael Sachs², Paolo Frumento², Martin Neovius¹, Karin E Smedby¹, Anders Ekbom¹, Petter Malmborg³, Jonas F Ludvigsson⁴

¹Karolinska Institutet, Department of Medicine Solna, Clinical Epidemiology Unit, Stockholm, Sweden
²Karolinska Institutet, Institute of Environmental Medicine, Stockholm, Sweden
³Sachsska Children’s Hospital, Department of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden
⁴Karolinska Institutet, Department of Medical Epidemiology and Biostatistics, Stockholm, Sweden

Objectives and study: Recent data suggest that adults with inflammatory bowel disease (IBD) are at no or only a slightly increased risk of death. A recent multi-national review identified more than 30 deaths in children with IBD predominantly due to infectious disease and cancer, but few studies have calculated absolute or relative risks for overall or cause-specific mortality in childhood-onset IBD.

Methods: In a nationwide cohort study, we estimated Hazard Ratios (HRs) through Cox regression for overall and cause-specific mortality in children diagnosed with IBD <18 years of age (n=9359) according to the Swedish National Patient Register 1964-2014. Separate HRs were estimated in patients with ulcerative colitis (UC; n=3364), Crohn’s disease (CD; n=3046) and in patients with a shift between UC/CD over time or indeterminate colitis (IBD-U; n=2949). Reference individuals matched for sex, age, calendar year and place of residence were drawn from the Swedish Total Population Register (n=92,344).

Results: During 136,902 person-years of follow-up, there were 291 deaths (213/100,000 person-years) among the IBD patients compared to 928 deaths among matched reference individuals (68/100,000 person-years). The corresponding adjusted HR was 3.18 (95%CI=2.78-3.62). HRs were highest in UC (4.71; 95%CI=3.87-5.71) with a two-fold increased mortality in CD (2.29; 95%CI=1.74-2.97) and IBD-U (2.45; 95%CI=1.90-3.13). The excess mortality remained statistically significant after >5 years of follow-up after initial IBD diagnosis (HR=3.30; 95%CI=2.86-3.80). The median age at end of follow-up in the main analyses was 27 years (interquartile range 21-38). Restricting our follow-up until the 18th birthday, there were 27 deaths among IBD patients corresponding to a 4.98-fold increased risk of death (95%CI=3.09-7.82), but a very small absolute risk. Mortality in childhood-onset IBD is difficult to compare over different time-periods, because of the obvious differences in age at end of follow-up. Mortality before the 18th birthday was however not significantly different when comparing the time-periods 1964-2001 and 2002-2014 (HR=5.49; 95%CI=2.91-9.96 and HR=4.40; 95%CI=2.08-8.73 respectively). The most common cause of death among IBD-patients was malignancy (131/291 deaths).

Conclusion: Children with IBD are at increased risk of death, both during childhood and later in life. However, the risk increase in absolute terms is small.
GASTROENTEROLOGY: Inflammatory bowel disease

G-eP-054

A prospective audit of biosimilar Infliximab use in paediatric IBD: no change in clinical effectiveness but an opportunity for significant cost savings!

Lisa Richmond1, Michelle L Wilson2, Lee Curtis3, Vikki Garrick1, Pamela Rogers4, Paul Henderson4, Rachel Taylor3, Richard Hansen1, David Wilson5, Richard Russell1

1Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
2University of Edinburgh, Child Life and Health, Edinburgh, United Kingdom
3Royal Hospital for Children, Gastroenterology, Glasgow, United Kingdom
4Royal Hospital for Sick Children, Paediatric Gastroenterology, Edinburgh, United Kingdom
5University of Edinburgh, Department of Pediatric Gastroenterology, Child Life and Health, Edinburgh, United Kingdom

Objectives and study: Biosimilar Infliximabs were licensed for use in paediatric inflammatory bowel disease in early 2015. A prospective safety and efficacy audit of biosimilar Infliximab (Remsima) was carried out in two Paediatric Gastroenterology networks between 2015 and 2016.

Methods: Prospective clinical data was collected from laboratory reports, electronic patient records and case notes of patients starting a biosimilar, IFX (Remsima) for the first time. The weighted Paediatric Crohn's Disease Activity Index (wPCDAI) and Paediatric Ulcerative Colitis Activity Index (PUCAI) were used to document disease activity at initiation and follow up. For analysis, calprotectin samples and C-Reactive Protein (CRP) values were limited to maximum and minimum assay values respectively. Costings for biosimilar and originator IFX were obtained from National Procurement Scotland. The statistics were calculated through Microsoft Excel and p values were recorded using the Mann-Whitney U test.

Results: 40 consecutive patients (60% male) commenced Remsima, equating to 190 infusions in total. 29 patients had Crohn's disease (CD) and 11 ulcerative colitis (UC)/inflammatory bowel disease unclassified (IBDU). The median age (IQR) at diagnosis was 12.7 yrs (10, 14) and 13.7 yrs (13, 16) at biosimilar IFX initiation.

The primary reasons for treatment in CD were: active luminal 76% (22/29), perianal – 14% (4/29) and other – 10% (3/29). For IBDU/UC: chronic refractory Disease – 64% (7/11) and acute severe colitis – 36% (4/11). 95% (38/40) of patients were on co-immunomodulator therapy and all were given IV hydrocortisone pre dosing. At initiation 43 % (17/40) were also on oral Prednisolone. Biosimilar IFX was associated with a significant clinical and biochemical improvement in CD post induction (see table).

1 patient had an acute Infusion reaction (AIR), an AIR per infusion rate of 1/190 (0.5%) and AIR per patient 1/40 (2.5%). Immediately after the 2nd Remsima infusion began, the patients face became flushed and throat felt tight. The infusion was discontinued and therapy changed. Infliximab levels were recorded as 25.9 mg/L with strongly positive antibodies.

The average cost saving per vial during this period was €150 compared to originator Infliximab, so we estimate a cost saving of around €57,000 during the study period.

Table:
## Clinical Data

<table>
<thead>
<tr>
<th></th>
<th>At initiation</th>
<th>At 12 week review</th>
<th>Comparative p value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ESR - Median (IQR)</strong></td>
<td>6 (N=40)</td>
<td>5 (N=26)</td>
<td>P=0.0009</td>
</tr>
<tr>
<td><strong>CRP- Median (IQR)</strong></td>
<td>5.5 (N=40)</td>
<td>1 (N=27)</td>
<td>P=0.0004</td>
</tr>
<tr>
<td><strong>Albumin - Median (IQR)</strong></td>
<td>35 (N=40)</td>
<td>38 (N=27)</td>
<td>P= 0.002</td>
</tr>
<tr>
<td><strong>Calprotectin- Median (IQR)</strong></td>
<td>840 (N=34)</td>
<td>250 (N=17)</td>
<td>P=0.008</td>
</tr>
<tr>
<td><strong>wPCDAI- Median (IQR)</strong></td>
<td>27.5 (N=29)</td>
<td>5 (N=21)</td>
<td>P = 0.002</td>
</tr>
<tr>
<td><strong>PUCAI- Median (IQR)</strong></td>
<td>45 (N=11)</td>
<td>23.8 (N=6)</td>
<td>P = 0.4</td>
</tr>
</tbody>
</table>

### Disease Classification (Crohn’s) % (n/N)
- Remission – 28% (8/29)
- Mild – 31% (9/29)
- Moderate – 28% (8/29)
- Severe – 13% (4/29)
- Remission – 67% (14/21)
- Mild – 28% (6/21)
- Moderate – 0% (0/21)
- Severe – 5% (1/21)

### Conclusion:
We have found that biosimilar IFX is as safe and effective as originator IFX, using our own regional and comparative national audit data. There are also associated significant cost savings. This baseline data is now enabling us to switch patients from originator to biosimilar IFX in our region, adopting the same prospective methodology to monitor effectiveness, safety and cost.

### Disclosure of interest:
- David Wilson - conflict with - MSD - Financial support for research, Abbvie - Lecture fees and Takeda - Consultancy
- Richard Russell - speaker’s fees, travel support, and participated in medical board meetings with Abbvie, NAPP and, Nestle.
- Richard Hansen - conflict with MSD - speakers fees
- Paul Henderson - Lecture fees from Falk
The natural history of pediatric onset IBD-unclassified and prediction of Crohn’s disease reclassification: a 27-year study

Firas Rinawi, Assa Amit, Rami Eliakim, Yael Mozer – Glassberg, Vered Nachmias Friedler, Yaron Niv, Yoram Rosenbach, Ari Silbermintz, Noam Zevit, Raanan Shamir

1Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach - Tikva, Israel
2Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel
3Sheba Medical Center -Tel Hashomer, Department of Gastroenterology, Tel Aviv, Israel
4Rabin Medical Center, Department of Gastroenterology, Petach Tikva, Israel
5Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Petach-Tikva, Israel

Objectives and study: A definitive diagnosis of Crohn's disease (CD) or ulcerative colitis (UC) in patients who were initially diagnosed as inflammatory bowel disease-unclassified (IBDU) remains challenging. Our aims were to describe the natural history of pediatric-onset IBDU patients during prolonged period of follow up and to identify associated predictors for CD reclassification among them.

Methods: In this retrospective single center study, out of 723 patients with pediatric onset IBD, we identified 53 patients (7.3%) diagnosed with IBDU at the Schneider Children’s Medical Center of Israel between 1986 and 2013. Potential predictors for CD reclassification including age at diagnosis, gender, clinical manifestations, disease extent, and laboratory findings were assessed.

Results: The median follow-up was 6.8 (± 6.7) years. Reclassification to CD was observed in 24/53 (45 %) of patients. The median interval from diagnosis to CD reclassification was 9.4 years. In 58% of these patients CD reclassification occurred within 5 years from diagnosis. Multivariate Cox models showed that familial history of CD and hypoalbuminemia at diagnosis were significantly associated with CD reclassification (HR 11.3, P = 0.02 and HR 5.3, P =0.03 respectively). All other assessed clinical, laboratory and endoscopic parameters did not serve as predictors for CD reclassification later on.

Conclusion: In our cohort, a substantial high proportion of pediatric onset IBDU patients were later rediagnosed as CD. Only a family history of CD and hypoalbuminemia could predict reclassification among IBDU patients.
Choice of corticosteroids or exclusive enteral nutrition as the first induction of remission therapy does not affect disease behaviour within two years of diagnosis

Malgorzata Sladek1, Rotem Sigall Boneh2, Gábor Veres3, Seamus Hussey4, Annamaria Staiano5, Federica Nuti6, Paolo Lionetti7, Sibylle Koletzko8, Noa Cohen_Dolev9, Arie Levine10

1Jagiellonian University Medical College, Department of Pediatrics, Gastroenterology and Nutrition, Cracow, Poland
2Wolfson Medical Center, Pediatric Gastroenterology and Nutrition Unit, Tel Aviv, Israel
3Semmelweis University, First Department of Pediatrics, Budapest, Hungary
4National Children’s Research Centre, National Centre for Paediatric Gastroenterology, Dublin, Ireland
5Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
6Fondazione Ircss Ca’ Granda Ospedale Maggiore Policlinico, Service of Pediatric Hepatology and Nutrition, Milano, Italy
7University of Florence, Meyer Children’s Hospital, Neurofarba Department, Gastroenterology and Nutrition, Firenze, Italy
8Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
9The E.Wolfson Medical Center, Pediatric Ibd Research Center, Holon, Israel
10Wolfson Medical Center, Department of Pediatric Gastroenterology, Holon, Israel

Objectives and study: Exclusive enteral nutrition (EEN) has been shown to be equivalent to corticosteroids (CS) for induction of remission in mild to moderate Crohn’s disease (CD) but superior for normal CRP remission and mucosal healing. Our goal was to evaluate if EEN or early immunomodulators (IMM) at diagnosis would reduce risk for early complicated disease in mild to moderate CD.

Methods: The GROWTH CD study (Growth, Relapses and Outcomes With THerapy) was designed to identify associations between treatments and early adverse outcomes by 24 months. Newly diagnosed children were evaluated at baseline, 8, 12, 78 weeks, and complications were recorded at week 104. Remission was defined as PCDAI ≤10 at both week 8 and week 12. Treatment was recorded at each visit. We evaluated intention to treat outcomes among patients receiving CS or EEN and outcomes for patients in remission with these treatments. Patients failing to obtain remission, with complicated behaviour at diagnosis, or requiring biologics by 12 week were excluded from the remission analysis.

Results: Among 152 mild to moderate children treated with either EEN or CS as a first line treatment (mean age 12.9 ±3.1 years), complications was already present in 19.7% (CS 18/91 (19.8%), EEN 12/61 (19.7%)). Baseline median PCDAI was slightly higher among CS (CS 30, EEN 25), p=0.002 while remission rates were higher in EEN treated patients, 51 (56.7%) CS vs. 43 (70%) EEN, p=0.08. Relapse rates for those achieving remission did not differ (20/49 (40.8%) CS vs. 14/42 (33.3%) EEN, p=0.46. Complications by two years developed in 34 (22.4%) and were higher with CS (CS 25/91 (29.7%); EEN 9/61 (15.5%), p=0.051). Early IMM did not affect complications which developed in 28/114 (24.6%) with IMM vs. 6/28 (21.4%) without IMM, p=0.73. Correcting for baseline complications and remission, we analysed 74 uncomplicated patients in CS or EEN induced remission. New complications developed in 6/40 (15%) CS vs. 6/34 (17.6%) EEN, p=0.91.

Conclusion: EEN and CS induce similar remission rates in mild to moderate CD. The choice of CS or EEN as a first line therapy does not seem to affect complicated disease behaviour if clinical remission is achieved. Immunomodulators do not seem to reduce the risk of complications by two years.

Supported by grants from ECCO and the Thrasher Research Fund
The relation of simple endoscopic score in Crohn’s disease and magnetic resonance enterography in children: Report from the ImageKids study

Batia Weiss¹, Dan Turner², Anne Griffiths³, Thomas Walters³, Izabela Herman-Sucharska⁴, Eva Maria Coppenrath⁵, Sudha Anupindi⁶, Alexander Towbin⁷, Jeffrey Hyams⁷, Kathy Obrien⁸, Javier Martin de Carpi⁹, Richard Russell¹⁰, Jared Silverstein¹¹, Michal Amitai¹²

¹Edmond & Lily Safra Children’s Hospital, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Pediatric Gastroenterology and Nutrition, Ramat Gan, Israel
²Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel
³The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
⁴Poland
⁵Munich, Germany
⁶Chop, Philadelphia, United States
⁷Connecticut Children’s Medical Center, Hartford, United States
⁸Halifax, Canada
⁹Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain
¹⁰Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
¹¹Providence, Rhode Island, Providence, United States
¹²Sheba Medical Center, Ramat Gan, Israel

Objectives and study: Failure of ileal intubation during colonoscopy impairs full evaluation of disease extent and severity in pediatric Crohn’s disease (CD). If mucosal healing is a goal of therapy then failure to examine the terminal ileum will be an impediment to full evaluation. It is unknown how to impute data in cases of missing ileal information using MRE and whether imputation is necessary or adequate at all. We therefore aimed to study the association between MRE and simple endoscopic score (SES-CD) patients as an ancillary sub-study of the prospective ImageKids study.

Methods: We used prospectively recorded data of pediatric CD patients collected for the ImageKids study. The patients underwent a baseline ileocolonoscopy followed by an MRE examination within 14 days. Data recorded on baseline included: clinical and disease characteristics, prior therapies, laboratory tests, gastroenterologist global assessment and the weighted Pediatric Crohn’s Disease Activity Index (wPCDAI). SES-CD items were scored at each colonic segment, with a total SES-CD score range of 0-60. Each MRE was scored independently by two experienced radiologists for severity of inflammatory disease activity and degree of stenosis based on a 100mm visual analogue scales (VAS) for each bowel section and globally for the entire bowel. The agreement between SES-CD and MRE was assessed for the ileocolon, and separately for each intestinal segment.

Results: A total of 240 children (age 11.5±3.3 years, with disease duration of 2.8±2.6 years, median 2.2 years, IQR 3.9) have been enrolled at 21 paediatric IBD international centres. In 43 children (18%) the ileum was not intubated during colonoscopy, of which 38 (88%) reached the right colon. In the entire cohort, the highest SES-CD scores was in the terminal ileum (3.6±3.7), followed by the right colon (2.2±2.8). The agreement between SES-CD < 3 and MRE-VAS <20mm was 69% in the terminal ileum (k=0.393, p<0.001), 70% in the right colon (k=0.293, p<0.001), 74% in the transverse colon (k=0.21 p<0.001), 74% in left colon (k=0.372, p<0.001) and 77% in the rectum (k=0.389, p<0.001). The MRE-VAS score for ileal damage was significantly higher in patients without ileal intubation (14.8 vs. 6.5mm; P=0.027). In 16 /43 patients without ileal intubation, the SES-CD was <3 in all colonic segments. The MRE-VAS of inflammation was 21.9±28.7 mm, MRE-VAS of stenosis 12.56±23.9 mm, and MRE-VAS of damage 9±16 mm in those patients.

Conclusion: In this international prospective multicentre IBD study the ileal intubation rate was 82% in pediatric CD. There is moderate agreement between SES-CD and MRE of the terminal ileum in children with CD. Patients in whom the ileum cannot be intubated, have a higher SES-CD of the right
colon and a higher score of ileal damage, suggesting that inability to reach the ileum in children with CD reflects a more severe disease of the ileum and right colon. In addition, some patients with a normal colonic examination and no ileal intubation may still have inflammatory and stenotic disease of the ileum. Therefore, when the ileum is not intubated, ignoring the ileal SESCD score or imputing the score of ‘0’ may bias the total score. MRE could provide an important supplementary outcome measure to colonoscopy in pediatric CD.
Individualised infliximab treatment guided by patient-managed eHealth in children and adolescents with IBD

Katrine Carlsen¹, Anders Paerregaard², Gunnar Houen³, Christian Jakobsen¹, Thomas Kallemose⁴, Lene Buhl Riis⁵, Pia Munkholm⁶, Anne Vibeke Wewer¹

¹Hvidovre Hospital, Department of Paediatrics, Hvidovre, Denmark
²Hvidovre University Hospital, Department of Paediatrics, and Genius Group, Copenhagen, Denmark
³Statens Serum Institut, København S, Denmark
⁴Hvidovre Hospital, Orthopaedic Surgery Department, Hvidovre, Denmark
⁵Herlev Hospital, Department of Pathology, Herlev, Denmark
⁶North Zealand Hospital, Department of Gastroenterology, Frederikssund, Denmark

Objectives and study:
The primary aim was to individualise the timing of infliximab (IFX) treatment in children and adolescents with IBD by means of a patient-managed eHealth solution www.young.constant-care.com. Secondary aims were to empower the patient to understand and take responsibility for his/her disease and to record the patients' ability to use and evaluation of the eHealth program.

Methods:
IBD patients, 10-17 years old, in ongoing IFX treatment, were prospectively included in an open label intervention study. Patients used the eHealth homepage www.young.constant-care.com. The disease burden was estimated weekly by a combination of patient-reported symptom score and faecal calprotectin (FC) level starting four weeks after the last infusion. The IFX-infusions were given with 4-12 weeks intervals and the weekly calculated disease burden determined the timing for the next infusion. Treatment intervals and trough levels of IFX concentration and antibodies were compared with a control group (standard IFX treatment). The results of blood analyses were blinded and analysed after the end of the trial.

A questionnaire evaluating patient/parent improvement in disease knowledge, disease management and satisfaction with the eHealth program was obtained after end of participation. eHealth adherence and Health Related Quality of Life (HRQoL) were also evaluated.

Results:
29 patients (10 UC, 19 CD; mean age 14.2 years, SD 2.17) were included in the eHealth group and 21 patients in the control group (4 UC, 15 CD, 1 IBD-unclassified; mean age 14.4 years, SD 3.3). 95 infusions were provided in the eHealth group (mean interval 9.5 weeks, SD 2.3), and 105 infusions were provided in the control group (mean interval 6.9 weeks; SD 1.4). A significant difference between treatment intervals was found (t-test: mean difference -2.56; CI95% -3.09:-2.03; p=<0.0001). Treatment intervals pr. patient altered during the eHealth participation.

IFX doses (mg/kg) per infusion did not differ between the two groups during the study (mixed effect model: estimate -0.01; CI 95% -0.10:0.08; P-value 0.81). The number of patients developing antibodies against IFX was not significant different comparing the eHealth (5 patients) and control group (2 patients) (Wilcoxon sum rank test: X², df=1, p-value=0.10).

The overall adherence to the eHealth program was 74% regarding the electronic entries of symptoms (827 out of 1123 expected) and 72% regarding FC samples (804 out of 1123 scheduled). Adherence decreased from the first to tenth treatment during the study from 86% (entries) and 80 % (FC) to 61% (entries and FC). Patient’s HRQoL did not differ between start and end of participation (mean [SD]: first score: 150 [15.6], last score 148 [18.0], t-test p-value=0.63).

None of the patients or parents felt unsafe using the eHealth program. 80 % of the patients felt they had achieved increased control of their disease and 63% had achieved better understanding and knowledge about her/his disease. 73 % of the parents experienced that their child had achieved a
better understanding and knowledge of the disease and 86% had achieved a better understanding of their child disease.

**Conclusion:**
Self-managed eHealth facilitated individualized timing of IFX treatments within treatment intervals of 4-12 weeks. Patient’s eHealth performance was acceptable. Both patients and parents obtained better knowledge and understanding of the disease course.
Urinary I-FABP is a suitable biomarker for early diagnostics of necrotizing enterocolitis

Stepan Coufal¹, Alena Kokešová², Helena Tlaskalova-Hogenova¹, Michal Rygi², Jiri Snajdauf², Miloslav Kverka¹

¹Institute of Microbiology of the Czech Academy of Sciences, V.V.I., Laboratory of Cellular and Molecular Immunology, Prague, Czech Republic
²2nd Faculty of Medicine, Charles University in Prague and Motol University Hospital, Department of Pediatric Surgery, Prague, Czech Republic

Objectives and study: Necrotizing enterocolitis (NEC) is a severe disease of the gastrointestinal tract (GIT) affecting mainly preterm neonates and neonates after surgery for congenital malformation of GIT. Current NEC diagnostics does not allow to timely distinguish NEC from other GIT disorders or sepsis. Since intestinal-fatty acid binding protein (I-FABP) reflects the rate of gut epithelium damage, we tested its suitability for early diagnostics of spontaneous and surgery-related NEC.

Methods: We included 42 individuals with suspected NEC and 12 healthy infants as controls. The urine samples were collected in 6-hour intervals for 48 hours from the moment of NEC suspicion or after surgery for congenital developmental malformation of GIT. Serum samples were collected at the moment of NEC suspicion and one week later. The I-FABP levels were determined with ELISA.

Results: Individuals suffering from NEC, including those with surgery related NEC, had significantly higher I-FABP levels than individuals suffering from sepsis or healthy individuals. The I-FABP levels did not differ between individuals suffering from spontaneous or surgery related NEC, both in serum and urine. There was a significant decrease of I-FABP in the course of successful therapy both in serum and urine. By addition of the I-FABP examination to the standard NEC diagnostics we revealed 9 radiologically and ultrasonographically negative patients, who developed NEC later. Analysis of I-FABP in urine has higher sensitivity than its analysis in serum.

Conclusion: I-FABP, especially urinary I-FABP, is suitable biomarker for the early diagnostics of both spontaneous and surgery related NEC.

Acknowledgement: This study was supported by IGA NT/13483 and GAUK no. 326815.
GASTROENTEROLOGY: Basic Science

G-P-002

Intestinal stem cell differentiation after bowel resection is regulated by Notch signaling in a rat model

Dror Berkowitz¹, Yulia Pollak², Igor Sukhotnik³

¹The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Dept of Gastroenterology, Bnai Zion Medical Center, Haifa, Israel
²Technion-Israel Institute of Technology, Haifa, Israel
³Technion - Inst. of Technology, Bnai Zion Medical Center, Haifa, Israel

Objectives and study: Notch signaling promotes differentiation to the absorptive cell lineage rather than to the secretory cell lineage. The objective of this study was to determine the role of Notch signaling in intestinal stem cell differentiation in a rat model of short bowel syndrome (SBS).

Methods: Male Sprague-Dawley rats were randomly assigned to one of two experimental groups of 8 rats each: Sham rats underwent bowel transection and re-anastomosis, SBS- rats underwent 75% small bowel resection. Rats were sacrificed on day 14. Illumina’s Digital Gene Expression (DGE) analysis was used to determine Notch signaling gene expression profiling. Notch-related gene and protein expression were determined using Real Time PCR, Western blotting and immunohistochemistry.

Results: From 7 investigated Notch-related (by DGE analysis) genes 6 genes were up-regulated in SBS vs control animals with a relative change in gene expression level of 20% or more. A significant up-regulation of Notch signaling related genes in resected animals was accompanied by a significant increase in Notch-1 protein levels (Western Blot) and a significant increase in NOTCH-1 and Hes -1 (target gene) positive cells (immunohistochemistry) compared to sham animals. Evaluation of cell differentiation has shown a strong increase in total number of absorptive cells (unchanged secretory cells) compared to control rats.

Conclusion: Two weeks after bowel resection in rats, stimulated Notch signaling directs crypt cells population toward absorptive progenitors.
Absence of intestinal microbiota in early life does not critically affect cholesterol metabolism in mouse offspring

Mirjam Lohuis, Uwe Tietge, Henkjan VERKADE

Dept of Paediatrics, University of Groningen, University Medical Center Groningen, Paediatrics, Groningen, Netherlands

Objectives and study: Microbiota influences the development of the metabolic system and impacts on efficiency of food uptake, diet-induced obesity, cholesterol absorption and excretion and bile acid composition. Antibiotic treatment during early development of mice perturbs the microbiota only transiently, but nevertheless causes long-lasting metabolic changes. We aimed to identify potential mechanisms underlying such long-lasting changes in metabolism. Therefore, we determined the effects of a germ-free versus conventional state during gestation and lactation on cholesterol metabolism in the offspring at adult age.

Methods: We used germ-free C57BL/6J mice and germ-free mice, that were conventionalized 5 weeks before mating for breeding. Male and female offspring of the germ-free group were conventionalized at weaning. At weaning, offspring originating from the germ-free (former GF) and the conventional (CV) group were individually housed. Between age 10 and 30 weeks, mice were challenged with a Western-type diet. We repeatedly measured body weight and performed glucose and insulin tolerance tests (GTT and ITT) before and after the dietary challenge. At age 28-30 weeks, we assessed the following cholesterol homeostasis parameters: dietary cholesterol intake, intestinal absorption, de novo synthesis, biliary secretion rate, and finally, bile composition and fecal excretion rate. We terminated mice at 30 weeks and harvested blood and organs.

Results: Body weight did not differ between CV and Former GF mice for both males and females over their whole lifetime. Similarly, the germ-free condition in early life did not affect either the GTT or the ITT, before and after the dietary challenge with Western-type diet. Interestingly, liver weight, lipoprotein distribution, food intake, fecal neutral sterol excretion, total biliary bile acid concentration, and intestinal cholesterol homeostasis were similar between the former GF and CV group. Former GF mice had a lower bile flow than CV mice (males -19%, p<0.05; females -23%, p<0.01), while lower biliary cholesterol secretion was only observed in Former GF males compared to CV males (-56%, p<0.05). However, a consistent and strong gender effect was found for many of the parameters studied: males had a higher body and liver weight, plasma lipoprotein-cholesterol content, and fecal neutral sterol excretion; females had a higher cholesterol absorption and fecal excretion.

Conclusion: This study demonstrates that complete absence of intestinal bacteria in mother and offspring during gestation and lactation does not influence glucose and cholesterol metabolism of the offspring in adulthood. The present germ-free and previous antibiotic results indicate that, in early life, a germ-free condition or administration of antibiotics differently affect adult metabolism. We hypothesize the presence of a specific microbiota composition mediates these programming effects.
The effect of Bifidobacterium animalis lactis HNO19 (DR 10) supplementation in women during pregnancy and lactation on breast milk DR10, IL-8 and infant’s gut mucosal integrity

Naomi Dewanto1, agus firmansyah2, Ali Sungkar3, Nani Dharmasetiawani4, Saptawati Bardosono5, Sudigdo Sastroasmoro6, siti kresno7, rulina suradi8, Dwi Prasetyo9

1Siloam Hospitals, Pediatric, Jakarta, Indonesia
2Gastrohepatology Division, Department of Child Health, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia
3University of Indonesia, Obstetri and Gynecology, Jakarta, Indonesia
4Budi Kemuliaan Hospital, Pediatric, Jakarta, Indonesia
5Faculty of Medicine University of Indonesia, Department of Clinical Nutrition, Jakarta, Indonesia
6Faculty of Medicine The University of Indonesia / Dr. Ciptomangunkusumo Hospital, Pediatrics, Jakarta, Indonesia
7University of Indonesia, Clinical Pathology, Jakarta, Indonesia
8University of Indonesia, Pediatric, Jakarta, Indonesia
9Dr. Hasan Sadikin General Hospital, Faculty of Medicine Padjadjaran University, Department of Child Health, Bandung, Indonesia

Objectives and study: Newborn infants have intestinal hyperpermeability because their gut mucosa is not fully mature yet. It is known that probiotics helps gut maturity. This study aimed to evaluate the effect of probiotic supplementation in mothers, with regards to probiotic presence and IL-8 concentration in breast milk, infant urine intestinal fatty acid binding protein (IFABP), as well as fecal α-1 anti-trypsin (AAT) and calprotectin at birth (V0) and at infant 3 months of age (V3).

Methods: This randomized, controlled trial was double-blind, two parallel groups, probiotic and placebo with 35 subjects in each group. The study was done at Budi Kemuliaan Hospitals and it’s satellite clinics from December 2014 until December 2015. We used Bifidobacterium animalis lactis HNO19 (commonly known as DR10) as the supplemental probiotic, as it is not a member of the normal flora.

Results: We found DR10 in colostrum at 5 subjects and 7 subjects in V3 breast milk probiotics group, but none in placebo group. Skin swab of DR10 were negative in both group. Median breast milk IL-8 in probiotic group compare to placebo group at V0 and V3 respectively were 2810,1 pg/mL vs 1516,4 pg/mL (p = 0.327) and 173,2 pg/mL vs. 132,7 pg/mL (p = 0.211). Infant urine IFABP 211,7 ng/mL vs. 842,5 ng/mL (p = 0.243) and 25,3 ng/mL vs. 25,1 ng/mL (p = 0.466). Infant stool AAT 136,2 mg/dL vs. 148,1 mg/dL (p = 0.466) and 24 mg/mL vs. 29,72 mg/mL (p = 0.545). Stool calprotectin 746,8 ng/mL vs. 4645,2 ng/mL (p = 0.233) and 378,6 ng/mL vs. 391,3 ng/mL (p = 0.888).

Conclusion: Probiotic DR10 were found in colostrum and 3 month-breast milk of women in the probiotic group, but no DR10 in placebo group. However, breast milk IL-8, the presence of other probiotics, and infant gut mucosal integrity were not significantly different between the two groups.
Presence of eosinophil cells in the lower gastrointestinal tract of healthy individuals

Zoltán Kiss¹, Bálint Tél¹, Péter Mátrai², Nóra Judit Béres¹, Andras Arato¹, Katalin Eszter Müller¹, Áron Cseh¹, Attila Szabo¹, Péter Hegyi³, Katalin Borka⁴, Gábor Veres¹

¹Semmelweis University, First Department of Pediatrics, Budapest, Hungary
²University of Pécs, Institute for Translational Medicine, Pécs, Hungary
³University of Pécs, Mta-Szte Tgrg & University of Szeged, Pécs, Szeged, Hungary
⁴Semmelweis University, Iind Dep. of Pathology, Budapest, Hungary

Objectives and study: Normal density of eosinophils in the gastrointestinal (GI) tract is unknown. Only exception is eosinophilic esophagitis where the cut-off is 15 eosinophil cell/High Power Field (HPF). There are several GI diseases with elevated eosinophil density, however, in the case of the lower gastrointestinal tracts there is no consensus on the normal levels of tissue eosinophil density. Publications vary highly in the value of empiric criteria 6-50 eosinophils/HPF. The aim of the current study was to review the available studies regarding eosinophil cell counts in healthy tissue specimen originating from lower GI fractions, in order to assess the validity of suggested diagnostic cut-offs widely used in clinical practice.

Methods: Pubmed, Scopus and Cochrane databases were screened after complex search criteria constructed with database specific syntaxes. The search was optimised to find all publications holding numeric data, including not only publications with a main topic of healthy tissue characterisation, but studies on various GI diseases where a healthy control group was incorporated.

All studies with numerical tissue eosinophil counts were addressed in detail. Studies using acceptable histologic methods, and reported metadata according to the patients were analysed qualitatively. Measurements for whole cell count with absolute values (mm²) and appropriately published results were incorporated to the quantitative analysis.

Results: The literature search resulted in 1026 publications. 25 relevant studies reported numerical values, 9 (36%) were excluded for incomplete data presentation. 16 studies were considered eligible for the quantitative part of the review. 16 studies were considered eligible for the quantitative part of the review. In summary the overall mean cell number was 6.28 (CI 5.26, 7.29) in the colon, 14.96 (CI 11.06, 18.87) in the small intestine. Subgroup analysis revealed a tendency of elevation in the means from distal to proximal segments of the colon. The means in the rectum, 1.35 (CI 0.62, 2.08) and the sigmoid colon, 2.85 (CI 0.47, 5.24) were under 6 cell/HPF. Subgroup analysis of adult and pediatric patients showed a slight difference of means with overlapping confidence intervals both in the case of the colon (adult: 4.84 (CI 3.53, 6.15), pediatric (7.47 (CI 5.83, 9.11)) and small intestines (adult: 18.38 (CI 12.06, 24.70), pediatric: 9.87 (CI 4.87, 14.87)). The counts of eosinophils in the lamina propria were higher in all segments (difference: 8.16 (CI 5.79, 10.53)) compared to surface epithelium).

Conclusion: The present review and meta-analysis does not support any of the higher cut-off values for tissue eosinophil number. According to the accumulated data, lower cut-off values might only be applicable for the rectum and sigmoid colon. The analysis suggests, that diagnostic cut-off between 20-25 eosinophil/HPF will not yield a high percentage of false positive diagnoses, provided that the sample collection and histologic assessment reaches a considerable homogeneity. It is of high importance in this regard, that empirical or consensus cut-offs should be presented in cell/mm² to avoid methodological bias in scientific publications and diagnostic procedures.
Dynamics of the gut Bifidobacterium microbiota during the first 3 years of life: a quantitative bird’s-eye view

Ravinder Nagpal1, Yuichiro Yamashiro1, Hirokazu Tsuji2, Takuya Takahashi2, Kazunari Kawashima3, Satoru Nagata4, Koji Nomoto2

1Juntendo University Graduate School of Medicine, Probiotics Research Laboratory, Bunkyo-Ku, Japan
2Yakult Central Institute, Kunitachi, Japan
3Gonohashi Obstetrics and Gynecology Hospital, Koto-Ku, Japan
4Tokyo Women’s Medical University, Paediatrics Medicine, Shinjuku, Japan

Objectives and study: Bifidobacteria represent a major element of infant gut microbiota and impart significant beneficial effects on infant’s gut, immune and metabolic health. However, quantitative data on the ontogenesis of gut Bifidobacterium population during early life and factors affecting this colonization is limited. In this milieu, we herein investigated the faecal carriage of eight signature Bifidobacterium species in healthy infants prospectively from first day to 3 years of life, and examined the effect of factors including birth mode, feeding type etc. on their colonization.

Methods: The study included 89 healthy term Japanese infants (vaginally-born: 76; C-section: 13) enrolled at Gonohashi Obstetrics and Gynecology Hospital, Tokyo. Faecal samples (≈1 g) at age 1 day, 7 days, 1, 3 and 6 months, and 3 years were collected into faecal collection tube containing RNAlater and were stored at 4°C until RNA extraction. Bifidobacterial groups and species viz. B. catenulatum group (B. catenulatum and B. pseudocatenulatum), B. longum, B. breve, B. bifidum, B. infantis, B. adolescentis, B. angulatum, and B. dentium were enumerated by using reverse-transcription-quantitative PCR assays targeting bacterial 16S rRNA molecules. The study was approved by the Institutional ethical committee, and prior written informed consent was obtained from the parents.

Results: About 21% of babies carried bifidobacteria at first day of life (mean bacterial count: 6.1±1.8 log10 cells/g faeces); but this count (and prevalence) gradually increased to 7.7±2.3 (62%), 8.3±2.1 (76%), 9.2±1.9 (97%), and 9.6±1.7 cells/g (99%) at age 7 days, 1, 3 and 6 months, respectively. At 3 years, all babies carried bifidobacteria (mean count: 9.7±1.0 cells/g). B. longum, B. breve, B. catenulatum group and B. bifidum were the first colonizers (detected at day 1). B. infantis, B. dentium and B. adolescentis appeared at day 7 whereas B. angulatum was detected only at 3 years. In terms of count as well as prevalence, B. longum, B. breve, and B. catenulatum group remained most dominant bifidobacterial clades throughout the study period. Compared to vaginally-born babies, cesarean-born babies had significantly or insignificantly lower carriage of bifidobacteria from age 7 days to 3 months, with difference being most prominent for B. catenulatum group. Interestingly, within vaginally-born babies, those who started formula-feed as early as first week of life had higher carriage of bifidobacteria during first 6 months as compared to those who were exclusively breast-fed during first 3 months. Further analyses revealed a significant negative correlation of bifidobacteria with enterobacteria and enterococci at one or more time-points.

Conclusion: Our study presents a quantitative bird’s-eye view of the age-related dynamics of typical infant-associated Bifidobacterium species in infant gut during the critical developmental window of life. The data further demonstrate the influence of various factors such as birth mode and feeding type on bifidobacterial colonization during infancy and early childhood, besides displaying the correlation pattern of bifidobacteria with other gut microbes. Given the fundamental role of gut microbes in various aspects of infant’s health, these data should prove to be informative and important for prospective studies on paediatric gastroenterology and nutrition in particular context to the gut microbiota.
**GASTROENTEROLOGY: Basic Science**

G-P-007

Evaluation of physical and emotional comfort of children undergoing electrostimulation of swallowing- initial report

Marta A. Biernacka¹, Ewa Winnicka², Magdalena Rakowska², Julita Borkowska³, Katarzyna Tomaszek³, Piotr Socha⁴

¹Children’s Memorial Health Institute, Department of Health Psychology, Warsaw, Poland
²Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
³Children’s Memorial Health Institute, Department of Neurology and Epileptology, Warsaw, Poland
⁴Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

**Objectives and study:** Dysphagia is a serious problem but often underestimated. Electrostimulation (ES) using VitalStim (VS) is one way of treatment for people with swallowing problems. However, it is mainly used for adults who well tolerate this kind of therapy and consider it as painless. There is a limited amount of research that analyses the use of this method for children. The aim of the study is to show that ES is well tolerated by children and positively assessed by parents.

**Methods:** 6 children with dysphagia (2 girls, 4 boys) aged 8 months to 7 years and their parents (6 women) aged 24 to 37 years participated in the study. Children underwent therapy in 5 day cycles repeated at least every 3 weeks. Every day there were two sessions, 30 minutes each. Each time the current values of electricity level were adjusted as close as possible to the discomfort limit, but not to exceed it. During evaluation of the discomfort limit, the main source of information came from parents. Before and after each treatment course of ES parents completed a questionnaire evaluating quality of life using Kiddy KINDL questionnaire. To assess the parents’ mood we used the adjective checklist UMACL.

**Results:** Statistical analysis showed that the quality of life of patients with dysphagia - in a subjective assessment of parents is significantly lower than reference values in the general population. Comparative analysis between the first and the second measurement of QoL (Kiddy Kindl) showed no statistically significant differences in psycho-physical comfort of patients. There was no statistically significant change in the patients’ parents mood during swallowing therapy using electrostimulation.

**Table:**

<table>
<thead>
<tr>
<th>Kiddy KINDL QoL</th>
<th>1-st assessment mean</th>
<th>2-nd assessment mean</th>
<th>Differences between 1-st and 2-nd assessment mean</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical well-being</td>
<td>38,5417</td>
<td>44,7917</td>
<td>-1,225</td>
<td>p = 0,275</td>
</tr>
<tr>
<td>Emotional well-being</td>
<td>40,6250</td>
<td>42,7083</td>
<td>-1,598</td>
<td>p = 0,576</td>
</tr>
<tr>
<td>Self- esteem</td>
<td>80,0000</td>
<td>77,5000</td>
<td>.431</td>
<td>p = 0,688</td>
</tr>
<tr>
<td>Family</td>
<td>56,2500</td>
<td>47,9167</td>
<td>1,136</td>
<td>p = 0,307</td>
</tr>
<tr>
<td>Friends</td>
<td>57,5000</td>
<td>62,5000</td>
<td>-.784</td>
<td>p = 0,477</td>
</tr>
<tr>
<td>School</td>
<td>78,1250</td>
<td>87,5000</td>
<td>-.600</td>
<td>p = 0,656</td>
</tr>
<tr>
<td>Disease</td>
<td>54,6875</td>
<td>53,1250</td>
<td>.333</td>
<td>p = 0,761</td>
</tr>
</tbody>
</table>
**Conclusion**: The results suggest that patients during swallowing therapy using VS do not experience emotional and physical discomfort. Moreover, parents’ mood remains stable during swallowing therapy. They don’t present a higher level of emotional tension during their children’s therapies. Parents’ emotions are important for maintaining physical and emotional comfort of the child during the treatment.
Hyperuricemia in children with acute gastroenteritis is caused by decreased urate excretion via ABCG2

Tomoyuki Tsunoda, Hirotaka Matsuo, Keiko Ooyama, Masayuki Sakiyama, Tsuyoshi Sogo, Teppei Takada, Aiko Nakashima, Akiyoshi Nakayama, Makoto Kawaguchi, Kenji Wakai, Hiroshi Ooyama, Ryota Hakan, Kimiyoshi Ichida, Ayano Inui, Shin Fujimori, Nariyoshi Shinomiya

Objectives and study: Hyperuricemia is often associated with acute gastroenteritis in children, however the mechanism was unclear. ATP-binding cassette transporter, subfamily G, member 2 (ABCG2) is a high-capacity urate transporter and expresses in both human intestine and kidney. The relationship of ABCG2 gene variants and the degree of its dysfunction has already been demonstrated and is known to cause gout and hyperuricemia, but the importance of intestinal urate excretion was not revealed in humans. The aim of this study is to clarify the physiological roles of intestinal urate excretion via ABCG2, and to investigate the pathophysiological mechanism of hyperuricemia in children with acute gastroenteritis.

Methods: Sixty-seven children with acute gastroenteritis and 106 maintenance hemodialysis patients, whose urate excretion must depend on intestinal excretion via ABCG2, were included in this study. Patients were not on medication for hyperuricemia. Genotyping of ABCG2 dysfunctional variants, Q126X and Q141K was performed in all patients. Based on estimated ABCG2 function for the following analyses, all of the participants were divided into three groups (full function, 3/4 function and ≤ 1/2 function of ABCG2).

Children with acute gastroenteritis were evaluated their degree of dehydration, and their serum uric acid (SUA) levels in acute and recovery period of gastroenteritis. In hemodialysis patients, to clarify the physiological role of intestinal urate excretion via ABCG2, SUA levels were measured just before maintenance hemodialysis.

This study was approved by the institutional ethical committees of institutes, and all procedures were performed in accordance with the Declaration of Helsinki with written informed consent from each participant or guardian.

Results: The mean SUA levels of the acute period of gastroenteritis were significantly higher than those of recovery period (8.8 mg/dl vs. 4.7 mg/dl, P = 2.3 × 10^{-12}). In the acute period, ABCG2 dysfunction significantly elevated SUA (7.5 mg/dl for full function, 9.6 mg/dl for 3/4 function and 10.6 mg/dl for ≤ 1/2 function, P = 6.3 × 10^{-3}), and the degree of dehydration also affected SUA (P = 1.6 × 10^{-3}). However, ABCG2 dysfunction was not associated with the degree of dehydration in the acute period and the significant association between ABCG2 dysfunction and SUA remained after the adjustment for the degree of dehydration (P = 7.8 × 10^{-3}), indicating that the association between ABCG2 dysfunction and SUA was not due to dehydration. Regarding the recovery period, there was a trend for SUA to increase by ABCG2 dysfunction (4.2 mg/dl for full function, 4.9 mg/dl for 3/4 function and 5.4 mg/dl for ≤ 1/2 function) without significance (P = 0.10).
In 106 hemodialysis patients, ABCG2 dysfunction significantly elevated SUA (7.1 mg/dl for full function, 7.9 mg/dl for 3/4 function and 8.4 mg/dl for ≤ 1/2 function, $P = 1.1 \times 10^{-4}$). However, in 106 health examination participants, ABCG2 dysfunction tended to elevate SUA without significance.

**Conclusion:** This study demonstrated the physiological role of intestinal urate excretion via ABCG2 in humans. Hyperuricemia in acute gastroenteritis is caused by decreased urate excretion in addition to dehydration which is generally considered to be a major cause of hyperuricemia. Intestinal inflammation of gastroenteritis can impair the function of intestinal urate excretion of ABCG2, which could be one of the mechanisms for hyperuricemia in acute gastroenteritis patients.

**Disclosure of interest:** Hirotaka Matsuo, Tappei Takada, Kimiyoshi Ichida, Nariyoshi Shinomiya have a patent pending based on the work reported in this paper. Other authors have declared that no competing interests exist.
Interleukin-6 and interleukin-17 gene polymorphism association with susceptibility to celiac disease

Ulas Emre Akbulut¹, Elif SAG², Alperhan Cebi³, Murat Cakir²

¹Kanuni Training and Research Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
²Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
³Karadeniz Technical University Faculty of Medicine, Department of Medical Biology, Trabzon, Turkey

Objectives and study: The aim of this study was to investigate polymorphisms in the genes encoding cytokines interleukin-6 (IL-6) (-572G/C) (rs1800796) and IL-17 (-197A/G) (rs2275913) in patients with celiac disease (CD) antigens DQ2-positive or DQ8-positive.

Methods: We compared the results with healthy controls to determine whether any of the polymorphisms have a role in susceptibility to CD. A total of 84 patients with CD (73 DQ2-positive and 52 DQ8-positive) and 83 healthy controls were enrolled in this study. The IL-6 (-572G/C) and IL-17 (-197A/G) polymorphisms were genotyped by polymerase chain reaction coupled with restriction fragment length polymorphism.

Results: Significant differences for the IL-6 (-572G/C) polymorphism were observed when we compared the following groups: CD with controls (p=0.018, OR: 5.47, 95 %CI: 1.161-25.800); DQ2-positive with controls (p=0.016, OR: 5.69, 95 %CI: 1.189-27.289); DQ8-positive with controls (p=0.005, OR: 7.36, 95 %CI: 1.498-36.195). We did not observe a statistically significant association between IL-17 (-197A/G) polymorphism and CD (P > 0.05).

Conclusion: The results of our study indicated that IL-6 (-572G/C) polymorphism may play a role in susceptibility to CD.
GASTROENTEROLOGY: Coeliac disease

G-P-011

Genetic predisposition to celiac disease and oral health: is there an association? Preliminary results of a large Italian screening in children

Roberta Annibali1, Anil Kumar Verma1, Alessandra Palpacelli1, Giada Delbaldo1, Elisa Franceschini1, Chiara Monachesi1, Marco Mascitti2, Andrea Santarelli2, Tiziana Galeazzi1, Simona Gatti1, Elena Lionetti2, Carlo Catassi1

1Università Politecnica Delle Marche, Department of Pediatrics, Ancona, Italy
2Università Politecnica Delle Marche, Department of Clinical Specialistic and Dental Sciences, Ancona, Italy

Objectives and study: HLA DQ2 and DQ8 are extremely common in the general population, despite their close association with some diseases, particularly celiac disease. This has raised the question whether these genes could be protective towards other common conditions. Some limited data have shown a possible influence of HLA DQ2 towards the development of dental caries. The aim of the study is to assess the prevalence of enamel defects, recurrent oral aphthous lesions and dental caries in a large cohort of age schoolchildren genetically predisposed to celiac disease (CD) in comparison with healthy controls (not predisposed) and children with CD.

Methods: students aged 5-10 years were invited to participate. A rapid, single PCR reaction HLA test (Celiac Gene Screen, Biodiagene Italy) on a single blood drop was used to identify subjects susceptible to CD (both HLA DQ2 and DQ8). In a second step serological tests were performed in HLA positive patients (including serum anti-transglutaminase (TTG), anti-endomisyum (EMA) and anti deamidated gliadin peptides (DGP) antibodies). CD was diagnosed according to the ESPGHAN guidelines. A dental examination was performed in school settings, by the same examiner. For the assessment of caries the DMFT (decayed-missed-filled teeths) and dmft index were used, for permanent and decidual teeths as appropriate. HLA positive (group 1), HLA negative (group 2) and celiac subjects (group 3) were compared.

Results: 1217 children have been enrolled and 1189 have been HLA screened so far (mean age: 8.06 years ± 1.58). Four hundred and sixty-eight patients were HLA positive (40.06 %), of these 362 underwent the serological evaluation. CD autoimmunity was found in 20 patients with 10 receiving a final diagnosis of CD. The overall prevalence of caries was 43.6%, with no difference detected in the 3 groups. The mean dmft was 1.35 ± 2.3, 1.2 ± 2, 0.91 ± 2 in group 1,2 and 3 respectively (p= NS). No statistical difference was found in the prevalence of reported oral aphthosis. The prevalence of enamel defects was similar in the 3 groups (group 1: 13.4%, group 2: 13.1%, group 3: 18%), with no difference in the severity of enamel hypoplasia.

Conclusion: preliminary data show that genes predisposing to CD (HLA DQ2/DQ8) do not seem to be associated with susceptibility to dental caries and other oral pathologies. Neither children with CD did show a particular risk of teeths and oral diseases compared to the other groups. Final results and analysis (multiple logistic regression) will further clarify these associations.
GASTROENTEROLOGY: Coeliac disease

G-P-012

Is Helicobacter pylori chronic infection associated with the severity of coeliac disease?

Efrat Broide¹, Vered Richter¹, Shay Matalon¹, Tzippy Shalem¹

¹The Kamila Gonczarowski Institute of Gastroenterology and Liver Diseases, Assaf Harofeh Medical Center, Tzrifin, Israel

Objectives and study: Various studies reported that lymphocytic gastritis may be associated both with coeliac disease (CD) and Helicobacter pylori (H. pylori) chronic infection. There are controversial reports regarding an inverse relationship between CD and H. pylori infection. As H. pylori may influence the inflammatory and immune response in the gut, we aimed to assess the prevalence of H. pylori infection in children with CD compared to non CD children and to explore a possible correlation between H. pylori infection and severity of CD.

Methods: All children aged 1-18, who were referred to upper endoscopy in Assaf Harofeh Medical Center within a 12 month period, were eligible for this prospective study. Demographic, clinical, endoscopic and histological features were reviewed. Gastric biopsies from the antrum and corpus were taken to investigate the presence of gastritis and H. pylori status by hematoxylin&eosin, Giemsa or immunohistochemistry staining and urease testing. CD was diagnosed according to the latest ESPGHAN criteria (positive serology and some evidence of villous atrophy). Histological severity of CD was assessed by estimation of villous atrophy and intraepithelial lymphocytes (IEL) number per 100 epithelial cells and were compared between children with and without H pylori chronic infection.

Results: Two hundred thirty two children were eligible for the study of them 102 were CD patients. CD patients were significantly younger compared to non CD patients: 7.3y (IQR 4.1-10.7) vs. 13 (IQR 8.8-15.6), p<0.001. The socioeconomic index (SEI) was higher in CD compared to non CD patients (0.54; IQR -0.01-1.17 and 0.15; IQR -0.31-0.7 respectively, p<0.001). Therefore, matching for age gender and SCI was done. Fifty children remained in each group. The mean age of CD patients was 9.08 (IQR 6.15-12.75) and 10 (IQR 5.73-12.89) in non CD patients. SEI was 0.5 (IQR 0.17-0.94) in CD and 0.64 (IQR 0.056-1.26) in non CD patients. The incidence of H. pylori infection was similar between both groups (11% in CD vs 13% in non CD patients). Among CD patients more were of short stature (p=0.013), and less patients had abdominal pain (p=0.043). Presence of chronic H. pylori infection had no impact on severity of CD. Among 102 CD patients with ≤75 IEL per 100 epithelial cells (75%), the HP prevalence was 21.6% compared to 17.6% in those CD patients who had >75 IEL per 100 epithelial cells (non-significant). Out of 32 CD patients with sub-total villous atrophy 23.7% had H. pylori chronic infection vs. 17.2% of 64 patients with total villous atrophy (not significant). Similar results were obtained while both parameters were combined.

Conclusion: Chronic H. pylori infection is not associated with the severity of CD. The protective effect of H. pylori against CD should be explored prospectively in potential celiac patients.
Use of non-invasive methods for monitoring the gluten-free diet adherence in paediatric coeliac disease

Isabel Casas¹, Alba Cebollero Agustí², Joana Carbonell Torremorell³, Silvia Miró⁴, Anna Puiggros Font², Vicente Morales Hidalgo³

¹Institut Catala DE LA Salut, Pediatric Gastroenterology, Barcelona, Spain
²Consorci del Laboratorio Intercomarcal Vilafranca del Penedès, Laboratory, Barcelona, Spain
³Institut Catala DE LA Salut, Pediatric Primary Care, Barcelona, Spain
⁴Consorci del Laboratorio Intercomarcal Vilafranca del Penedès, Laboratory, Barcelona, Spain

Objectives and study: Coeliac disease (CD) is a genetically induced disease in which there is a permanent intolerance to gluten, which causes severe damage to the intestinal mucosa. The only available treatment is a lifelong strict gluten-free diet (GFD). Our aim was to evaluate the measurement of gluten immunogenic peptides (GIP) in stools as a marker of GFD adherence and compare it with traditional methods.

Methods: We performed a prospective study including 24 patients with paediatric CD (<15 years) in a primary care setting. GIP in stool and serological anti-tissue transglutaminase Ig A (tTG), anti-deamidated gliadin peptid Ig A (DGPA) and anti-deamidated gliadin peptid IgG (DGPG) were measured simultaneously. GIP in stool was measured by iVYCheck GIP Stool immunochromatography (iVYDAL). The detection limit of the immunochromatographic strip is 0.3 ug GIP / g feces. The levels of tTG, DGPA, DGPG were determined by the Menarini® chemiluminescence technique with the Zenit RA team.

Results: The median of age was 8.8 years. 54% were girls. 8.3% had detectable GIP levels in stools. Elevated titres of anti-tTG IgA (median: 24.5 U/ml) were found in 17%. Titres of anti-DGPA (median: 16.5 U/ml) and anti-DGPG (median: 42.6 U/ml) were positive in 12.5% respectively. Of the 2 patients GIP- stools positive one had serological markers positive. 83.3% patients with positive serology were GIP-stools negative.

Conclusion: In conclusion we have observed that GIP in stools is a useful marker for detecting transgressions in CD with negative serology. Patients GIP-stools negative with positive serology would indicate adherence to the diet. Although not was target of the study, we observed a great acceptance of parents because it is a non-invasive test.
Health related quality of life: cross-cultural differences

Josefa Barrio Torres¹, Mª Luz Cilleruelo Pascual², Enriqueta Roman Riechmann³, Cristina Fernandez⁴, Luisa Mearin⁵

¹Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
²Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
³Hospital Universitario Puerta Hierro (Majadahonda), Paediatric Gastroenterology Unit, Madrid, Spain
⁴Hospital Universitario Clínico San Carlos, Epidemiology, Madrid, Spain
⁵Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands

Objectives and study: Health Related Quality of Life (HRQOL) has awakened interest among researchers. The first specific questionnaire for celiac children (CDDUX) was created in Holland and has been adapted by research groups in several countries. We previously used this adapted questionnaire and a generic one (the Kidscreen questionnaire) to evaluate QOL in Spanish celiac children.

Our objective is to compare our results with those obtained by other groups using these two questionnaires.

Methods: A systematic PubMed search was conducted in November 2016 for studies of HRQOL in celiac children. Studies that used the Celiac Disease (CD) specific CDDUX and the generic Kidscreen questionnaires, were included. Data related to HRQOL scores were extracted and compared with the results obtained in our study.

Results: CDDUX: We found 3 publications from other groups that used CDDUX (table)

In general, the Spanish children with CD and their parents perceived their HRQOL as similar to the Brazilian but significantly worse than the Argentinian and better than the Dutch.

The Spanish and the Brazilian children perceived their HRQOL as “neutral”, the Argentinian children as “good” and the Dutch children as “bad”.

The Spanish, Brazilian and Argentinian parents perceived their children’s HRQOL as “neutral”, but the Dutch parents perceived it as “bad”.

All the groups showed the best scores in the scale “communication” with the exception of Brazilian parents that scored it as “bad”. The worst scores for all the countries were obtained in the scale “having CD”.

There were only significant differences in appreciation of HRQOL between children and parents in Argentina and the Netherlands.

Kidscreen: There is only a Swedish group that have used Kidscreen⁵. The Swedish children had better scores than the Spanish children in 8 out of 10 dimensions, in the other 2 dimensions the scores were similar between the 2 groups.
Table: HRQOL in celiac children and their parents using CDDUX

<table>
<thead>
<tr>
<th>CDDUX</th>
<th>SPAIN¹</th>
<th>BRAZIL²</th>
<th>HOLLAND³</th>
<th>ARGENTINA⁴</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=214</td>
<td>N=33</td>
<td>N=510</td>
<td>N=193</td>
</tr>
<tr>
<td>Scores</td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>total</td>
<td>Children</td>
<td>55.5</td>
<td>12.7</td>
<td>57.6</td>
</tr>
<tr>
<td></td>
<td>Parents</td>
<td>54.8</td>
<td>12.3</td>
<td>45.4</td>
</tr>
<tr>
<td>Having CD</td>
<td>Children</td>
<td>46.5</td>
<td>13.1</td>
<td>44.0</td>
</tr>
<tr>
<td></td>
<td>Parents</td>
<td>49.8</td>
<td>12.6</td>
<td>45.4</td>
</tr>
<tr>
<td>Communicatio</td>
<td>Children</td>
<td>72.0</td>
<td>16.9</td>
<td>71.3</td>
</tr>
<tr>
<td></td>
<td>Parents</td>
<td>69.6</td>
<td>15.6</td>
<td>38.4**</td>
</tr>
<tr>
<td>Diet</td>
<td>Children</td>
<td>51.7</td>
<td>17.3</td>
<td>57.6</td>
</tr>
<tr>
<td></td>
<td>Parents</td>
<td>50.0</td>
<td>15.7</td>
<td>52.3</td>
</tr>
</tbody>
</table>

(¹)  p<0.05. (**) p<0.01

Conclusion: 1.- There are significant differences in the perception of HRQOL in celiac children among different countries.

2.- These differences could be related to the different awareness and health resources offered to those with CD (for example availability of gluten free products and the differences in the free prescriptions for gluten-free food products). There are intercultural differences that also could affect the perception of QOL.

3.- Further studies are necessary to better identify these differences.

GASTROENTEROLOGY: Coeliac disease

G-P-015

Plasma citrulline levels are a useful marker of mucosal recovery after the starting of a gluten free diet in newly diagnosed coeliac pediatric patients

Elene Larrea¹, Juan Diaz², Santiago Jimenez², Cristina Molinos³, Sara Bueno³, Belen Prieto⁴, Carlos Bousoño⁵

¹Centro de Salud de Tolosa, Pediatrics, Tolosa, Spain
²Hospital Universitario Central de Asturias, Pediatric Gastroenterology and Nutrition, Oviedo, Spain
³Hospital de Cabueñes, Pediatrics, Gijon, Spain
⁴Hospital Universitario Central de Asturias, Biochemistry, Oviedo, Spain

Objectives and study: Citrulline is a nonessential amino acid synthesized by the enterocytes, which has been proposed as a potential marker of intestinal absorptive surface. The aim of this study was to evaluate the usefulness of plasma citrulline levels in children with celiac disease (CD) at diagnosis and as a marker of mucosal recovery after starting a gluten-free diet (GFD).

Methods: A prospective observational study including a total of 38 newly diagnosed celiac patients according to the ESPGHAN 2012 criteria, aged less than 14 years. The plasma levels of citrulline were determined by ion exchange chromatography before the implementation of a GFD and afterwards between the third and the sixth month after starting the GFD. Hemoglobin, ferritin and albumin levels, IgA Anti-tissue transglutaminase (ATTG) and anti-gliadin IgG levels (AG) were determined simultaneously. Statistical analysis: paired t test, Pearson correlation coefficient. A p value < 0.05 was deemed statistically significant.

Results: Twenty patients (14 women) were able to obtain the two study samples. They presented a median age of 6 years (range: 1-13 years). There was a significant increase in mean levels of citrulline after starting the GFD, from 26.1 to 35.9 nmol/ml (p = 0.001). In 17 of the 20 patients (85%) citrulline levels increased after the establishment of the GFD. There was an inverse non significant relationship between ATTG and AG and citrulline levels at diagnosis (pearson correlation coefficient -0.25; p = 0.14 and 0.22 respectively). There was no association between citrulline levels and somatometric variables (weight, height and BMI Z scores) or the nutritional biochemical parameters analyzed.

Conclusion: The establishment of a gluten-free diet in the celiac pediatric patient is followed by an increase in plasma citrulline levels, which could indicate its usefulness as a marker of mucosal recovery in these patients.

Disclosure of interest: The study was funded by a grant of the Instituto de Salud Carlos III (reference number I12/02768)
Objectives and study: Celiac disease (CD) is an autoimmune inflammatory condition. The choroid is the vascular layer of the eye, lying between the retina and sclera. SD OCT is used to acquire high-resolution cross-sectional scans of the retina, choroid and retinal nerve fiber layer and becomes an important tool for diagnosing and managing chorioretinal diseases. Autoimmunity, circulating immune complex in the eye tissue are the possible mechanism of eye involvement. The aim of this study was to assess subfoveal choroidal thickness (CT) celiac patients (adherence to the gluten-free diet (GFD), nonadherence to the GFD), comparing it with age- and gender-matched healthy controls using SD-OCT.

Methods: 42 celiac patients and 42 healthy patients was conducted. Celiac patients were divided into two groups (adherence to GFD and nonadherence to GFD).

Results: Subfoveal CT was thinner in EmA(+) or anti-TG2(+) eyes than EmA(-) or anti-TG2(-) celiac patients but it was not statistically significant. The mean subfoveal CT values in eyes with CD, whose diagnosis time was longer than 60 months were thinner than shorter 60 months. Longer duration of GFD was associated with adherence difficulty and thinner CT (r=-0.15, p=0.34). Adherence GFD was %88.2 for children under 60 months old and %57.1 for children over 60 months old.

Conclusion: In conclusion, in addition to other extraintestinal manifestations of CD, retinal disease may develop CD patients, whose diagnosis time is longer than 60 months, nonadherence to the GFD and antibody positivity. We recommend to evaluate these patients in terms of retinal damage.
Evaluation of psychological situations, quality of life and parental attitudes of children with celiac disease

Güzide Doğan¹, Sermin Yalın Sapmaz², Yeliz Cagan Appak³, Masum Öztürk⁴, Yeşim Yiğit⁵, Beyhan Cengiz Özyurt⁶, Erhun Kasırğa⁷

¹Celal Bayar University School of Medicine, Department of Paediatric Gastroenterology, Manisa, Turkey
²Celal Bayar University School of Medicine, Department of Child and Adolescent Psychiatry, Manisa, Turkey
³Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, İzmir, Turkey
⁴Faculty of Medicine, Celal Bayar University, Department of Child Psychiatry, Manisa, Turkey
⁵Faculty of Medicine, Celal Bayar University, Department of Pediatrics, Manisa, Turkey
⁶Celal Bayar University School of Medicine, Department of Public Health, Manisa, Turkey

Objectives and study: Gluten-free diet negatively affects the quality of life in children with celiac disease (CD) and may cause anxiety and depression in both patients and their parents.

It is aimed to compare psychological symptoms, quality of life perception, depression and anxiety severities, parental attitudes and family activities of celiac patients with the healthy controls.

Methods: Thirty six celiac patients and 36 healthy children and their parents were prospectively evaluated for their quality of life and their psychological status. The sociodemographic data form, the strengths and difficulties questionnaire, Pediatric Quality of Life Inventory (PedsQL), the Family Assessment Scale (FAS), Parent Attitude Research Instrument (PARI), the State-Trait Anxiety Inventory (STAI) (for mothers) and the Beck Depression Inventory (BDI) (for mothers) were questioned.

Results: The mean BDI and STAI scores of parents were found significantly higher in CD group than in the control group. PARI's extreme maternity, rejection of housewife, and pressure and discipline severity were found significantly higher in CD group than in the control group. For PedsQL, all the quality of life subscale scores were found to be lower in patients with CD compared to control group except for physical health total score.

Conclusion: Because child is a social-psychological-biological whole, children with CD should be evaluated together with their family. Parents also under psychopathologic risk, therefore appropriate mental support must be provided. Further studies are needed to evaluate children with CD and their parents on this subject.
**GASTROENTEROLOGY: Coeliac disease**

**G-P-018**

DQ2/DQ8 negative celiac disease children in Spain: data from a prospective national registry

Ester Donat¹, Felix Sanchez Valverde², Enriqueta Román Riechmann³, José Ignacio García Burriel⁴, Isabel Polanco⁵, Francisco Javier Eizaguirre Arocena⁶, Rosaura Leis Trabazo⁷, Honorio Armas Ramos⁸, Salvador García- Calatayud⁹, Rosa Solaguren¹⁰, Patricia Barros García¹¹, Ruth García Romero¹², Luis Oritoza del Castillo¹³, Josefa Barrio¹⁴, Pedro Urruzuno¹⁵, Gemma Castillejo¹⁶, Idoia Hualde Tapia¹⁷, Jose Carlos Salazar Quero¹⁸, Gonzalo Galicia Poblet¹⁹, Cecilia Martinez Costa²⁰, Mª Luz Cilleruelo Pascual³, Carmen Ribes Koninckx²¹  

¹La Fe Universitari i Politecnic Hospital, Pediatric Gastroenterology Unit, Valencia, Spain
²Hospital Virgen del Camino, Pediatric Gastroenterology Unit, Pamplona, Spain
³Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
⁴Complejo Hospitalario Universitario de Vigo (Xeral-Cies), Pediatric Gastroenterology Unit, Vigo, Spain
⁵Hospital Universitario la Pazspa, Pediatric Gastroenterology Unit, Madrid, Spain
⁶Hospital de Donostia, Paediatric Gastroenterology Unit, Donostia-San Sebastian, Spain
⁷Complejo Hospitalario Universitario Santiago, Pediatric Gastroenterology Unit, Santiago de Compostela, Spain
⁸Hospital Universitario de Canarias, Pediatric Gastroenterology Unit, La Laguna (Tenerife), Spain
⁹Hospital Marqués de Valdecilla, Pediatric Gastroenterology Unit, Santander, Spain
¹⁰Hospital Virgen Salud, Pediatric Gastroenterology Unit, Toledo, Spain
¹¹Hospital San Pedro de Alcántara, Pediatric Gastroenterology Unit, Caceres, Spain
¹²Miguel Servet Children's Hospital, Paediatric Gastroenterology and Nutrition Unit, Zaragoza, Spain
¹³Hospital Universitario la Candelaria, Pediatric Gastroenterology Unit, Tenerife, Spain
¹⁴Hospital Universitario de Fuenlabrada, Pediatric Gastroenterology Unit, Madrid, Spain
¹⁵Hospital Universitario Doce de Octubre, Pediatric Gastroenterology Unit, Madrid, Spain
¹⁶Hospital Universitario Sant Joan de Reus, Pediatric Gastroenterology Unit, Reus, Spain
¹⁷Hospital Txagorritxu, Pediatric Gastroenterology Unit, Vitoria, Spain
¹⁸Hospital Virgen del Rocio, Gastroenterology, Hepatology and Nutrition Unit, Sevilla, Spain
¹⁹Hospital Universitario de Guadalajara, Pediatric Gastroenterology Unit, Guadalajara, Spain
²⁰Hospital Clínico Universitario, Pediatric Gastroenterology Unit, Valencia, Spain
²¹La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

Objectives and study: The presence of the HLA-DQA1*05 and HLA-DQB1*02 alleles (encoding HLA-DQ2.5) and/or HLA-DQA1*03 and HLA-DQB1*03:02 (encoding HLA-DQ8) characterizes celiac disease (CD). Testing negative for both HLA-DQ types makes a diagnosis of CD very unlikely. The majority of HLA no DQ2.5/8 patients possess one of the alleles encoding HLA-DQ2.5. The aim of the study is to assess the prevalence of HLA DQ2.5 and DQ8 negativity in CD paediatric patients of our country.

Methods: Data were obtained from a nationwide prospective registry of new paediatric CD cases in Spain.

Results: From 1/01/2011 till 20/09/2016 a total of 4872 new CD cases were prospectively reported by clinical investigators pertaining to 68 Paediatric Gastroenterology Units (PGUs) distributed all over the country and participating in the national survey. From them 3393 patients were HLA typed by PCR, thus data from the 2 alleles were available and were considered for evaluation.

239 (7.04%) were no DQ2/DQ8. Out of these 152 patients had none of the alleles encoding neither for HLA-DQ2.5 nor for DQ8, representing 4.4% of the total cases evaluated and 63% of the no DQ2.5/DQ8. 54 additional cases were DQ2.2 (11 out of 54 in homozygosis) and 33 more had at least one allele encoding for HLA-DQ2.5, together representing 36% of the DQ2/DQ8 negative cases.

Conclusion: According to the European genetic cluster on CD, 6% of CD were non-HLA-DQ2, and 93% of them were encoding at least 1 chain of HLA-DQ2.5. Large differences have been observed.
among European countries, the frequency of negative cases ranging from 0% to 12.5%. Thus overall our data fit into previous reported percentages (1, 2) although the proportion of cases bearing one of the alleles encoding for HLA-DQ2.5 is higher than in other series. Still pathophysiology of CD in these cases is a real challenge although we may speculate on the implication of a different repertoire of gluten-specific T cells recognizing different immunogenic peptides than in DQ25/DQ8 positive coeliac patients.


Objectives and study: The immune mechanism of coeliac disease (CD) is still not completely clarified. Recently, several immunoglobulin G4 (IgG4) related clinical disorders are defined with tissue infiltration by IgG4 positive plasma cells. Also, these plasma cells were found in duodenal biopsy specimens of some CD patients. A significant correlation between serum IgG4 levels and morphologic damage was observed in adult CD cases recently. The aim of this study was to evaluate the clinical value of serum IgG4 levels in children with CD.

Methods: In this multicentre, cross-sectional study, children diagnosed as CD and age and sex matched healthy subjects with normal gastric and duodenal histology were recruited. CD patients were classified into two groups according to their dietary adherence determined by anti-tissue transglutaminase IgA (TTG IgA) levels: Good gluten free diet (GFD) adherence and poor GFD adherence. Samples for complete blood count, C-reactive protein, immunoglobulin G and A, IgG4 were obtained from all patients. Patients with selective IgA deficiency, diabetes mellitus, acute infection, other accompanying systemic disease and younger than 36 months were excluded.

Results: A total of 64 CD patients (27 with good GFD adherence and 37 with poor GFD adherence, mean age: 9.5±3.6 years, 54.7% female) and 42 healthy subjects (mean age: 8.7±4.8 years, 47.6% female) were studied. TTG IgA and IgG4 values of CD and control groups are demonstrated in table 1. Serum IgG4 levels were significantly higher in CD patients (p<0.01). Serum IgG4 levels of healthy subjects and good GFD adherence cases were statistically similar (p>0.05) while they were statistically lower than the poor GFD adherence cases (p<0.01). Serum IgG4 was correlated with serum TTG IgA levels ($r^2=0.425$, $p<0.01$). Further assessing this correlation, in ROC analysis, area under the curve was 0.901, the sensitivity and the specificity of IgG4 was 91.9% and 77.8% respectively for the cut off value of 216.5 mg/L.

Table: Table 1 – TTG IgA and IgG4 values of CD and control groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>TTG IgA (U/mL) (mean±SD)</th>
<th>IgG4 (mg/L) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy subjects</td>
<td>4.13±2.8</td>
<td>224.1±260.3</td>
</tr>
<tr>
<td>CD good GFD adherence</td>
<td>8.55±7.3</td>
<td>243.24±131.3</td>
</tr>
<tr>
<td>CD poor GFD adherence</td>
<td>219.7±84.4</td>
<td>772.1±702.1</td>
</tr>
</tbody>
</table>

Conclusion: As far as we know, this represents the first report of serum IgG4 levels in children with CD. We found that serum IgG4 levels are higher in CD cases especially with poor GFD adherence and it is correlated with TTG IgA levels.
Repigmentation of white hair and eyelashes in childhood coeliac disease

Mariam Ghughunishvili¹, Nugzar Uberi¹, Michael Lentze²

¹Givi Zhvania Academic Pediatric Clinic, Tbilisi State Medical University, Tbilisi, Georgia
²Children's Hospital Medical Center, University of Bonn, Department of Pediatrics, Bonn, Germany

Objectives and study: There are minimal reports published about hair color changes in patients with coeliac disease. Only in two adults with celiac disease hair graying and repigmentation after a gluten free diet were published. In children hair discoloration in coeliac disease has not been described in contrast to dermatological changes like vitiligo and alopecia areata.

Methods: A 6 years old girl (height P90, weight P50) was seen because of white hairs growing within her black hair since 1 year on scalp and on eyelashes. The skin showed no vitiligo, no history of halo nevi as well as no signs for tuberous sclerosis, neurofibromatosis type I, sarcoidosis or keratoconjunctivitis. The girl was without any medication. She also had no abdominal pain, no heartburn or epigastric pain. Blood investigation showed: TTG-IgA-antibodies 168 mg/dl (reference range: <10,0), deamidated gliadin IgG-antibodies: 21 U/ml (reference range: <7.0), deamidated Gliadin IgA-abs - 18 U/ml (reference range: <7.0). The intestinal biopsy showed a total/subtotal atrophy of villous (Marsh 3a/b). In the gastric biopsy chronic gastritis with Helicobacter pylori (H.p.) bacteria in the mucosa was noted by histology. The diagnosis of coeliac disease was established and child was put on gluten free diet. Within 10 month on a gluten free diet repigmentation of hair on scalp and on eyelashes without any other therapy (figure 1 and 2) was seen. As for the finding of a chronic gastritis with helicobacter pylori bacteria in the gastric mucosa of this girl, it should be noted that the prevalence of H.p. in children in Georgia is 72%. Because she had no ulcers or abdominal symptoms, she was not treated with antibiotics and proton pump inhibitors according to the guidelines of ESPGHAN and NASPGHAN. She was only on a gluten free diet.

Results: Within 10 month on a gluten free diet repigmentation of hair on scalp and on eyelashes without any other therapy (figure 1 and 2) was seen.

Figure 1: White hair in a 6 years old girl before (A) and 10 months after introduction of a gluten free diet (B)

Figure 2: White eyelashes in a 6 years old girl before (C) and 10 months after introduction of a gluten free diet (D)
Conclusion: Coeliac disease is an autoimmune, lifelong gluten-sensitive intestinal enteropathy, which often manifests with extra-intestinal symptoms, including skin and rarely hair. In this 6 year old girl we report the effectiveness of gluten-free diet on the repigmentation of the white hair and eyelashes 10 months after introduction of a gluten free diet. Children with precocious white hair or eyelashes should therefore be investigated for underlying coeliac disease.
GASTROENTEROLOGY: Coeliac disease

G-P-021

HLA typing and serological screening for coeliac disease in type 1 diabetes children

Chloé Girard¹, Aurélie De Percin¹, Carole Morin¹, Maeva Talvard¹, Claire Le Tallec¹, Olives Jean-Pierre¹, Emmanuel Mas²

¹Centre Hospitalier Universitaire Toulouse, Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, Toulouse, France
²Centre Hospitalier Universitaire de Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, and Genius Group, Toulouse, France

Objectives and study: Patients with type 1 diabetes (T1D) are considered at high-risk for developing coeliac disease (CD). The purpose of our study was to determine the prevalence of CD among children who were followed in our unit for T1D using the recent ESPGHAN guidelines, and avoiding some intestinal biopsies.

Methods: We performed a prospective monocentric study, which included 663 T1D children between June 2014 and June 2016. We considered CD according to serological (tissue transglutaminase (TGA) and endomysium antibodies) and genetic (HLA DQ2 and DQ8) results. Children were included either at the time of T1D diagnosis or during their follow up. We looked for clinical and biochemical signs of CD, and for T1D characteristics.

Results: Children’s age ranged from 11 months to 18 years. CD was confirmed in 32 of 663 patients with T1D, with a prevalence of 4.8%. CD was excluded in 619 children and remained uncertain for 12 children, who had positive TGA without required criteria. We found that 95% of T1D children had positive HLA DQ2 and/or DQ8 haplotypes, which was 2.4 time higher than in the general population.

Conclusion: Intestinal biopsy should be avoided to confirm CD in the majority of T1D children. Silent forms of CD are frequent and screening is recommended for all patients. Importantly, repeated TGA assessment is required in HLA genetically predisposed T1D patients, while it is unnecessary in 5% of them who were HLA DQ2 and DQ8 negative.
Epitopes of human and microbial transglutaminases are shared by celiac disease sera

Patricia Jeremias¹, Kai Prager², Sandra Neidhöfer³, Aaron Lerner⁴, Torsten Matthias¹

¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Aesku.Diagnostics GmbH & Co. Kg, Wendelsheim, Germany
³Aesku. Kipp Institute, Wendelsheim, Germany
⁴B. Rappaport School Medicine, R&d, Haifa, Israel

Objectives and study: The consumption of microbial transglutaminase (mTg) in Western diet is expanding. mTg shares multiple functional similarities with human endogenous tTg. However, immunogenic comparison of the two enzymes in celiac disease (CD) is lacking.

Methods: Complexing mTg and gliadin results in mTg neo-epitope (mTg neo). The complexes were purified by asymmetric flow field-flow fractionation and confirmed by multi-angle light scattering and SDS-PAGE. Sera of 81 CD patients and 81 healthy controls were analysed using the following ELISAs: AESKULISA® tTg New generation (tTg neo-epitopes) IgA and IgG, AESKULISA® Gliadin IgA and IgG, AESKULISA® DGP IgA and IgG and AESKULISA® s against mTg and mTg neo-epitopes (Research use only (RUO) Kits as IgA and IgG).

Results: Purified mTg-neo IgG and IgA (AUC=0.92, 0.93, respectively) showed an increased immunoreactivity compared to single mTg and gliadin (p<0.001) but similar immunoreactivity to the tTg-neo IgG and IgA ELISA (AUC=0.94, 0.95, respectively). Using a competition ELISA, the mTg neo-epitopes and tTg neo-epitopes have identical outcomes in CD sera. They are both showing a decrease in optical density of 55±6% (p<0.0002). Sera with high antibody titre [U/ml] against the tTg neo-epitope show also high antibody activities of the mTg neo-epitope. In addition, vice versa indicating the presence of similar epitopes within the Tg-gliadin complexes.

Conclusion: mTg and tTg display a comparable immunopotent epitope. mTg neo-epitope IgA and IgG antibodies are immunogenic in CD. If substantiated, it will affect the food industry additive regulation.
The role of serology testing and HLA genotyping in the diagnosis of coeliac disease in Slovak cohort. Can duodenal biopsies be omitted?

Jarmila Kabatova, Rastislav Hustak, Stanislava Blažičková, Vladimir Bosak

1Gastroenterology Center, Piešťany, Slovakia
21st Faculty of Medicine, Charles University, Prague, Czech Republic
3Laboratória S.R.O., Piešťany, Slovakia
4Faculty of Health Studies and Social Work, Trnava, Slovakia

Objectives and study: The recent ESPGHAN (European Society of Paediatric Gastroenterology, Hepatology and Nutrition) guidelines for the diagnosis of coeliac disease (CD) allow to avoid duodenal sampling in certain clinical situation. Nevertheless, regional specifications for the diagnosis of CD almost in European countries may differ. Currently, in Slovak Republic, small-bowel biopsy is still requested for determination of CD, while genetic testing is still omitted. The aim of study was to validate diagnostic yields of the tissue transglutaminase antibody (anti-tTG), endomysium (EMA) antibody tests and the genotyping of HLA-DQ2/HLA-DQ8 for the ESPGHAN non-biopsy criteria in paediatric CD cohort.

Methods: We performed a retrospective analysis in a group of 258 CD patients (172 female, 86 males, age 2-18 years) with consecutive duodenal biopsy. Histology reports were graded according to the Marsh classification (Marsh 0-1 n=25; Marsh 2-3 n=233). Blood samples were tested for IgA, anti-tTG IgA (ELISA, Inova Diagnostics USA), EMA (indirect IF, Euroimmun) and HLA-DQ alleles associated with CD (EUROArray, Euroimmun).

Results: 181 patients (70%) were symptomatic and 93% (168/181) of them had at least moderate or higher grade of duodenal villous atrophy. Patients with anti-tTG IgA >10x upper limit of normal (ULN) had markedly increased likelihood of more advanced small-intestine villous atrophy (odds ratio 13.5). Sensitivity, specificity and accuracy of combination anti-tTG IgA >10x UNL and EMA positive reached 78.9% (95% CI, 70.1-85.8), 87.5% (95%CI, 46.7-99.3) and 79.5% (72.3-86.7), respectively. In our cohort at-risk HLA were 217 patients (84.1%), which is slightly lower than in others populations. A total of 58 of them (26.7%) were positive for both DQ haplotypes (DQ2+DQ2, DQ2+DQ8; table). It confirms the importance of the gene dosage in predisposition to CD. In applying non-biopsy criteria to our cohort, 33.3% (86/258) of symptomatic individuals with anti-tTG IgA >10x ULN, EMA positive and with HLA-DQ2 or/and HLA-DQ8 alleles could have been initially diagnosed without an intestinal biopsy.

Table:

<table>
<thead>
<tr>
<th>Histology grading</th>
<th>Total n = 217</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>DQ2</td>
</tr>
<tr>
<td>Marsh 0-1</td>
<td>41</td>
</tr>
<tr>
<td>Marsh 2</td>
<td>8</td>
</tr>
<tr>
<td>Marsh 3a</td>
<td>9</td>
</tr>
<tr>
<td>Marsh 3b</td>
<td>8</td>
</tr>
<tr>
<td>Marsh 3c</td>
<td>13</td>
</tr>
</tbody>
</table>

Conclusion: Our findings suggest that CD could be diagnosed without the need of duodenal sampling in one third of selected patients according ESPGHAN guidelines. HLA-DQ genotyping can be included in the algorithm of CD and national guidelines for CD diagnosis should be reviewed.
Patients with potential coeliac disease showing persistent negative serology maintain some intestinal hallmarks of coeliac disease

Valentina Discepolo¹, Maria Antonia Maglio², Maria Rosaria Del Vecchio¹, Serena Scapaticci¹, Andrea Di Siena¹, Roberta Mandile¹, Luigi Greco³, Riccardo Troncone³, Renata Auricchio³

¹University Federico II, Department of Translational Medical Sciences, Section of Paediatrics, Naples, Italy
²University Federico II, Department of Translational Medical Sciences, Section of Paediatrics & European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
³University of Naples "Federico II", Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Naples, Italy

Objectives and study: Natural history of potential celiac disease (PCD) is still under investigation. We observed that a subgroup of those subjects show a persistent normalization of serum anti-TG2 antibodies levels during follow-up despite staying on a gluten containing diet (GCD). These patients could have been “false positive” or, on the contrary, be primed to gluten and, despite being seronegative, at risk for future evolution to celiac disease (CD). In the present study we investigated PCD patients who became persistently seronegative looking for intestinal abnormalities of the mucosal immune response likely to be gluten-related.

Methods: In our cohort of 330 PCD, 86 subjects had a biopsy at time of diagnosis (when serum anti-TG2 were positive) and subsequently became persistently seronegative during follow-up. Only 8 out of 86 seronegative PCD had also a second biopsy after a median period of 24 months (when serum anti-TG2 were negative). All the biopsies have been evaluated for Marsh scoring and CD25+, CD3+ and γδ+ cells counts by immunohistochemistry. Intestinal anti-TG2 IgA antibody deposits were assessed by double immunofluorescence.

Results: 86/330 (26%) PCD children became seronegative during follow up (median 42.3 months) on a GCD. 36/86 (41%) became negative in the first 24 months of follow-up. Statistical differences were observed in HLA class risk (lower), anti-TG2 titer (lower), γδ infiltration (lower) and anti-TG2 intestinal deposits (less intense) in PCD who became seronegative compared to PCD who remained serologically positive over time.

8 out of 86 seronegative PCD had two biopsies, the first biopsy at diagnosis, when serum anti-TG2 were positive, and the second after normalization of serum anti-TG2 antibodies. Overall, 50% of these patients did not change Marsh score over time, while 37.5% showed an improvement (from M1 to M0) in parallel with normalization of anti-TG2 antibody levels. Only 1/8 (12.5%) patient from M0 became M1. Moreover a significant decrease (p=0.047) in the number of CD25+ cells infiltrating the small intestinal lamina propria, while no difference in the number of intraepithelial CD3+ cells and γδ+/CD3+ ratio were observed upon normalization of serum anti-TG2 antibody levels. Of interest, despite normalization of serum anti-TG2 levels, we still observed the presence of intestinal anti-TG2 antibody deposits although less intense.

Conclusion: In this study, we showed that PCD patients who developed a persistent normalization of serum titers over time, despite being on a GCD, continued to show signs suggesting an abnormal mucosal immune response, most likely gluten-dependent. Our results suggest that patients who have showed, during their lifetime, positive CD-associated serology continue to require careful follow-up.
Prevalence and factors associated with the long-term follow-up of coeliac disease diagnosed in childhood

Laura Kivelä¹, Sointu Alin¹, Marja-Leena Lähdeaho¹, Markku Mäki¹, Katri Kaukinen², Kalle Kurppa¹

¹University of Tampere and Tampere University Hospital, Tampere Centre for Child Health Research, Tampere, Finland
²University of Tampere, School of Medicine, Tampere, Finland

Objectives and study: Regular follow-up of coeliac disease is recommended to detect possible complications and dietary lapses. Crucial period in the long-term coping is transition and transfer of care from paediatric to adult providers, an issue that is very scarcely studied. We investigated the prevalence and factors associated with the follow-up and its long-term significance.

Methods: A questionnaire was sent to 588 adults with a childhood diagnosis of coeliac disease. Besides the frequency of follow-up, the survey contained questions about demographic data, time of coeliac disease diagnosis, clinical presentation at diagnosis, current self-experienced health and physical activity, presence of coeliac disease-associated and other comorbidities and possible complications, membership of coeliac society and adherence to gluten-free diet. Diagnostic information was confirmed from the medical records.

Results: Altogether 175 (30%) patients responded. Of them, 25% had regular follow-up while the rest were followed only occasionally or not at all. Patients with a follow-up were diagnosed significantly later than those without (median year of diagnosis 2003 vs 1997, p<0.001), whereas the groups did not differ in gender, age or clinical presentation at diagnosis, distribution of gastrointestinal symptoms and presence of coeliac disease-associated complications. At current evaluation those with a follow-up were less often smokers (12% vs 38%, p=0.002) and more often asthmatics (19% vs 7%, p=0.040). There were no significant differences in other co-morbidities or complications, general health, physical activity and membership of coeliac society, but the followed subjects tended to have more diabetes (14% vs 6%, p=0.119) and thyroidal diseases (16% vs 8%, p=0.139) and less depression (7% vs 15%, p=0.202). The proportion of patients on a strict diet was similar (82% vs 79%), but all non-adherent patients were those without a follow-up.

Conclusion: Most coeliac disease patients diagnosed in childhood remain inadequately followed later in life, although the situation seems to be improving. Even though the majority of those without a regular follow-up appear to cope rather well, there might be a subgroup who would need a special attention.

References:
The structure of iron-deficiency conditions in children with celiac disease in dependence on the atrophy degree of mucous membrane of the small intestine

Leonid Klimov¹, Marina Stoyan¹, Victoria Kuryaninova¹, Irina Zakharova², Vyacheslav Kashnikov³, Elena Gerasimenko¹, Ekaterina Zavyalova¹, Yulia Dmitrieva², Mariam Botasheva¹

¹Stavropol State Medical University, Stavropol, Russian Federation
²Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation
³City Children's Clinical Hospital Named after G.K. Filippsky, Stavropol, Russian Federation

Objectives and study: The analysis of relationship between the degree of mucous membrane damage of the small intestine (MMDSI), the titer of antibodies to tissue transglutaminase (tTG) and iron deficiency (ID) in children and adolescents in the period of clinical manifestation of celiac disease (CD).

Methods: 87 children and adolescents at the age of 8 months to 17 years with newly diagnosed CD were enrolled in this study. 41 (47.1%) of these participants were boys and 46 (52.9%) were girls. The diagnosis was established according criteria of ESPGHAN (1990, 2012). The diagnostics of ID included the determination of blood count, serum iron, serum ferritin, transferrin levels. Iron-deficient anemia (IDA) was characterized by the reduced levels of hemoglobin, serum iron, serum ferritin, and increased levels of transferrin, but latent iron deficiency (LID) was defined by the decrease in serum iron and serum ferritin with normal hemoglobin levels. IDA was detected in 20 (23.0%) patients, LID — 48 (55.2%), and 19 (21.8%) patients had no laboratory signs of ID. Depending on the stage of MMDSI atrophy in accordance with Marsh-Oberhuber classification, the patients were divided into 3 groups. The first group consisted of 19 (21.8%) children with Marsh type 3A, the second — 30 (34.5%) patients with Marsh 3B, the third — 38 (43.7%) children with Marsh 3C.

Results: The average level of tTG IgA in the patients of study groups was (X±m): 30.9±5.6 U/l; 56.1±8.7 U/l and 101.8±11.4 U/l, respectively. The maximum level of tTG IgA detected in case of Marsh 3C, exceeds significantly the parameters of patients with MMDSI atrophy, corresponding to Marsh 3A (p<0.001) and Marsh 3B (p<0.005). The levels of tTG IgG to a lesser extent depend on the stage of MMDSI damage: this parameter was 14.1±2.5 U/l in the first group, 23.8±4.5 U/l (p>0.05) — in the second, 36.3±of 5.6 U/l (p<0.01) — in the third group. There was the direct correlation between the stage of atrophy according to Marsh and the levels of tTG IgA (r=0.43, p<0.001), and to a lesser extent — tTG IgG (r=0.29, p<0.02). The cases of ID (IDA and LID) were detected with overall frequency of 12 (63.2%) among the patients of the first group; 22 (73.3%) — in the second group, and 34 (89.5%) — in the third group. In the structure of ID with types of Marsh 3A and Marsh 3B, the cases of ID without anemia (LID) are the most common, but IDA rate increases in cases of Marsh 3C. In patients with total MMDSI atrophy (Marsh 3C), the rate of IDA is 7.9-fold higher (p<0.01) than in children with Marsh 3A and 4.2-fold higher than in patients with Marsh 3A (p<0.01). Among the patients with IDA, MMDSI atrophy corresponding to Marsh 3C, is found in 80.0% cases, and in children without ID, the rate of MMDSI atrophy is as low as just 21.1% (p<0.001). The correlation analysis revealed an inverse relationship between the stage of jejunum atrophy and hemoglobin (r=-0.26, p<0.02), serum iron (r=-0.32, p<0.005), and serum ferritin (r=-0.50, p<0.001) levels.

Conclusion: In children and adolescents with CD, during the increase in the degree of MMDSI atrophy, ID rate is progressively on the rise. The titers of tTG IgA and IgG elevate according to the increase in damage of jejunum mucous membrane and correlate with MMDSI atrophy. The maximal negative correlation between the degree of MMDSI atrophy and serum ferritin levels, reflecting body iron stores is observed. The predictable depletion of body iron stores and IDA development, are to the greatest extent typical for the patients with total atrophy corresponding to Marsh 3C.
HLA-DQ in patients with coeliac disease living in south Russia

Leonid Klimov¹, Victoria Kuryaninova¹, Marina Stoyan¹, Irina Zakharova², Yulia Dmitrieva², Elena Gerasimenko¹, Ekaterina Zavyalova¹

¹Stavropol State Medical University, Stavropol, Russian Federation
²Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation

Objectives and study: to assess frequency and HLA-haplotype structure in celiac patients who live in the south of Russia. To identify age of celiac disease manifestation and sexual characteristics, depending on the haplotype.

Methods: HLA-typing (PCR) was performed in 112 children living in the south of Russia (Stavropol Territory, Republic of Ingushetia, Republic of Chechnya, Kabardino-Balkar Republic). The diagnosis of celiac disease was set for all children in accordance with ESPGHAN 1999, 2012 criteria.

Results: Total of 112 people, 55 boys (49.1%), 57 girls (50.1%), average age of 53.4 ± 4.4 months. HLA-positive patients accounted for 106 patients (94.6%). Among children with a positive haplotype most often encountered allele was DQ 2 - 67 children (59.8%), DQ 8 - 18 people (16.1%), DQ 7 - 11 (9.8%), incomplete DQ allele 2 - 10 (8.8%) children. DQ 2 is more common in girls – 39 (68.4%), DQ 8 – boys 13 (23.6%). The average age of celiac disease onset respectively amounted to: DQ 2 – 26.6 ± 3.9 months (men = 26, 38.8%), DQ 8 – 24.4 ± 9.1 months (men = 13, 72.2%), DQ 7 – 8.8 ± 1.7 months (men = 5, 45.5%; p = 0.007 vs DQ 2), incomplete DQ allele 2 – 11.9 ± 3.3 months (men = 6, 60.0%; p < 0.05 vs DQ 2). The DQ2 allele was presented by DQ2.5 (28, 41.8%), combination of DQ2.5 with DQ2.2 (11, 16.4%). In 12 patients DQ2 (17.9%) was presented only by alleles DQA1*201 DQB1*201 (DQ2.2). 12 patients (17.9%) had combination of DQ2 with DQ7 and 4 patients – combination DQ 2 with DQ 8 (6.0%).

Conclusion: thus, in the south of Russia overall prevalence of celiac disease predisposition alleles is different from the European, but is characterized by increased incidence of DQ 8.
Comparison of the reliability of 17 celiac disease associated biomarkers to reflect intestinal damage

Aaron Lerner¹, Patricia Jeremias², Sandra Neidhöfer³, Torsten Matthias²

¹B. Rappaport School Medicine, R&d, Haifa, Israel
²Aesku. Kipp Institute, Research, Wendelsheim, Germany
³Aesku. Kipp Institute, Wendelsheim, Germany

Objectives and study: In view of the increasing importance of serological biomarkers for screening and diagnosing celiac disease (CD), lack of back-to-back comparison, and reliability of isolated or combined antibody test systems to reflect intestinal damage in children with CD, their differential performances were evaluated.

Methods: AESKULISA® Gliadin (AGA), AESKULISA® DGP (DGP), AESKULISA® tTg “New Generation” (Neo-epitope tTg complexed to gliadin= tTg-neo), tTg (for in house research purpose only), AESKULISA® mTg neo-epitope and mTg (RUO). Anti-endomysial antibodies (EMA) were checked by immunofluorescence (AESKUSLIDES® EMA). The results were compared to the degree of intestinal injury, using the revised Marsh criteria.

Results: Most assays were able to discriminate between patients with low and high degree of intestinal damage. Comparing the different correlations between CD associated IgA and IgG antibodies’ isotypes, the tTg-neo IgA (r=0.6165, p<0.0001) and tTg-neo check (r=0.6492, p<0.0001) stood out, significantly, as the best indicators of the intestinal damage in CD. EMA-IgA, tTg and DGP check and mTg-neo IgG correlated nicely to the mucosal injury.

Conclusion: It is suggested that tTg-neo IgA/IgG antibodies should be used preferably to reflect intestinal damage during screening and diagnosing childhood CD. EMA-IgA, tTg, DGP checks and mTg-neo IgG liters followed the tTg-neo check performance. mTg-neo IgG presents a new serological biomarker for CD.
Eosinophilic esophagitis associated with coeliac disease in children

D’Abramo Fulvio Salvatore1, Francesca Gagliardi2, Fernanda Cristofori3, Isabella Mezzina4, Massimiliano Praitano5, Stefania Castellana5, Vincenzo Rutigliano2, Domenico Piscitelli2, Ruggiero Francavilla6

1Ospedale Giovanni XXIII, Bari, Italy
2University of Bari, Bari, Italy
3Ss. Annunziata Hospital / Pediatric Department, Taranto, Italy
4Università DI Bari, Italy, Interdisciplinary Department of Internal Medicine- Pediatric Section, Bari, Italy
5San Paolo Hospital, Department of Pediatrics, Bari, Italy
6University of Bari, Bari, Italy

Objectives and study: Recent studies have found different rates of eosinophilic esophagitis (EoE) in patients with Celiac disease (CD) ranging from 1.2 to 10.7% and higher than in the general population. The aim of the present study was to prospectively investigate the prevalence of EE with CD in a large group of celiac children over a 8 years period.

Methods: All 465 children (age: 1-14 years) undergoing endoscopy in the suspect of CD between January 2008 and October 2016 received oesophageal biopsies to exclude EoE (>15 eosinophils/HPF on lower/proximal esophageal biopsies). The presenting symptoms, laboratory evaluations, endoscopic and histopathological findings of these children were analyzed.

Results: 398 children (85,6%) were available for the analysis; 5 were diagnosed with EoE and CD (1,25%); therefore the prevalence is at least 35 times higher than in the paediatric population of our geographical area (0,031%; p<0,0001). We found that male gender (p<0,05), history of allergy (p<0,05), presence of endoscopic features suggestive of EoE (p<0,0006) and lower TTG-IgA at CD diagnosis (36,6 vs. 142,4 UI/ml; p<0,04) were associated with higher risk of EoE in CD. Gluten-free diet (GFD) resolved the histological features of EoE in 2 (40%) after 12 months.

Conclusion: Our data support the association between EoE and CD. Male gender, history of allergy, endoscopic features and low levels of TTG-A but not oesophageal symptoms might be use to increase the suspect of EoE in CD children. GFD is able to improve histology in less that half of the cases.

Conflict of interest: no conflict of interest to declare
Intestinal anti-tissue transglutaminase2 antibodies in patients with diagnosis other than coeliac disease

Maria Antonia Maglio¹, Fabiana Ziberna², Rosita Aitoro³, Virginia Bassi⁴, Giuliana Lania⁵, Erasmo Miele⁶, Valentina Discepolo⁴, Tarcisio Not², Riccardo Troncone¹, Renata Auricchio¹

¹University Federico II, Department of Translational Medical Sciences, Section of Paediatrics & European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
²Institute for Maternal and Child Health - Ircs "Burlo Garofolo", Paediatric Department, Trieste, Italy
³University of Naples "Federico II", Department of Translational Medical Science, Naples, Italy
⁴Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy

Objectives and study: Anti-tissue-transglutaminase2 antibodies (anti-TG2) are sensitive and specific biomarkers for celiac disease. They are produced in the intestine and it has been suggested that in early phases of the disease they may be present only at the intestinal level. Furthermore, their intestinal deposits have been proposed to be predictive of future evolution to villous atrophy. Aim of this work has been to investigate intestinal anti-TG2 antibodies in patients with normal serum levels of such antibodies and to relate their presence to imunohistochemical markers of gluten-dependent enteropathy.

Methods: For 136 patients (66=m, mean age 7 years) with normal serum levels of anti-TG2 antibodies undergoing small intestinal biopsy in the years 2001-2015, OCT embedded biopsies and organ culture supernatants were available. 98, 32 and 6 subjects presented Marsh 0, 1 or 3a mucosae, respectively. They had final diagnosis other than CD [gastroesophageal reflux (n=52), gastrointestinal functional disorders (n=32), type 1 diabetes (T1D; n=19), HP infection (n=10), eosinophilic esophagitis (n=8), first degree relatives of CD patients (n=6), iron deficiency anemia (n=2), failure to thrive (n=2), inflammatory bowel disease (n=2), autoimmune hepatitis (n=2)]. Intestinal production of anti-TG2 antibodies was investigated detecting mucosal anti-TG2 antibody deposits by immunofluorescence and by ELISA measurement of the same antibodies secreted into organ culture supernatants. Furthermore, phage antibody libraries were created from intestinal samples of 10 subjects and were analysed for the anti-TG2 response. Finally, intraepithelial density of CD3+ and γδ TCR+ cells, γδ TCR/CD3 ratio and density of lamina propria CD25+ cells were evaluated by immunohistochemistry in duodenal mucosa of 32 patients with positive intestinal anti-TG2 antibodies (Group A) and of 31 negative patients (Group B) that served as controls.

Results: Twenty out of 136 (14.7%) patients showed only intestinal anti-TG2 deposits, 13/136 (10.0%) secreted high levels of such antibodies into culture supernatants, 5 (3.7%) resulted positive to both techniques. In total 33/136 (24.2%) patients with normal serum levels of anti-TG2 antibodies produced, only at intestinal level, specific-CD autoantibodies. Analysis of antibody libraries from intestine confirmed the mucosal production of anti-TG2 antibodies in 8/10 patients that were positive to at least one of the above-mentioned tests, while no anti-TG2 antibodies were isolated from intestinal libraries of two patients negative to both the above-mentioned tests. Immunohistochemistry showed that only density of lamina propria CD25+ cells was significantly (p<.05) higher in Group A vs group B. Moreover, 13/32 (41%) subjects in group A showed TCR-γδ/CD3 ratio over cut-off, their diagnosis being type 1 diabetes (n=4), functional gastrointestinal disorders (n=7), eosinophilic esophagitis (n=2).

Conclusion: Production of anti-TG2 antibodies is not absolutely specific for celiac disease. Subjects with anti-TG2 deposits and/or production of anti-TG2 antibodies in culture supernatants have more often an inflamed mucosa. However, we cannot exclude that in some of these patients the presence of such antibody is gluten related.
High cumulative incidence of coeliac disease in a childhood-onset inflammatory bowel disease cohort from northern Stockholm County?

Petter Malmborg¹, Maja Ideström², Cecilia Zetterström², Natalia Mouratidou³, Henrik Arnell⁴

¹Sachsska Children’s Hospital, Department of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden
²Karolinska University Hospital, Astrid Lindgren Children’s Hospital, Department of Women’s and Children’s Health, Karolinska Institutet, Stockholm, Sweden
³Karolinska University Hospital, Astrid Lindgrens Children’s Hospital, Stockholm, Sweden
⁴Karolinska University Hospital, Alb Children’s hospital, Paediatric Gastroenterology, Hepatology & Nutrition, Se-141 86 Stockholm, Sweden

Objectives and study: Some register studies have demonstrated an association of inflammatory bowel disease (IBD) with increased risk of coeliac disease (CD) [1]. Upper endoscopy with duodenal biopsies is recommended in the diagnostic work-up of children with suspected IBD [2]. Here we report the cumulative incidence of CD by age in a population-based childhood-onset IBD cohort.

Methods: Medical records of all 256 patients diagnosed in the period 1993-2007 with childhood-onset IBD (<16 years) in northern Stockholm County were scrutinized from birth until 2011. The patients in the cohort were born between 1978 and 2006. At the end of the study period the median age of the patients was 20.0 (4.5-32.1) years.

During the study period 242 (95%) of the patients were examined with upper endoscopy and 204 (80%) of the patients were also re-endoscoped at least once. Ten of the remaining 14 patients, not examined with upper endoscopy, were tested negatively for CD-associated antibodies at least once during the study period.

Patients were diagnosed with CD according to ESPGHAN’s diagnostic recommendations during the study period [3].

The cumulative incidence of CD in the IBD cohort by age was estimated by the Kaplan-Meier method.

Results: Twelve patients in the cohort (six girls and six boys) were diagnosed with coeliac disease; three of them had ulcerative colitis and nine had Crohn’s disease. The median age at CD-diagnosis in the cohort was 12.1 (1.7-16.7) years. None of the patients were diagnosed with CD in adult age (>17 years).

CD was diagnosed prior to IBD diagnosis in two patients, at diagnostic IBD work-up in ten patients and at re-endoscopy, due to symptoms suggestive of worsening intestinal inflammation, in one patient.

The cumulative incidence of CD in the childhood-onset IBD cohort at 5 years of age was 0.4% (CI 0.0-2.5), at 15 years 4.5% (CI 2.4-8.0), and at 25 years 4.9% (CI 2.7-8.5).

The estimated cumulative incidence of CD at thirteen years of age in our childhood-onset IBD cohort was not statistically significantly different from the prevalence of CD in a cross sectional study of twelve year old school-children in Sweden born 1995 (3.2% versus 2.9% (p=0.86)) [4].

Conclusion: In an international perspective our study demonstrates a high cumulative incidence of CD by age in a population based childhood-onset IBD cohort. However, the estimated cumulative incidence of CD in our cohort was similar to the prevalence found among children in a national contemporary cross-sectional school study. Hence, our study does not lend any support to a clinically important association of childhood-onset IBD with increased risk of CD.

The association of childhood-onset IBD with increased risk of CD in register studies could be expected to be heavily biased by the routine use of upper endoscopy in the diagnostic work-up of children with IBD.
Serum brain derived neurotrophic factor (BDNF) in children with coeliac disease

Daphne Margoni¹, Kelly Michalakakou², Eleni Angeli³, Panagiota Pervanidou³, Christina Kanaka-Gantenbein⁴, George Chrousos⁵, Ioannis Papassotiriou⁶, Eleftheria Roma⁷

¹University of Athens, First Department of Paediatrics, Athens, Greece
²Department OF Clinical Biochemistry, “Aghia Sophia” Children’s Hospital, Athens, Greece
³University of Athens, Athens, Greece
⁴3rd Department of Paediatrics, 1st Department of Pediatrics, University of Athens, Aghia Sophia Children’s Hospital, Athens, Greece
⁵University of Athens School of Medicine, First Department of Pediatrics, Aghia Sophia Children’s Hospital, Athens, Greece
⁶Department OF Clinical Biochemistry, “aghia Sophia” Children’s Hospital, Athens, Greece
⁷National and Kapodistrian University of Athens, First Department of Paediatrics, Athens, Greece

Objectives and study: Brain Derived Neurotrophic Factor (BDNF) is a neurotrophin linked with neuronal plasticity, having a protective role in the nervous system. It is abundant in the central nervous system, but it is also expressed in tissues of the gastrointestinal tract. Coeliac disease (CD), characterized by intestinal inflammation, has an increased prevalence of neurological and mental disorders. The aim of this study was to evaluate the serum BDNF levels of coeliac patients at diagnosis, of those on a Gluten Free Diet (GFD) for more than one year and of healthy controls, as well as to identify possible differences between the three groups.

Methods: Fifty newly diagnosed patients with CD (aged 8.6±3.7 yrs, 64.0% females), thirty-nine CD patients on GFD for more than one year (aged 10.4±3.4 yrs, 71.8% females) and 36 healthy controls (aged 8±1.7 yrs, 33.3 % females) were included in the analysis. For eight patients from the newly diagnosed group, all the parameters were measured again after more than one year on a GFD. Along with anthropometric evaluation and standard blood chemistry, serum BDNF levels were measured by means of immunoenzymatic technique.

Results: Patients at diagnosis had significantly higher BDNF levels compared to healthy controls (26,110 ± 8,204 pg/ml vs 19,630 ± 8,093 pg/ml respectively, p<0.001). Patients on a GFD for more than one year had significantly higher BDNF levels compared to healthy controls (28,860 ± 7,992 pg/ml vs 19,630 ± 8,093 pg/ml respectively, p<0.001). Patients at diagnosis had significantly lower BDNF levels compared to those on a GFD for more than one year (26,110 ± 8,204 pg/ml vs 28,860 ±7,992 pg/ml, respectively, p=0.02). For the patients measured before and after initiation of a GFD, no statistical significance was reached regarding BDNF levels, (26,780 ± 10,244 pg/ml vs 25,660 ± 7,732 pg/ml respectively, p>0.3).

Conclusion: Serum BDNF levels in our analysis, are higher in patients with CD compared to those of healthy controls, regardless of their status of gluten consumption. The elevation of serum BDNF levels in coeliac patients could be attributed to a potential protective response to the local inflammation of the intestine.
GASTROENTEROLOGY: Coeliac disease

G-P-033

Antibodies against neo-epitope tTg complexed to gliadin outperform the uncomplexed anti-tTg to follow rheumatic arthritis patients

Torsten Matthias¹, Patricia Jeremias¹, Sandra Neidhöfer², Aaron Lerner³

¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Aesku. Kipp Institute, Wendelsheim, Germany
³B. Rappaport School Medicine , R&d, Haifa, Israel

Objectives and study: Rheumatoid arthritis (RA) is a high-risk disease for celiac disease (CD), sharing multiple aspects. IgA-tTg autoantibody is a classical marker for CD, however, it has many false positives. Anti neo-epitope tTg complexed to gliadin is a reliable biomarker for CD and it has never been compared to the IgA-tTg performance and false positivity in naïve and treated RA population.

Methods: 135 RA adult patients, mean age 55 ±12.7 years, F/M 1:0.2, respectively, from the ADAPTHERA study cohort, where studied in naïve patients and longitudinally at 3 follow up visits. ADAPTHERA is a network to improve patient care and to find new biomarkers for RA. Patients were tested using the following ELISAs detecting either IgA, IgG or both (IgA+IgG): tTg (for in house research purpose only) and AESKULISA® tTg New Generation (tTg neo-epitope).

Results: In the naïve patients, on the first visit after diagnosis and along the follow up under pharmaceutical therapy, for 3 consecutive visits, the % positivity of the IgA-tTg (Visit 1, 2, 3, 4 , 6.7 %, 3.1 %, 4.6 %, 7.0 %, respectively) was significantly higher than in the tTg-neo antibodies (Visit 1, 2, 3, 4, 2.2 %, 0.8 %, 1.1 %, 2.8 %, respectively, p<0.05).

Conclusion: Determinations of CD associated autoantibodies in naïve and treated RA groups reveal that IgA-tTg is less specific for CD in relation to the lower false positivity of its competitor (anti tTg neo-epitope antibodies) in RA patients’ sera. This is also mirrored by IgA-tTg’s higher false positivity rate.

Disclosure of interest: Dr. Torsten Matthias: conflict because he is the CEO of AESKU.Diagnostics GmbH&Co. KG.
Objectives and study: Variable esophageal abnormalities are often reported during the diagnostic gastroscopy in celiac disease. We investigated the frequency and significance of such findings in a large group of pediatric celiac disease patients.

Methods: Reported endoscopic irregularities and histopathologic results of systemically taken esophageal biopsies were compared between 316 children with celiac disease and 981 disease controls. Further, association between the esophageal findings and other clinical and histological features of the disease were investigated in celiac disease patients.

Results: Endoscopic esophageal findings were rarer in celiac disease (3%) than in unspecific abdominal pain (6%), Crohn’s disease (6%), mastocytosis (7%), H. Pylori (7%), ulcerative colitis (10%), gastroesophageal reflux disease (22%) and eosinophilic esophagitis (EoE, 38%). Prevalence of histological changes was as follows: abdominal pain 9%, H. pylori 14%, celiac disease 17%, ulcerative colitis 18%, Crohn’s disease 18%, mastocytosis 20%, reflux 32% and EoE 100%. Two celiac children had a suspicion of EoE but the other esophageal findings were unspecific. Reflux symptoms were more common in celiac children with esophageal findings than those without (5.7% vs 0.8%, p=0.035), whereas the groups did not differ in demographic data, family history of celiac disease, clinical presentation, severity of villous atrophy, growth parameters and celiac disease serology or other laboratory parameters.

Conclusion: Histopathological findings of esophagus are rather common in celiac disease. However, except for EoE they are mostly without major clinical significance, and children with or without esophageal pathologies do not differ in any other disease features except the prevalence of reflux.
Diagnostic accuracy of a point-of-care screening test for coeliac disease

Zrinjka Mišak1, Iva Hojsak1, Oleg Jadresin1, Sanja Kolacek2

1Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
2Zagreb University Medical School, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia

Objectives and study: It has been shown that point-of-care (POC) screening tests for celiac disease (CD) have excellent diagnostic accuracy, although not superior to anti-tissue transglutaminase (anti-tTG) or endomysial antibodies. Majority of previous studies used tissue transglutaminase based POC test on study populations with high prevalence of CD (1). The aim of this study was to evaluate the performance of POC test for deamidated gliadin peptides (DGP) and total immunoglobulin A (IgA) level (SimtomaX, Augurix, Switzerland) in population of children with symptoms or positive family history suggestive of CD.

Methods: Children who were evaluated for CD (because of symptoms or associated diseases suggestive of CD or positive family history) and who underwent upper endoscopy from October 2015 to October 2016 in Children's Hospital Zagreb were prospectively enrolled into the study. All included patients performed POC for DGP and IgA level, serologic test for anti-tTG and duodenal biopsy. Exclusion criteria were already known CD, patient adhering to gluten-free diet, having another autoimmune disease, or not having signed informed consent.

Results: In total, 103 patients were included in the study (64 female; mean age 9.7 years (0.6-17.9)). Serologic antibody tests were positive in 23 children (22%), while CD was diagnosed (biopsy proven) in 19 patients (18%). POC test for DGP and IgA level was positive in 26 patients (25%) and had sensitivity of 100% and specificity of 91.7% when compared to biopsy results. Further analysis is shown in Table 1. Not even one patient had false negative POC test result. However, 7 patients had false positive POC test: one had dermatitis herpetiformis and positive serology but negative biopsy, three had positive serologic DGP, but negative tTG and negative biopsy while in the remaining three patients tTG and biopsy were negative and DGP was not determined.

Table:

<table>
<thead>
<tr>
<th></th>
<th>In relation to biopsy</th>
<th>In relation to serologic anti-tTG</th>
</tr>
</thead>
<tbody>
<tr>
<td>sensitivity</td>
<td>100%</td>
<td>95.65%</td>
</tr>
<tr>
<td>specificity</td>
<td>91.67%</td>
<td>95%</td>
</tr>
<tr>
<td>positive predictive value</td>
<td>73.08%</td>
<td>84.62%</td>
</tr>
<tr>
<td>negative predictive value</td>
<td>100%</td>
<td>98.7%</td>
</tr>
<tr>
<td>positive likelihood ratio</td>
<td>12</td>
<td>19</td>
</tr>
<tr>
<td>negative likelihood ratio</td>
<td>0</td>
<td>0.05</td>
</tr>
<tr>
<td>accuracy</td>
<td>93.2%</td>
<td>95.15%</td>
</tr>
</tbody>
</table>
**Conclusion:** In this prospective study, POC test for DGP and IgA level performed in population with CD prevalence of 18% showed good diagnostic accuracy, excellent sensitivity and high positive likelihood ratio when compared to biopsy results. Owing to high negative predictive value it may be used to rule out CD in children with symptoms suggestive of the disease.

Reference:

Evaluation of gut-vascular barrier by plasmalemna vesicle-associated protein-1 measurements in patients with celiac disease and abnormal serum alanine transaminase

Luigina De Leo¹, Samuele Naviglio², Serena Vatta¹, Elisa Benelli³, Giacomo Stera³, Daniela Santon⁴, Fabiana Ziberna¹, Stefano Martelossi¹, Antonio Di Sabatino⁵, Alessandro Ventura¹, Tarcisio Not¹

¹Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Paediatric Department, Trieste, Italy
²University of Trieste, PhD School in Reproductive and Developmental Sciences, Trieste, Italy
³University of Trieste, Trieste, Italy
⁴Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Trieste, Italy
⁵San Matteo Hospital, Pavia, Italy

Objectives and study: A gut-vascular barrier (GVB) has been recently identified. GVB controls the translocation of macromolecules across intestinal blood endothelial cells to flow to portal vein and it seems to play a pivotal role in the regulation of the gut-liver axis. Plasmalemna vesicle-associated protein-1 (PV-1) has been proposed as a marker of abnormal GVB permeability. Very recently, it has been observed a higher PV-1 expression in the intestinal mucosa of patients with celiac disease (CD) and elevated serum alanine transaminase (ALT) compared with CD-patients with normal serum ALT, suggesting a GVB’s involvement in the liver damage. The objective of this study is to investigate PV-1 levels in serum samples and in intestinal biopsies from untreated-CD patients with normal or high ALT and from patients suffering from minor gastrointestinal complaints. We also verified the effect of the gluten free diet (GFD) on the PV-1 serum concentration.

Methods: Sera and intestinal biopsies from 20 untreated-CD patients with high ALT (>40 U/l) (group A), 24 untreated-CD patients with normal ALT (group B) and 40 patients suffering from minor gastrointestinal complaints (group C) were included in the study. PV-1 was measured in serum samples and in intestinal specimen homogenates by ELISA assay. Intestinal PV-1 expression was also evaluated by quantitative reverse transcription polymerase chain reaction (qRT-PCR) and the results were reported using the ∆∆Ct comparative method. Statistical differences between groups were evaluated with t test.

Results: PV-1 has been measured by ELISA assay in intestinal biopsy homogenates from patients of group A (3.7±1 ng/ml), group B (4.27±1 ng/ml) and group C (3.4±1.4 ng/ml) with significant difference between group B and group C (p=0.008). qRT-PCR assay of intestinal biopsies demonstrated no differences among the three study groups (2-∆∆Ct: 1.16 group A, 1.15 group B and 1 group C). Serum PV-1 concentrations were 1.09±0.9 ng/ml in group A, 0.66±1 ng/ml in group B and 0.34±0.52 ng/ml in group C. Statistically significant differences were observed between group A and group B (p=0.03) and between group A and group C (p=0.0005). Serum samples of 12/20 patients of group A were retested after at least one year of GFD: PV-1 serum concentration significantly decreased (0.9±0.9 ng/ml in gluten containing diet vs 0.10±0.3 ng/ml in gluten free diet; p=0.01) with concomitant serum ALT reduction (75±40 U/l in gluten containing diet vs 21.2±23.5 in gluten free diet; p=0.002).

Conclusion: Our results showed for the first time that PV-1 is detectable in serum samples and it is more expressed in CD-patients with abnormal ALT enzyme. Moreover, in CD-patients with elevated ALT PV-1 is more expressed in serum samples and not at the intestinal level suggesting that PV-1 might be released by the hepatic vascular system and not by the intestinal one. Of interest, the GFD reduces the PV-1 concentrations with concomitant ALT normalization. Finally, PV-1 might be a marker of gluten dependent liver damage.
Antibodies against a tissue transglutaminase neo-epitope for the diagnosis of celiac disease in children

Jiri Nevoral1, Ondrej Hradsky2, Jan Lastovicka3, Eva Neubertova4, Jiri Bronsky5

1University Hospital Motol, 2nd Medical School, Charles University, Pediatrics, Prague, Czech Republic
2University Hospital Motol, Paediatrics, Prague, Czech Republic
3University Hospital Motol, 2nd Medical School, Charles University, Department of Immunology, Prague, Czech Republic
4Biolab Praha, Prague 6, Czech Republic
5Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic

Objectives and study: Recently, reports have been published regarding a new serological test in which tissue transglutaminase in complex with gliadin, representing a neo-epitope and antibodies (anti-TG-neo-IgA+IgG), have been evaluated with improved reliability for pediatric celiac disease (CD) compared with currently used tissue transglutaminase antibodies (anti-TG-IgA). The aim of this study was to assess the accuracy and benefits of the new test in comparison with currently used anti-TG-IgA.

Methods: Fifty-eight children with suspected CD and 13 children suffering from functional abdominal pain without suspicion of CD were examined. Serum samples from all children were simultaneously tested for endomysial antibodies (EMA)—anti-TG-IgA and anti-TG-neo-IgA+IgG (AESKULISA CeliCheck New Generation IgA+IgG, AESKU Diagnostics, Wendelsheim, Germany). Gastroscopies with biopsies were also performed concurrently, and histological findings were evaluated according to the Marsh classification.

Results: When evaluating ROC curves we did not find a significant difference between both ROCs (AUC for anti-TG-IgA, 0.996; AUC for anti-TG-neo-IgA+IgG, 0.989; p = 0.23). Specificity for anti-TG-neo-IgA+IgG was 0.914 (95CI, 0.845–0.983) and for anti-TG-IgA 0.948 (95CI, 0.879–1). The population positive predictive value was 0.055 for the former assay, and 0.089 for the latter.

Conclusion: We were unable to confirm that anti-TG-neo-IgA+IgG provides improved reliability for CD diagnosis in children. We were unable to confirm that anti-TG-neo-IgA+IgG provides improved reliability for CD diagnosis in children. On the contrary, the new test had a lower specificity than the hitherto used anti-TG-IgA measurement.

Supported by research grants VZ FNM 00064203/6001 and GA UK No. 136215.
GASTROENTEROLOGY: Coeliac disease

G-P-038

Serologic tests in patients with suspected coeliac disease in Rio de Janeiro

Lílian Nobre Ferro e Silva Ulloa¹, José Junqueira¹, Clemax Couto Sant’Anna¹, Mariana Aires¹

¹Universidade Federal Do Rio de Janeiro - Instituto de Puericultura e Pediatria Martagão Gesteira, Departamento de Pediatria, Rio de Janeiro, Brazil

Objectives and study: To determine the clinical and laboratory profiles of patients with diagnostic suspicion of celiac disease (CD) of a pediatric gastroenterology outpatient clinic of a university hospital in Rio de Janeiro.

Methods: This descriptive retrospective study analyzed the medical records of all patients with suspected CD and all patients with confirmed CD treated at the service to determine their clinical and laboratory profiles. Patients who presented CD symptomatology and positive serology for CD underwent upper gastrointestinal endoscopy with biopsy. CD diagnosis was based on histopathological examination, which evidenced villous atrophy.

Results: A total of 181 patients with signs and symptoms suggestive of CD were analyzed. Sixty patients composed the CD group, and 121 patients composed the non-CD group (NCD) either because of negative serology or negative histopathological test. The CD group had 36 (60%) females and 24 (40%) males, and the NCD group had 58 (47.9%) females and 63 (52.2%) males. The mean ages of the CD and NCD groups were 4.4 and 5.5 years, respectively. In the CD group, 32 patients had difficulty gaining weight (p = 0.001), 31 had chronic diarrhea (p = 0.004), 23 had abdominal distension (p = 0.002), and 7 had mood swings (p = 0.006), symptoms which were significantly more prevalent in this group. The CD group had the following serologic results: anti-gliadin antibodies (AGA) AGA IgA positive (p = 0.0003), AGA IgG positive (p = 0.005), endomysial antibodies (EMA) EMA IgA positive (p <0.0001), EMA IgG positive (p = 0.002), anti-tissue transglutaminase (anti-tTG) anti-tTG IgA positive (p <0.0001), and IgA deficiency (p = 0.001), all more common in the CD group.

Table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Sensitivity %</th>
<th>Specificity %</th>
<th>PPV %</th>
<th>NPV %</th>
<th>Accuracy %</th>
</tr>
</thead>
<tbody>
<tr>
<td>AGA IgA</td>
<td>45</td>
<td>86,8</td>
<td>69,2</td>
<td>70,6</td>
<td>70,2</td>
</tr>
<tr>
<td>AGA IgG</td>
<td>55,8</td>
<td>65,9</td>
<td>54,2</td>
<td>67,3</td>
<td>61,7</td>
</tr>
<tr>
<td>EMA IgA</td>
<td>42,4</td>
<td>97,8</td>
<td>93,3</td>
<td>70,3</td>
<td>74,6</td>
</tr>
<tr>
<td>EMA IgG</td>
<td>40</td>
<td>100</td>
<td>100</td>
<td>60</td>
<td>68,4</td>
</tr>
<tr>
<td>Anti-tTG IgA</td>
<td>83,7</td>
<td>93</td>
<td>83,7</td>
<td>93</td>
<td>90,2</td>
</tr>
<tr>
<td>Anti-tTG IgG</td>
<td>50</td>
<td>100</td>
<td>100</td>
<td>90</td>
<td>90,9</td>
</tr>
</tbody>
</table>

Sensitivity and specificity found in the present study. PPV - positive predictive value. NPV - negative predictive value. LR – likelihood ratio.
Conclusion: The signs and symptoms that most frequently required serology to confirm CD were difficulty gaining weight, diarrhea, and abdominal distension. Anti-tTG IgA was the best test for diagnosing symptomatic patients and screening patients at risk, such as those with genetic syndromes, autoimmune diseases, and first-degree relatives with CD. The CD group had positive serology for CD, that is, their AGA, EMA, and anti-tTG IgA were significantly higher than those of the NCD group.
Prospective multicentric evaluation of the response to initial hepatitis B virus vaccination and revaccination in children with coeliac disease

Thaïs Rousseff¹, Els Van De Vijver², Saskia Van de Velde³, De Bruyne Ruth³, Myriam Van Winckel³, Petra Schelstraete⁴, Stephanie Vanbiervliet³

¹Ghent University Hospital, Paediatrics, Ghent, Belgium
²Antwerp University Hospital, Paediatric Gastroenterology, Antwerp, Belgium
³University Hospital Ghent, Paediatric Gastroenterology and Hepatology, Ghent, Belgium
⁴Ghent University Hospital, Paediatric Pneumology and Infectious Diseases, Ghent, Belgium

Objectives and study: Coeliac disease (CD) is an autoimmune disease characterized by immune mediated inflammatory damage of the small intestinal mucosa, precipitated by the ingestion of gluten-containing foods. Nonresponse following Hepatitis B virus (HBV) vaccine in a healthy population is 4-10% and can partially be explained by genetic predisposition, especially Human leukocyte antigen (HLA) DQ2 and DQ8 alleles seem to play a primary role. It is known that more than 95% of coeliac patients possess these HLA genotypes. Consequently, a lower immunisation rate after HBV vaccine is seen in coeliac patients. The aim of this study is to prospectively map the responses to HBV vaccine in children with CD. We also investigated if there is a relationship between the patients’ responses to HBV vaccination and the dietary compliance.

Methods: At the moment of annual follow-up, we performed a blood analysis and measured the antihepatitis B surface antibodies (antiHBs AB) in children with CD followed at the paediatric gastroenterology department of the university hospital of Ghent and Antwerp, between 2015 and 2016. Subjects with antiHBs AB <10 U/L were considered non-responders. Non-responders were advised to take a single intramuscular HBV vaccine booster. Response was checked at the next annual appointment. Compliance to gluten free diet (GFD) and CD activity were monitored as usual, using serum anti-transglutaminase antibody levels (a-TG AB). The results were compared to the 4-10% non-response reported in literature.

Results: 91 children with CD were included of which 29% (n=26) were male. The mean age at diagnosis of CD was 6.0 years (range 1–16 years) and 9.3 years (range 3-17 years) at measurement of antiHBs AB. Of the 38 (42%) responders to vaccination, 25 (66%) showed low response (10-100 IU/L), 11 (29%) intermediate response (100-1000IU/L) and 2 (5%) a high response (>1000 IU/L). More than half of the patients were non-responders (53 (58%)). Until now, for only 14/53 (26%) non-responders, antiHBs AB were available after intramuscular revaccination. Of those 57% (n=8) acquired immunity after a single HBV booster. The a-TG AB were still positive in 20/91 (22%) CD patients. The a-TG AB ranged from 11-392 U/mL (normal value <7U/mL). Twelve of them (60%) were non-responders. Control antiHBs AB titre after booster vaccination was available for 3/12. At control all had normal a-TG AB and 2/3 became responders.

Conclusion: Non-responsiveness to HBV vaccination was more frequently found in children with CD compared to the literature reported non-response. Since more than half of the CD patients have an insufficient response to HBV vaccination this should be checked. A single booster injection was able to induce a response in more than 50% of patients. Furthermore, compliance to the prescribed GFD may possibly improve the immune response to HBV vaccination in children with CD.
Ptosis and ‘Alice in Wonderland’ syndrome as presenting symptoms of coeliac disease

Irene Oldenburger1, Caroline Meine Jansen2, Marloes Bongers3, Roderick Houwen1, Victorien Wolters1

1University Medical Center/Wilhelmina Children's Hospital, Department of Pediatric Gastroenterology, Utrecht, Netherlands
2Hospital Groene Hart, Department of Pediatrics, Gouda, Netherlands
3St Jansdal Hospital, Department of Pediatrics, Harderwijk, Netherlands

Coeliac disease (CD) is traditionally described as a malabsorption syndrome presenting with a triad of chronic diarrhoea, weight loss and abdominal distension. However, nowadays it is recognized as a systemic disease. Hence, neurologic conditions are also reported in association with CD. Most mentioned are cerebellar ataxia and peripheral neuropathy. Other manifestations include inflammatory myopathies, myelopathies, encephalopathy, stiff-man syndrome, epilepsy, autism and migraine. The prevalence of neurological dysfunction in adults with CD is estimated between 10-22.5% and is unknown in children.

We report 2 children with CD who presented with ptosis and Alice in Wonderland syndrome. The first child was diagnosed with CD at the age of 11 months with classical symptoms, tTG of 11 U/ml, negative EMA and Marsh 3A on biopsy. She was incomp liant with the gluten free diet and lost to follow up. After 9 years she presented with ptosis of her left eye since 5 years, her tTG was 128 U/ml. Within months after starting a glutenfree diet the ptosis of her left eye and keratoconjunctivitis disappeared completely.

The second child was a 9 year old girl who suffered from visual complaints since 6 months and small stature. She experienced daily episodes in which she sees objects larger (micropsia), smaller (micropsia), closer (pelopsia) or at a further distance (teleopsia) than in reality, also known as the Alice in Wonderland syndrome. Her tTG was 128 U/ml, she was EMA positive and her biopsy showed Marsh 3B. Furthermore, IgG-EBV was positive and IgM-EBV was negative as a result of an infection 2 years earlier. Her visual complaints resolved within a few months after starting a glutenfree diet.

We hypothesize a relationship between these remarkable neurological symptoms and CD since in both cases complaints disappeared upon a glutenfree diet. The underlying immunological mechanism responsible for this manifestation is probably similar to the characteristic gliadin mediated T-cell response known in CD. We could diagnose our patients with CD because they had typical mucosal changes in their small intestinal biopsy. However, neurological symptoms may also present in the absence of an enteropathy which poses diagnostic challenges. We reported these cases to emphasize that CD can present very atypically. Performing CD-serology in case of inexplicable neurologic findings may diagnose patients with CD who would have been missed otherwise.
GASTROENTEROLOGY: Coeliac disease

G-P-041

Review of coeliac disease presentation in a tertiary centre: Manchester, UK

Gracinda Oliveira¹, Rajiv Mohan¹, Andrew Fagbemi²

¹Royal Manchester Children's Hospital, Gastroenterology, Manchester, United Kingdom
²Royal Manchester Childrens Hospital, Department of Paediatric Gastroenterology, Manchester, United Kingdom

Objectives and study: Coeliac disease (CD) is an immune-mediated disorder with a multiform presentation and therefore a challenging diagnosis. Our purpose is to review the clinical presentation, laboratory and histological findings of paediatric CD and to assess clinical response, IgA tissue transglutaminase antibody (IgA tTG) and growth after 12 months of gluten-free diet (GFD).

Methods: Children with previously established or newly diagnosed CD, admitted in a tertiary centre from April 2014 to April 2016 were recruited. 312 patients were identified, 153 were excluded because of repeated admissions, diagnosis made in a different hospital, unconfirmed diagnosis or being over 18y. A total of 159 patients were included. Data was collected retrospectively from electronic medical records and clinical notes. Oslo classification was used for clinical profile and Modified Marsh Classification was applied for duodenal biopsy interpretation. Data were analyzed with SPSS version 20.0, using absolute and relative frequencies for categorical variables, means and standard deviation (SD) for continuous variables and ANOVA test for variance analysis.

Results: Children aged 1 to 18y were included (mean±SD: 8.50±4.47y, 69% girls). Disease presentation was classical in 60% (mean±SD: 7.87±4.47y), non-classical in 25% (mean±SD: 9.17±4.08y), subclinical in 10% (mean±SD: 10.85±4.50y), and 5% classified as potential CD (mean±SD: 7.88±5.13y). Non-classical and subclinical profiles had a higher mean age at presentation but not statistically significant (p-value 0.24). Predominant gastrointestinal features at presentation included abdominal pain (58%), diarrhoea (43%), bloating (27%), constipation (23%), weight loss (29%), failure to thrive and lethargy (20% each). A simultaneous diagnosis of anaemia (23%), type 1 diabetes mellitus (9%), IgA deficiency (5%), hypothyroidism (4%), genetic syndromes (4%) and other disorders, namely atopic (27%), neurodevelopmental (13%) and rheumatologic (7%) was found. Family history of CD was positive in 24%. CD-specific serologic testing (tTG or endomysial antibody-EMA) and esophagogastroduodenoscopy were performed in 99%. Histology revealed modified marsh 2 or 3 (a,b,c) enteropathy in 94% and normal in 6% though positive for HLA typing. Ferritin was low in 63% (<15 uG/L). There was a moderate to severe deficiency of 25-hydroxy-vitamin D in 62%. All patients were referred to a dietician. Clinical improvement at 12 months of GFD was complete in 51% and partial in 49%. IgA tTG normalized after 12-30 months of GFD in 45%. On growth assessment at diagnosis and after 12-28 months of GFD, 100% had height increase (mean±SD: 7.11±4.43 cm) and 96% weight gain (mean±SD: 5.60±4.91 kg).

Conclusion: Overall, these findings outline the diverse clinical presentations of paediatric CD that should be considered irrespective of age. Increased clinician's awareness will enable an early diagnosis and treatment, with subsequent symptom and growth improvement.
GASTROENTEROLOGY: Coeliac disease

G-P-042

Gallstones in children with coeliac disease: a multi center cohort

Esra Polat¹, Nevzat Aykut Bayrak², Gunsel Kutluk¹, Burcu Volkan³, Ozge Kaba⁴

¹Kanuni Sultan Suleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Diyarbakir Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
³Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
⁴Kanuni Sultan Suleyman Research and Training Hospital, Paediatrics, Istanbul, Turkey

Objectives and study: Although it is more prominent in adults, gallstones (GS) have been increasingly diagnosed in children lately. It is known that functional or organic alterations in the whole gastrointestinal tract might influence the motility of the gut and the gallbladder (GB). Hence, it is suggested that impaired GB motility in coeliac disease (CD) GB motility would predispose to GS formation. The aim of the study is to evaluate the relation between GS formation and CD in children.

Methods: In this multicenter, cross-sectional study, incidental GS cases admitted between September 2015 and August 2016 in paediatric gastroenterology outpatient clinics were evaluated. The patients with cystic fibrosis, hemolytic disease, progressive familial intrahepatic cholestasis, under 24 months and without consent were excluded. demographic data was recorded and blood samples were obtained for anti-tissue transglutaminase (tTG) IgA for CD. Endoscopic biopsy for CD was suggested if necessary. At the same time the patients with celiac disease was evaluated by abdominal ultrasonography for GS.

Results: Of 15413 paediatric gastroenterology outpatient visits, 428 (2.8%) had GBS and 342 cases (mean age: 7.69±4.3 years, 51% girls) were eligible for the study. tTG IgA levels were high in 46 (7.3%, mean:54.7±13.9 U/mL) patients and CD was detected in 1 of 38 children (11 years old girl, BMI z-score: -3.79, 16mm GS, tTG IgA>300 U/mL) undergone biopsy. Also, a total of 271 CD patients (mean age: 10.1±3.9 years, 46.1% girls) were enrolled and 10 cases had GBS (frequency:3.6%, median age:13.2 years, 60% girl, mean tTG: 223±57.4 U/mL). CD cases with GS had significantly lover BMI z-scores than other CD cases, as well as non-CD patients with GS (-2.49±0.23, -0.68±0.74, 0.46±0.83 respectively, p<0.05). GS diameter was significantly larger in CD cases (17.75±8.4 mm vs. 7.8±7.3 mm, p<0.05).

Conclusion: Our cohort shows that; CD can be detected in patients with GS. Especially, GS cases with malnutrition should be evaluated for CD. Besides, CD patients with moderate to severe malnutrition and high tTG IgA levels might benefit an evaluation for GS.
Detection and quantification of gluten immunogenic peptides in faeces of infants and their relationship with the diet

Maria Roca\textsuperscript{1}, Esther Donat\textsuperscript{2}, Etna Masip\textsuperscript{2}, Begoña Polo\textsuperscript{2}, Paula Crespo Escobar\textsuperscript{3}, Victoria Fornes\textsuperscript{4}, Carmen Ribes Koninckx\textsuperscript{2}

\textsuperscript{1}Instituto de Investigación Sanitaria La Fe, U. Enfermedad Celiaca e Inmunopatología Digestiva, Valencia, Spain
\textsuperscript{2}La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
\textsuperscript{3}Hospital Universitari I Politecnic La Fe, Valencia, Spain
\textsuperscript{4}Instituto de Investigacion Sanitaria La Fe, Unidad de Bioestadística, Valencia, Spain

Objectives and study: To establish cut-off values of gluten immunogenic peptides (GIP) in faeces through two novel analysis methods, which are promising tools to detect dietary transgressions in CD patients on a gluten free diet.

Methods: Faecal samples were obtained from 48 healthy infants. Group 1 comprises 32 infants, aged 0 to 6 months, which had never ingested gluten. Of these 15 were exclusively breastfed (BF) and 8 had mixed feeding, all mothers with regular gluten consumption; 9 received infant formula (IF). Group 2 includes 16 infants, aged 6 to 24 months, who consumed unrestricted gluten containing cereals.

48 fecal samples (1/infant) were analyzed by using a rapid immunochromatographic test: iVYCheck GIP Stool, limit of detection 0.3\textmu gGIP/g faeces (Biomedal), and an enzyme-linked immunosorbent assay (ELISA): iVYLISA GIP-S, measuring range: 0.156-5\textmu gGIP/g faeces (Biomedal), both based on the antigliadin 33-mer monoclonal antibody.

Results: In group 1, by ELISA all infants presented values <0.156\textmu gGIP/g, and by immunochromatographic test the results were also negative, i.e. 100\% specificity for both methods. In group 2, the daily gluten intake calculated from a dietary questionnaire ranged from 0.5g to 10.5g/day. By ELISA all infants had values >0.156\textmu gGIP/g faeces, mean being 11.15 \textmu gGIP/g (range 0.56-46.79). The immunochromatographic test was negative in 4/16, thus sensitivity being 75\%. The Kappa Fleiss concordance index (Kappa = 0.79) indicates a moderate concordance between both methods. Additionally in group 2 we found a significant correlation (p = 0.03) between the mean daily gluten intake and the concentration of GIP in faeces.

Conclusion: According to our results both methods are highly specific, however the ELISA test displays a higher sensitivity. Although we found a significant correlation between the amount of gluten consumed and GIP recovery in faeces, more studies are needed specifically in individuals following a gluten free diet before generalizing the use of these methods for routine control in celiac patients.

Study funding by Asociación de Celiacos y Sensibles al gluten de la Comunidad de Madrid.
What factors influence the resolution of symptoms in celiac patients

Naire Sansotta¹, Hilary Jericho², Karine Amirikian³, Stefano Guandalini²

¹University of Verona, Department of Life and Reproduction Sciences, Section of Paediatrics, Verona, Italy
²University of Chicago, Department of Pediatrics, Section of Gastroenterology, Hepatology, and Nutrition, Chicago, United States
³University of Chicago, Department of Pediatrics, Chicago, United States

Objectives and study:
The aim of our study was to evaluate the efficacy of the gluten free diet (GFD) in resolving gastrointestinal and extra-intestinal manifestations and identify predictors for persistence of symptoms in children and adults with celiac disease (CeD) at the University of Chicago (UofC).

Methods: We conducted a retrospective chart review of the UofC Celiac Center clinic from January 2002 to May 2015. We included the following gastrointestinal (GI) symptoms: abdominal pain, bloating, constipation, diarrhea, failure to thrive/weight loss, nausea, reflux and vomiting. Among extra-intestinal (EI) manifestations we analyzed: abnormal liver enzymes, arthralgia/arthritis, dermatitis herpetiformis, alopecia, fatigue, headache, anemia, stomatitis, myalgia, psychiatric disorders, rashes, seizures, neuropathy, short stature, delayed puberty, osteoporosis, and infertility.

Non-adherence to the GFD was assessed through patient self-reporting and evaluation of celiac serologies.

Duration of symptoms (“no symptoms,” symptoms<5 years” or “symptoms>5 years), duration of diet and the presence of other significant comorbidities were also recorded.

Results: From 827 celiac patients in our database, 554 met inclusion criteria (biopsy confirmed CeD or clinical symptoms consistent with CeD plus TTG >10ULN and positive EMA without biopsy), of them 277 pediatric (< 18 years).

Long duration of symptoms, age>18 yrs old, female sex, negative family history of CeD and non-adherence to a GFD were the most important significant predictors of failure to clinically improve.

Conversely, duration of the diet and our examined comorbidities (including type 1 diabetes, food allergy and thyroid disease) did not appear to be statistically related to a patient’s rate of symptom resolution. See table 1.
### Table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>Symptom (%)</th>
<th>OR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>346</td>
<td>58</td>
<td>1.74</td>
<td>1.16-2.61</td>
<td>P = 0.0074</td>
</tr>
<tr>
<td>Male</td>
<td>131</td>
<td>42</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Age at diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;18 yrs</td>
<td>277</td>
<td>34</td>
<td>1.00</td>
<td>1.77-3.72</td>
<td>P = 0.0001</td>
</tr>
<tr>
<td>&gt;18 yrs</td>
<td>277</td>
<td>56</td>
<td>2.57</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>GFD strict</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>426</td>
<td>50</td>
<td>1.00</td>
<td>1.28-3.72</td>
<td>P = 0.0060</td>
</tr>
<tr>
<td>not</td>
<td>51</td>
<td>71</td>
<td>2.42</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of symptoms prior to diagnosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5yrs</td>
<td>370</td>
<td>48</td>
<td>1.00</td>
<td>1.44-3.56</td>
<td>P = 0.0004</td>
</tr>
<tr>
<td>&gt;5yrs</td>
<td>107</td>
<td>67</td>
<td>2.26</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Family history of CeD</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>152</td>
<td>39</td>
<td>1.00</td>
<td>1.47-3.24</td>
<td>P = 0.0001</td>
</tr>
<tr>
<td>No</td>
<td>325</td>
<td>58</td>
<td>2.19</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Duration of diet</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt;5yrs</td>
<td>353</td>
<td>51</td>
<td>1.00</td>
<td>0.80-1.83</td>
<td>P = 0.3442</td>
</tr>
<tr>
<td>&gt;5yrs</td>
<td>124</td>
<td>56</td>
<td>1.21</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Type 1 diabetes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>20</td>
<td>50</td>
<td>0.92</td>
<td>0.37-2.25</td>
<td>P = 0.8555</td>
</tr>
<tr>
<td>No</td>
<td>457</td>
<td>52</td>
<td>1.00</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Thyroid disease</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>426</td>
<td>51</td>
<td>1.00</td>
<td>0.82-2.70</td>
<td>P = 0.1857</td>
</tr>
<tr>
<td>No</td>
<td>51</td>
<td>60</td>
<td>1.49</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other comorbidities</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>367</td>
<td>49</td>
<td>1.00</td>
<td>0.99-2.36</td>
<td>P = 0.0531</td>
</tr>
<tr>
<td>Yes</td>
<td>110</td>
<td>60</td>
<td>1.53</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Food allergies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>433</td>
<td>51</td>
<td>1.00</td>
<td>0.73-2.57</td>
<td>P = 0.3240</td>
</tr>
<tr>
<td>Yes</td>
<td>44</td>
<td>59</td>
<td>1.37</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** On a strict GFD, children report greater rates of both GI and EI symptom resolution as compared to adults with greater rates of improvement in GI over EI symptoms. Longer duration of symptoms prior to diagnosis as well as poor adherence to the GFD predisposed a patient to poor symptom resolution. Early recognition of CeD and close attention to diet adherence may help in symptom resolution.
Current situation of celiac disease adults, diagnosed during childhood, 30 years later and the relationship with the compliance with de gluten free diet

Ignacio Ros¹, Monica López Campos¹, Ruth García Romero¹, Eduardo Ubalde Sainz¹, María Luisa Baranguan¹, Jose Miguel Martinez de Zabarte¹

1Miguel Servet Children's Hospital, Pediatric Gastroenterology and Nutrition Unit, Zaragoza, Spain

Objectives and study: To evaluate the relationship between the gluten free diet (GFD) compliance and the symptoms, laboratory tests result, bone mineral density and the presence of autoimmune diseases of adult patients diagnosed in childhood with celiac disease at our centre, at least 25 years ago.

Methods: Patients with celiac disease (CD) diagnosed in childhood at our centre between 1979 and 1990, following the ESPGHAN guidelines in force (at least 3 biopsies). Patients were given a clinical interview, genetic testing, blood tests and bone densitometry (spine DXA). The local ethics committee approved the project. All patients signed informed consent.

Results: The patients that had been diagnosed between 1970 and 1990 were 68, we managed to contact 56, and 54 of them agreed to participate (Current age: 32.61 ± 8.64 years old, age at time of diagnosis: 13.28 ± 9.29 months old).

All the patients followed a strict GFD during childhood. Currently 56% of patients assured to follow a strict GFD, even though only 31% performed it correctly, 22% of them considered their diet was gluten-restricted and 22% of patients had an unrestricted gluten diet. 70% claimed to have no symptoms through gluten intake. Medical supervision was finished after completing the pediatric controls in 63% of patients.

No significant differences were observed between the degree of compliance with the GFD and the presence of symptoms (diarrhea, asthenia, and constipation), the presence of other diseases or the inflammatory and nutritional laboratory values. Also, no differences were found in the presence of osteoporosis, or in other autoimmune disorders.

Duodenal biopsies were performed in half of cases (6 cases) of the uncontrolled gluten diet patients, all of them being strictly normal.

Conclusion: The degree of compliance with the gluten-free diet in adult patients diagnosed with celiac disease in childhood was very low.

Contrary to what was expected, we did not find a greater number of symptoms, complications, laboratory abnormalities, or autoimmune diseases in patients with lower dietary compliance.

It is surprising that our celiac patients diagnosed in childhood currently present completely normal biopsies in spite of taking gluten, although this data has already been described in other studies.
**Objectives and study:** Familial Mediterranean fever and celiac disease share many common clinical features for example; diarrhea, abdominal pain, arthralgia, and arthritis. Both of the diseases are associated with many inflammatory and auto-immune conditions, as well. A diagnosis of celiac disease in patients with FMF could be challenging due to many common clinical features. We present a 15-year-old male, diagnosed with familial Mediterranean fever before 6 years, recently diagnosed with celiac disease.

**Methods:** Our patient with familial Mediterranean fever was admitted to the pediatric emergency unit many times, with complaints of recurrent widespread, and epigastric abdominal pain in the last month. Acute phase reactants were in normal limits at consecutive blood analysis. His family history revealed that his brother has celiac disease. The previous celiac serology for our case had been done when he was 10 years old and the result was found as negative. Due to the presence of severe epigastric tenderness and pain, gastroduodenoscopy was performed and then multiple small intestinal biopsies were obtained.

**Results:** After gastroduodenoscopy procedure, tissue transglutaminase antibody IgA level was re-analysed, tissue transglutaminase antibody level was found as positive (> 300 U/ml). The pathology result was compatible with Marsh 3 classification, so celiac disease was diagnosed.

**Conclusion:** The diagnosis of celiac disease is difficult in patients with familial Mediterranean fever because both of the diseases have similar clinical symptoms. Even if previous screening is negative for celiac disease as in this case, celiac disease should be considered particularly in patients with familial Mediterranean fever who have similar clinical symptoms, and a positive family history for celiac disease.
Evaluation of hearing loss in pediatric celiac patients

Yasin Sahin¹, Cengiz Durucu², Derya Aydin Sahin³

¹Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Gaziantep University, Medical Faculty, Otorhinolaryngology, Head and Neck Surgery, Gaziantep, Turkey
³Gaziantep University, Medical Faculty, Pediatric Cardiology, Gaziantep, Turkey

Objectives and study: Celiac disease (CD) is a chronic immune-mediated enteropathy caused by the ingestion of gluten in genetically predisposed individuals. In some reports, sensorineural hearing loss (SNHL) has been identified as an extraintestinal symptom of CD. We aimed to further investigate the possible association between CD and SNHL by examining a greater number of pediatric CD patients.

Methods: The study was carried out from March to September 2014 and included 110 pediatric patients with biopsy-confirmed CD (220 ears) and 41 age- and sex-matched controls (82 ears); participants were evaluated by tympanometry and pure tone audiometry (frequency, 250–8000 Hz frequency).

Results: Audiometric bone conduction thresholds were significantly different between the CD patients and the controls (p < 0.05), but there were no significant differences in pure tone averages for air conduction (p > 0.05). When the results for CD patients were analyzed according to duration of disease (≤36 months and >36 months), a significant difference in bone conduction thresholds (p < 0.05) was noted, with significant increments at the later stages of disease. However, this difference was not sufficient to define clinical hearing loss, as the pure tone average thresholds remained below 20 dB.

Conclusion: These results indicate that subclinical hearing loss may be present in children with CD, which could presage more serious hearing impairments at older ages and later stages of the disease. Hearing screenings should be recommended for children with CD in order to prevent the potentially unfavorable effects of hearing loss on the emotional, behavioral, cognitive, and sensorimotor development of these patients.

Disclosure of interest: This manuscript was published in International Journal of Pediatric Otorhinolaryngology (2015; 79: 378–381), but it is not presented in any congress or meeting. We want to present it in this ESPGHAN meeting.
The frequency of the celiac disease in patients with juvenile idiopathic arthritis

Yasin Sahin¹, Sezgin Sahin², Kenan Barut³, Fugen Cullu Cokugras³, Tulay Erkan⁴, Amra Adrovic², Tufan Kutlu⁵, Ozgur Kasapcopur²

¹Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Istanbul University, Cerrahpasa Medical Faculty, Pediatric Rheumatology, Istanbul, Turkey
³Istanbul University Cerrahpasa Medicine Faculty, Department of Paediatric Gastroenterology, Istanbul, Turkey
⁴Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
⁵Istanbul University Cerrahpasa Medicine Faculty, Pediatric Gastroenterology Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: We aimed to assess the frequency of celiac disease (CD) in patients with juvenile idiopathic arthritis (JIA).

Methods: This prospective study was carried out from October 2015 to August 2016 and included 96 patients with JIA. We used 85 age- and sex-matched healthy subjects as a control group. Patients were evaluated in terms of clinical and laboratory findings of CD. Levels of total IgA and tissue transglutaminase (tTG) IgA antibody were measured in both patients and control groups. Those with increased level of tTG IgA were further tested for anti-endomysium IgA antibodies (EMA). Gastroduodenoscopy and intestinal biopsy were planned for a definite diagnosis of CD in patients with positive EMA.

Results: Of the 96 patients in this study, 56 (58.3%) were female, and 40 (41.7%) were male. The mean age and weight were 11.58±4.59 years and 38.69±15.53 kg, respectively. Thirty-four of our patients (35.4%) had oligoarticular form of JIA, 29 (30.2%) had polyarticular form, 12 (12.5%) had enthesitis-related arthritis (ERA) form, 11 (11.5%) had systemic form, and 10 (10.4%) psoriatic form. Sixteen of our patients (16.6%) were not using any drugs during the study. Neither EMA IgA antibodies were analysed nor gastro-duodenoscopy was performed because no patients were positive for tTG IgA. There was no difference in terms of tTG levels between between the patients using NSAIDs or other drugs. In the control group: 50 subjects (58.8%) were female and 35 (41.2%) were male. Only one subject from the control group was positive for tTG IgA but EMA positivity was not detected.
**Table:**

Table I. Demographic and laboratory characteristics of patients and healthy controls

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=96)</th>
<th>Healthy controls (n=85)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
<td></td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>11,58±4,59</td>
<td>11,31±4,51</td>
<td>0.694</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>143,18±22,60</td>
<td>141,86±22,69</td>
<td>0.696</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>38,69±15,53</td>
<td>38,42±15,53</td>
<td>0.907</td>
</tr>
<tr>
<td>Hemoglobine (mg/dL)</td>
<td>12,44±1,33</td>
<td>12,80±1,47</td>
<td>0.095</td>
</tr>
<tr>
<td>MCV</td>
<td>81,61±5,10</td>
<td>80,26±4,36</td>
<td>0.055</td>
</tr>
<tr>
<td>Plt (/mm(^3))</td>
<td>307,41±91,63</td>
<td>285,33±75,33</td>
<td>0.074</td>
</tr>
<tr>
<td>tTG IgA (U/ml)</td>
<td>1,04±1.42</td>
<td>1,55±2.44</td>
<td>0.097</td>
</tr>
<tr>
<td>Total IgA (mg/dl)</td>
<td>153,95±77,24</td>
<td>134,96±59,76</td>
<td>0.065</td>
</tr>
<tr>
<td>Age at diagnosis (yrs)</td>
<td>6,44±4,17</td>
<td>-</td>
<td></td>
</tr>
</tbody>
</table>

*Plt=thrombocytes, MCV= mean corpuscular volume, tTG=tissue transglutaminase*

**Conclusion:** We did not find CD in children with JIA. According to our results, we think that there is no relationship between celiac disease and JIA disease in children. Larger studies are needed to provide healthier interpretation.
GASTROENTEROLOGY: Coeliac disease

G-P-049

Depression and quality of life in mothers of child with celiac disease

Nergiz Sevinc¹, Ahmet Öztürk¹, Eylem Sevinç²

¹Erciyes University Public Health, Kayseri, Turkey
²Kayseri Training and Education Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Kayseri, Turkey

Objectives and study: Just like other chronic diseases, Celiac disease (CD) affects physical, mental, and social lives as well as health-related quality of life of children. The purpose of this study was to evaluate depression and the quality of life in mothers with children suffering from celiac disease compared with those who have healthy children. To our knowledge, this study is the first report of the assessment of depression and quality of life (QoL) in mothers of child with CD

Methods: Mothers having a celiac child (n = 93) and mothers having a healthy child (n = 93) were enrolled. Short-Form Health Survey (SF-36) Questionnaire and Beck Depression Inventory (BDI) were used to assess depression and QoL of mothers.

Results: The mean score on the BDI of mothers with celiac child and control were 21 (min-max:0-50) and 8 (min-max: 0-32) respectively. The mothers of children with celiac disease had significantly lower QoL scores in SF-36 for all subscales and higher levels of depression by using BDI (p<0.05). There was a positive correlation between economic status and SF-36 mean scores in celiac group. Furthermore we detected that there was a negative correlation between SF-36 mean scores and BDI mean scores in celiac group. There were no statistical significance between celiac group and controls for age, sociodemographic and familiar characteristics (p>0.05).

Conclusion: The findings of this study indicated that celiac disease has a severe impact on mother QOL and psychological health. Increased depression levels affected with badly in mother's quality of life. We think that the mothers with celiac child might be evaluated by a psychiatrist for an optimal quality of life and mental health.
The frequency of the celiac disease among children with familial Mediterranean fever

Yasin Sahin¹, Amra Adrovic², Kenan Barut², Tufan Kutlu¹, Fugen Cullu Cokugras³, Sezgin Sahin², Ozgur Kasapcopur², Tulay Erkan⁴

¹Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Istanbul University, Cerrahpasa Medical Faculty, Pediatric Rheumatology, Istanbul, Turkey
³Istanbul University Cerrahpasa Medicine Faculty, Department of Paediatric Gastroenterology, Istanbul, Turkey
⁴Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: We aimed to assess the frequency of celiac disease (CD) in patients with Familial Mediterranean Fever (FMF) followed up at our clinic. By this way, we wanted to explore if the screening for CD is necessary among patients with childhood FMF.

Methods: This is a prospective study performed in the time period from October 2015 to March 2016. A total of 303 patients followed up with the diagnosis of FMF were included in the study. Ninety-eight sex- and age-matched healthy subjects were used as a control group. Levels of total IgA and tissue transglutaminase (tTG) IgA antibody were measured in both patients and control groups. Those with increased level of tTG IgA were tested for anti-endomysium IgA antibodies (EMA). Patients with positive EMA underwent gastro-duodenoscopy and intestinal biopsy for a definite diagnosis of CD.

Results: A total of 303 childhood FMF patients we included in the study. One hundred fifty-two patients (50.2%) were male and 151 of them (49.8%) were female. In the control group: 50 subjects (51%) were male and 48 of them (49%) were female. Only 9 of 303 patients (2.9%) were positive for tTG IgA. Patients positive for tTG IgA were then tested for EMA IgA antibodies and only one of them (0.3%) had a positive result. This patient underwent gastro-duodenoscopy. The pathological report was compatible with Marsh 0 classification score for the diagnosis of CD. Two subjects from the control group were positive for tTG IgA but none of them had positive EMA antibodies.

Conclusion: We did not find CD in the large cohort of childhood FMF patients. This study reports the lack of association between FMF and CD in childhood. It points out that screening for CD could be unnecessary for the patients with childhood FMF.
**GASTROENTEROLOGY: Coeliac disease**

G-P-051

**A rare cause of protein-losing enteropathy: celiac disease**

Yasin Sahin¹, Fatih Varol², Nuray Kepil³, Tulay Erkan⁴, Tufan Kutlu¹

¹Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Istanbul University, Cerrahpasa Medical Faculty, Pediatric Emergency, Istanbul, Turkey
³Istanbul University, Cerrahpasa Medical Faculty, Pathology, Istanbul, Turkey
⁴Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

**Objectives and study:** We present a case, who had a protein losing enteropathy, recently diagnosed with celiac disease to underline that celiac disease should be considered as a rare presenting cause of protein losing enteropathy as in this case.

**Methods:** Our patient had admitted to the hospital with complaints of vomiting, swollen eyelids, abdominal pain, and distension. She had this complaints for one week. After evaluation, hypoalbuminemia was found, but protein loss was not detected in the urine analysis. Pleural effusion and ascites were detected in abdominal ultrasonography. Albumin infusion was administered two times with a dose of 1 g/kg. After that, she was referred to our hospital for further evaluation and treatment.

**Results:** When the patient came to our hospital, we detected edema in eyelids, ascites, and pretibial edema in the physical examination. In laboratory analysis, hemoglobin 10.6 g/dl, MCV 69.1, platelet 289,000/mm³, AST 38, ALT 19, total protein 4.4 g/dl, albumin 3.5 g/dl, triglycerides 386 mg/dl, total cholesterol were 91 mg/dl, and no proteinuria was detected. We found a high albumin levels, because of receiving albumin infusion at the first hospital. One day after admission, serum albumin level decreased to 2.6 g/dl. Gastroduodenoscopy was performed on our patient to evaluate in terms of etiology of protein losing enteropathy. We observed the disappearance of normal mucosal patterns, scalloped duodenal folds macroscopically. Four biopsies from the duodenum, and one biopsy from the bulb was taken, and celiac disease was considered. And then total IgA, tissue transglutaminase, and anti-endomisium antibody levels were detected as 22.3 mg/dl, 300 U/ml and positive, respectively. The pathology result was compatible with Marsh classification 3, so celiac disease was diagnosed. Gluten-free diet was started. Five days after gastroduodenoscopy, total protein and albumin levels were 3.0 g/dl, 2.1 g/dl, respectively. Albumin infusion was not administered, and she complied with a strict gluten-free diet. In 7 days of hospitalisation, edema on eyelids disappareared, ascites and pretibial edema decreased and the patient was discharged. After 10 days, she had no complaints, there was no ascites, and swollen eyelids in physical examination. Also pretibial edema decreased. Total protein level was 5.5 g/dl, and albumin level was 3.7 g/dl.

**Conclusion:** Although it is a rare reason, celiac disease should be considered as a cause of protein losing enteropathy as in our case.
GASTROENTEROLOGY: Coeliac disease

G-P-052

The frequency of celiac disease in children with autoimmune thyroiditis

Yasin Sahin¹, Olcay Eviyaoglu², Tulay Erkan³, Fugen Cullu Cokugras⁴, Oya Ercan², Tufan Kutlu¹

¹Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Istanbul University, Cerrahpasa Medical Faculty, Pediatric Endocrinology, Istanbul, Turkey
³Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
⁴Istanbul University Cerrahpasa Medicine Faculty, Department of Paediatric Gastroenterology, Istanbul, Turkey

Objectives and study: Although the presence of autoimmune thyroiditis (AT) in celiac disease (CD) has been well documented, CD in AT has been less reported especially in children. We aimed to investigate the frequency of CD in children with AT.

Methods: Sixty six patients with AT were enrolled in the study. Age- and sex-matched 66 healthy children were used as a control group. Patients were evaluated in terms of clinical and laboratory findings of CD. Firstly, total IgA and tissue transglutaminase antibody (tTG) IgA were measured in both groups. Then anti-endomysial antibody (EMA) IgA was analysed in patients with tTG positivity. Patients with positive EMA underwent gastroduodenoscopy and intestinal biopsy for a definitive diagnosis of CD.

Results: Sixty six patients with AT (52 female, 14 male) aged 14.68±3.18 years, and sixty six healthy children (43 female, 23 male) aged 13.61±3.46 years were enrolled. IgA deficiency was found in four patients, then tTG IgG measured was found negative. tTG IgA was found positive in only three (4.5%) patients, then EMA IgA was screened, and seropositivity was found in only one (1.5%) patient. Gastroduodenoscopy was performed on this patient, multiple small intestinal biopsies was obtained. The result of pathology was consistent with Marsh 3 classification, so CD was detected. Also, a patient with AT had been diagnosed with CD previously. No CD was detected in control group.

Table:

<table>
<thead>
<tr>
<th>Patient no</th>
<th>tTG IgA (U/ml)</th>
<th>Total IgA (mg/dl)</th>
<th>EMA IgA</th>
<th>Pathology</th>
<th>Thyroid function status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1*</td>
<td>300</td>
<td>126</td>
<td>+</td>
<td>Marsh 3</td>
<td>hypothyroid</td>
</tr>
<tr>
<td>2</td>
<td>300</td>
<td>158</td>
<td>+</td>
<td>Marsh 3</td>
<td>euthyroid</td>
</tr>
<tr>
<td>3</td>
<td>42.4</td>
<td>120</td>
<td>-</td>
<td>-</td>
<td>hypothyroid</td>
</tr>
<tr>
<td>4</td>
<td>16.2</td>
<td>135</td>
<td>-</td>
<td>-</td>
<td>euthyroid</td>
</tr>
</tbody>
</table>

⁴tTG=tissue transglutaminase, EMA= anti-endomysium antibodies
*The patient diagnosed with Down syndrome

Conclusion: Two (3.0%) of sixty-six patients with AT were found to have CD. According to the results, we believe that there was a close relationship between CD and AT disease, but larger studies are needed to provide healthier interpretation.
The frequency of celiac disease in children with colchicine-resistant familial Mediterranean fever

Yasin Sahin1, Kenan Barut2, Tufan Kutlu1, Fugen Cullu Cokugras3, Amra Adrovic2, Sezgin Sahin2, Tulay Erkan4, Ozgur Kasapcopur2

1Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
2Istanbul University, Cerrahpasa Medical Faculty, Pediatric Rheumatology, Istanbul, Turkey
3Istanbul University Cerrahpasa Medicine Faculty, Department of Paediatric Gastroenterology, Istanbul, Turkey
4Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: Familial Mediterranean fever (FMF) and celiac disease (CD) share many common clinical features such as abdominal pain, diarrhea, arthralgia and arthritis. Also, both of the diseases are associated with many inflammatory and autoimmune diseases. There are two studies investigating the frequency of CD in patients with FMF. According to our knowledge, there is no study investigating the frequency of CD in patients with colchicine-resistant familial Mediterranean fever (crFMF). It can be difficult to diagnose CD in patients with crFMF because of having similar clinical findings. For this reason, we aimed to investigate the relationship between CD and crFMF disease.

Methods: This prospective study was carried out from October 2015 to August 2016. A total of 24 patients with crFMF were included in the study. We used 60 sex- and age-matched healthy subjects as a control group. Levels of total IgA and tissue transglutaminase (tTG) IgA antibody were measured in both patients and control groups. Those with increased level of tTG IgA were tested for anti-endomyosium IgA antibodies (EMA). Gastroduodenoscopy and intestinal biopsy were planned for a definite diagnosis of CD in patients with positive EMA.

Results: Of the 24 patients in this study, 18 (75.0%) were female, and 6 (25.0%) were male. The mean age and weight were 12.28±4.79 years and 41.04±17.35 kg, respectively. Only 4 (16.6%) of 24 patients were positive for tTG IgA. Patients with positive for tTG IgA were then tested for EMA IgA antibodies and EMA positivity was not detected in any of patients. In the control group; 45 subjects (75.0 %) were female and 15 (25.0%) were male. Only one (1.6%) subject from the control group was positive for tTG IgA but EMA positivity was not detected. No IgA deficiency was detected in both patients and control groups.

Conclusions: We did not find CD in 24 children with crFMF. According to our results, we think that there is no relationship between celiac disease and crFMF disease in children.
Role of High Mobility Group Box 1 (HMGB1) as a non-invasive biomarker of gut inflammation in a cohort of paediatric celiac patients at diagnosis and during follow-up

Chiara Maria Trovato¹, Francesca Palone², Roberta Vitali², Laura Stronati³, Salvatore Cucchiara⁴, Monica Montuori¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsichiatry, Rome, Italy
²Enea, Radiobiology and Human Health, Rome, Italy
³Sapienza University of Rome, Cellular Biotechnology and Hematology, Rome, Italy
⁴Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy

Objectives and study: Coeliac disease (CD) is a immune-mediated systemic disorder. Fecal high mobility group box 1 (HMGB1) has been suggested to be a novel non-invasive biomarker of gut inflammation. We aimed to assess the reliability of fecal HMGB1 in detecting intestinal damage in children with CD at diagnosis and during the follow-up.

Methods: Stool samples from 37 children (M: 14; F:23) with CD at the diagnosis were analysed; samples from 24 of 37 subjects were obtained and analysed also during follow-up. Western-Blot analysis was performed in assessment of fecal HMBG1.

Results: Fecal HMGB1 was positive in all of 37 children at the diagnosis. During the follow-up, the value of HMGB1 decreased in 21 of 24 stool samples analyzed. Significant difference (Wilcoxon signed-rank test, p<0.01) was observed between diagnosis and follow-up; correlation between anti-tissue transglutaminase (anti-tTG) IgA and HMGB1 band intensity was observed, but failed to reach statistical significance (Spearman's rank correlation coefficient, rho = 0.416, p = 0.1027).

Conclusion: Fecal HMGB1 in coeliac patients at diagnosis and during follow-up could be a valid noninvasive biomarker of gut inflammation. Our results need validation through a study involving a greater population. Furthermore, analysis of HMGB1 may be used as a complementary tool for serum evaluation of coeliac disease.
The frequency of celiac disease in Turkish children with systemic lupus erythematosus

Yasin Sahin¹, Sezgin Sahin², Amra Adrovic², tulay erkan³, tufan kutlu¹, Kenan Barut³, Fugen Cullu Cokugras⁴, Ozgur Kasapcopur²

¹Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Istanbul University, Cerrahpasa Medical Faculty, Pediatric Rheumatology, Istanbul, Turkey
³Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
⁴Istanbul University Cerrahpasa Medicine Faculty, Department of Paediatric Gastroenterology, Istanbul, Turkey

Objectives and study: We aimed to assess the frequency of celiac disease (CD) in patients with systemic lupus erythematosus (SLE).

Methods: This prospective study was carried out from October 2015 to August 2016 and included 50 patients with SLE. We used 41 age- and sex-matched healthy subjects as a control group. Patients were evaluated in terms of clinical and laboratory findings of CD. Levels of total IgA and tissue transglutaminase (tTG) IgA antibody were measured in both patients and control groups. Those with increased level of tTG IgA were further tested for anti-endomysium IgA antibodies (EMA). Gastroduodenoscopy and intestinal biopsy were planned for a definite diagnosis of CD in patients with positive EMA.

Results: Of the 50 patients in this study, 44 (88.0%) were female, and 6 (12.0%) were male. The mean age and weight were 15.49±3.39 years and 50.72±13.31 kg, respectively. Thirteen (60.0%) of our patients were receiving corticosteroids, and four (8.0%) were receiving no therapy at the time of the study. Only three (6.0%) of our patients were positive for tTG IgA. Patients with positive for tTG IgA were then tested for EMA IgA antibodies and none of them had a positive result. No gastroduodenoscopy was performed. In the control group: 34 subjects (82.9%) were female and 7 (17.1%) were male. Only one (2.4%) subject from the control group was positive for tTG IgA but EMA positivity was not detected. There was no difference between the patients and controls in terms of tTG levels (p> 0.05). Also, there was no difference between the patients who did and did not use steroids in terms of tTG levels (p> 0.05).

Conclusion: We did not find CD in children with SLE. According to our results, we think that there is no association between celiac disease and SLE in children. Larger studies are needed to provide more valid interpretation.
The incidence of celiac disease in type 1 diabetes depends on diabetes duration

Mordechai Slae, Azi Romem, David Strich, Michael Wilschanski

1Hadassah Hebrew University Medical Center, Pediatric Gastroenterology, Jerusalem, Israel
2Hebrew University, Pediatrics, Jerusalem, Israel
3Hebrew University, Pediatric Endocrinology, Jerusalem, Israel

Objectives and study: The prevalence of celiac disease (CD) in children with diabetes mellitus type 1 (DM1) ranges from 1.6 – 12.3%. In most cases, CD is diagnosed by screening tests in patients with no clinical symptoms. Due to the high prevalence in this population, it is recommended to perform periodic tests, but there is no scientific basis for the frequency of performance of such tests. The purpose of this study was to investigate the incidence of the appearance of CD in children with DM1 and to identify risk factors for the development of CD.

Methods: All celiac antibody screening tests and small bowel biopsy results taken from 1998 until 2015 were collected from patients with DM1. Based on these results, the prevalence of celiac antibodies and the yearly incidence following the diagnosis of DM1 was computed. Identification of the risk factors for CD were also recorded.

Results: The charts of 314 children diagnosed with DM1 were examined. 31 (9.87%, 95% CI 6.8-13.7) were found to have positive celiac antibodies. 25 of those underwent small bowel biopsy. 16 were positive, 7 negative and 2 were inconclusive. In 6 patients, biopsy was not performed, 2 of whom were diagnosed because of high levels (10 times normal) of antibodies, in 3 there was a spontaneous normalization of celiac antibodies with no dietary treatment, and 1 was lost to follow-up. Kaplan-Meier survival analysis showed that the probability of developing antibodies increases with the length of time after diagnosis of DM1 and reaches a peak of 17.69% after 13 years. A total of 18 subjects were diagnosed with CD (5.73%, 95% CI 2.7-7.8), 3 were diagnosed at initial diagnosis of DM1. Kaplan-Meier survival analysis showed that the probability of developing CD increases with the length of time after diagnosis of DM1 and reaches a peak of 8.49% after 5.3 years. In the celiac group, the average age of diagnosis of DM1 was 7.22 years as opposed to 9.78 years in the non-celiac group (p=0.02). There was no correlation between gender or other familial auto-immune disorders.

Conclusion: This study shows that screening for CD is recommended at diagnosis of DM1 and thereafter yearly for the following 5 years only. There is no benefit for screening after 5 years after diagnosis of DM1. Early age of diagnosis of DM1 is a risk factor for developing CD.
Iron deficiency anemia and coeliac disease: the role of DMT1 IVS4+44CA polymorphism

Carlo Tolone¹, Caterina Strisciuglio¹, Giulia Bellini¹, Grazia Cirillo¹, Crescenzo Coppola¹, Alfonso Papparella¹, Francesca Rossi¹

¹Second University of Naples, Department of Woman, Child and General and Specialistic Surgery, Naples, Italy

Objectives and study: Iron-deficiency anemia (IDA) is often recorded in newly diagnosed coeliac disease (CD) and may persist for variable periods after beginning of a gluten free diet. IDA may also be the only clinical feature of CD in absence of classical symptoms such as diarrhea or weight loss. Since CD is an immune-mediated disorder largely focused in the proximal small intestine, it can compromise iron absorption that occurs mostly in the duodenum. Interestingly, many coeliac patients, even with severe grade of villous atrophy, do not present IDA.

Recently it has been shown that also reduced expression of different regulatory proteins critical in iron uptake may be responsible of IDA in CD.

The most important apical uptake transporter of inorganic iron is the divalent metal transporter DMT1. It was demonstrated that a missense mutation in DMT1 in rodents causes an IDA; IDA caused by DMT1 mutations was also identified in human subjects. Moreover, previous studies have reported an association between DMT1 IVS4+44C/A polymorphism and the increased risk of some diseases such as Wilson's disease, age related macular degeneration and Parkinson's disease. It has also been demonstrated in a Turkish population that the polymorphism of DMT1 IVS4+44C/A is associated with inter-individual variations in blood iron.

The aim of our study was to investigate the association between the DMT1 IVS4+44C/A polymorphisms and IDA in a paediatric cohort of CD patients.

Methods: The study was carried out on 410 South Italian children with CD referred from January 1989 to December 2015 to the Department of Paediatrics of the Second University of Naples. Demographic and clinical data of each patient were retrospectively collected from medical records and an interview including a questionnaire at the time of enrollment.

All data (age at diagnosis, Hb, MCV, serum iron, IgA anti TTG, mucosal damage) were collected blind to the DMT1 IVS4 polymorphism. Diagnosis of IDA was performed if Hb and MCV were < 3°th (- 2 DS) by age and sex and low serum iron (IST < 0,151; ferritin < 10 ng/ml). Diagnosis of CD was performed according to the ESPGHAN criteria (typical histological findings on duodenal biopsies and positive serological test specific for CD). This study included only patients with all data at diagnosis and that underwent to duodenal biopsies.

DMT1 IVS4 polymorphism analysis was performed in 387/410 patients.

Results: We analyzed a cohort of 410 children with CD at diagnosis (M 164), 137 of them (33,4%) with IDA. There was significant difference between CD IDA and CD non-IDA patients in lower median age at diagnosis (49,2 ± 43,7 months), lower Hb level (p-value 0,0164), MCV (p-value 0) and all the parameters related to iron absorption (p-value 0); there was no difference in the level of specific antibodies (p-value 0,21) or in the grade of villous atrophy (p-value 0,79). 33 children (8,53%) resulted homozygote AA; 21/33(63,64%) were AA with IDA.

Conclusion: We report for the first time in CD patients an association between IDA and DMT1 IVS4+44C/A polymorphism. Such variant was more frequent in CD anemic patients compared to CD not anemic (5,43% vs 3,10%), and it was associated with a significantly higher odds ratio to develop IDA compared to AC and CC genotype (OR 3,7; CI 95%; 1.77-7.85). CD patients with IDA were also significantly younger at the diagnosis than non anemic patients. Interestingly, there was no difference in the level of specific antibodies or in the grade of villous atrophy between patients with or without IDA.
**GASTROENTEROLOGY: Coeliac disease**

G-P-058

**Celiac disease in children with peptic ulcer**

Gokhan Tumgor¹, Mehmet Agin¹, Figen Doran², Salih Cetiner³

¹Cukurova University Medical Faculty, Dept of. Pediatric Gastroenterology, Hepatology and Nutrition, Adana, Turkey
²Cukurova University Medical Faculty, Pathology, Adana, Turkey
³Cukurova University Medical Faculty, Dept. of. Medical Biology, Adana, Turkey

**Objectives and study:** Injury to the duodenum and jejunal mucosa is observed in the majority of cases of celiac disease. The incidence of peptic ulcer associated with celiac disease reported in the literature is low, and generally appears in the form of case reports. The purpose of this study was to investigate the incidence of celiac disease in cases of childhood celiac disease and to compare these subjects with non-celiac ulcer patients in terms of clinical and laboratory values.

**Methods:** Upper GIS endoscopy was performed in 1760 cases at the Çukurova University Faculty of Medicine Pediatric Gastroenterology Department, Turkey, between January 2012 and January 2016. Two hundred fifty patients (14%) were diagnosed with celiac disease on the basis of endoscopic and histopathological findings, and 74 (4%) were diagnosed with peptic ulcer. Serum anti-tissue transglutaminase antibodies IgA (tTGA), anti-endomysial antibodies IgA (EMA) and serum IgA were studied in the 74 patients diagnosed with peptic ulcer. Gastric and duodenum biopsy specimens were stained with hematoxylin and eosin and examined for the presence of *H. pylori* infection and celiac disease.

**Results:** tTGA and EMA (+) were determined in 22 (29%) of the 74 cases in which peptic ulcer was identified at upper GIS endoscopy, and celiac disease was confirmed histopathologically. *H. pylori* was positive in 14 (63%) of the celiac cases and in 23 (44%) of the non-celiac cases. The difference was not statistically significant (p=0.12). The level of *H. pylori* (-) celiac patients with ulcer among all cases of ulcer was 10.8% (8/74; 10.8%). The prevalence of celiac disease among all *H. pylori* (-) ulcer cases was 21% (8/37). *H. pylori* positivity was determined in 44 of our celiac disease cases without ulcers (44/228, 19%), and a statistically significant difference was determined in comparison with celiac disease cases with peptic ulcer (p=0.000). Hemoglobin, MCV and ferritin values were significantly low in the celiac group. There was no difference between the two groups in terms of other laboratory values.

**Table:**

<table>
<thead>
<tr>
<th>Peptic Ulcus</th>
<th>Celiac disease</th>
<th>nonCeliac disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>H. pylori (+)</td>
<td>H. pylori (-)</td>
</tr>
<tr>
<td></td>
<td>H. pylori (+)</td>
<td>H. pylori (-)</td>
</tr>
</tbody>
</table>

**Conclusion:** The incidence of celiac disease increased in cases with peptic ulcer. Cases of peptic ulcer identified at endoscopy should also be evaluated in terms of celiac disease.
Bone mineral density and vitamin D treatment in patients with coeliac disease

Burcu Volkan¹, Nevzat Aykut Bayrak², Atilla Çayır³

¹Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
²Diyarbakir Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
³Erzurum Regional Training and Research Hospital, Department of Pediatric Endocrinology, Erzurum, Turkey

Objectives and study: Impaired bone health is a common entity in children with coeliac disease. Numerous studies have assessed bone status in CD, both at diagnosis and after (gluten free diet) GFD. It is observed that children with CD have a lower bone mass at diagnosis compared to healthy controls and have revealed complete recovery or significant but incomplete improvement of BMD following diet therapy. The aim of this study was to investigate the bone mineral density (BMD) (before and after treatment in children with CD) and osteopenia treatment response in children with CD.

Methods: This multi-center study investigated patients with CD. Demographic data such as height, weight and diet compliance were obtained from physical examination and patient questionnaires. Blood samples for anti-tissue transglutaminase IgA (anti-tTG IgA), 25-hydroxy vitamin D, calcium, phosphate, magnesium, alkaline phosphatase (ALP) and PTH were assayed. BMD of the lumbar spine was measured in all subjects. Depending on the results, patients were given either stoss therapy and calcium support or 400 U/day vitamin D and calcium support. Patients with normal BMD and vitamin D levels were observed without treatment. Parameters were studied again after treatment.

Results: Three hundred sixteen CD patients (mean age, 12.2±2.8 years; 59.8% female) were included. Demographic data and biochemistry of cases are shown in Table 1. Based on BMD results, 46.5% of patients were normal, 33.2% were diagnosed with osteopenia and 20.3% with osteoporosis. One hundred thirty-one patients attended regular follow-ups, and their results were evaluated after treatment. Vitamin D (before: 18.4 ± 9.1, after: 22.1 ± 9.8, p=0.004), PTH (before:66.8 ± 43.8, after:54.2 ± 22.8, p=0.007) and tTG IgA (before: 94.6 ±101.6, after:64.5 ±83.1, p=0.003), levels were significantly improved in both therapy groups. No vitamin D support was given to 7.6% of the 131 patients attending follow-ups, while 43.5% received stoss therapy and calcium support and 42.9% received 400 U/day vitamin D and calcium support. There was no significant change in BMD in the untreated group (BMD1: -0.39±0.87, BMD2: -1.04±0.84, P>0.05), Control BMD improved significantly in the patients receiving stoss therapy and 400 U/day vitamin D (BMD1: -1.77±1.21, BMD2: -0.47±1.18, p<0.05) vs (BMD1: -0.6±1.15, BMD2: - 0.18±1.09, p<0.01).
**Conclusion:** BMD of the 400 U vitamin D and stoss group were both improved at the end of the study, however the improvement was more statistically significant in 400 U vitamin D group. The reason might be the continuing vitamin D support in 400 U vitamin D group, besides the patients in the stoss group had more severe osteopenia. Meanwhile, the normal mean bone mass of the untreated group turned into osteopenia state at the end of the study. As a result, bone mineralization seems to be a highly dynamic process. We think that maintaining vitamin D and calcium support in physiological doses after stoss therapy will contribute still further to improvement of BMD in patients with CD.

**Table 1:** Demographic data and biochemistry of celiac patients

<table>
<thead>
<tr>
<th></th>
<th>Celiac Patients (n=316)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diet time (year)</td>
<td>3.3 ± 2.8</td>
</tr>
<tr>
<td>Height Z score</td>
<td>-1.78±1.43</td>
</tr>
<tr>
<td>Weight Z score</td>
<td>-2.01±1.43</td>
</tr>
<tr>
<td>BMI Z score</td>
<td>1.27±1.09</td>
</tr>
<tr>
<td>Calcium</td>
<td>9.6 ± 0.54</td>
</tr>
<tr>
<td>Phosphate</td>
<td>4.6 ± 0.67</td>
</tr>
<tr>
<td>Magnesium</td>
<td>1.87 ± 0.29</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>20.2±9.9</td>
</tr>
<tr>
<td>PTH</td>
<td>64.4±35.6</td>
</tr>
<tr>
<td>ALP</td>
<td>229.8±83.1</td>
</tr>
<tr>
<td>BMD Z score</td>
<td>-1.05±1.24</td>
</tr>
</tbody>
</table>
Prevalence of asthma and allergic disease in patients with inflammatory disease compared to celiac disease

Nafiye Urganci¹, Fatma Yavuz Yılmaz², Sebnem Ozdoğan³, Merve Usta¹

¹Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
²Sisli Etfal Training and Research Hospital, Department of Pediatrics, Istanbul, Turkey
³Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Thoracic Medicine, Istanbul, Turkey

Objectives and study: Increased incidence of atopy and asthma has been reported in autoimmune disease such as celiac disease and inflammatory bowel disease (IBD). There is no published literature comparing the frequency of asthma and allergic disease in celiac and IBD patients. In this study we aimed to investigate the frequency of asthma and allergic disease in IBD compared to celiac disease with ISAAC questionnaire.

Methods: This cross-sectional study was conducted between May 2015 and August 2015 at the Pediatric Gastroenterology Clinic of Sisli Hamidiye Etfal Research and Training Hospital. A total of 153 patients (70 with IBD and 83 with celiac disease) were included in the study. The age range of the cases was between 6 and 18 years. The validated ISAAC questionnaire in Turkish was obtained from patients with celiac disease and IBD.

Results: A total of 153 patients (70 with IBD and 83 with celiac disease) were involved. 52.9% of patients were female and the mean age was 13.21±3.80 years. The prevalence of wheeze was 26.6% at any time (24.3% in IBD and 28.9% in celiac disease), (p>0.005) and 18.2% for the last 12 months (17.1% IBD, 19.3% celiac disease), (p>0.005). The prevalence of allergic rhinitis was 31.5% at any time (41.4% in IBD and 33.7% in celiac disease), (p>0.005). Long-term use of nasal steroids was 16.9% (15.7% IBD, 18.1% celiac), (p>0.005). Atopic dermatitis was found in 7.1% (1.5% IBD, 12% celiac), (p<0.005).

Conclusion: The frequency of asthma and allergic disease were similar in both children with IBD and celiac disease. We think that asthma and atopy frequency are similar in both patient groups.
The relation between clinical presentation, serology, histology and duodenal deposits of tissue transglutaminase antibodies in celiac disease

Batia Weiss¹, Nurit Loberman-Nachum², Camila Avivi³, Ilana Weinraub⁴, Avishay Lahad⁵, Akiva Fradkin⁴, Yoram Bujanover⁵, Iris Barshack⁷, Michael Schvimer³

¹Edmond & Lily Safra Children's Hospital, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Pediatric Gastroenterology and Nutrition, Ramat Gan, Israel
²Edmond and Lily Safra Children's Hospital, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Pediatric Gastroenterology Unit, Tel-Aviv, Israel
³Sheba Medical Center, Tel-Hashomer, Institue of Pathology, Ramat Gan, Israel
⁴Edmond and Lily Safra Children's Hospital, Tel Hashomer, Pediatric Gastroenterology Unit, Ramat Gan, Israel
⁵Edmond and Lily Safra Children's Hospital, Tel-Hashomer, Ramat-Gan, Israel
⁶Ranaana, Israel
⁷Sheba Medical Center, Tel Hashomer, and Sackler Faculty Of Medicine, Tel-Aviv University, Institute of Pathology, Tel-Aviv, Israel

Objectives and study: The characteristic autoantibodies to tissue transglutaminase (TTG) in celiac disease (CD) are produced at the intestinal level and deposited on the extracellular TTG before passing into the circulation. Deposits of immunoglobulin (Ig)A anti-TTG are present in 96% of CD patients with overt disease. Data correlating TTG antibody titers with mucosal deposits of anti-TTG and severity of duodenal involvement are limited. Our aim was to examine the relation between serum anti-TTG, mucosal anti-TTG, histological features and clinical presentation in children with CD.

Methods A single-center retrospective study of CD patients diagnosed between January 2012 and December 2014. Four intestinal and one duodenal bulb biopsies were routinely obtained during endoscopy. Marsh classification and immunohistochemical staining for anti-TTG were performed and reviewed by one pathologist. Demographic data, presenting symptoms and serum TTG antibody levels were retrieved. The patients were classified as monosymptomatic or polysymptomatic according to their clinical presentation. The intensity of mucosal anti-TTG stain was classified separately in the lamina propria and in the epithelium.

Results: Out of 200 patients diagnosed with CD, complete data were available for 100 patients: 37 Males, age 7.2±4.0 years, 54 monosymptomatic, and 46 polysymptomatic (age 8.1±3.8 vs 6.3±4.1years, p=0.026). Serum anti-TTG levels were not significantly different between patients with single or multiple symptoms. Marsh 2-3c was more prevalent in patients with multiple symptoms (93% vs 78%, p =0.028). The intensity of mucosal anti-TTG deposits correlated with serum anti-TTG levels, but not with the clinical presentation.

Conclusion: Deposits of TTG in duodenal mucosa correlate with serum anti-TTG levels and with Marsh classification, but not with the type of clinical presentation.
GASTROENTEROLOGY: Coeliac disease

G-P-063

Haemolysis interferes with detection of IgA-antibodies against tissue transglutaminase

Johannes Wolf¹, Norman Händel², Thorsten Kaiser³, Johannes Remmler³, Thomas Mothes¹

¹Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, Medical Faculty of the University and University Hospital Leipzig, Leipzig, Germany
²Univ.-Kinderklinik Leipzig, Leipzig, Germany
³Institute of Laboratory Medicine, Clinical Chemistry and Molecular Diagnostics, University Hospital Leipzig, Leipzig, Germany

Objectives and study: Tissue transglutaminase (TTG) represents the autoantigen of coeliac disease (CD). The autoantibodies, IgA-antibodies against tissue transglutaminase (IgA-aTTG) are present in the serum of the patients and represent highly sensitive and specific markers to confirm or exclude CD. Laboratory assays for measurement of the autoantibodies apply the recombinant TTG coated to plastic surfaces to capture the antibodies. Haemolysis (HL) is one of the most common pre-analytical factors influencing the results of laboratory diagnostics. Therefore, free haemoglobin is routinely quantified in parallel to most biochemical assays by calculation of an HL index (HI) (1 index point = ~1 g free haemoglobin per 100 ml). TTG is abundant in erythrocytes and released upon HL into the serum. The released erythrocytic TTG can interfere with binding of IgA-aTTG to the coated recombinant TTG. The manufacturers of the IgA-aTTG assays recommend discarding samples with evident HL (HI up to 100). The current study will serve to improve the interpretation of IgA-aTTG measurement in samples affected by HL.

Methods: To simulate different levels of HL, we isolated, washed, and lysed erythrocytes from whole-blood and determined the HI. To estimate the effect of HL on different IgA-aTTG concentrations, we selected seven HL-free serum samples from biopsy-confirmed children with CD with low (group 1), five samples with intermediate (group 2) and five samples with high concentration of IgA-aTTG (group 3). The concentration of IgA-aTTG - expressed as multiples of upper limit of normal (xULN) applying a cut-off of 20 U/ml - was in the first group 1 to 5xULN, in the second group 5 to 10xULN and in the third group 10 to 15xULN. Sera were spiked with a dilution series of haemolysate resulting in a HI of 12.5, 25, 50, 100, 200, 400 and 800. As control, each sample was spiked with a serum without IgA-aTTG and without HL. Test kits for measurement of IgA-aTTG of two different manufacturers were investigated. A decrease of IgA-aTTG concentrations of at least 10% (twofold of mean interassay variations) was considered to be significant.

Results: We observed a significant reduction of IgA-aTTG after addition of haemolysates. The critical HI threshold was 25 (not visible) for group 1, 70 for group 2, and 100 for group 3. IC₅₀ (HI at which the IgA-aTTG concentration was decreased by 50%) for group 1 and group 2 was determined at an HI of 300 and 700, respectively. For group 3, a maximum decrease of 25% was observed at an HI of 800. Notably, one sample of group 1 with borderline IgA-aTTG values was false-negative even at HI 12.5 and IgA-aTTG in two samples decreased below the cut-off at an HI between 200 and 300. From January 2015 to December 2016, 1102 sera were tested both for IgA-aTTG and HI. Of these, 316 sera (28.7%) had an HI ≥25 giving the possibility of interference with assay of IgA-aTTG.

Conclusion: To the best of our knowledge, IgA-aTTG is the first autoantibody species which became known to be influenced by HL. The gastroenterologist should interpret IgA-aTTG results below the 10xULN with caution if the HI is ≥25. Different kinds of misinterpretation of results due to HL are possible: 1) False negativity especially in case of borderline IgA-aTTG values. 2) Misestimation of the compliance of gluten-free diet in case IgA-aTTG is reduced due to HL at follow-up. 3) Diagnosis of CD without biopsy not possible because IgA-aTTG was reduced below 10xULN if the HI is >100.
Assessment of vitamin A status among newly diagnosed coeliac disease patients

Yael Weintraub¹, Amir Ben Tov¹, Anat Yerushalmy Feler², Dror Weiner¹, Gad Dotan³, Ronit Lubetzky⁴, Shlomi Cohen¹

¹“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Paediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
²Tel Aviv Sourasky Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
³Tel Aviv Sourasky Medical Center, Division of Ophthalmology, Tel Aviv, Israel
⁴“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatrics, Tel Aviv, Israel

Objectives and study: Coeliac disease (CD) is a systemic immune-mediated disorder triggered by dietary gluten in genetically susceptible persons. Clinical features of CD are protean and reflect its systemic nature. Nutritional deficiencies described among coeliac patients include vitamin B12, folic acid and fat soluble vitamins. Vitamin A, a fat soluble vitamin, is abundant in our daily nutrition. In cases of malnutrition or malabsorption, vitamin A deficiency (VAD) may commence, as is the case in certain coeliac patients. VAD at a subclinical and often unnoticed level is extremely widespread in developing countries. Recent data reveals scares cases of VAD among chronic paediatric patients in developed countries as well.

We encountered several patients that presented preliminary with VAD. Medical investigation revealed CD as the aetiology of the deficiency. Since such profound cases are scares in developed countries, we seeked to determine vitamin A status among patients with CD upon diagnosis.

Objectives: to assess the prevalence and degree of VAD among newly diagnosed CD patients in comparison to paediatric patients evaluated endoscopically for gastrointestinal symptoms in which CD has been ruled out.

Methods: a prospective cohort study, among children 1-18 years old evaluated endoscopically for GI complaints. The primary endpoint was serum VA levels along with Haemoglobin (Hb), C-reactive protein (CRP), ferritin, IgA and vitamin D levels. Histopathological examination conformed CD diagnosis and Marsh Score was determined in relevant cases. CD cases were compared to non-CD cases.

Results: 79 children were evaluated endoscopically. 46 children were diagnosed with CD on the base of histopathology findings and 32 served as controls, (1 non conclusive). No difference was found regarding Vitamin A levels, Hb and CRP. True VAD was diagnosed in 4.3% of coeliac group and in 9.7% of the controls, a non-statistical significant difference (P value 0.642). TTG were higher in the coeliac group (median 200 vs. 0.1, P value <0.001). Ferritin and Vitamin D levels were lower in the coeliac group compared to controls (mean 16.71 vs. 25.59, p value 0.005 and median 26 vs. 32, p value 0.002, respectively).

Conclusion: Overall, the risk for VAD in CD at diagnosis was not higher than in the control group. Therefore, we cannot recommend routine Evaluation of vitamin A in newly diagnosed CD patients.

In our study, we found a significant number of children with true VAD. VAD, considered by the WHO as an isolated problem of developing countries nowadays, requires further prevalence assessment in developed countries.
Contribution of bulb biopsy in the diagnosis of coeliac disease in Algerian children

Abdelghani Yagoubi\textsuperscript{1}, Safa Chorfi Baiod\textsuperscript{1}, Reda Djidjid\textsuperscript{2}, Zine-Charaf Amir\textsuperscript{3}, Fadila Benhassine\textsuperscript{1}

\textsuperscript{1}Bologhine Ibn Ziri Hospital, Pediatrics, Algiers, Algeria
\textsuperscript{2}Beni Messous University Hospital, Immunology, Algiers, Algeria
\textsuperscript{3}Mustapha University Hospital, Pathology, Algiers, Algeria

Objectives and study: Coeliac disease (CD) is a very common immune-mediated enteropathy triggered by the ingestion of gluten in genetically susceptible individuals. Its diagnosis needs a confirmation by histology which classically involves duodenal biopsies. Many studies have shown the value of bulb biopsies and current recommendations are to do duodenal and bulb biopsies. The aim of our study was to evaluate the contribution of bulb biopsies in the diagnosis of CD in our practice.

Methods: We included prospectively and consecutively 26 children between April 2012 and April 2016. All these children under normal diet had a positive celiac serology performed by the same immunology lab; A high anti-tissue transglutaminase (anti-tTG) IgA level for children over 2 years of age and a high anti-deamidated gliadin peptid (anti-DGP) IgA level for infants (positive if \( \geq 20 \) IU/ml by ELISA for both). Digestive endoscopy (Fujinon EG 530FP or Olympus Evis P230) was performed after at least 6 hours of fasting. During the procedure, we collected 2 bulb biopsies and 2 biopsies from the descending duodenum. Histological analysis was performed by the same pathologist, according to the modified Marsh classification. The diagnosis of CD was retained in the presence at least of Marsh type 2.

Results: From the 26 patients included, CD was diagnosed in 14 patients and ruled out in the other 12 children (Marsh type 0). In CD group, the mean age was 8 y with a sex ratio of 1,3. Chronic diarrhea was the main symptomatic manifestation (8/14 cases) and 3 cases were asymptomatic (type1 diabetes, Turner syndrome, sister with CD). None of these patients had IgA deficiency. 12 children had high anti-tTG titers ranging from 6 to 50 times the upper limit of normal (ULN) and 2 infants had anti-DGP titers 5 and 7 times ULN. Upper GI endoscopy found duodenal mosaic pattern in 7 cases with bulb nodular pattern in 6 of them. Otherwise, a normal appearance was found in 50%. In 13/14 patients, histological findings were similar in bulb and descending duodenum (Marsh type 3a in 1 case, Marsh type 3b in 6 cases and Marsh type 3c in 6 cases). In one symptomatic infant, we found a severe lesion in the bulb (Marsh type 3c) and a normal finding (Marsh type 0) in the descending duodenum. All symptomatic children improved after gluten-free diet.

Conclusion: CD-related histological lesions are always found in the bulb and sometimes only present in this site. In our practice and awaiting further studies, bulbar and duodenal biopsies will be systematically performed to improve the diagnosis of CD.
Concentration of anti-HBs in previously immunized coeliac patients - does a gluten free diet make a difference?

Eyal Zifman¹, Noam Zevit², Merav Heshin-Bekenstein³, Dan Turner⁴, Raanan Shamir², Ari Silbermintz⁵

¹Pediatric Gastroenterology Clinic, Meir Medical Center, Kfar Saba, Israel
²Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Petach-Tikva, Israel
³Shaare Zedek Medical Center, Pediatric Department, Jerusalem, Israel
⁴Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel
⁵Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach-Tikva, Israel

Objectives and study: Universal immunization has helped decrease the burden of chronic hepatitis B virus (HBV) infection. Coeliac disease (CD) patients have been shown to have high rates of non-protective HBsAb concentration despite receiving recommended vaccination regimens. The cause for these low concentrations is unclear, and has been attributed to the genetic milieu of CD patients as well as their gluten consumption prior to diagnosis. We evaluated the effect of gluten free diet (GFD) on HBsAb concentration among previously immunized CD patients.

Methods: We examined the HBV antibody concentration of 413 CD patients retrospectively. All children received the standard hepatitis B vaccine regimen as infants and none had received a booster dose prior to inclusion nor had evidence of HBV infection. We extracted demographic data as well as HBsAb concentration for all patients and evaluated the temporal relationship of HBsAb concentration to the time on a GFD and age.

Results: Overall, 413 CD patients were evaluated, 156 before and 257 after initiation of GFD. None had evidence of prior HBV infection. After excluding non-compliant patients (reflected by persistently elevated coeliac serology), 156 and 217 patients were retained in the 2 groups. Mean age at HBsAb concentration measurement for those before and after GFD initiation was 6.5±4.1 yrs and 8.4±3.9yrs, respectively (p<0.001). There was no gender difference between the groups. The median time of HBsAb measurement was 0.4 months (IQR: 0-2.3 months) before and 16.2 months (IQR: 7-33 months) after initiation of GFD, respectively. The HBsAb concentration was <10mIU/mL (non-protective) in 79 (50.6%) and 121 (55.7%) of patients before and after GFD initiation, respectively (p =0.35). Age was the only influencing factor for non-protective HBsAb concentration. Neither being on GFD nor the gender had any effect on non-protective HBsAb rates.

Conclusion: Adherence to GFD does not affect rates of non-protective HBsAb concentration in children with CD. As such, HBsAb determinations may be performed at any time in children with CD.
Acute pancreatitis in Saudi children: case series over 20 years from a single Saudi tertiary pediatrics center

Maher Al Hatlani

1King Abdullah Children Hospital, Pediatrics, Riyadh, Saudi Arabia

Abstract Objectives: Because there is no single Saudi data on natural history of pediatric acute pancreatitis, we studied prevalence, etiology, severity, and outcome of acute pancreatitis.

Methods: Over 20 years, consecutive children with Acute Pancreatitis (AP) diagnosed in King Abdullah Specialized Children Hospital and King Abdul-Aziz Medical City at the National Guard Health Affairs, Riyadh, Saudi Arabia. Retrospective chart review to include all pediatric patients (Age < or = 14 years old) diagnosed with primary (first attack) acute pancreatitis from January 1994 to April 2015. A total number of fifty-two patients were included. Demographics, clinical features, management, and outcome were collected. Analysis of variance was used to compare continuous variables and χ or Fisher exact test for categorical variables.

Results: Fifty encounters, in which AP was the primary admitting diagnosis. The median age at diagnosis was 7 years (range 1.3-14.9). The mean length of admission was 10.5 days, with a median of 6 days (standard deviation of 13.14). Only 9 patients had recurrence of AP.

Of the 50 cases There were 22 cases (44%) that are idiopathic, 11 induced by gallstones (22%), 3 pancreatic divisum (6%), 2 familial hyperlipidemias (4%), 2 Diabetic Ketoacidosis (4%), 2 Post-ERCP (4%), 2 are drug-induced (4%), 1 choledochal cysts (2%), 1 familial hypertriglyceridemia (2%), 1 herbal therapy (2%), 1 common bile duct sludge (2%), 1 trauma (2%), 1 viral infection (2%).

94% of the patients presented with abdominal pain, 76% with vomiting, 20% with nausea, 8% with fever, 8% with jaundice, 2% with constipation.

Abdominal X-Ray was ordered only 42% of the cases, all of which were normal radiological findings. Ultrasound had a normal finding in 18.42% of the patients, while only 12 patients (15.79%) did not have US study. 14.47% has an enlarged, bulky, prominent and swollen pancreas on US, 11.84% had gallstone, 7.89% had peritoneal fluid, 5.26% had dilated common bile duct, 3.95% fluid “rim around the pancreases.

Conclusion: Although still relatively uncommon in Saudi Arabia, on average there is 2-3 cases of childhood AP diagnosed every year in our institute, the natural history, prevalence, etiology, severity, and outcome of pancreatitis are comparable to the western countries.
Clinical presentation, etiology, treatment and management of pancreatitis in children: 7 years experience

Yeliz Cagan Appak¹, Miray Karakoyun¹, Gülşah Soydan², Nursel Akmaz², Maşallah Baran¹

¹Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, İzmir, Turkey
²Tepecik Training and Research Hospital, Department of Paediatric, İzmir, Turkey

Objectives and study: Pancreatitis is defined as the histological presence of inflammation within the parenchyma of the pancreas. There is limited literature on acute pancreatitis, acute recurrent pancreatitis and chronic pancreatitis in children. The aim of this study was to evaluate etiologic factors, clinical features, treatment and management of pancreatitis in children.

Methods: Retrospective analysed in hospitalized children who were diagnosed with pancreatitis between May 2009 - September 2016. All data of pancreatic attacks contains clinical presentation, biochemical analysis, imaging tests, used treatment and etiologies were recorded from patient’s files.

Results: 63% of the patients were female and their mean age was 9.8±4.8 years. The most common symptoms were abdominal pain (%85.2) and vomiting (%66.6). The most common etiologic cause of pancreatitis was idiopathic (%59.3). 29.6% of the patients had acute recurrent episodes of pancreatitis. In the half of patients with recurrent pancreatitis didn’t found any etiologic factors. When recurrent attacks of 27 patients included in the study, a total of 44 pancreatic attacks were recorded and the average time between episodes was 10.1±13.6 month. The number of attacks was highest in a patient who had pancreas divisum and cystic fibrosis. Amylase in 86% and lipase 92.7% of the patients were detected more than 3 times than normal level. Amylase and lipase levels normalized at the mean 13.7±18 days of attacks. The average duration of hospitalization was 17.7±37.6 days. Somatostatin was used in 65.9% of the attacks and there was no significant difference was determined in the duration of normalization of pancreatic enzymes between patients given and not given somatostatin (p=0.79). All patients stopped feeding at the onset of pancreatitis attack and need of total parenteral nutrition for 36.1% of the patients. Two pancreatic divisum anomaly, one pseudocyst and one choledochal cyst were found in imaging studies. Genetic analysis were evaluated in patients with recurrent pancreatitis, PRSS and SPINK mutations were not observed while CFTR mutation was detected in one patient.

Conclusion: In acute and recurrent episodes, no etiological cause was found in half of the patients. Somatostatin treatment has not been shown to be effective in improving pancreatitis attacks. There is need for controlled works in this subject.
Hereditary pancreatitis in children- rare but important problem

Grzegorz Oracz¹, Karolina Wejnarska¹, Elwira Kolodziejczyk¹, Jaroslaw Kierkus²

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
²The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland

Objectives and study: Hereditary Pancreatitis (HP) is a rare inherited condition. We reviewed our experience over the last 25 years. The aim of our study was to evaluate the clinical course of HP in children.

Methods: 340 children with chronic pancreatitis, hospitalized since 1988 to 2016, were enrolled into the study. The medical records of these patients were reviewed for data on the presentation, diagnostic findings and endoscopic treatment. All children were screened for the PRSS1 gene mutations.

Results: Hereditary pancreatitis was diagnosed in 59 patients (17.5%) (37 girls and 22 boys; aged 0.8-17; mean-9.8 years). PRSS1 gene mutations were found in 43 patients. We detected R122H/- in 18, R122C/- in 14, N29I/- in 5, E79K/- in 3, R116C/- in 2 and A16V/- in 1 patient. Family history was positive in 54 children with HP (92%). In 16 patients without mutations diagnosis of HP was made when the patients satisfied the requirements of the family history. In 7 patients we found SPINK1 mutation (N34S/-), in 7 CTRC (G60G/-), in 1 CFTR mutation (delF508/-). There was no difference in age of the disease onset between HP group and non-HP group (8 vs. 9.1 years; NS). In children with PRSS1 mutation ERCP had mean 2° Cambridge grade, vs. 1.6°, p<0.05. Therapeutic intervention, including both surgical and endoscopic intervention, was more frequent in the HP group (75% vs. 35%; p<0.05). Pancreatic duct stenting was done in 21 children with HP (36% vs. 26%; p<0.05). ESWL was performed more frequent in HP group (10% vs. 3%; p<0.05).

Conclusion: Hereditary pancreatitis in children has worse clinical course than CP in children without PRSS1 mutations.
Pancreatic enzyme replacement therapy in cystic fibrosis: dose, variability and coefficient of fat absorption

Joaquim Calvo Lerma¹, Etna Masip², Sandra Martínez-Barona¹, Victoria Fornes³, Carmen Ribes Koninckx²

¹Instituto de Investigación Sanitaria La Fe, Valencia, Spain
²La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
³Instituto de Investigación Sanitaria La Fe, Unidad de Bioestadística, Valencia, Spain

Objectives and study: pancreatic enzyme replacement therapy (PERT) remains a backbone in the nutritional treatment of Cystic Fibrosis. Currently there is a lack of an evidence-based tool that allows for dose adjustment. Although theoretical PERT adjustment recommendations are extensively disseminated, these have a limited scientific foundation according to the new European guidelines. Currently, the only two criteria for PERT dosage are the fat content of the meal or the body weight. Although recent studies have proven there is no clear co-relationship between PERT dosage and the coefficient of fat absorption (CFA), other variables other than nutritional status mainly, have not been considered. Therefore, the aim of the present study was to assess the long-term influence of both the dose of PERT and the variability in this dosage on the coefficient of fat absorption.

Methods: retrospective study including 16 paediatric patients with three consecutive visits to the hospital in a year. Dietary fat intake was assessed through a specifically developed 4-day food and enzymes record and fat in stools was determined by means of a 3-day stools collection. CFA was calculated. A beta regression model was build up to explain the association between the coefficient of fat absorption and the interaction between PERT dose, referred as enzyme to substrate ratio (E/S) expressed in lipase units/ g dietary fat (LU/g) and its intra-patient variability (standard deviation).

Results: Patients included maintained an adequate nutritional status the mean median BMI value of the 3 visits being 15.7kg/m² (15.1,17.1). A total of 192 food records were obtained (16 patients, 4-day food record and 3 visits) from which 1152 meals were characterised (5 to 7 meals a day) in terms of E/S, nutritional composition and energy value of the foods registered. Considering the total enzyme dose (E/S) in every meal, day, visit and patient, we found a median global E/S of 719.4 (interquartile range 451.5, 1205) LU/g of fat with an intra-patient variability (SD E/S) of 616.7 (308.1, 1516) LU/g among different meals. The global median CFA value of all registrations and for all patients was 89.7% (84.88, 93.31), with very little variability among records. Coefficient of fat absorption increased with E/S as long as the variability in the dose was low. In contrast, even at the highest E/S values, the coefficient of fat absorption decreased when the variability was high. The study of the interaction did not reach statistical significance but showed a strong association (p=0.09).

Conclusion: the variability in the E/S adjustment should be taken into consideration when performing studies on PERT efficiency. In the light of our outcomes, a higher efficiency in PERT dosage could be achieved by trying to maintain a constant E/S rather than by only attempting at finding an optimal figure of lipase units per gram of fat.
Amylase, lipase and white blood cell count at presentation are predictors of severity of acute pancreatitis in children

Tut Galai¹, Shlomi Cohen², Anat Yerushalmy Feler³, Yael Weintraub¹, Dror Weiner¹, Achiya Amir³

¹“Dana-Dwek” Children’s Hospital, Tel Aviv Sourasky Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
²“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
³Tel Aviv Sourasky Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel

Objectives and study: Acute pancreatitis (AP) in children is an etiologic heterogeneous disease. AP ranges in severity from mild disease, to a moderate and severe inflammation with local and systemic complications mandating prolonged hospitalization and invasive procedures. Several prognostication models exist in adults, however, several reports demonstrated their futility in paediatric population. Data regarding predicting factors of severity in children is limited. This study aimed to investigate laboratory markers at presentation as predictors of disease severity.

Methods: A retrospective study of all children (<18y) hospitalized with AP between January 1995 to December 2015 was conducted. AP diagnosis was based on the Acute Pancreatitis Classification Working Group guidelines-2013. Patient demographics, clinical, laboratory and imaging data were reviewed. The primary outcomes were disease severity, hospitalization duration and endoscopic and surgical interventions.

Results: 68 children with a total number of 117 hospitalizations for AP were identified, including 59 (59.3% males, median age 135 months, interquartile range 70-186) children with first episode hospitalizations. Etiologies included medications in 12 (20.34%), cholelithiasis in 6 (10.1%), structural anomalies in 3 (5.08%) and trauma in 3 (5.08%). However in 35 (59.3%) patients etiology remained idiopathic. 51 patients (86.4%) had mild and 8 had moderate or severe disease. Median duration of hospitalization was 6 days (range 4-8). 55 (93.2%) children were treated conservatively, 3 (5%) underwent therapeutic endoscopic intervention and 1 (1.69%) underwent surgery. 14 (23.73%) children had AP recurrence. There was no mortality. Patients with moderate/severe AP had higher WBC, amylase and lipase levels at presentation compared to patients with mild AP (23.8 vs. 11.1, p=0.032; 1376 vs. 313, p=0.05; and 1200 vs. 363, p=0.041, respectively). WBC > 14.2, amylase > 1200 and lipase > 1200 (OR 2.9, 7.4, 5.3, respectively) predict a moderate/severe disease.

Conclusion: AP in children is generally a mild disease amenable to conservative management. In as 59.3% of episodes the etiology is idiopathic. Surrogate markers of pancreatic inflammation- WBC, amylase and lipase at presentation are predictors of disease severity.
Objectives and study: To describe the frequency, etiology, clinical feature, and risk factors of acute recurrent pancreatitis (ARP) at a reference children’s hospital.

Methods: Chart review of all patients with acute recurrent pancreatitis seen during a 10 year period at the Pediatric National Institute of Mexico City.

Results: We found 115 cases of pancreatitis in that period of time, 64 patients had acute pancreatitis, 1 chronic pancreatitis an 48 patients with ARP.

We studied the characteristics of the patients with ARP. The admission per year was a mean of 8.18 cases (min 1, max 13). Most of the patients were female 67% (n=32). The mean age of diagnosis of the first event of ARP was 11 years (min 2, max 16).

The nutritional conditions were classified with body mass index according to CDC growth charts 50% of the patients (n=24) were eutrophic, 27.1% (n=13) had obesity, 12.5% (n=6) had overweight, 8.3% (n=4) had mild malnutrition, and 2.1% (n=1) moderate malnutrition.

All of the patients complained of abdominal pain, followed by 62.5% with nausea, 54.2% vomit, only 6.3% presesented fever.

All the patients had elevated levels of amylase and lipase. We found 14.58% (n=7) with hypercholesterolaemia and 31.25% (n=15) with hypertrigliceridaemia and none with hypercalcaemia. Of the patients with obesity and overweight, all of them presented hypertrigliceridaemia, 23.07% and 16.67% repectively presented hypercholesterolaemia.

About hereditary factors, only one case had familiar history positive to pancreatitis but the genetic mutations couldn’t be done. One case had abdominal trauma as a risk factor for ARP. Most of the medical records of patients with ARP (83.33%) did not present associated diseases; metabolic syndrome was registered in 3 cases (6.25%), 2 cases (4.16%) with Systemic Eritematous Lupus, one case (2%) with Antiphospholipid Syndrome.

Concerning to drugs intake, 85.41% of the cases did not consume any drug, meanwhile 2 consumed prednisone and micofenolic acid, 1 prednisone, azatioprine and acenocumarine, 1 consumed only valproic acid, 1 consumed acid valproic and sertraline, 1 only metilfenidate, 1 metformine and bezafibrate.

Imaging studies: ultrasound was performed in all of the patients, finding 22.91% with biliary lithiasis and 50% as normal; magnetic resonance cholangio-pancreatography was performed in 44 patients, finding 7 dilatated biliary tract, 2 stenosis of pancreatic duct, and the rest reported as normal; 11 patients underwent to endoscopic retrograde cholangio-pancreatography finding in five patients the main pancreatic and secondary duct morphology was distorted with irregular, narrow or dilated segments; in ten patients endoscopic ultrasound was performed finding 4 cases with choledocal microstones.

We found that the most frequent risk factors for ARP was biliary lithiasis in 29% (n=14), structural abnormalities in 19%, metabolic causes in 15%, toxic drug exposure in 10%, with 21% (n=10) as idiopathic etiology or none risk factor associated.
**Conclusion:** In our experience, we found that 42% of patients with acute pancreatitis had recurrent episodes of acute pancreatitis. Most of them with biliary stones and idiopathic etiologies.

Also 39.6% of the patients had overweight or obesity, that could be considered as a risk factor in ARP, also all of them presented hypertriglyceridaemia

Early detection of the underlying cause may favor a complete resolution of the disease, as in the case of biliopancreatic abnormalities or biliary stones.
Determinants of vitamin K deficiency in non-supplemented cystic fibrosis patients

Patrycja Krzyzanowska¹, Slawomira Drzymala-Czyz¹, Nataliya Rohovyk², Lyudmyla Bober², Jerzy Moczko³, Marta Rachel⁴, Jaroslaw Walkowiak¹

¹Poznan University of Medical Sciences, Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland
²Lviv Cystic Fibrosis Centre, Lviv, Ukraine
³Poznan University of Medical Sciences, Department of Computer Science and Statistics, Poznan, Poland
⁴Provincial Hospital No. 2, Allergology Outpatient Department, Rzeszow, Poland

Objectives and study: Vitamin K deficiency is highly prevalent in cystic fibrosis (CF) patients despite its supplementation. Moreover, no reliable risk factors for its appearance are known. In the present study we aimed to assess the risk factors for vitamin K deficiency in a unique group of CF patients who have never received vitamin K supplementation.

Methods: The study group comprised 79 CF patients aged 0.4-25.3 years. In all subjects the concentration of prothrombin induced by vitamin K absence (PIVKA-II) and the percentage of undercarboxylated osteocalcin (u-OC) were determined.

Results: PIVKA-II and u-OC were abnormal in 56 (70.9%) and 45 (57.0%) patients, respectively. Patients with elevated PIVKA-II were significantly older (p=0.0184) and had lower Z-score values for body weight (p=0.0297) than those with its normal concentrations. On the other hand, patients with normal and pathological percentages of u-OC did not differ. Abnormal PIVKA-II and u-OC appeared more frequently in subjects with two severe CFTR mutations and with worse nutritional status. Multiple linear and forward stepwise regression analyses did not reveal strong predictive factors of vitamin K deficiency.

Conclusion: Vitamin K deficiency is highly prevalent in the natural course of cystic fibrosis. Its occurrence cannot be predicted from the clinical picture alone.
Objectives and study: Despite of the rising incidence of pediatric pancreatitis (PP) in the last decade, there is still lack of information (studies) concerning the management of childhood onset pancreatitis. Most of the guidelines are based on clinical trials performed on adults. The Pediatric Section of the Hungarian Pancreatic Study Group aimed to initiate a prospective international observational clinical trial (APPLE - Analysis of Pediatric Pancreatitis) (i) to understand the genetic factors of all forms of pancreatitis occurred under 18 (APPLE-R), and (ii) to collect a critical mass of clinical data and biomedical research samples from children suffering from AP (APPLE-P).

Methods: The study has (i) been discussed and agreed in our latest international meeting (http://pancreas.hu/sites/info/files/conferences/ALPD2014-Program.pdf), (ii) received the relevant ethical permission, (iii) been registered at the ISRCTN registry (ISRCTN35618458, ISRCTN89664974) which is a primary clinical trial registry recognised by WHO. The study is open for all centres. All clinical research forms are available at our webpage http://pancreas.hu/en/studies.

Results: APPLE-R: 45 acute (AP), 18 recurrent acute (RAP) and 14 chronic pancreatitis (CP) cases were enrolled yet. Concerning the etiology, biliary 17%, drug-induced 7%, trauma 4%, alcohol 2%, other 26% were identified, however 44% of the cases still remained idiopathic. In 54 cases, genetic analyses of PRSS1, SPINK1, CFTR and CTRC genes have been completed. Genetic alterations in PRSS1 were found in 4 cases (all CP), in SPINK1 in 8 cases (5 RAP and 3 CP), in CFTR in 1 case (CP) and in CTRC in 25 cases (5 AP, 6 RAP and 7 CP). In 5 CP patients mutations in two genes were observed (5 SPINK1-CTRC, 1 PRSS1-SPINK, 1 CFTR-CTRC).

Conclusion: Positive genetic alteration was found in 72% of the idiopathic and 38% of the non-idiopathic groups. Our results suggest that genetic testing should be performed in all children suffering from pancreatitis. The study is still ongoing, more patients are crucially needed.
Acute pancreatitis in children: single center experience over 10-year period

Elif Sag¹, Ulas Emre Akbulut², Hatile Sonay Yalçın Comert³, Elif Bahat Ozdogan⁴, Süleyman Caner Karahan⁵, Murat Cakir¹

¹Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
²Kanuni Training and Research Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
³Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Surgery, Trabzon, Turkey
⁴Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Nephrology, Trabzon, Turkey
⁵Karadeniz Technical University, Faculty of Medicine, Dept. of Biochemistry, Trabzon, Turkey

Objectives and study: Acute pancreatitis (AP) is the inflammation of the pancreatic parenchyma and is characterized by the presence of inflammatory cell infiltrate, and varying degrees of cellular apoptosis, necrosis and hemorrhage. It is defined as the requiring 2/3 of following: (i) abdominal pain, (ii) serum pancreatic enzymes ≥3UNL (iii) imaging findings consistent with AP. In recent years; increase prevalence of AP in children has been reported worldwide due to clinical awareness of in children admitted with acute abdominal pain. Herein; we evaluated the demographic and clinical findings, incidence and outcome of the children with AP in our unit since 2005.

Methods: Medical records of the children with AP were reviewed. Patients were defined as recurrent AP if the symptoms of the patient recurrence at least one month after improving AP attack. Additionally, incidence analysis of AP was made (number of “patients with AP”/“hospitalized patients”) in three time spans (2005-2008, 2009-2012 and 2013-2016).

Results: 63 patients (50.8% female, 9.6 ± 4.8 years) were admitted with 87 AP attacks. Abdominal pain was present in 98.9%, elevated pancreatic enzymes in 95.6% and radiological findings in 72.4%.

Systemic diseases (HUS, HSP) (14.3%), trauma (11.1%) and drugs (6.3%) were the most common etiological factors. Etiological factor could not identified in 25.4% patients. The course of the disease was mild according to DeBanto criteria in 79.4% of the attack. Three patients (4.8%) had necrotizing pancreatitis. Ten patients (15.9%) experienced 24 recurrent AP attacks within the 10 months (range; 1-24 months). No risk factors including age, gender, etiology and laboratory findings was identified associated with recurrence of AP. Increased pancreatic size (28.5%), peripancreatic fluid (17.5%), increased echogenicity (12.7%) and pancreatic pseudocysts (11.1%) were the most common radiological findings (USG, CT and MRCP) at initial AP attack.

Enteral nutrition was discontinued in all patients (6.1±6 day, 2 to 30 days), octreotide infusion were used in 54 attacks and antibiotics in 58 attacks. Surgery was performed to 6 patients. Complications were developed in 31 patients (49.2%); early (septic shock, cavitary effusion and GI bleeding) in 10 patients (15.9%), late (pancreatic fluid, pseudocysts, necrosis and abscess) in 14 patients (22.2%) and both early and late in 7 patients (11.1%). Four patients were died during follow-up (6.3%), but all were related with the primary diseases (2 HUS, 1 suffocation, 1 multiple trauma). Patients with and without complications were compared and found that the rate of mortality (6.3% vs. %0), time to start enteral nutrition (8.2±6.7 days vs. 3.7± 2.2days), duration of hospitalization (25.3±22.3 days vs. 15.3±19.3 days) and CRP levels at initial admission (4.1±4.7 mg/dl vs. 1.4±1.8 mg/dl) were higher in patients with complication (p=0.001, p=0.001, p=0.01, p=0.04, retrospectively). The incidence of AP was increased in 2013-2016 compared to other spans (0.14%, 0.13% and 0.37%, respectively and p=0.029, p=0.036).

Conclusion: Systemic diseases and trauma are the major causes of AP in children. As compared to adults, AP is generally a mild disease in children, and the mortality is mainly related with the primary disease. Mortality, duration of hospitalization and time to initiate enteral nutrition are increased in the presence of complications. As in previous studies, the incidence of AP is steadily increased.
The frequency of the celiac disease in Turkish children with cystic fibrosis

Yasin Sahin, Tulay Erkan, Tufan Kutlu, Nuray Kepil, Ayse Ayzit Kilinc, Fugen Cullu Cokugras, Haluk Cokugras

Istanbul University, Cerrahpasa Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Istanbul University, Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Istanbul University, Cerrahpasa Medical Faculty, Pathology, Istanbul, Turkey

Istanbul University, Cerrahpasa Medical Faculty, Pediatric Pulmonology, Istanbul, Turkey

Istanbul University Cerrahpasa Medicine Faculty, Department of Paediatric Gastroenterology, Istanbul, Turkey

Objectives and study: There are very few studies investigating the incidence of celiac disease (CD) in patients with cystic fibrosis (CF) in the literature. To our knowledge, there are no studies investigating the frequency of CD in Turkish children with CF. We aimed to assess the frequency of CD in Turkish children with CF.

Methods: This prospective study was carried out from October 2015 to December 2016. A total of 71 patients with CF were included. We used 73 sex- and age-matched healthy subjects as a control group. Levels of total IgA and tissue transglutaminase (tTG) IgA antibody were measured in all groups. Those with increased level of tTG IgA were tested for anti-endomysium IgA antibodies (EMA). Patients with positive EMA underwent gastroduodenoscopy and intestinal biopsy for a definite diagnosis of CD.

Results: Only 8 of 71 patients (11.2%) were positive for tTG IgA. Patients positive for tTG IgA were then tested for EMA IgA antibodies and only four of them (5.6%) had a positive result. Those patients underwent gastro-duodenoscopy. The pathological report was compatible with Marsh 2 classification score for the diagnosis of CD in two of them who had also a positivity of HLA-DQ2. For this reason, latent celiac disease was considered in those patients. Marsh 0 classification score was detected in the other two patients. Three (4.1%) subjects from the control group were positive for tTG IgA but none of them had positive EMA antibodies, so the further assessment was unnecessary.

Conclusion: Of the 71 CF patients, two (2.8%) had latent celiac disease. The frequency of CD was detected as 1/35.5 in children with cystic fibrosis. Our results suggest that there is a association between CD and CF. Although we have a small number of cases, we recommend that all patients with CF should be evaluated for CD. Larger studies are needed to provide more valid interpretation.
Is chronic pancreatitis in children a multifactorial disease?

Karolina Wejnarska¹, Elwira Kolodziejczyk¹, Grzegorz Oracz¹

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland

Objectives and study: The etiology of chronic pancreatitis (CP) in children is more diverse than in adults. The major cause of CP are gene mutations (PRSS1, SPINK1, CFTR, CTRC, CPA1), other important etiological factors include anatomical defects of the pancreatic duct, lipid disorders and diseases of the biliary tract. As it was proven, most of these factors increase the risk of the disease and the other coexisting cause has to appear to develop CP. The aim of the study was to analyze the coexistence of risk factors in etiology of CP in children.

Methods: A total of 324 patients with CP, hospitalized from 1988 to 2016 were enrolled into the study. Medical records were reviewed for data on presentation, diagnostic findings and treatment. All children were screened for mutations in major pancreatitis-associated genes (SPINK1, PRSS1, CFTR, CTRC).

Results: Multiple risk factors of CP were found in 85 children (26.2%). Median age of the disease onset was 8.1 years (range 2.1-16.4). Seventy four patients (87%) had 2 risk factors of CP, in 6 children (7%) more than 2 causes were found. Fourteen patients with PRSS1 mutation, which is proven to be direct cause of hereditary pancreatitis, had other risk factors of CP. Nine of them had mutation in second gene associated with pancreatitis (CTRC n= 5, SPINK1 n=3, CFTR n=1). Three children had anatomic defect (pancreas divisum n=2, ansa pancreatica n=1), 1 patient had a history of choledocholithiasis, 1 had hypertriglyceridemia. Twenty two children (25.9%) was found with two or more coexisting gene mutations, moreover 4 patients of that group had another risk factor (1 child with anatomical defect, 1 with hypertriglyceridemia, 1 with anatomical defect and choledolithiasis). In 39 children (45.9%) with gene mutation, other gene than PRSS1, we found coexisting anomalies such as: anatomical defect n=24 (1 patient had additionally hypertriglyceridemia as a third potential cause of CP), biliary tract diseases n=5, lipid disturbances n=10. In group of 10 children without gene mutations anatomical defects were diagnosed with biliary diseases n= 4 patients, lipid disturbances n=3 children and both n=1. The coexistence of lipid disturbances and biliary track diseases were found in 2 patients.

Conclusion: The etiological factors of CP in children are diverse. According to the results obtained in our study, CP in children is a multifactorial disease and the “double hit” hypothesis has a strong grounds. However, determining which risk factor is crucial in etiopathogenesis of CP is unenforceable.
Childhood pancreatitis: a multicenter study

Bilge Sahin Akkelle1, Ozlem Kalaycik Sengul1, Burcu Volkan2, Nevzat Aykut Bayrak3, Esra Polat4, Gunsel Kutluk4, Engin Tutar1, Deniz Ertem1

1Marmara University School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
2Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
3Diyarbakir Children's Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
4Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: Acute pancreatitis presents with abrupt onset abdominal pain and elevation of pancreatic enzymes, and characterized by inflammation and interstitial edema of pancreas. In children, the prevalence of acute pancreatitis varies between 1/7,500-28,000. While alcohol consumption and gallbladder diseases comprise the etiology in up to %80 of acute pancreatitis etiology in adults, its etiology in children is multifactorial. In addition to trauma which is a well known factor for childhood pancreatitis, drugs, infections, metabolic-genetic and anatomical defects are associated with even greater risk. However, the etiology remains unknown in many patients.

The aim of this multicenter study was to outline the epidemiologic, etiologic and clinical features of patients diagnosed with pancreatitis

Methods: Between January 2010 and December 2016, a total of 101 patients who had the diagnosis of pancreatitis in 4 different pediatric gastroenterology units in Turkey were retrospectively reviewed. Patient records regarding demographic features, etiology, progression, duration of hospitalization and prognosis were analyzed.

Results: At diagnosis, the mean age of the children with pancreatitis was 9.58 ± 4.13 years and %55.4 was females. Cholelithiasis and drugs were the most common etiologies for pancreatitis in this group, and were etiologic factors in more than 25% of the cases (table). In this cohort, pancreatitis associated with hyperlipidemia, trauma and anatomic anomalies of pancreas were similar in percentage. The etiology could not be identified in %37.6 (38/101) of the cases. One patient with a history of pancreatitis in his relatives had PRSS mutation, hence had the diagnosis of hereditary pancreatitis.

Of all patients, 19 (%19) had recurrent episodes of pancreatitis. Besides cholelithiasis (%15) and hypertriglyceridemia (%15), cystic fibrosis, autoimmunity and congenital anatomical defects were the other etiological factors among patients with recurrent pancreatitis, while the etiology in 37.6 % of patients could not be identified. The mean duration of hospitalization was 14.6 ± 15 days. Four out of 101 patients developed pseudocyst during follow up, and one of them experienced multiorgan failure. Three patients with severe course underwent surgery (1 pancreaticoduodenectomy, 1 pancreas resection and 1 pseudocyst drainage).
Table:

<table>
<thead>
<tr>
<th>Etiology of pancreatitis (n=101)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholelithiasis</td>
<td>14 (13.9%)</td>
</tr>
<tr>
<td>Drugs (valproic acid, phenobarbital, azathiopurine, L-asparaginase)</td>
<td>13 (12.9%)</td>
</tr>
<tr>
<td>Cystic fibrosis</td>
<td>6 (5.9%)</td>
</tr>
<tr>
<td>Autoimmune</td>
<td>6 (5.9%)</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Trauma</td>
<td>5 (5%)</td>
</tr>
<tr>
<td>Other (anatomical anomaly, viruses, malignancy, Kawasaki dis., hydatid cyst)</td>
<td>14 (13.9%)</td>
</tr>
<tr>
<td>Not identified</td>
<td>38 (37.6%)</td>
</tr>
</tbody>
</table>

**Conclusion:** The prevalence of pancreatitis is increasing among children; however etiology remains obscure in many patients. Classical knowledge of trauma being the most common etiology in children should be regarded with caution according to the results found in our study group. In this cohort, cholelithiasis and drugs were most commonly identified etiological factors. Hence drugs with pancreatic toxicity should be carefully monitored.

The rate of recurrent pancreatitis was 19% in this cohort which indicated a close follow-up of children with acute pancreatitis for recurrence.
Electrophysiological tests in CF Diagnosis- Nasal Potential Difference is more predictive than sweat test

Mordechai Slae\textsuperscript{1}, Michael Cohen\textsuperscript{1}, Michael Wilschanski\textsuperscript{1}, Hannah Freedman\textsuperscript{1}

\textsuperscript{1}Hadassah Hebrew University Medical Center, Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: Cystic fibrosis is associated with defective cAMP-mediated (CFTR) Cl\textsuperscript{-} secretion and an accelerated rate of basal Na\textsuperscript{+} transport across epithelial membranes resulting in a change in transepithelial potential difference (PD) that can be measured in the nasal epithelium, the Nasal Potential Difference test (NPD). The sweat chloride concentration is still the gold standard for diagnosis of CF. NPD is now one of the criteria for the diagnosis of CF in questionable cases. The aim of this study was to compare the diagnostic outcome of a cohort of patients with questionable CF phenotypes referred for electrophysiological testing.

Methods: Patients with suspected CF were referred between 2003 and 2014 who performed sweat test and NPD in one tertiary center. Sweat test was defined as <40mmol/L normal, borderline 40-60 and positive >60mmol/L. The measurement of $e\Delta\text{chlor}/\Delta\text{amil}>0.7$ was defined as an abnormal NPD while $e\Delta\text{chlor}/\Delta\text{amil}<0.7$ was defined as a normal NPD. Final diagnosis was defined as registration in the National CF Registry.

Please copy and paste the corresponding text here.

Results: 449 patients underwent both NPD and sweat tests. 246 had sweat < 40, 33 had >60 and 170 had 40-60. Of the 449 patients, 375 had normal NPD and 74 abnormal, 26 of 375 are in the CF registry. Of the 74 diagnosed as abnormal, 21 are in the CF registry. The sensitivity of NPD is 44.7% and specificity 86.8% with negative predictive value of 93% This is better than the sweat test which has sensitivity of 45.4%, specificity of 58.1% and negative predictive value of 88.8%. There were 8 patients with a normal sweat test and abnormal NPD of which 5 are registered as CF. There were 83 patients with a positive sweat test and normal NPD of which 5 are in the CF registry. The sensitivity of NPD in this group is 50%, specificity is 96.2%, positive predictive value 62.5% and negative predictive value of 93.9%. Of the 170 patients with borderline sweat test, 5 out of 140 (3.6%) with normal NPD are in the registry while of the 31 patients with abnormal NPD, 7 (23%) are in the registry. Please copy and paste the corresponding text here.

Conclusion: In patients with a questionable diagnosis of CF, the NPD is very useful and is best at ruling out the diagnosis in the presence of a false positive sweat test. Please copy and paste the corresponding text here.
Nasal potential difference in young children is feasible

Mordechai Slae¹, Michael Cohen¹, Hannah Freedman¹, Michael Wilschanski¹

¹Hadassah Hebrew University Medical Center, Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: The diagnosis of cystic fibrosis is based on characteristic clinical symptoms and either a positive sweat test or identification of related mutations on each of Cystic Fibrosis Transmembrane Conductance Regulator (CFTR) gene alleles. A significant number of patients have no definite diagnosis, having possibly related symptoms, borderline sweat test and no identifiable known mutation on the CFTR gene. Nasal Potential Difference (NPD) is an established method of diagnosis in these patients. Until now standard values for very young patients have not been developed and validated. The aim of this study was to evaluate the feasibility of NPD in young children.

Methods: The standard protocol for NPD was adapted for young children. In the standard protocol infusions of amiloride, chloride-free and isoproterenol are for 3 minutes. In the current protocol this was reduced to 2 minutes so the entire test is completed in 10 minutes.

Results: 35 children aged 2 months to 3 years of age were enrolled in the study. Diagnoses included Failure to thrive (15), chronic diarrhea (6), respiratory problems (10), meconium plug (2). Mean sweat test was 53mmol/L. The NPD was abnormal (e_∆chlor/∆Amil>0.7 was defined as an abnormal NPD while e_∆chlor/∆Amil<0.7 was defined as a normal NPD) in 6 patients and these children were referred for follow up in CF Centers. The procedure was tolerated in all children.

Conclusion: NPD is feasible in very young children and may be useful in the diagnosis of CF in questionable cases.
Assessment of nutritional status in children with cystic fibrosis

Laura Trandafir¹, Mihaela Moscalu², Otilia Frasinariu³, Dana Anton-Paduraru³

¹“Sant Mary” Clinical Emergency for Children Hospital, Pediatric Department, Iași, Romania
²University of Medicine and Pharmacy “Grigore T. Popa”, Preventive Medicine and Interdisciplinarity Department, Iasi, Romania
³University of Medicine and Pharmacy Grigore T. Popa Iasi, Paediatrics Department, Iasi, Romania

Objectives and study: The importance of nutritional intervention for children with cystic fibrosis (CF) is well recognised. Improved nutritional status early in life is associated with better long term evolution in patients with CF. The authors evaluated the nutritional status of children with CF in a Regional Center in Eastern Romania.

Methods: We performed a retrospective study included 34 children with CF, 65% boys and 35% girls, followed between January 2014 - May 2016. Mean age of disease diagnosis was 44.81 months ± 25.3SD (min.: 2 weeks; max.: 185 months). Nutritional status was assessed based on weight, height, weight and height Z score. Pulmonary function was evaluated by determining FEV₁ in children older than 6 years and frequency of respiratory infections. Body mass index (BMI) was calculated and nutritional status was defined according to CDC recommendations. We followed the nutritional status correlate with age at diagnosis, age at disease onset, impaired lung function, frequency of lung infections and number of hospitalizations. The categorical variables were expressed as absolute frequency and relative frequency. Data were analyzed using SPSS V.21 software.

Results: Mean BMI was 14.79 ± 2.47 kg/m², with minimum values of 10.33 and maximum 20.54 kg/m². 50% of analyzed cases showed BMI values below 14.67 kg/m². From the study group, 20.5% had malnutrition and 41.1% had short stature with low weight-for-height. Lower age at onset was significantly correlated with disease severity (r=−0.696). The result of multiple logistic regression analysis showed that the nutritional status was significantly influenced by repeated respiratory infections (β =−0.434, p = 0.0045, 95% CI) and early age of symptoms onset. Nutritional status correlated with identified mutations analize not confirmed the classical patterns of evolution.

Conclusion: The worse nutrition is associated with late aged of diagnosis and early respiratory infections of children with CF. In order to improve nutritional status and a better clinical evolution is necessary to introduce newborn screening programs. The prevalence of overweight and obesity is high in preschool-aged children, especially in urban areas. These results are part of a nutritional screening study conducted in kindergarten to identify children and adolescents with overweight and obesity.
Successful conservative management of a complete traumatic pancreatic duct rupture: an ERCP-guided approach

Valerio Balassone¹, Simona Faraci², Kalid Alreheili³, Francesca Rea⁴, Annachiara Iolanda Contini³, Erminia Francesca Romeo⁵, Filippo Torroni⁶, Giovanni Federici di Abriola⁴, Renato Tambucci⁵, Giulia Angelino⁴, Paola De Angelis⁴, Tamara Caldaro⁶, Luigi Dall'Oglio⁶

¹Bambino Gesù Children Hospital, Irccs, Digestive Surgery and Endoscopy Unit, Rome, Italy
²Bambino Gesù Children Hospital, Digestive Endoscopy and Surgery Unit, Rome, Italy
³Bambino Gesu Children Hospital, Digestive Surgery and Endoscopy, Rome, Italy
⁴Bambino Gesù Children's Hospital, Irccs, Digestive Surgery and Endoscopy Unit, Rome, Italy
⁵Bambino Gesù Children's Hospital, Irccs, Unit of Digestive Surgery and Endoscopy, Inflammatory Bowel Disease Group, Rome, Italy
⁶Bambino Gesù Children's Hospital, Digestive Surgery and Endoscopy Unit, Rome, Italy

Objectives and study: Pancreatic injuries with complete Wirsung’s duct rupture (CWDR) are uncommon finding in abdominal blunt trauma. A pancreatic trauma must be suspected when dynamics of trauma, blood tests and symptoms are suggestive. Diagnosis is generally confirmed by ultrasounds and computed-tomography. For total distal rupture, without the involvement of the ampulla, a distal pancreatectomy was the purposed strategy in past decades. The role of ERCP in children with CWDR has been aimed to confirm the duct rupture (by the extravasation of contrast) and for therapy. The use of plastic stent for pancreatic trauma is a matter of debate because of the increased risk of bleeding and infections.

Methods: retrospective case report.

Results: A 8-year-old male was referred to our emergency department because of vomiting and abdominal pain following a mild blunt trauma caused by a bike handle-bar. Blood tests showed amylase and lipase elevation (>500 IU/L) and computed tomography confirmed a distal pancreatic rupture with main duct involvement and a renal hematoma (American Association for Surgery in Trauma - AAST Grade 4 of 5). Because of the clinical stability, we decided to admit the patient and to plan an Magnetic Resonance Cholangiopancreatography. The CWDR was confirmed and, in addition, the ERCP confirmed a small contrast extravasation from a distal duct laceration. By advancing a hydrophilic guide-wide in the distal part of the main duct, we confirmed a compound laceration. To avoid risk of late bleeding of sphincterotomy and possible stent-related infections, we limited our treatment to a pancreatic sphincterotomy and a nose-pancreatic drainage placement. According to good clinical condition, we started an early re-feeding and the patient initially needed an insulins supplement. During the hospital stay (10 days in total) a complete recovery of the pancreas endocrine function was obtained and the patient was discharged after the removal of nose-pancreatic drainage. A pancreatic pseudocyst of 8x5 cm was demonstrated at the 1st follow up abdominal ultrasound. We decided again for a conservative treatment of the pseudocyst, despite a slight volume improvement, during the subsequent controls. The 4-months abdominal ultrasound confirmed the complete resolution of the pseudocyst and a total recovery of the main pancreatic duct. Clinical condition of the child was completely satisfactory at the 5th month follow up visit.

Conclusion: We reported our successful management in a child with complete pancreatic duct rupture treated by an ERCP-guided drainage after the confirmation of a compound laceration. Our findings are supportive for a stepwise conservative management based on clinical condition and ERCP findings. According to our experience, ERCP stent placement should be reserved for complicated duct rupture or after the failure of pancreatic drainage.
Feasibility and safety of placement of fully covered self-expandable metal stent for refractory benign dominant main pancreatic ductal strictures in children

Sujin Cho¹, Sunghee Lee², Insook Jeong², Seakhee Oh², Kyungmo Kim²

¹Asan Medical Center, Pediatrics, Seoul, Korea, Rep. of South
²Seoul Asan Medical Center, Seoul, Korea, Rep. of South

Objectives and study: Commercially available fully covered self-expandable metal stents (FCSEMS) are being widely used in pancreatico-biliary stricture in adult population. This retrospective study is to explore the feasibility and safety of temporary placement of a newly designed, fully covered self-expandable metal stent in refractory benign pancreatic ductal strictures in children.

Methods: Five patients with dominant main pancreatic ductal stricture (upstream dilatation > 6 mm) of chronic pancreatitis (CP) who were refractory to plastic stent trial previously were enrolled. Three male and 2 female were enrolled. Median age was 12y (10-18y). ERCP with temporary (3~10 months) FCSEMS placement (Hanarostenteq T-shaped, M.I. Tech, Korea) were done and endoscopic removal of FCSEMSs was performed with a snare or rat-tooth forceps. Outcome was measured with feasibility, safety, and morbidity retrospectively.

Results: Successful FCSEMS placement was performed in all enrolled patients. The diameter of stents were 6 mm in all and length were 4,4,5,7,7 cm respectively. There was no occurrence of pancreatic sepsis, pancreatitis, cholestasis, and mortality among any patients. Proximal migration and distal migration were not observed. FCSEMSs were removed from 5 of 5 patients without stent migration. Improvement or resolution of the pancreatic ductal strictures was confirmed in all 5 patients on follow-up ERCP. Mean diameter of the stricture change 1.18 mm to 3.82 mm and that of upstream dilatation changed 9.02 mm to 6.22 mm after stenting.

Conclusion: Three to six -months placement of FCSEMSs in patients with refractory benign pancreatic ductal strictures may be feasible and safe in children. A further investigation with ideal number of patients will be necessary.
Fiberoptic endoscopic evaluation of swallowing in children with dysphagia. Relation between endoscopic findings, feeding outcomes and videofluoroscopic swallow study results

José Vicente Arcos-Machancoses¹, Johanna Martínez Osorio¹, Mariela Mercedes de Los Santos¹, Raquel García Ezquerra¹, Sergio Pinillos Pisón¹, Javier Martín de Carpi¹

¹Hospital Sant Joan de Déu, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain

Objectives and study: Fiberoptic endoscopic evaluation of swallowing (FEES) is an instrumental tool developed to assess swallowing function in patients with feeding disorders, as an adjunct to clinical observation and videofluoroscopic swallow study (VFSS). It enables anatomical evaluation of pharynx and larynx without radiation exposure and, moreover, allows the observer to study functional movements of the hypopharynx and vocal cords, secretion management and laryngeal reflexes. Our purpose is to describe our experience with FEES in children and the relationship between its findings, feeding outcomes and VFSS results

Methods: We completed a retrospective review in patients who underwent FEES from June 2015 to November 2016. The FEES procedure is carried out by a team including a gastroenterologist, a nurse and a speech therapist (ST). Flexible laryngoscopy is performed through transnasal way. The ST presents food of different textures, mixed with blue colouring to aid in visualization. FEES is only stopped if serious impairment of swallowing safety is detected or patient fails to cooperate. The following abnormalities are noted: 1) anatomical or functional movement anomalies in pharynx and larynx, 2) lack of secretions management ability, 3) altered proprioception, 4) premature entry of the bolus over the base of the tongue, 5) penetration or aspiration of material below the true vocal folds and 6) residue of the bolus in the vallecula and pyriform sinus. Feeding status was documented in the last follow up visit and placed into one of these categories: total oral intake with or without food texture adaptation, partial oral intake with tube feeding supplementation, or nothing by mouth (NPO). Dysphagia characterization agreement between FEES and VFSS was assessed by the kappa index with linear weighting. Logistic regression was used to compare clinical diagnoses and FEES findings to the final feeding status.

Results: Forty-seven patients underwent FEES after clinical swallowing evaluation. Dysphagia to both liquids and solids was the main indication, in up to 38.3% of patients. Age ranged from 1 to 19 years. In 7 patients, FEES was stopped because of apparent significant aspiration but no complications were detected afterwards. Pre-FEES feeding recommendations were based on VFSS in 38.3%. Aspiration pneumonitis, indicating significant swallowing security impairment, was present in 23.4%. Findings suggesting larynx cleft were noted in 9 patients, all of whom were derived to anatomical airway assessment by the ENT specialist, who confirmed it in 6 cases. Only 3 patients required VFSS after the FEES to complete swallowing assessment. The kappa index for results in VFSS and FEES regarding swallowing security and efficacy was 0.494 and 0.345 respectively, showing a fair/moderate agreement. Two out of five patients with neither aspiration nor penetration in VFSS were found to have security impairment in FEES. No cases were detected the opposite way. Description of aspiration or penetration with liquids (odds ratio –OR– 5.7, p-value 0.014) and honey-thick food (OR 7.5, p-value 0.014) significantly increased the risk of NPO. Neither baseline neurological nor neuromuscular disorders modified the likelihood of achieving total oral feeding status.

Conclusion: In children with dysphagia, FEES findings can predict middle term feeding status better than clinical diagnoses. FEES provide complementary information to VFSS and can be performed safely at patient’s bedside.
Bean syndrome: a three-case series

CARLOS CUADROS¹, Stephania Peña¹, Juana María Quevedo¹, Flora Zarate², Monserrat Cazares¹, Roberto Cervantes², Jaime Ramirez²

¹Instituto Nacional de Pediatria, Gastroenterology and Nutrition, Mexico, Mexico
²Instituto Nacional de Pediatria, Pediatric Gastroenterology and Nutrition, Mexico, Mexico

Objectives and study: To describe the clinical presentation of 3 patients with Bean syndrome.

Methods: A case series of 3 patients with Bean syndrome attended at Instituto Nacional de Pediatría, México.

Results: Cases
1- A 9 year-old male with history of Hemangioma on right hand at birth, referred for study of hematoquezia at 4 years old. PE: vascular neoformations on gluteal area, shoulders and forearms. Endoscopic study with multiple vascular malformations in the esophagus, stomach and colon. He required application of cyanocrylate at the gastric fundus. During the follow-up he presented an episode of melena with bleeding injury at antrum was observed at endoscopic control, 1% polidocanol was applied. No new episodes of digestive bleeding have occurred.

2- A 11 year-old female with a chest cutaneous hemangioma detected at birth. She was referred for study of chronic anemia and microscopic gastrointestinal bleeding (GIB) at 11 years old. PE: vascular neoformations in stomach, duodenum, jejunum, colon and rectum, without active bleeding. To date, the patient has not experienced new episodes of macroscopic GIB.

3- A 14 years old male with history of Kasabach-Merritt syndrome who required resection of cutaneous hemangioma on the back when he was 1 year old. Referred at 8 years old for the assessment of an upper and lower GIB causing anemia. PE: vascular neoformations in head, glans and lower limbs. Endoscopic study showed vascular malformations in gastroesophageal junction, stomach, duodenum, ileum and rectum. Coagulation was performed with argon plasma in the stomach and duodenum. Episodes of GIB causing chronic anemia, so an endoscopic capsule was performed finding justapyloric antral angiodysplasia and multiple blue nesus in jejunum and ileum. Argon plasma was injected by enteroscopy. However, GIB causing chronic anemia and therefore jejunoileal resection was performed at 9 years old. Evolution was favorable, without new episodes of GIB.
Table: Clinical and endoscopic findings are summarized in the following table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>1</th>
<th>2</th>
<th>3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Age (years)</td>
<td>9</td>
<td>11</td>
<td>14</td>
</tr>
<tr>
<td>Gastrointestinal clinical presentation</td>
<td>Hematochezia</td>
<td>Microscopic GIb</td>
<td>Melenas and hematochezia</td>
</tr>
<tr>
<td>Vascular malformation at birth</td>
<td>Hemangioma on right hand</td>
<td>Chest Hemangioma</td>
<td>Hemangioma on back</td>
</tr>
<tr>
<td>Skin lesions</td>
<td>Gluteal region, Shoulders and forearms</td>
<td>Trunk, limbs and Gluteal region</td>
<td>Head, glans and lower limbs.</td>
</tr>
<tr>
<td>Digestive lesions</td>
<td>Esophagus, stomach and colon</td>
<td>Stomach, duodenum, jejunum, colon and rectum</td>
<td>Gastroesophageal junction, stomach, duodenum, jejunum, ileum and rectum</td>
</tr>
<tr>
<td>Evolution</td>
<td>1 episode of GIb</td>
<td>No GIb</td>
<td>Multiple GIb episodes</td>
</tr>
<tr>
<td>Treatment</td>
<td>Application of 1% cyanoacrylate and polidocanol</td>
<td>Oral iron</td>
<td>2 argon plasma injections and jejunoleal resection</td>
</tr>
</tbody>
</table>

Conclusion: Bean syndrome diagnosis requires a high suspicion due to its low frequency. In patients with chronic anemia, GIb, cutaneous and gastrointestinal hemangiomas Bean syndrome should be suspected. Early identification of patients with multiple cutaneous lesions and endoscopy findings is part of the diagnosis. The most serious complication is the potentially fatal GIb. Its treatment depends on the location and magnitude of the lesions. Endoscopic diagnosis and treatment of conditions has now supplanted a number of surgical procedures.
Intestinal involvement and subsequent development of lymphoma in activated phosphoinositide 3-kinase syndrome case

Simona Faraci¹, Alessia Scarselli², Francesca Rea¹, Maia De Luca², Erminia Romeo¹, Valerio Balassone¹, Tamara Caldarò¹, Filippo Torroni¹, Giovanni Federici di Abriola¹, Renato Tambucci¹, Anna Chiara Contini¹, Giulia Angelino¹, Rita De Vito³, Paola de Angelis¹, Luigi Dall’Oglio¹, Caterina Cancrini²

¹Bambino Gesù Children’s Hospital, Irccs, Digestive Surgery and Endoscopy Unit, Rome, Italy
²Bambino Gesù Children’s Hospital, Irccs, University Department of Pediatrics, Unit of Immune and Infectious Diseases, Rome, Italy
³Bambino Gesù Children’s Hospital, Irccs, Department of Pathology and Molecular Histopathology, Rome, Italy

Objectives and study: Activated phosphoinositide 3-kinase δ syndrome (APDS) is a new autosomal-dominant primary immunodeficiency (PID) caused by a heterozygous gain-of-function mutation in the PIK3CD gene which determines PI3Kδ hyper-activation, predisposing to multiple types of B-cell lymphomas. We report our experience in the management of an APDS2 (c.1425+1G>T) case of a 30 years old girl, diagnosed six months ago. The patient presented an early intestinal involvement IBD-like. Subsequently, she developed lymphoma. Usually, in APDS patients, endoscopy is performed in according to clinical symptoms.

Methods: retrospective case report.

Results: Since early life, the patient presented recurrent sino-pulmonary infections, diffuse lymphadenopathy. When she was 10-year old, immunological investigations showed CD4+ naive lymphopenia and dysgammaglobulinaemia. Therefore a monthly immunoglobulin infusion treatment was started. At 18 years, because of a diagnosis of Hodgkin’s lymphoma, she was treated by chemotherapy and radiation therapy with the development early menopause. At 24 years she presented abdominal pain and bloody diarrhoea. Endoscopic evaluations showed colonic micro-erosions and multiple sessile polyps. Histology was suggestive for an IBD-like with a general hyperplasia. Capsule enteroscopy uneventful. She started mesalazine with annual endoscopic follow up. The patient was asymptomatic and in good general condition for 4 years. During the last colonoscopy, a polypoid mass was identified and piece meal polypectomy was performed. Histological finding of diffuse large B-cell lymphoma. Bone marrow aspirate was normal. The patient was referred to an adult centre and she is now candidate to chemotherapy.

Conclusion: The activation of PI3Kδ signalling contributes to B and T cell proliferation and neoplastic transformation. Recent reports have underscored that APDS patients have a high incidence of lymphoma, especially in young adult patients. In these patients, clinical and laboratory manifestations suggestive of LPD should prompt clinicians to consider early and alternative diagnostic tools including serial needle biopsies of the lymph-nodes, endoscopy and involvement of a multidisciplinary team with a strict gastrointestinal follow up even in the absence of symptoms.
The use of haemostatic spray in a child with high-risk nonvariceal bleeding

Nataruks Chaijitraruch1, Piyapan Prueksapanich2, Sureeporn Jangsirikul2, Rungsan Perknimitr2, Voranush Chongsrisawat1

1King Chulalongkorn Memorial Hospital, Chulalongkorn University, Paediatrics, Bangkok, Thailand
2King Chulalongkorn Memorial Hospital, Chulalongkorn University, Medicine, Bangkok, Thailand

Objectives and study: Gastrointestinal haemorrhage from nonvariceal bleeding in paediatrics is a rare but life-threatening condition. Haemostatic spray (Hemospray®) is a novel method that has been shown promising efficacy in achieving hemostasis in adult. However, data in paediatrics is scarce. This case report aimed to demonstrate the use of Hemospray® as an adjunct therapy to treat a child with refractory gastrointestinal bleeding secondary to duodenal ulcer.

Method: Case report

Results: An 11 year-old girl with autoimmune sclerosing cholangitis and ulcerative colitis was admitted for liver transplantation. She had end-stage liver disease with portal hypertension, and pancytopenia due to hypersplenism. Acute renal failure which required renal replacement therapy was noted on day 1 after transplantation. On day 5, she had melena and coffee-ground nasogastric content. She was haemodynamically stable but haemoglobin dropped from 80 to 47 g/L, platelets and prothrombin time were 34 x10^9/L, and 15 seconds, respectively. She was started on intravenous drips of pantoprazole and octreotide. Urgent upper endoscopy showed grade II oesophageal varices without haemorrhagic sign, nonbleeding portal hypertrophic gastropathy and oozing hemorrhage at duodenal bulb possibly a Dieulafoy lesion. Adrenaline injection and heater probe were applied to the duodenal lesion. Two banding ligations were performed on oesophageal varices. The following day, she developed haematemesis in which generalized erythematous with active oozing at duodenal bulb was again visualised at endoscopy and the bleeding was stopped with an argon plasma coagulation. After 2 days, a third episode of massive bleeding occurred despite full support of blood components and medical therapy. There was no evidence of extravasation on angiogram. A duodenal ulcer with adherent clot surrounded by friable mucosa was identified. Adrenaline injection followed by Hemospray® was applied resulting in transient haemostasis which recurred at 72 hours. Diffuse ooze in duodenum and bleeding duodenal ulcer was successfully stopped with combination of adrenaline, Hemoclips® and Hemospray® (Figure 1). Post procedure, her haemodynamic was stable and had no complication. She is well with no further evidence of bleeding after 1-month follow up.
Figure 1: Upper endoscopy images of the patient. (A) Adherent clot with active oozing in duodenal bulb. (B) Duodenal ulcer after adrenaline injection and clot removal. (C) Post Hemoclip® application. (D) Post Hemospray® application.

Conclusion: The use of haemostatic spray in combination with conventional endoscopic therapy (adrenaline and haemostatic clips or thermal device) seems to be a promising therapeutic method in children with nonvariceal bleeding particularly in a refractory bleeding owing to its simplicity and safety.
Diagnostic endoscopy in children with gastrointestinal symptoms: indications and outcomes - prospective study

Ahmed Kadir¹, David Rawat², Sandhia Naik³, Nick Croft⁴

¹Royal London Hospital / Queen Mary's University, Paediatric Gastroenterology, London, United Kingdom
²The Royal London, Paediatric Gastroenterology, London, United Kingdom
³Royal London Hospital, London, United Kingdom
⁴Queen Mary's University, London, United Kingdom

Objectives and study: The aim of the study was to prospectively evaluate the prediction of abnormalities for first upper GI endoscopies and colonoscopies done in children and to correlate the indication for the procedure with expected contributive yield in clinical practice. A second aim was to examine variation of practice in decision making for GI endoscopy nationally in the UK

Methods: This study was a descriptive, prospective analysis, conducted at the department of paediatric gastroenterology, Royal London Children's Hospital Barts Health NHS Trust. All children who had first upper GI endoscopies and colonoscopies from April 2016 to June 2016 were included. Exclusion criteria were any interventional procedures. A standard questionnaire was filled in by the clinician at the time of requesting the endoscopy for prediction of abnormalities, which was compared to macroscopic and histology findings. At the time of endoscopy the endoscopist defined the macroscopic outcomes as normal or abnormal which were recorded. 2 consultant histopathologist were involved in analysis of all biopsy specimens which were reviewed in a weekly multidisciplinary meeting.

To examine the possibility of differences in clinical decision making we also created an online survey of 6 different cases and through the endoscopy working group of BSPGHAN, a link for the survey was sent to paediatric gastroenterologist (consultants and trainees) throughout the United Kingdom. The survey was anonymized.

Results: A total of 63 children had endoscopies in the period of 3 months, 14 children had repeat endoscopies therefore were excluded from the study leaving 49 children. Out of 49 children 28 (57.1%) were male and 21 (42.9%) were female. 26 children had upper GI endoscopies, 8 had colonoscopies and 15 children had both procedures. Our study suggested that the most common symptom for which upper GI endoscopy was requested were symptoms of upper abdominal pain (34%), for colonoscopy was rectal bleed (76%) and for request of both upper GI and colonoscopy was generalised abdominal pain (47%). Histological findings were abnormal in 46% of children with upper abdominal pain, 30% of children with reflux symptoms, 20% of children with rectal bleed and all endoscopies were normal in children with symptoms of vomiting. The predictability of a normal endoscopy (32.65%) was more accurate as compared to the predictability of abnormal histology findings (23%).

Conclusion: Our study is the largest prospective clinical evaluation of paediatric OGD, colonoscopy and upper and lower endoscopy in a UK tertiary paediatric gastroenterology unit. We still need a larger prospective multicentre studies in order to develop appropriate guideline for patient selection to maximise diagnostic yield.
Preemptive surgery for impending aorto-oesophageal fistula after button battery ingestion

Raffi Lev-Tzion1, Eldad Erez2, Roman Bass3, Yaron Armon4, Ruth Cytter-Kuint5, Naama Bogot5, Dan Turner6

1Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
2Hadassah Medical Center, Pediatric Cardiothoracic Surgery, Jerusalem, Israel
3Shaare Zedek Medical Center, Pediatric Intensive Care Unit, Jerusalem, Israel
4Shaare Zedek Medical Center, Pediatric Surgery, Jerusalem, Israel
5Shaare Zedek Medical Center, Radiology, Jerusalem, Israel
6Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: One of the most feared outcomes after button battery ingestion is the occurrence of an aorto-oesophageal fistula with sudden onset of catastrophic bleeding. This complication may occur up to 28 days after ingestion and carries a reported mortality rate of nearly 100%.

Methods: We report a preemptive surgical intervention to prevent this deadly event.

Results: Case Presentation: A 4-year old boy presented to the emergency room after swallowing a 22 mm diameter button battery. The battery was removed endoscopically less than three hours after ingestion. Deep ulcerations were demonstrated at the points of contact in the distal esophagus. He was admitted to the pediatrics ward and closely supervised; throughout his hospital course he remained asymptomatic.

MRI evaluation of the esophagus performed on day 8 showed extensive burn damage to the esophagus including two deep ulcers; one of the ulcers was positioned in the esophageal wall adjacent to the aorta, without perforation. Two follow-up MRI studies over the next 10 days showed no improvement, with no clearly visible plane of separation between esophagus and aorta. Given these findings, it was decided to proceed with surgery to protect the aortic wall from penetration. A left thoracotomy incision was made and an intercostal muscle flap was dissected free and positioned between the aorta and esophagus. Surgery was uneventful and the patient was discharged on soft mechanical diet. Repeat endoscopy at 4 weeks showed a nearly healed ulcer and by 6 weeks he resumed a normal diet and was discharged from followup.

Conclusion: It is still unclear how to predict who will develop an aorto-oesophageal fistula after button battery ingestion and how to prevent its occurrence. The recent NASPGHAN guidelines are likely to result in an increase in the number of MRI studies performed after button battery removal and thus more cases of potential fistula events will be discovered; each of these cases presents a therapeutic dilemma. Protective intercostal muscle flap might be considered in select cases of impending aorto-oesophageal fistula.
How can we reduce the anxiety of children before gastroscopy

Nevzat Aykut Bayrak¹, Burcu Volkan², Cahit Ucar³, Duygu Kara⁴, Sedat Yıldız⁴

¹Diyarbakir Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
²Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
³Inönü University School of Medicine, Department of Physiology, Malatya, Turkey
⁴Erzurum Regional Training and Research Hospital, Anesthesiology and Reanimation, Erzurum, Turkey

Objectives and study: Gastrointestinal (GI) endoscopy is a useful modality for the diagnosis and treatment of various paediatric gastrointestinal disorders. It can cause severe anxiety, fear, pain and stress in children. Like adults, many paediatric patients are anxious about pain associated with endoscopy. Medical staff should therefore explain the procedures in the light of these findings. The purpose of this study was to determine whether anxiety levels of paediatric patients who undergo endoscopy are reduced after aspects of the examination have been explained.

Methods: Children undergoing gastroscopy under sedoanalgesia for various reasons were included in the study. Cases were divided into two groups; patients to whom aspects of the examination were not explained (Group 1) and those to whom the examination was explained (Group 2). In order to determine anxiety levels, three saliva specimens were obtained to examine saliva cortisol levels (SCL): first at any time on the day before the procedure, others just before and after endoscopy. Anthropometric measurements were performed, and history of additional chronic disease was investigated. Anxiety scores before endoscopy were calculated (Yale Preoperative Anxiety Scale Modified). Patients were monitored throughout sedoanalgesia, and duration of endoscopy, sedation and recovery and total propofol dosage were recorded.

Results: A hundred nineteen children undergoing gastroscopy (age 10.9±3.2 years; 43.7% male) constituted Group 1 and 65 children (age 11.2±3.1 years; 50.8% male) constituted Group 2. Group data are shown in Table 1. Anxiety score, propofol dosage, duration of recovery, basal SCL, SCL before endoscopy and SCL after endoscopy were significantly higher in Group 1 (p<0.05).

Table: Characteristics of the study groups

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n=119)</th>
<th>Group 2 (n=65)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anxiety score</td>
<td>10.1±2.7</td>
<td>8.03±1.7</td>
<td>0.001</td>
</tr>
<tr>
<td>Length of procedure</td>
<td>9.1±1.9 min</td>
<td>8.6±1.9 min</td>
<td>0.18</td>
</tr>
<tr>
<td>Propofol dosage</td>
<td>3.9±1.6 mg/kg</td>
<td>2.9±0.8 mg/kg</td>
<td>0.001</td>
</tr>
<tr>
<td>Duration of recovery</td>
<td>11.2±4.3 min</td>
<td>8.9±4.3 min</td>
<td>0.001</td>
</tr>
<tr>
<td>Basal SCL</td>
<td>16.1±19.7 ng/ml</td>
<td>9.7±5.7 ng/ml</td>
<td>0.001</td>
</tr>
<tr>
<td>SCL before endoscopy</td>
<td>36.4±32.5 ng/ml</td>
<td>12.2±10.5 ng/ml</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>SCL after endoscopy</td>
<td>20.2±19.4 ng/ml</td>
<td>13.6±11.1 ng/ml</td>
<td>0.013</td>
</tr>
</tbody>
</table>

Conclusion: Patients who were not explained about aspects of the examination were more anxious, their duration of recovery was longer, and propofol dosage was higher. It is important for the attending physician to carefully explain the aspects of the examination in order to decrease the patient anxiety and avoid probable complications related to patient stress and sedoanalgesia.
Endoscopic retrograde pancreatography performed by pediatric endoscopists - single centre experience

Marek Woynarowski¹, Patryk Lipiński¹, Maciej Dadalski², Violetta Wojno¹, Mikołaj Teisseyre¹, Grzegorz Oracz¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
²The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland

Objectives and study: The experience with endoscopic retrograde cholangiopancreatography (ERCP) in pediatric population is limited. The aims of the study are to evaluate indications, results, and safety of ERCP in children performed for pancreatic indications by pediatric endoscopists at the single pediatric endoscopy referral center.

Methods: This is a retrospective review of patients’ medical records who had undergone ERCP between Jan 2014 and Dec 2016. Data on demographics, indications, procedures performed during ERCP, and complications were collected.

Results: A total of 70 children underwent 154 examinations. The patients’ age ranged from 3 to 18 years (mean±SD: 12.5±3.6) and body weight from 12 to 100 kg (45.0±19.6). The minority (n=25) of patients underwent a single procedure, whereas 45 patients underwent more than one intervention (15 had 2 ERCPs, 8 had 3 ERCPs, 11 had 4 ERCPs, 5 had 5 ERCPs, 1 had 6 ERCPs).

The main indication for ERCP was chronic or recurrent pancreatitis (n=66, including 3 with the pancreatic cyst, 8 with pancreas divisum and 1 with cystic fibrosis). 4 patients had ERCP following surgery for pancreas disease (n=2), retroperitoneal tumor (n=1), or abdominal trauma (n=1). 6% (n = 10) of the ERCPs were performed as emergency procedures.

ERCP goal was achieved in 92% of procedures while unsuccessful or partially successful pancreatic duct cannulation occurred in 8% (n=13). 4 patients had successful cannulation of minor ampulla. The following procedures were carried out: sfincterotomy (n=33), pancreatic stent implementation (n=94), removal of previously inserted pancreatic stent (n=88), removal of pancreatic duct deposits using basket or balloon (n=17), dilatation of pancreatic duct stenosis with rigid or balloon dilator (n=16).

The complication rate was 6% including duodenum perforation (n=1), acute pancreatitis (n=2), abdominal pain with transient elevation of pancreatic enzymes (n=7). There were neither late complications nor mortality related to ERCP.

Patients were discharged home 2 to 15 days (4.5±2.4) after ERCP. 4 patients reached 18 years of age and were referred to adults’ centers. 24 patients completed the treatment with ERCP. 9 patients were referred for surgical treatment and 35 patients continue ERCP therapy improving pancreatic duct drainage.

Conclusion: The failure and complications rates of ERCP performed for pancreatic indications by pediatric endoscopists in the children’s center are comparable to those observed in centers for adults. ERCP is a safe and effective procedure for pediatric patients.
ENDOSCOPIC RETROGRADE CHOLANGIOGRAPHY PERFORMED BY PEDIATRIC ENDOSCOPISTS - SINGLE CENTRE EXPERIENCE

Marek Woynarowski, Patryk Lipiński, Maciej Dadalski, Violetta Wojno, Mikołaj Teisseyre, Grzegorz Oracz

1 The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
2 The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland

OBJECTIVES AND STUDY: The experience with endoscopic retrograde cholangiopancreatography (ERCP) in pediatric population is limited. The aims of the study are to evaluate indications, results, and safety of ERCP in children performed for biliary indications by pediatric endoscopists at the single pediatric endoscopy referral center.

METHODS: This is a retrospective review of patients’ medical records who had undergone ERCP between Jan 2014 and Dec 2016. Data on demographics, indications, procedures performed during ERCP, and complications were collected.

RESULTS: A total of 89 children underwent 146 examinations. The patients’ age ranged from 1 to 18 years (mean±SD: 11.8±5.0) and body weight from 8 to 90.5 kg (40.4±22.0). The majority (n=47) of patients underwent a single procedure, whereas 38 patients underwent more than one intervention (22 had 2 ERCPs, 11 had 3 ERCPs, 4 had 4 ERCPS, 1 had 6 ERCPs).

ERCP were performed for the following indications: cholelithiasis (n=45); cholestasis (n=16, including 11 in the course of primary sclerosing cholangitis); post-liver transplantation biliary complications (n=11); common bile duct extension (n=8), liver injury (n=3), liver hilum tumor (n=5) and multiple liver abscesses (n=1). 30% of ERCP (n=44) were performed as urgent procedures.

ERCP goal was achieved in 91% (n=133) procedures while cannulation of the ampulla failed in 6% (n=9) or was partially possible in 3% (n=4). The following interventions were carried out: sphincterotomy (n=78), biliary stent implementation (n=78), removal of previously inserted biliary stent (n=57), extraction of biliary stones using basket or balloon (n=47), dilatation of biliary duct strictures by rigid or balloon dilator (n = 23). Biliary tract tissue sample (brush smear or biopsy) was taken in 4 patients and in one subject material was diagnostic for sarcoma.

The complication rate was 6% including aspiration pneumonia (n=1), bile duct or duodenum perforation (n=2) and mild pancreatitis (n=6). There were neither late complications nor mortality related to ERCP.

Patients were discharged home 2 to 24 days (4.9±3.0) after ERCP. 5 patients reached the age of 18 years and was referred to adults’ centers. In 28 patients ERCP was found final therapeutic procedure with no further treatment. 20 patients had undergone further surgical interventions (cholecystectomy, Re-LTx). 36 patients continue therapy with repeated ERCP for biliary tract drainage.

CONCLUSIONS: The failure and complications rates of ERCP performed for biliary indications by pediatric endoscopists in the children’s center are comparable to those observed in centers for adults. ERCP is a safe and effective procedure for pediatric patients.
Blue rubber bleb nevus syndrome: a challenging cause of gastrointestinal bleeding

Ahmed Megahed¹, Mohammad Ezz El-Regal¹, Suzy Abd El-Mabood², Mona Abd El-Latief³, Ashraf Abd El-Rahman⁴

¹Mansoura University Children’s Hospital, Mansoura University, Pediatrics, Gastroenterology, Hepatology and Nutrition, Mansoura, Egypt
²Mansoura University Children’s Hospital, Mansoura University, Pediatrics, Mansoura, Egypt
³Mansoura University Children’s Hospital, Mansoura University, Pediatrics, Gastroenterology, Hepatology and Nutrition, Mansoura, Egypt
⁴Mansoura University Children Hospital, Radiology, Mansoura, Egypt

Objectives and study: Blue Rubber Bleb Nevus Syndrome (BRBNS) is a rare condition characterized by multiorgan venous malformations, particularly skin and the gastrointestinal (GI) tract that could manifest by intractable GI bleeding. Surgery may be the optimum choice if lesions are few in number; however multiple extensive GI lesions are a real challenge. Sirolimus had been effectively used, owing to its antiangiogenic effect, in some case reports.

Methods: This is a report of a 4.5 years old Egyptian boy with BRBNS. Clinical, laboratory, imaging and endoscopic findings together with Sirolimus response were reported.

Results: A 4.5 years old Egyptian boy, who was presented with newly evolving skin lesions since the age of 3 months, associated with visceral, deep tissue and extensive GI lesions. Left lower limb MRI showed multiple small intra-muscular lesions seen within the quadriceps and calf muscles with altered marrow signal at the mid shaft femur. Abdominal CT discovered multiple enhancing hepatic focal lesions scattered at both lobes largest seen at segment IV (2.2 X1.8 cm). Push enteroscopy demonstrated extensive small bowel and colonic involvement by lesions of variable sizes and shapes. Over the last 2 years this patient suffered from intractable melena and bleeding per rectum, blood transfusion dependency. Treatment with sirolimus resulted in a significant improvement of his condition. Hemoglobin level was maintained over 10gm/dl, cessation of transfusions with very good drug tolerance and minimal side effects. A noticeable reduction in the number and size of GI lesions on relook endoscopy after 3 months treatment as well as skin lesions. Meanwhile sirolimus withdrawal trial after 6 months therapy failed, requiring its continuation.

Figure: Enteroscopic pictures of BRBNS lesions: (A) Second part of duodenum; (B) Proximal small intestine.

Conclusion: In spite being rare, BRBNS can manifest with a challenging GI bleeding. Sirolimus treatment is seeming promising in extensive bowel lesions.

Disclosure of interest: None of the authors has any conflict of interest to declare.
Diagnostic evaluation and management of obscure gastrointestinal bleeding in children- a single centre experience

Natalia Nedelkopoulou1, Sara Isoldi2, Sean Marven3, Govind Murthi3, Richard Lindley3, Dalia Belsha2, Sishu Sharma2, Prithviraj Rao4, Priya Narula4, Mike Thomson1

1Sheffield Childrens NHS Foundation Trust, Paediatric Gastroenterology, Sheffield, United Kingdom
2Sheffield Children's Hospital, Paediatric Gastroenterology, Sheffield, United Kingdom
3Sheffield Childrens NHS Foundation Trust, Paediatric Surgery, Sheffield, United Kingdom
4Sheffield Children's Hospital NHS Foundation Trust, Paediatric Gastroenterology, Sheffield, United Kingdom

Objectives and study: Failure to identify the cause of gastrointestinal (GI) bleeding at upper GI endoscopy and ileo-colonoscopy poses a diagnostic and therapeutic challenge to the clinician. We present our 6-year experience on the management of obscure GI bleeding (OGIB) in children.

Methods: The records of pediatric patients with OGIB who underwent diagnostic evaluation and management in our Centre between 2010-2016 were reviewed

Results: 19 patients (9M) aged 8m-16y (median 8.5y) were identified. The presenting symptoms included hematochezia (10), melaena (7), haematemesis (3), collapse secondary to GI bleed (2), refractory iron deficiency anaemia (4), recurrent abdominal pain (3) and hypoalbuminaemia (1). 7 patients received blood transfusions and 5 octreotide/terlipressin. 13/19 had been investigated in other tertiary centres with upper GI endoscopy (EGD) +/- ileo-colonoscopy (13), wireless capsule enteroscopy (WCE) (5), Meckel's scan (3), CT angiogram (3), laparotomy (2) and laparoscopy (2), technetium-99m red blood cell scan (1) and barium follow through (1). 2 had had a segment of the colon removed. The interval between initial presentation and referral to our Centre ranged from 4d to 10 years (median 16.5m). All patients had endoscopic reassessment with upper GI endoscopy and ileo-colonoscopy in our Unit. The diagnostic work up included WCE (16), antegrade and retrograde double balloon enteroscopy (DBE) (11), laparoscopic assisted enteroscopy (5), CT angiography (1), CT abdomen (1), Meckel's scan (1) and endoscopic ultrasound (EUS) (1). In 2 patients no cause was identified and in one the bleeding was attributed to severe esophagitis. 4/19 were diagnosed with polyposis syndromes (Peutz-Jeghers in 2 and juvenile in 2) with small bowel involvement. 2 underwent lap-assisted enteroscopy and had excision of of Meckel's diverticulum. The diagnosis, diagnostic modality and management in 10/19 are shown in table 1.
### Table: Diagnosis, diagnostic modality and management of OGIB

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>Diagnostic Modality</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>Concentric stenoses and ulcers in small bowel</td>
<td>Lap-assisted enteroscopy</td>
<td>Referral for genetic testing SLCO2A1</td>
</tr>
<tr>
<td>Patient 2</td>
<td>Blue rubber bleb naevus (gastric body)</td>
<td>EGD</td>
<td>APC*, endoclip, proximal gastrectomy</td>
</tr>
<tr>
<td>Patient 3</td>
<td>Aphthoid ulcers (distal ileum)</td>
<td>DBE</td>
<td>Treatment for Crohn’s disease</td>
</tr>
<tr>
<td>Patient 4</td>
<td>Perianastomotic ulcer (history of gastroschisis)</td>
<td>Ileo-colonoscopy</td>
<td>APC, endoclip</td>
</tr>
<tr>
<td>Patient 5</td>
<td>Angiodysplastic lesions (colon)</td>
<td>Ileo-colonoscopy</td>
<td>Referral for resection</td>
</tr>
<tr>
<td>Patient 6</td>
<td>Perforated gastric duplication cyst - colic fistula</td>
<td>CT abdomen</td>
<td>Resection</td>
</tr>
<tr>
<td>Patient 7</td>
<td>Threadworms in small bowel</td>
<td>DBE</td>
<td>Mebendazole</td>
</tr>
<tr>
<td>Patient 8</td>
<td>Lymphangiectasia</td>
<td>DBE</td>
<td>Conservative treatment</td>
</tr>
<tr>
<td>Patient 9</td>
<td>Jejunal varices</td>
<td>DBE</td>
<td>Banding</td>
</tr>
<tr>
<td>Patient 10</td>
<td>Arteriovenous malformation (rectum)</td>
<td>EUS</td>
<td>Steroid injection</td>
</tr>
</tbody>
</table>

*APC: argon plasma coagulation

**Conclusion:** In our case series the cause of OGIB/anaemia was identified in 89% of the cases. Advances in small bowel imaging with WCE, DBE, radiographic imaging and close collaboration between gastroenterologists and surgeons have improved the diagnosis and outcomes of OGIB in children. The importance of restarting the diagnostic process, with no preconceptions of possible sources of blood loss, is emphasized when a patient is referred from another tertiary centre.
Pan-enteric clearance of large number of polyps is feasible even with pan-enteroscopy: a case report of a 6 month old with >150 polyps removed at one procedure

Natalia Nedelkopoulou¹, Huw Jenkins², Richard Lindley³, Govind Murthi³, Mike Thomson¹

¹Sheffield Childrens NHS Foundation Trust, Paediatric Gastroenterology, Sheffield, United Kingdom
²Cardiff and Vale University Health Board, Department of Paediatric Gastroenterology, Cardiff, United Kingdom
³Sheffield Childrens NHS Foundation Trust, Paediatric Surgery, Sheffield, United Kingdom

Objectives and study: Juvenile polyposis syndrome is a rare disorder in children characterized by multiple hamartomatous polyps in the alimentary tract. We present here an interesting case of a 6m old male infant with juvenile polyposis syndrome and protein losing enteropathy with two possible new mutations

Methods: The medical record of the infant that was referred to our Centre for further management of juvenile polyposis syndrome was reviewed.

Results: The 6m old infant presented to the local hospital with bloody, mucousy diarrhoea, hypoalbuminaemia (15mg/dL) and microcytic anaemia (Hb 65g/dL). He was treated for cow’s milk protein allergy, but there was no clinical or biochemical improvement. He received 1 blood transfusion and parenteral nutrition and was treated for sepsis. Meckel’s scan was negative and abdominal USS showed multiple thickened bowel loops and intermittent short segment intussusception. At 8 months, upper GI endoscopy (EGD) and ileo-colonoscopy (IC) revealed 2 polyps in the stomach, 1 in the duodenum and 15 in the colon, both pedunculated and sessile. Histology confirmed the features of juvenile polyps and barium meal and follow through was negative for small bowel polyps. Genetic testing detected a 1.6Mb copy number loss of the long arm of chromosome 10 (from q23.2 to q23.31) including loss of both the BMPR1A and PTEN OMIM Morbid genes. Colectomy was suggested, but family was keen on conservative treatment.

At 9 months EGD, wireless capsule endoscopy (WCE), IC and polypectomy occurred in our Centre. 3 juvenile gastric polyps and 23 colonic polyps were noted at endoscopy and small bowel polyps on WCE. At 11 months antegrade and retrograde double balloon enteroscopy (DBE), multiple polypectomy, and on conversion to mini-laparotomy assisted enteroscopy over 100 small bowel polyps were identified. At 13m, a further mini-lap-assisted enteroscopy with a view to total polyp clearance occurred: 8 small sessile gastric polyps were noted, 145 small bowel polyps and 21 colonic polyps were removed. Haemostasis was achieved. 6 weeks later, albumin remains stable at 32mg/dL and Hb at 104g/dL. Endoscopic reassessment and WCE has occurred revealing no significant polyp regrowth and regular re-assessment is planned.

Conclusion: This is the youngest child described with juvenile polyposis syndrome and loss of both BMPR1A and PTEN OMIM Morbid genes. Safe and effective polyp clearance was achieved but it remains to be seen if this aggressive phenotype will prevent long term endoscopic management.
Could general anesthesia modify efficacy yield of wireless capsule endoscopy in children?

Cecile Yakovleff¹, Beatrice Bruneau², Marc Bellaiche¹, Alexis Mosca¹, Solene Ganousse¹, Christine Martinez-Vinson¹, Jean-Pierre Hugot¹, Jerome Viala³

¹Robert-Debré Hospital / Assistance Publique - Hôpitaux de Paris, Pediatric Gastroenterology Department, Paris, France
²Robert-Debré Hospital / Assistance Publique - Hôpitaux de Paris, Department of Anaesthesia, Intensive Care, Paris, France
³Robert-Debré Hospital, Assistance Publique - Hôpitaux de Paris, Departments of Pediatric Digestive and Respiratory Diseases, Paris, France

Objectives and study: Wireless Capsule Endoscopy (WCE) is a non-invasive tool for small bowel exploration in many diseases which can be deployed in the duodenum by endoscopy under anesthesia. Our aims were to compare the diagnostic yield, completion rate and small bowel transit time (SBTT) in case of swallowed or endoscopically placed WCE.

Methods: We retrospectively collected procedure and anesthesia charts for all the WCE performed in our tertiary center between November 2001 and March 2015. The WCE were endoscopically placed in children < 8 years or > 8 years after a failure to swallow the device, or in case of simultaneous endoscopy under anesthesia. Children were anesthetized mainly using halogenated agents, propofol and sufentyl.

Results: 142 swallowed WCE (Ingestion group) and 120 deposed WCE (Deposit group) were included. WCE were most frequently performed for inflammatory bowel diseases (27.9%), intestinal bleeding (36.3%) and polyposis (13%) in both groups. The diagnostic yield for small bowel lesions was similar in Ingestion and Deposit groups (55.6% vs 45.7%, p = 0.15). The SBTT was longer in Deposit group (280.4 ± 128 min vs 242 ± 100 min, p = 0.008) but completion rate was not differed in both groups (78.9% vs 83.3%, p = 0.36). The recording time was longer in Deposit group (488 ± 138 min vs 436 ± 110 min, p = 8x10⁻⁵). The diagnostic yield and the completion rate of WCE were similar whatever were the anesthetics used or the duration of the procedure.

Conclusion: endoscopic deployment under general anesthesia of WCE did not modify the diagnostic performance of small bowel exploration, even in deep and prolonged anesthesia. As the transit time was longer in endoscopically deposed WCE, the recording time should be prolonged to obtain a complete small bowel exploration and maintain a high diagnostic yield.

laetitia marie petit¹, Franziska Grunder², Jessica Ezri³, Anne Aspirot⁴, Christophe Faure⁵

¹Hopitaux Universitaires de Geneve, Pediatrics, Geneva, Switzerland
²Hopital Sainte Justine, Service de Gastro-Entérologie Pédiatrique, Montréal, Canada
³Centre Hospitalier Universitaire Vaudois, Unité de Gastro-Entérologie Pédiatrique, Lausanne, Switzerland
⁴Hopital Sainte Justine, Service de Chirurgie Viscérale, Montréal, Canada
⁵Chu Sainte Justine, Paediatric Gastroenterology, Hepatology and Nutrition, Montreal, Canada

Objectives and study: Upper endoscopy (EGD) with esophageal biopsies is recommended to evaluate systematically patients with esophageal atresia (EA). However, the diagnostic yield of EGD is unknown in this population. We aimed to report the diagnostic value of EGD in a cohort of EA patients prospectively followed in a tertiary EA Clinic with evaluation of potential risk factors for abnormal endoscopic findings.

Methods: We studied prospectively a cohort of 77 paediatric patients with ATOE born between 01.01.2005 and 31.12.2014. End of follow up was 16.07.2016. Indication for EGD was the presence of clinical symptoms and/or systematic follow-up, in accordance to published guidelines. Pathologies in form of peptic oesophagitis, eosinophilic oesophagitis (EoE) and metaplasia were confirmed by histology and reported during FU.

Statistical univariate analysis was performed by using SAS® University edition program. Chi-square test, Fisher’s exact was used for qualitative variables and non parametric one way test for continuous variables. P.value <0.05 is considered as statistically significant.

Results: In the population of 77 (44 boys) children with repaired ATOE, the median follow up(FU) time was 4.39 years. 71 patients (39 boys) (92.2%) had at least one endoscopy during FU. Median age at study end or date of very last FU: 4.9y, range 1-10.9y. At median time of FU of 4.9y, more than 95% of patients underwent at least one endoscopy. 6 patients had never an endoscopy to date during FU, but in all of them an endoscopy is scheduled. In patients with anastomotic stricture, the appearance of the stricture was before onset of histological complications. Totally 35 patients (49%, 19 boys) had histological complications in form of peptic esophagitis (n=29), eosinophilic esophagitis(n=12), and/or gastric metaplasia(n=8).

Median time to appearance of histological complications in patients without anastomotic stricture vs in patients with anastomotic stricture was 3.94 vs 2.95y respectively. Long gap atresia (OR 5.04, p=0.02), complications after surgery (anastomotic leak, refistula) (OR 4.89, p=0.01), recurrent anastomotic stricture (>3 episodes) (OR 7.33, p=0.002) are associated positively with appearance of histological complications. In patients with peptic oesophagitis (n=29), recurrent anastomotic stricture (OR 3.67, p=0.03) and anastomotic leak (OR 4.24, p=0.01) are positively associated with this pathology.

Conclusion: Prospective FU in a cohort of children with ATOE showed high number of endoscopic follow up, and 45 % of any histological complications among them. Recurrent anastomotic strictures, occurring mostly during the first 2 years after surgery, and early complications after surgery appear to be risk factors for abnormal histological findings and allow to draw indication for repetitive endoscopic FU.
Comparison of ileal intubation rates and diagnostic yields in ileocolonoscopy between four tertiary paediatric gastroenterology centres in the United Kingdom: a multicentre retrospective cohort study

Amit Saha\(^1\), Lakshmipriya Selvarajan\(^2\), Huey Miin Lee\(^3\), Manjula Velayudhan\(^4\), Shishu Sharma\(^5\), Dharam Basude\(^6\), John Fell\(^7\), Babu Vadmalayan\(^8\), Mike Thomson\(^9\)

\(^1\)Kings College Hospital NHS Trust, Paediatric Hepatology, Gastroenterology and Nutrition, London, United Kingdom
\(^2\)Bristol Royal Hospital for Children, Paediatric Gastroenterology, Bristol, United Kingdom
\(^3\)The Royal London Hospital, Paediatric Gastroenterology, London, United Kingdom
\(^4\)Sheffield Childrens Hospital, Paediatric Gastroenterology, Sheffield, United Kingdom
\(^5\)Sheffield Children's NHS Foundation Trust, Gastroenterology, Sheffield, United Kingdom
\(^6\)University Hospital Bristol, Paediatric Gastroenterology, Bristol, United Kingdom
\(^7\)Chelsea and Westminster Hospital, Department of Paediatric Gastroenterology, London, United Kingdom
\(^8\)King's College Hospital, Paediatric Liver, GI and Nutrition Centre, London, United Kingdom
\(^9\)Sheffield Childrens NHS Foundation Trust, Paediatric Gastroenterology, Sheffield, United Kingdom

Objectives and study: Gastrointestinal endoscopy is integral to the diagnosis and management of paediatric inflammatory bowel disease (PIBD). With increasing numbers of paediatric endoscopies performed worldwide, terminal ileum intubation (TII) rate at ileocolonoscopy has been gaining increasing importance, and indeed now constitutes a pivotal mandate in the revised Porto Criteria to improve IBD diagnosis, establishing itself as an integral part of PIBD management. It also has a critical role in contributing to the diagnostic yield of ileocolonoscopy, both by its positive and negative findings.

Several service evaluation studies have looked at TII rates and diagnostic yields in individual centres, and the factors influencing the same. In our study, we have compared this data amongst four major paediatric gastroenterology centres in the UK, in order to identify practice variations and local factors that may influence these outcomes, with a view to using this knowledge to further improve practice nationwide.

Methods: A service evaluation study was originally conducted in Sheffield Children's Hospital, UK, where data was collected randomly in 147 patients to evaluate the diagnostic yield of ileocolonoscopy in children. Subsequently, further data was collected as per an agreed proforma across three other paediatric gastroenterology training units in the UK – Bristol, Chelsea & Westminster (London) and Kings College Hospital (London). 50 consecutive cases were selected from each of these 3 centres and data collected retrospectively. The number of procedures per list, both scheduled and actually performed, was also reviewed for its impact on TII rates. The data was compiled and analysed on excel sheet and TII rates and other parameters, including normal findings, were evaluated. While the arithmetic mean was used as the measure of central tendency, the diagnostic yield was calculated from the Sheffield data and the sensitivities, specificities, positive predictive values (PPV) and negative predictive values (NPV) from all the other centres were calculated for comparison.

Results: Data from a total of 297 children who underwent endoscopy across 4 UK centres were analysed. The common indications were abdominal pain, chronic diarrhoea, per-rectal bleeds, reassessment of known PIBD and surveillance in post transplant patients. The diagnostic yield from Sheffield was 18.9% and 32.6% for esophagogastroduodenoscopy and ileocolonoscopy respectively in this cohort. Overall, the endoscopic procedures had comparable sensitivities, specificities, PPV and NPV across all centres, as per Table 1.
**Conclusion:** Our data suggests that full paediatric ileocolonoscopy in UK tertiary centres seem to be adhering well to established guidelines, with an overall high ileal intubation rate (>95%) across all centres, without any significant impact of the number of procedures done per list, use of scope guide or use of scope stiffener. With over half the ileocolonoscopies being normal, appropriate selection of cases is paramount, as is small bowel imaging in appropriate settings in order to further improve the diagnostic yield. Further studies looking at international trends and practices will throw light on how
robustly PIBD is being managed on a global scale.

| Table 1 |
|----------------------|-----------------|-----------------|-----------------|-----------------|
| **Number** | Bristol | Kings | Sheffield | Chelsea | Cumulative |
| 50 | 50 | 147 | 50 | 297 |
| **Mean age (years)** | 10.5 | 11.8 | 9.58 | 11.85 | 10.49 |
| **M:F ratio** | 1.6:1 | 1.5:1 | 1:1.42 | 2.8:1 | 1.15:1 |
| **Average no. of procedures/list (scheduled)** | 5.36 | 4.68 | 7.0 | 6.1 | 5.38 |
| **Average no. of procedures/list (performed)** | 5.3 | 4.32 | 6.4 | 5.68 | 5.10 |
| **Upper GI abnormalities (macroscopy)** | 14/43 (32.5%) | 12/50 (24%) | 35/147 (23.8%) | 13/41 (31.7%) | 74/281 (26.33%) |
| **Upper GI abnormalities (histology)** | 26/43 (60.4%) | 16/48 (33.33%) (2 not done) | 36/147 (24.4%) | 17/41 (41.4%) | 95/279 (34.05%) |
| **Lower GI abnormalities (macroscopy)** | 23/50 (46%) | 34/50 (68.7%) | 33/103 (32%) | 31/50 (62%) | 121/253 (47.8%) |
| **Lower GI abnormalities (histology)** | 29/50 (58%) | 28/49 (58.33%) (2 not done) | 23/103 (22.33%) | 31/60 (52%) | 111/261 (42.5%) |
| **Scope Type** | Fujinon | Olympus | Olympus | Olympus |
| **Scope guide used** | No | No | Yes | No |
| **Scope stiffener used** | No | No | Yes | No |
| **TII rate** | 42/44 (96%) (6 not indicated) | 48/50 (96%) | 144/147 (98%) | 40/47 (85%) (3 not indicated) | 274/288 (>95%) |
| **Normal ileocolonoscopy** | 21/50 (42%) | 20/50 (40%) | 70/103 (67.9%) | 19/50 (38%) | 130/253 (51.38%) |
| **Sensitivity** | 75% | 73.3% | 71.4% | 94.5% | 77.8% |
| **Specificity** | 90% | 77.7% | 71.4% | 92.3% | 77.3% |
| **PPV** | 91.30 | 84.61 | 65.21 | 97.22 | 79.87 |
| **NPV** | 74.07 | 63.63 | 76.90 | 85.71 | 75.17 |
Severe esophageal injury due to doxycycline ingestion in a girl 17 years old

Hussein Shamaly¹, Alaa Abu Sharki¹, Nazih Asli², Adib Habib³

¹Saint-Vincent De Paul French Hospital, Pediatric Gastrointestinal Unit, Nazareth, Israel
²Saint-Vincent De Paul French Hospital, Pediatric Cardiology, Nazareth, Israel
³Saint-Vincent De Paul French Hospital, Pediatrics, Nazareth, Israel

Objectives and study: We present a girl 17 years old who was admitted to Pediatric Department three days post ingestion of 2 pills of Doxycycline with chest pain, dysphagia, refusal to eat, without vomiting, diarrhea, cough or fever

Methods: The girl suffered from chest pain which was aggravated by deep respiration and movement. She is known as healthy girl but she took 2 tablets of Doxycycline for face acnea 3 days before this admission

Clinical examination was within normal limits except for pain on palpation and compression of chest wall, especially in midsternum

Blood tests for CBC, liver function tests, amylase, creatin kinas (CPK), troponin, chest & ribs x-ray within normal limits.

Cardiac consultation including EKG and heart echocardiography also normal

She was treated first with PPI (Proton pump inhibitor) intravenously without improvement. During 2 days of treatment an aggravation was observed with severe chest pain, difficulty in moving, complete refusal to eat. At this time an upper endoscopy was performed which showed large erosion and circular ulcer on the mid esophagus

Results: Complete fast of eating and high dose PPI intravenously were recommended with progressive improvement through next days with discharge from the department 3 days later.

Repeat endoscopy one month later with complete healing of the esophageal lesion

Conclusion: The drug-induced esophagitis is not rare and should be suspected in all patients presenting with chest pain and dysphagia. Physicians must warn the patients to take the pills and capsules with enough liquid and in the upright position.
**Gastroenterology: Endoscopy**

G-P-100

**Crohn's disease duodenal stricture: mitomycin C and endoscopic balloon dilatation**

Shishu Sharma¹, Mike Thomson², Arun Urs³

¹Sheffield Children's NHS Foundation Trust, Gastroenterology, Sheffield, United Kingdom  
²Sheffield Children's NHS Foundation Trust, Paediatric Gastroenterology, Sheffield, United Kingdom  
³Sheffield Children's Hospital NHS Foundation Trust, Sheffield, United Kingdom

**Objectives and study:** Approximately one third of Crohn's disease (CD) cases develop a stricture within 10 years of diagnosis. [1] Endoscopic balloon dilatation (EBD) is being widely used for dilatation of oesophageal and intestinal strictures in IBD. [2] However, there are no case reports or series published about the use of EBD for duodenal stricture in paediatric CD and the evidence is limited to adult literature only. [3-4] A case of 12 year old boy with CD with duodenal stricture managed effectively with EBD is presented here.

**Methods:** A 12 year old boy first presenting at 11 years of age with 7 months history of abdominal pain, vomiting and diarrhoea. The initial endoscopy showed mild thickening of duodenum and terminal ileum (TI) with histological findings of ulceration and acute inflammation with villous architectural distortion in the duodenum and TI. A diagnosis of CD was made and the patient was commenced on appropriate treatment. The MRI was not suggestive of any stricture. Poor compliance was an issue. A reassessment endoscopy after 8 months continued to show thickening in duodenum and ulcers in TI but the histopathology showed acute duodenitis only. Regular Infliximab was commenced but diarrhoea and abdominal pain persisted. Further endoscopy 1 year later revealed a 2mm diameter stricture in the first part of the duodenum. Adalimumab was started, however vomiting quickly ensued. Duodenal EBD was then undertaken to 10mm under radiological control. This resulted in immediate symptom resolution with consequent weight gain. Mitomycin C anti-fibrotic (0.5mg/ml) was applied topically post-dilation via the endoscope. The duodenum was reassessed with repeat endoscopy after 6 weeks and demonstrated a 10-12mm calibre. (Figures)

**Discussion:** Duodenal Crohn’s has been reported to occur in 0.5 to 4% patients with Crohn’s Disease. Duodenal stricture is a rare complication of Crohn’s Disease and can lead to symptoms of gastric outlet obstruction. This is usually managed by surgical procedures such as resection, bypass procedures or stricturoplasty which are associated with significant morbidity. As compared to surgical procedures, Endoscopic Balloon Dilatation of short segment duodenal strictures is associated with less complication.

**Conclusion:** To our knowledge this is the first ever reported case of successful EBD of the duodenum in paediatric Crohn’s disease including the application of topical Mitomycin C and hence avoidance of more invasive options of surgical resection or stricturoplasty.

**References:**


G-P-101

Short Bowel Syndrome: importance of the colon for energy salvage

Sabine Abi Abboud1, Laurence Barbot-Trystram2, Solène Artru3, Lorenzo Norsa3, Cécile Lambe3, Cécile Talbotec3, Bénédicte Pigneur3, Florence Lacaille4, Hélène Lengline3, Elie Abi Nader3, Yves Agrain5, Christophe Chardot5, Frank Ruemmele3, Nathalie Kapel2, Olivier Goulet3

1Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
2Hôpital La Pitié Salpêtrière, Coprologie Fonctionnelle, Paris, France
3Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
4Necker-Enfants Malades, Gastroenterology-Hepatology- Nutrition, Paris, France
5Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Chirurgie Viscérale Pédiatrique, Paris, France

Objectives and study: Intestinal failure (IF) is a state of severe intestinal malabsorption requiring parenteral nutrition (PN) for survival. The leading cause of IF is short bowel syndrome (SBS). This study aims to show whether the presence of the colon makes a difference in children with SBS, and to find correlations between intestinal absorption rate, citrulline level, anatomy of the remnant bowel and parenteral nutrition dependency.

Methods: Twenty-three SBS children were included in this study and divided into two groups according to the presence or absence of the colon. Bowel length, citrulline plasma levels, intestinal absorption rate [by using three days stool balance analysis] and PN dependency index [by using the index Non Protein Energy Intake (NPEI)/Resting Energy Expenditure (REE) by Schofield formula], were assessed. Regression analysis and student t tests comparing variables were performed.

Results: Patients with colon (n=14) had significantly shorter remnant small bowel as compared with those without colon (n=9) (29.25 ± 25.64 vs. 60.88 ± 22.54 cm; P < 0.003) and lower fecal sodium losses (48.5 ± 28.07 vs. 85.88 ± 18.98 mmol/l; P < 0.002). No difference was found between the groups for the percentage energy absorption (63.4 ± 19.0 vs 66.4 ± 15.4% respectively), while citrulline plasma levels showed only a tendency to be higher in SBS without colon (19.1 ± 12.17 vs. 14.4 ± 9.72 µmol/l; P = 0.17). PN dependency was not significantly different between neither groups, nor the total energy intake from oral or enteral nutrition. No correlation was found between the different parameters, although the citrulline level correlates with the small bowel length in the group with colon (r² = 0.57).

Conclusion: By using three days stool balance analysis, this study demonstrates for the first time in SBS children, the role of the colon in energy salvage in addition to water- electrolytes absorption. It emphasizes the importance of early restoration of intestinal continuity and preservation of intestinal microbiota.
**Clinical Heterogeneity of IPEX: a retrospective study of 31 patients**

Rémi Duclaux-Loras, Fabienne Charbit-Henrion, Jan Nowak, Sophie Collardeau-Frachon, Christophe Malcus, Pierre Ray, Benoist De Neve, Frederic Rieux-Laucat, Nadine Cerf-Bensussan, Olivier Goulet, Alain Lachaux, Frank Ruemmele

1. Imagine Institut, Inserm Umr 1163 - Intestinal Immunity, Paris, France
2. Assistance Publique Hôpitaux de Paris, Hôpital Necker-Enfants Malades, Department of Pediatric Gastroenterology, Paris, France
3. Poznan University of Medical Science, Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland
4. Hospices Civils de Lyon, Hôpital Femme Mère Enfant, Department of Pathology, Lyon, France
5. Hospices Civils de Lyon, Hôpital Edouard Herriot, Laboratory of Immunology, Lyon, France
6. Centre Hospitalier-Universitaire de Grenoble, Department of Genetic and Procreation, Grenoble, France
7. Assistance Publique Hôpitaux de Paris, Hôpital Necker-Enfants Malades, Paediatric Haematology, Immunology Unit, Paris, France
8. Imagine Institut, Inserm Umr 1163 - Immunogénétique des Maladies Auto-Immunnes Pédiatriques, Paris, France
9. Imagine Institute, Inserm Umr 1163 - Intestinal Immunity, and Genius Group, Paris, France
10. Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
11. Hôpital Femme Mère Enfant du Chu de Lyon, Pediatric Gastroentgy, Hepatology Nutrition Unit Reference Centre for Wilson Diseaseroloe, Lyon, France
12. Hôpital Necker Enfants Malades, Department of Pediatric Gastroenterology, Université Paris Descartes, Sorbonne Paris Cité, Aphp, Paris, France

**Objectives and study:** Immune dysregulation, polyendocrinopathy, enteropathy, X-linked (IPEX) syndrome is an autoimmune genetic disorder caused by mutations of the forkhead box protein 3 gene (FOXP3), a key regulator of immune tolerance. The aim of this study was to describe the clinical heterogeneity of the disease in a French cohort of 31 patients.

**Methods:** Multicentric retrospective study of patients diagnosed with IPEX syndrome due to FOXP3 mutation from 1980 to 2015.

**Results:** Thirty-one children coming from 27 families were included. Twelve cases are reported for the first time. Even if the median was 1.5 month, age at disease onset was heterogenous [1st-3rd quartile; 0-84 months] and spread out from before birth (two foetal deaths in the 19th and 24th week of gestation) up until after 1 year of age (three patients at 13 month, 60 and 84 months). Symptoms at onset included: diarrhea (n = 19; 60%), diabetes (n = 7; 23%), skin lesions (n = 2; 6%) and nephropathy in one patient (3%). During the course of the disease: 28 patients (93%) presented diarrhoea, also 24 (80%) skin lesions, 13 (43%) diabetes mellitus, 10 (33%) severe food allergy, 9 (30%) a haematological disorder, 8 (27%) a nephropathy and 4 (13%) hepatitis. Autoantibodies to autoimmune enteropathy-related 75kDa antigen (AIE75kDa) were found in 25 patients (90%). Seven out of eleven investigated subjects (64%) had a regulatory T-cell number deficiency. Twenty-three various genomic mutations were identified in the cohort, 5 of which have not yet been described in the literature (c.23+1 G>A, c.23+5G>A, c.152G>A, c.264delC, c.1015C>T). During the follow-up (5 [0.6-22.0] years) 12 patients died (39%) at a median age of 3.5 [0-10.5] years. The 14 patients in whom symptoms at least partially resolved (46%) were under the following treatment: sirolimus (n = 3), no immunosuppression (n = 3), tacrolimus (n = 3), hematopoietic stem cells transplantation (HSCT) (n = 2), triple immunosuppression consistently including mycophenolate mofetil and cyclosporine (n = 1; 8%).

**Vol. 64, Supplement 1, April 2017** 286
Conclusion: We could confirm, in a large cohort, the significant phenotypic heterogeneity among patients carrying FOXP3 mutations. We described patients with different clinical presentations but with common genotype indicating lack of correlation genotype-phenotype and thus implying a possible role of additional factors (epigenetic modifier) in determining disease severity. Rapid diagnosis is necessary since it permits aggressive, combined immunosuppressive therapy and opens the way to early HSCT. For these reasons, access to NGS diagnostics of early-onset ileitis and colitis should be provided in the appropriate clinical settings.
Tufting enteropathy: clinical characteristic and outcome, experience of tertiary care center in Saudi Arabia

Badr Al Saleem¹, Amna Ahmed¹, Ali Asery¹, Abdulrahman Al Hussaini¹, Nurah Al Banyan², Mosa Fagih²

¹King Fahad Medical City, Pediatric Gastroenterology, Hepatology & Nutrition, Riyadh, Saudi Arabia
²King Fahad Medical City, Pharmacy, Riyadh, Saudi Arabia

Objectives and study: Tufting enteropathy (TE), also known as intestinal epithelial cells dysplasia is a rare autosomal disease. It presents with intractable diarrhea in the neonatal period which require parenteral nutrition (PN). The intestinal epithelial cells characterized by dysplasia and tufting without inflammation associated with villous atrophy.

Aim: The aim of this study is to describe the characteristics of clinical and laboratory features and outcome of patients with TE at tertiary care institution in Saudi Arabia (SA)

Methods: This is a retrospective study, reviewing the TE patient’s files who are diagnosed by gene test (EPCAM) or has characteristic histopathology features and family history of TE. At King Fahd Medical City, Riyadh, SA in the period, from May 2004 until May 2016.

Results: Twenty-four patients with TE have been identified. The median age at the onset of the diarrhea 7 days and median age at presentation 3.6 months. Fifteen (63%) were female, all were Saudi, all full term except one, and average birth weight 2.94 kg. All presented with severe failure to thrive, metabolic acidosis and normal serum albumin. Three were refused admission and discharged against medical advises and died. Twenty one have been followed. One went for bowel transplant and died and two refused parenteral nutrition(PN). Eighteen(86%) still survived (90%).The median follow up was 4.5 years(8.0 month-10.5 year).

Conclusion: TE should be considered in the preferable diagnosis of infants presenting with neonatal intractable diarrhea, severe failure to thrive and normal serum albumin. Favorable outcomes is possible with PN. To the best of our knowledge, this is the largest series about TE patients.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-P-104

Differences in gut microbiota profile in patients with chronic cholestasis and healthy infants and their correlation with fat malabsorption and gut integrity

Fatima Safira Alatas¹, Hanifah Oswari¹, Agus Firmansyah¹

¹Gastrohepatology Division, Department of Child Health, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Objectives and study: Bacterial translocation from the gastrointestinal tract is central to current concepts of endogenous sepsis in obstructive cholestasis and cirrhosis. In this study we evaluate gut microbiota profile and their correlation with fat malabsorption and gut integrity.

Methods: We evaluate feces samples from chronic cholestasis and healthy infants to know their fat malabsorption, gut microbiota composition, and gut integrity, then compare between the 2 groups.

Results: Fifty-seven infants (27 cholestasis and 30 healthy) were evaluated. There were significant difference in mean body weight of infants with cholestasis (7932.39; SD: 3416.2 grams) VS healthy infants (11453.3; SD: 4012.3 grams), \( P = 0.001 \); nutritional status, \( P \leq 0.0001 \), and middle chain triglyceride dominant infant formula, \( P \leq 0.0001 \). Feces evaluation showed a significant higher fat composition (+2 and +3), \( P \leq 0.0001 \) and fecal calprotection level in cholestatic (81.32; SD:61.6 microgram/g faeces) VS healthy infants (47.37; SD:47.3 microgram/g faeces), \( P = 0.021 \). In accordance with fecal calprotectin level, there were a significant difference between the 2 groups in composition of *Bifidobacteria sp.* and *E. Coli sp.*, \( P = 0.005 \).

Conclusion: Significant differences were found in body weight, nutritional status, feces fat composition, fecal calprotection level and gut microbiota profile between chronic cholestasis and healthy infants. Further studies needed to evaluate the interaction between gut and liver axis in infants with cholestasis.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-P-105

Nutritional strategies and microbiota as risk factors for necrotizing enterocolitis in very preterm infants

Jean-Christophe Roze1, Pierre-Yves Ancel2, Patricia Lepage3, Laetitia Martin-Marchand2, Ziad Anabhan3, Johanne Delannoy4, Jean-Charles Picaud5, Alexandre Lapillonne6, Julio Aires4, Mélanie Durox2, Dominique Darmaun7, Josef Neu8, Marie-José Butel9

1 Nantes University Hopistal, Neonatology, Nantes, France
2 Epidemiology and Statistics Sorbonne Paris Cité Reserach Center, U1153, Paris, France
3 Inra, Umr 1319, Jouy-En-Josas, France
4 University Paris Descartes, Ea4065, Paris, France
5 Hospices Civils de Lyon, Neonatology, Lyon, France
6 Necker Enfants Malades Hospital, Neonatology, Paris, France
7 Inra, Umr 1280, Nantes, France
8 University of Florida, Neonatal Medicine, Gainesville, United States
9 University Paris Descartes, Paris, France

Objectives and study: The pathophysiology of necrotizing enterocolitis (NEC) remains poorly understood. We aimed at a better understanding of the role of feeding strategies and intestinal microbiota composition in the development of NEC.

Methods: We used data from a prospective, nationwide population-based observational study, EPIPAGE 2. Individual characteristics observed before Day 7 were used to build a propensity score for the risk of NEC after Day 7. We secondly characterized NICU profiles concerning the rate of progression of enteral feeding and breastfeeding policy, defined according the difference between observed and expected percentage rate of breastfed infants at Day28. Thirdly, we analyzed the relationship between these strategies and the onset of NEC after day 7. Finally, an ancillary propensity-matched case control study, EPIFLORE, was performed in 20 of the 64 NICUs, analyzing the intestinal microbiota by classical and pyrosequencing methods.

Results: Among the 3161 preterm infants, 106 developed NEC (Bell’s stage 2 or 3) after Day 7. Low gestational age, APGAR score less than 7 at 5 minutes of life, circulatory failure requiring fluid expansion and analgesia using sevoflurane during the 7 first days were significantly associated with NEC. The issuance of stools at least once a day, after the first stool and during the first 7 days, was associated with a lower risk of NEC thereafter (adjusted odds ratio, aOR=0.5, 95%CI:0.3-0.8), p=0.001). Slower and intermediate rates of progression of enteral feeding strategies were associated with a higher risk of NEC (aOR = 2.5, 95%CI: 1.3-4.9, p=0.009, and aOR=2.2, 95%CI:1.2-3.9, p=0.01, respectively). Microbiota analyses were performed in 16 cases and 78 propensity matched controls. By culture, at a species level, a specific Clostridium species, i.e. neonatale, and Staphylococcus aureus were significantly associated with NEC.

Conclusion: During the first 7 days, circulatory failure requiring fluid expansion and slow rate of progression of enteral feeding were associated with an increased risk to develop NEC after day 7. At a given level of risk, colonization by Clostridium neonatale and/or Staphylococcus aureus is significantly associated with NEC.
Protein-losing enteropathy after Fontan operation: enteric capsule findings and management with atrial pacing

Kyriaki Papadopoulou-Legbelou1, Maria Kavga1, Irene Katsanika2, Evagelia Karaiskou1, Konstantinos Thomaidis3, Maria Fotoulaki4

14th Department of Paediatrics, Aristotle University, Papageorgiou Hospital, Thessaloniki, Greece
2Dietetics Department, Papageorgiou Hospital, Thessaloniki, Greece
3Papanikolaou General Hospital, Thessaloniki, Greece
4Aristotle University of Thessaloniki, 4th Department of Paediatrics, Papageorgiou Hospital, Thessaloniki, Greece

Objectives and study: Protein losing enteropathy (PLE) is characterized by abnormal enteric loss of plasma proteins. Various risk factors have been hypothesised for the development of PLE, including the presence of chronically elevated right atrial pressure and low cardiac output.

Methods and results: We report a case of PLE in a girl with congenital heart disease and Fontan operation, whose clinical manifestations were improved after the implantation of a pacemaker. At the age of 11 she presented peripheral oedema. Blood tests revealed hypoalbuminemia (serum albumin 2.5 g/dl, normal range 3.8-5.4 g/dl), lymphopenia and hypogammaglobulinemia. The extensive investigation showed normal renal and liver function, but α1-antitrypsin excretion in stool was indicative for PLE (448mg/dl, normal values <54 mg/dl). Findings from a video capsule endoscopy were compatible with PLE showing a “starry-sky” reflexion pattern of the small intestine. A high protein and low fat supplemented with medium-chain triglyceride diet was initiated and transient clinical improvement occurred, but her albumin levels continued to be low (2.9 g/dl) for the next 2 years. Because of heart rhythm disorders (sinus node dysfunction) at the age of 13, a permanent epicardial pacemaker was implanted. After this, the α1-antitrypsin excretion in stool was decreased, with a significant increase in serum albumin concentration (3.9g/dl).

Conclusion: An enteric video capsule study is useful to demonstrate the PLE findings. Atrial pacing is a way to increase cardiac output and should be considered as a part of treatment for patients with PLE after Fontan procedure.
Comparison between syndromic and non-syndromic congenital tufting enteropathy: an ultrastructural point of view

Julie Salomon¹, Florence Campeotto¹, Danielle Canioni², Delphine Delacour³, Olivier Goulet¹

¹Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
²Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Anatomopathologie, Paris, France
³Institut Jacques Monod, Cnrs Umr 7592 Laboratoire Cam, Paris, France

Objectives and study: Congenital Tufting Enteropathy (CTE) is a rare and incurable disease responsible for chronic intestinal insufficiency as well as diarrhoea persisting at fasting, characterized by specific histological epithelial tufts. In 80% of the cases of our cohort, digestive symptoms are isolated and attributed in 73% of CTE patients to EPCAM mutations, whereas 20% of CTE patients, which are mutated for Spint2/HAI-2, present a syndromic form of the disease including keratitis, atresia or fistulas, and other sporadic anomalies. We aimed at studying the ultrastructural defects in both CTE clinical forms studying intestinal biopsies of patients mutated either for one or the other gene.

Methods: Using transmission electron microscopy, we finely studied the ultrastructure of duodenal biopsies of patients mutated either for EPCAM (n=3) or SPINT2/HAI-2 (n=3), in comparison with control biopsies (n=3).

Results: We found out that the apical absorptive domain (i.e. the brush border) and the basolateral domain (i.e. cell-cell and cell-basal lamina interfaces) are deeply perturbed in both genetic situations. In addition to common perturbations, we could distinguish specific defects of each CTE clinical form. Moreover, the inactivation of SPINT2/HAI-2 results in an abnormal nuclear shape and excess of centrioles, suggesting of cell division defects.

Conclusion: This study highlights cellular defects that could well explain intestinal insufficiency and chronic diarrhoea presented by both phenotypic forms of CTE. Moreover, the syndromic SPINT2/HAI-2 mutated form harbours additional cues of division defects that would be in coherence with the particular clinical severity of this form compared to the EPCAM-mutated form. Syndromic form of CTE has been questioned as it is said to resemble syndromic form of Congenital Sodium Diarrhoea (CSD) both phenotypically and genetically. As the observation of characteristic CTE lesions, namely “tufts”, requires an expert eye, the diagnosis has indeed wandered between syndromic CTE and syndromic CSD. Showing here common ultrastructural anomalies of syndromic and non-syndromic CTE, our study pleads in favour of attributing the SPINT2/HAI-2-mutated syndromic form to CTE. Nevertheless, to our knowledge, there is no published analysis to date of ultrastructural defects of syndromic CSD (nor non syndromic CSD) that would add to this thought. It thus stresses the need for ultrastructural analyses of rare diseases knowing that genetics cannot on its own clearly classify.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-P-108

Paediatric eosinophilic oesophagitis in Ireland - a 10 year review of incidence, presenting symptoms, phenotype and management at diagnosis

Ashling O'Malley1, Francesca Keane2, Alice Casey1, Karina O'Flynn2, Sheila Sugrue1, Michael McDermott1, Maureen O'Sullivan3, Tara Raftery4, Michael Mahony5, Shoana Quinn6, Annemarie Broderick7, Billy Bourke5, Seamus Hussey8

1Dublin Institute of Technology, Dublin, Ireland
2University College Dublin, Dublin, Ireland
3Our Lady's Children's Hospital Crumlin, Department of Pathology, Dublin, Ireland
4National Centre for Paediatric Gastroenterology, Dublin, Ireland
5The Children's Ark, Paediatric Department, University Hospital Limerick, Limerick, Ireland
6Tallaght Children's Hospital, Dublin, Ireland
7Our Lady's Children's Hospital, Crumlin, Dublin, Ireland
8National Children's Research Centre, National Centre for Paediatric Gastroenterology, Dublin, Ireland

Objectives and study: Eosinophilic oesophagitis (EoE) is a poorly understood, chronic immune-mediated condition caused by eosinophilic infiltration of the oesophagus. Limited international epidemiological data suggest incidence is increasing, however to-date no Irish national paediatric national data are available. The objectives were to establish the national incidence of paediatric EoE in Ireland from January 2006 to December 2015, and to profile symptoms, phenotype, and management at diagnosis.

Methods: Patients diagnosed with EoE were identified using endoscopy and histological records from the three nationally approved centres where paediatric endoscopy takes place – Our Lady’s Children’s Hospital Crumlin, Tallaght Children’s Hospital and Limerick University Hospital. Incidence was calculated using 2011 census data from the Central Statistics Office. A retrospective chart review was performed collecting relevant data. Analysis was performed based on age (<6 years vs. ≥6 years) at diagnosis.

Results: Overall, 358 children were diagnosed with EoE and full chart data was available on 339 patients (95%). An increase in incidence over time was observed from 2006-2015, from 2.0 to 3.3 per 100,000/year. Male: female ratio was 3:1, and 36% were <6 years at diagnosis. Presenting symptoms differed based on age. The most common symptom overall was abdominal pain (46%), occurring significantly more frequently in those ≥6 years (P<0.001); vomiting was significantly more common in those <6 years (P<0.001). Other presenting symptoms were dysphagia (25%), gagging (23%) and reflux (21%). An inflammatory phenotype was predominant (93%). The majority were treated with swallowed fluticasone propionate (78%) at diagnosis. Dietary manipulation and oesophageal dilation were not widely performed.

Conclusion: This is the first national population-based study of paediatric EoE in Ireland, showing increasing incidence and a male preponderance. Over one third were <6 years and there were marked age specific differences in presenting symptoms at diagnosis. Inflammatory phenotype was prevalent and pharmacological treatment was used most frequently. Further research is necessary regarding the outcomes of this national cohort.
Possible cow’s milk proteins allergy in severe necrotizing enterocolitis leading to short bowel syndrome in term neonates

Lorenzo Norsa1, Cecile Lambe1, Cécile Talbotec1, Thao Pham1, Florence Campeotto1, Christophe Dupont2, Olivier Goulet1

1Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
2Necker Children’s Hospital, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France

Objectives and study: Necrotizing enterocolitis (NEC) is a very serious condition that may lead to small bowel syndrome and resulting in dependency to parenteral nutrition (PN). The cause of NEC in term babies is not known but the role of cow’s milk allergy has been suggested. We aimed to analyze possible factors involved in the development of NEC in term babies.

Methods: A retrospective convenience study enrolled all patients with SBS due to NEC and who required long term PN from 2000 in our tertiary referral center. We analyzed their medical history in terms of well recognized NEC risk factors (prematurity, intrauterine growth retardation, ventilation, neonatal intensive care unit stay, cardiac malformations) and of diagnostic elements of cow’s milk allergy.

Results: In a total of 32 patients enrolled, only 3 did not have any of recognized NEC risk factors. 1/ A 5-year old boy had had extensive bowel resection for NEC occurring at 45 days of life while being at home. He had been fed a hydrolyzed formula during the first days of life due to a history of anaphylactic shock due to cow’s milk allergy in his sister and milk protein had been reintroduced shortly before the development of NEC. This patient is still on home PN but tolerated milk protein reintroduction after the first year of life. 2/ A 3-year old boy had had a history of failure to thrive in the first month of life, treated with cow’s milk protein elimination. NEC occurred at 46 days of life, 5 days after milk proteins introduction. An allergologic work-up revealed raised total IgE and positive cow’s milk protein specific IgE. He is currently PN dependent with elimination of cow’s milk protein. 3/ A 2-year old boy had developed NEC with multiple digestive perforations the second day of life after switching from human milk to cow’s milk based formula. Total IgE and cow’s milk proteins specific IgE were found elevated during hospitalization. His treatment currently associates PN and cow’s milk protein’s avoidance.

Conclusion: NEC leading to PN nutrition dependency may occur in term neonates without risk factors. Cow’s milk protein allergy could play a role in the development of NEC in such patients.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-P-110

Implementation of a food allergy clinic in Medellin, Colombia: the first three years of experience

Catalina Ortiz1, Carlos Fernando Chinchilla Mejía1, Edna Trejos Cabrera1, Paula Andrea Roldan Cano1, Juan Camilo Perez Cadavid1, Katerine Henao Roldán1

1Hospital Pablo Tobón Uribe, Medellín, Colombia

Objectives and study: Food allergies and eosinophilic gastrointestinal disorders are considered emerging diseases so that there are no precise data of the incidence of this disease in our country. We describe the implementation of the first food allergy clinic in our country, where in a simultaneously way a paediatric gastroenterologist, clinical allergologist, paediatric nutritionist examine and educate the patients and their families.

Methods: Cross sectional retrospective study of patients below 18 years of age included in the food allergy clinic at the Pablo Tobon Uribe Hospital in Medellin, Colombia from January 2014 to September 2016. Distribution by sex, age, therapeutic group and overall results.

Results: We analyzed the clinical charts of 133 patients. We distributed patients by sex, finding a dominant population by the male sex with 79 patients (59.3%) compared to the female patients 54 (40.7%). The patients were divided into age groups as follows: < 1 year: 56 patients (42.1%), from 1.1 to 5 years: 51 patients (38.3%), from 5.1 to 10 years: 19 patients (14.2%), >10 years: 7 patients (5.2%). The dominant group of age was the one belonging to children under 1 year of age. With regard to the prevalence of food allergies, through report of positive IgE inmunoCAP- Phadia we found: 85 patients (64%) with cow milk protein allergy, 33 with egg allergy (24.8%), 11 with white fish allergy (8.2%), 9 patients allergic to soy, maize and oat (6.75%), 7 with allergy to wheat (5.3%), 6 with allergy to dried fruit (4.5%), 4 with allergy to chicken meat (8.2%) and 2 patients allergic to crustaceans (1.5%). In the group of the eosinophilic gastrointestinal disorders, the population was represented in the following way: 48 patients with allergic proctocolitis (36%), 23 patients with eosinophilic duodenitis (17.2%), 2 in which the initial presentation was a duodenal ulcer, 18 patients with eosinophilic esophagitis (13.5%), 11 patients with eosinophilic gastritis (8.2%), 3 patients with food protein induced enterocolitis (2.25%) and 1 patient with eosinophilic ileitis (0.7%) without significant difference in the distribution by sex. It is important to clarify that several patients had more than one eosinophilic disorder. All the diagnoses were made by the study of biopsies by upper and lower endoscopy except in cases of allergic proctocolitis. In the group of proctocolitis allergic, we have 6 patients who required hospitalization and transfusion with red blood cells. We had 9 cases of urticaria and anaphylaxis as initial manifestation, 3 cases with hypereosinophilic syndrome and 1 case of scalded skin.

Conclusion: Food allergies and eosinophilic gastrointestinal disorders are diseases that are on the rise. We need local statistics of each country to be able to deploy diets directed to the management of these disorders. The creation of the first food allergy clinic in our country contributes to the wellbeing of the patient and his family.
Faecal calprotectin as non-invasive marker for graft versus host disease after paediatric allogeneic haematopoietic stem cell transplantation

Dagmar Berghuis¹, V. Bekker², Jaap A. Bakker³, A Lankester¹, Robbert Bredius¹, Joachim Schweizer¹

¹Willem-Alexander Children’s Hospital/Leiden University Medical Center, Leiden, Netherlands
²Willem-Alexander Children’s Hospital/Leiden University Medical Center, Pediatrics, Leiden, Netherlands
³Leiden University Medical Center, Department of Clinical Chemistry and Laboratory Medicine, Leiden, Netherlands

Objectives and study: Allogeneic haematopoietic stem cell transplantation (HSCT) is a potentially curative treatment option for children with a variety of haematological, oncological and immunological diseases. Graft versus host disease (GVHD) of skin, gut, liver and lungs is a major cause of post-transplantation mortality and morbidity. GVHD is diagnosed by clinical symptoms and histology, necessitating invasive procedures including endoscopy and biopsy. No non-invasive markers are available for diagnosis and/or treatment monitoring in children with GVHD. Faecal calprotectin (FC) reflects intestinal mucosal inflammation of any origin. In allogeneic HSCT in adults, FC has shown to be a marker for acute (steroid-resistant) GVHD in symptomatic patients. No firm data exist for paediatric patients. We aimed to evaluate the feasibility of prospective FC measurement as a non-invasive marker for diagnosis and treatment in children with GVHD.

Methods: A prospective, observational, single centre study was started in July 2015. The study was approved by the local medical ethics committee. Faecal samples were collected weekly from two weeks before until four weeks after HSCT and monthly thereafter up to six months after HSCT. FC levels were measured by a fluorescent immune assay, according to manufacturer’s instructions. Clinical symptoms were prospectively evaluated and managed according to local guidelines. If GVHD was suspected on clinical grounds, histological confirmation was obtained. First line therapy for GVHD consisted of corticosteroids. In case of steroid-resistant disease, more advanced immune modulation was applied.

Results: By December 2016, 21 paediatric allogeneic HSCT patients (age 0-17 years) were included. Five patients developed histologically confirmed GVHD: acute GVHD of skin and gut (n=2, one patient with steroid-resistant disease), acute GVHD of skin only (n=1); chronic GVHD of lung only (n=1) and acute GVHD of skin followed by chronic oromucosal GVHD (n=1). Without exception and regardless of gut involvement, GVHD occurrence was accompanied by rises in FC levels to values >100 ug/g (range 108-1600 ug/g). FC levels correlated with clinical and histological grading. Moreover, adequate response to therapy was consistently reflected by return of FC levels to values <100 ug/g. FC levels could not be used to predict or diagnose GVHD due to increased FC levels in 11/16 patients with post-transplant complications other than GVHD such as viral reactivation and pulmonary or gastro-intestinal infections.

Conclusion: FC levels do not accurately predict GVHD but reflect GVHD occurrence and correlate with clinical and histological grading in paediatric allogeneic HSCT patients. FC levels increase in case of GVHD regardless of gut involvement, supporting a central role for (subclinical) intestinal inflammation in GVHD initiation. Although, in this interim analysis, FC lacks sensitivity to diagnose GVHD, FC may serve as a non-invasive marker for monitoring therapy response and, thereby, reduce the need for repeated invasive procedures including endoscopy and biopsy.
Seven-year clinical experience of congenital diarrhoeal disorders: difficulty and importance of genetic diagnosis


Konya Research and Training Hospital, Department of Pediatric Gastroenterology, Konya, Turkey
Akdeniz University Medical School, Department of Pediatric Gastroenterology, Antalya, Turkey
Ataturk University Medical School, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
Necmettin Erbakan University School of Medicine, Department of Pediatric Allergy and Immunology, Konya, Turkey
Ankara University School of Medicine, Paediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
Konya Research and Training Hospital, Department of Pediatrics, Konya, Turkey
Hôpital de la Timone Enfant, Service de Pédiatrie Multidisciplinaire, and Genius Group, Marseille Cedex 05, France
Université Aix-Marseille, Ap-Hm, Marseille, France
Université Libre de Bruxelles, Brussels, Belgium
Section of Child’s Health, University of Florence, Department of ‘neurofarba’, Florence, Italy
Institute of Biomedical and Clinical, Exeter, United Kingdom
Kremlin-Bicêtre University Hospital, Paris, France
Medical University of Innsbruck, Innsbruck, Austria
Synlab, Medical Genetics, Lausanne, Switzerland
Uniklinikum Freiburg, Freiburg, Germany
Medical University of Vienna, Department of Pediatrics and Adolescent Medicine, Vienna, Austria
Akdeniz University, Faculty of Medicine, Department of Pediatric Gastroenterology, Antalya, Turkey

Objectives and study: Congenital diarrhoeal disorders (CDD) are a heterogeneous group of severe enteropathies comprising over 50 rare monogenic diseases that share early-onset intractable diarrhoea as a main characteristic. A precise diagnosis depends on genetic analysis. Only limited data appear in the literature; therefore, we present our experience with patients with CDD.

Methods: We retrospectively analysed data from two centres for patients whose clinical, laboratory or histological features matched those of one of the four groups of CDD, according to the mechanism involved in the pathogenesis. Clinical and genetic diagnoses, as well as outcomes, were noted.

Results: We defined 34 patients as having CDD. The mean onset of diarrhoea was 5.8 ±10.8 months. For 4 (11.7%) patients, diarrhoea started after 1 year of age. The mean diagnostic delay, namely the description of diarrhoea as ‘congenital’, was 10.8 ±17.5 months. Most initial diagnoses were acute viral gastroenteritis (n=8), food allergy/food protein-induced enterocolitis syndrome (n=8), coeliac disease (n=3), Bartter syndrome (n=1) and Langerhans cell histiocytosis (n=1). The requirement for at least one hospitalisation and for parenteral nutrition were 97% (33/34) and 73.5% (25/34), respectively, prior to CDD diagnosis.

While 23 different genes in 21 patients were sequenced, diagnosis by sequencing of a single gene was possible only in seven (20.5%) patients (abetalipoproteinaemia, chylomicron retention disease, congenital chloride diarrhoea, enteric anendocrinosis, IL-10 deficiency, IPEX syndrome, and trichohepatoenteric syndrome). Whole exome sequencing in two patients provided one further diagnosis (LRBA deficiency) and targeted gene panel sequencing for three patients revealed one LRBA deficiency and one DGAT-1 deficiency. The mean diagnostic delay for specific diagnosis of these 10 patients was 37.2 ±47.3 months. Twelve (35.3%) patients died due to complications caused by diarrhoea. The rate was lower for genetically confirmed cases (2/10 vs. 10/24); however, the
difference was not statistically significant. A comparison of the demographic and clinical features of patients according to their specific genetic diagnosis is presented in Table 1.

**Conclusion:** Although patients with CDD have a fairly high morbidity and mortality rate, genetic diagnosis can be confirmed for a restricted number of patients via single-gene sequencing when specific clinical, laboratory or histopathological features are present. However, due to the rarity and clinical heterogeneity of these diseases, we recommend the use of more powerful genetic approaches, including targeted gene panels, to accelerate diagnosis, facilitate management and improve patient outcome. Whole exome sequencing could be preferable in some cases.

**Table:** The comparison of demographic and clinical features for genetically diagnosed and undiagnosed cases

<table>
<thead>
<tr>
<th></th>
<th>Genetically diagnosed (n:10)</th>
<th>Genetically undiagnosed (n:24)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (f)</td>
<td>6/10</td>
<td>13/24</td>
<td>0.529</td>
</tr>
<tr>
<td>Presence of consanguinity</td>
<td>8/10</td>
<td>17/24</td>
<td>0.462</td>
</tr>
<tr>
<td>Mean onset of diarrhoea (months)</td>
<td>6.8 ±14.6</td>
<td>5.4 ±9.1</td>
<td>0.741</td>
</tr>
<tr>
<td>Mean first admission time (months)</td>
<td>8.0 ±14.9</td>
<td>7.8 ±11.8</td>
<td>0.973</td>
</tr>
<tr>
<td>Mean diagnostic delay for CDD (months)</td>
<td>19.6 ±24.1</td>
<td>7.2 ±12.9</td>
<td>0.059</td>
</tr>
<tr>
<td>Mean hospitalisation / parenteral nutrition requirements (n)</td>
<td>10/10</td>
<td>23/24</td>
<td>0.706</td>
</tr>
<tr>
<td></td>
<td>7/10</td>
<td>18/24</td>
<td>0.538</td>
</tr>
<tr>
<td>Mean diagnostic delay for specific genetic diagnosis (months)</td>
<td>37.2 ±47.3</td>
<td>-</td>
<td>N.D.</td>
</tr>
<tr>
<td>Outcome (death)</td>
<td>2/10</td>
<td>10/24</td>
<td>0.211</td>
</tr>
</tbody>
</table>
LRBA deficiency as a cause of severe autoimmune myositis, myocarditis and early intestinal failure with the need of long-term parenteral nutrition

Filip Fencl1, Barbora Vlková1, Jana Tejnická1, Jana Kayserová2, Josef Zamecnik3, Markéta Vlčková4

1Department of Paediatrics, 2nd Faculty of Medicine, Charles University in Prague and University Hospital Motol, Prague, Czech Republic
2Department of Immunology, 2nd Faculty of Medicine, Charles University in Prague and University Hospital Motol, Prague, Czech Republic
3Department of Pathology and Molecular Medicine, 2nd Faculty of Medicine, Charles University in Prague and University Hospital Motol, Prague, Czech Republic
4Department of Biology and Medical Genetics, 2nd Faculty of Medicine, Charles University in Prague and University Hospital Motol, Prague, Czech Republic

Objectives and study: LRBA (Lipopolysaccharide-Responsive and Beige-like Anchor) deficiency is a condition based on biallelic loss of function mutation in the gene LRBA (4q31.3). The spectrum of clinical manifestations is broad, comprising of recurrent respiratory, gastrointestinal (GIT), skin infections and autoimmune disorders (idiopathic thrombocytopenic purpura, autoimmune hemolytic anemia or autoimmune enteropathy). Intestinal symptoms may vary from chronic diarrhea to severe malabsorption leading up to intestinal failure (IF) with need of parenteral nutrition (PN).

Patients, Methods, Results: We present two sisters with LRBA deficiency.

Patient 1. At six months of age she presented with repeated respiratory infections and prolonged secretory diarrhoea with the necessity of partial/total PN. Common causes of malabsorption were ruled out. GIT infections were diagnosed repeatedly. Laboratory examinations showed hypogammaglobulinemia (IgG 1.77, IgA 0.07, IgM 0.45 g/l, IgE <30 IU/ml), positive ASCA, slightly lowered B cell counts (5-7%). Being seven years old, she presented with autoimmune thyroiditis and started to show signs of progressive myopathy. Muscle biopsy revealed an autoimmune inflammatory myopathy. Corticosteroid treatment was initiated, but the muscle injury progressed further, and resulted in diaphragmatic paralysis with respiratory insufficiency and heart failure, causing her death at eight years of age. Autopsy revealed not only severe inflammatory myopathy, but also lymphocytic myocarditis.

Patient 2. At six months of age she began failing to thrive and a month later presented with prolonged vomiting and diarrhoea. Edemas evolved due to severe hypoproteinemia. Immunologic findings showed severe hypogammaglobulinemia (IgG 0.48, IgM 0.31, IgA <0.27 g/l). Intestinal biopsy proved duodenal villous atrophy combined with thinned mucosa, lymphoplasmacytic and eosinophilic infiltration of lamina propria and decrease in digestive enzymes. Corticosteroid therapy had no effect. PN led to gradual improvement of nutritional status. She had repeated respiratory, GIT and urinary tract infections, repeated catheter sepses and exit site abscesses.

Whole exome sequencing and Sanger sequencing a homozygous truncating LRBA mutation in both sisters. Both parents were healthy heterozygous carriers of the mutation. Consequently, Abatacept treatment was initiated, the patient is in partial remission, tolerates oral intake in combination with partial PN and thrives.

Conclusion: LRBA deficiency represents an extremely rare cause of IF in children. We demonstrate two sisters with genetically proven LRBA deficiency which caused IF in infancy and was associated with the need for long-term PN. All patients with diarrhoea and IF of unknown etiology should undergo LRBA gene testing. One of our patients suffered from severe autoimmune myositis and myocarditis, which led to her death. These findings have not yet been described in a LRBA deficient patient.
Maternal depression from infancy to toddlerhood. Does it affect feeding, sleeping and defecation problems in toddlers?

Gizem Ondalikoglu¹, Gokhan Baysoy²

¹Istanbul Medipol University School of Medicine, Pediatrics, Istanbul, Turkey
²Istanbul Medipol University School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: Postpartum depression (PPD) might affect the growth and development of children. Postpartum depression is common in mothers of sick children even though the disease is physiologic such as reflux, colic or infant constipation. Long term effects of PPD on growth and development of toddlers, children and adolescents were demonstrated. In this ongoing study, we tried to evaluate the impact of continuation of maternal depression into toddlerhood on the sleep, feeding, and constipation problems in toddlers.

Methods: Children above 2 years of age whose mothers were routinely screened for PPD by validated Turkish version of Edinburgh PPD scale in their first visit to pediatric gastroenterology clinic (when infant was <1 year of age) between October 2014 to January 2015 were called back for another evaluation. Mothers were requested to fill Beck depression scale, Behavioral Pediatric Feeding Assessment scale, The Child Vulnerability Scale, a validated Turkish version of Rome III criteria for constipation, Brief Screening Questionnaire for Infant Sleep Problems, and demographic data.

Results: Of the 140 eligible mothers, 125 could be contacted. Up to now, 42 of them were responded and filled the questionnaires. Of the 42 mothers 30.9% had PPD at the first visit and 19.0% had depression at the second time point. Postpartum depression significantly increased the risk of maternal depression during toddlerhood. Most of the infants had organic disease in the first evaluation (73.8% vs 26.2%). Prevalence of feeding, sleeping problems and constipation were 53.4%, 47.6%, and 23.8% respectively in the second evaluation. Gender, number of siblings, nature of first admission (physiological vs. organic), monthly income, smoking, antenatal depression history, prematurity, admission to neonatal intensive care unit (NICU) were not found to be related to feeding, sleeping and defecation problems. Feeding problem was more common in toddlers with hospitalization history (other than NICU) (p=0.02). Feeding problems and constipation were not related to vulnerability, and Beck depression score. Sleeping problem was not related to vulnerability but it was related to Beck depression score (p=0.02).

Conclusion: Postpartum depression is a significant risk factor for the persistence of maternal depression in toddlerhood. Appropriate screening, support and treatment must be provided to mother. Not only organic but also physiological problems in infancy are related to feeding, sleeping, and defecation problems in toddlerhood regardless of mothers depression status.
Amino acid formula as a new strategy for diagnosing cow’s milk allergy: how far is this strategy dominant?

Vanessa Cristina Castro Rodrigues¹, Ary Lopes Cardoso², José Vicente Spolidoro³, Ana Paula Moschione Castro⁴, Mario Vieira⁴, Otavio Clark⁵, Mauro Morais⁶

¹Postgraduate Program of Nutrition, Escola Paulista de Medicina, Universidade Federal de São Paulo, São Paulo, Brazil
²Instituto Da Criança, Hospital Das Clínicas, Universidade de São Paulo, São Paulo, Brazil
³Escola de Medicina - Pontifícia Universidade Católica Do Rio Grande Do Sul (Pucrs), Hospital Moinhos de Vento, Porto Alegre, Brazil
⁴Escola de Medicina - Pontifícia Universidade Católica Do Paraná (Pucpr), Hospital Pequeno Príncipe, Curitiba, Brazil
⁵Evidências/Kantar Health Company, Campinas, Brazil
⁶Escola Paulista de Medicina, Sao Paulo, Brazil

Objectives and study: To evaluate the influence between amino acid formula (AAF) and extensively hydrolyzed formula (EHF) price ratios in the total cost for the diagnosis and treatment of cow’s milk allergy (CMA).

Methods: In pharmacoeconomics the term dominant is defined as the most effective and lower cost alternative. A pharmacoeconomic model recently published (J Med Econ 2016;19:1027-14) showed that the use of AAF as a diagnostic elimination diet in infants with suspected CMA is a dominant strategy when compared with EHF and soy-based formula (SF). Both strategies differ only regarding diagnostic elimination diet, and once CMA is confirmed patients would receive EHF or SF as a treatment elimination diet with AAF being reserved for those not responding to other formulas. The model considered duration of symptoms and direct costs (i.e. formulas, medical consultations, oral food challenge test, drugs and laboratory tests) of both strategies until patients develop spontaneous tolerance to cow’s milk or reach 36 months of age. Although the price per can of AAF was almost twice that of EHF, the strategy using AAF was considered dominant (lower cost and higher effectiveness). In this study, formulas represented around 95% of total costs.

Based on this pharmacoeconomic model a cost simulator was developed (Evidências®, Kantar Health Company) in order to calculate total cost of both strategies according to resources and procedures costs (formulas, drugs, medical consultations, laboratory tests and oral food challenge).

In the present study the impact of AAF price variation was evaluated in the total cost of treatment maintaining the prices per can of SF (R$18,50) and EHF (R$85,18). The other costs were not considered.

Results: The table shows the results according to AAF price variation. The strategy that uses AAF as diagnostic elimination diet remains dominant until the price per can of AAF reaches three times (R$256,40) that of EHF.
Table:

<table>
<thead>
<tr>
<th>SF</th>
<th>EHF</th>
<th>AAF</th>
<th>Price ratio</th>
<th>Average cost per patient with suspected CMA (R$)</th>
<th>Difference (R$)</th>
<th>Lower cost</th>
</tr>
</thead>
<tbody>
<tr>
<td>18.50</td>
<td>85.18</td>
<td>127.77</td>
<td>1:1.5</td>
<td>2.998,97</td>
<td>2.629,93</td>
<td>-369,04</td>
</tr>
<tr>
<td>18.50</td>
<td>85.18</td>
<td>170.36</td>
<td>1:2.0</td>
<td>3.209,40</td>
<td>2.962.01</td>
<td>-247,39</td>
</tr>
<tr>
<td>18.50</td>
<td>85.18</td>
<td>212.95</td>
<td>1:2.5</td>
<td>3.419,83</td>
<td>3.294.10</td>
<td>-125,73</td>
</tr>
<tr>
<td>18.50</td>
<td>85.18</td>
<td>256.40</td>
<td>1:3.01</td>
<td>3.634,51</td>
<td>3.632,89</td>
<td>-1.62</td>
</tr>
<tr>
<td>18.50</td>
<td>85.18</td>
<td>257.25</td>
<td>1:3.02</td>
<td>3.638,71</td>
<td>3.639,52</td>
<td>+0.81</td>
</tr>
<tr>
<td>18.50</td>
<td>85.18</td>
<td>340.73</td>
<td>1:4.0</td>
<td>4.051,17</td>
<td>4.290,43</td>
<td>+239.26</td>
</tr>
</tbody>
</table>

SF, soy-based formula; EHF, extensively hydrolyzed formula; AAF, amino acid formula; CMA, cow’s milk allergy. *Followed by oral food challenge and treatment with EHF or SF according to Brazilian Food Allergy Guidelines.

**Conclusion:** The strategy that uses AAF in the diagnostic elimination diet followed by an oral food challenge is a dominant pharmacoeconomic approach since the price of AAF does not exceed three times the price of EHF. Above this price, this strategy becomes more expensive although it continues to provide less duration of symptoms (higher effectiveness).

**Disclosure of interest:** VCCR was employee of Support Advanced Medical Nutrition until September 2015. ALC, JVS, APMC, MV and MM are consultants and speakers for Support Advanced Medical Nutrition. OC is employee of Evidências, which is a company specialized in Pharmacoeconomics that was contracted by Support Advanced Medical Nutrition to develop the cost simulator.
Comparisons of microbiota in small bowel and stool between irritable bowel syndrome patients and healthy subjects

Pi-Feng Chang¹, Yu-Cheng Lin¹, Kevin Liu¹

¹Far Eastern Memorial Hospital, Pediatrics, New Taipei, Taiwan

Objectives and study: Several studies suggested that colonic microbiota have impacts on irritable bowel syndrome (IBS) patients. However, the knowledge about the association of small intestine (SI) microbiota with IBS is limited. We aimed to investigate the gut microbiota composition of SI and stool in IBS patients.

Methods: Biopsies of jejunum mucosa by enteroscopy and faecal samples from 28 IBS patients and 19 healthy controls were analysed by next-generation sequencing method. Student’s t-test and χ²-test were used for the comparisons of continuous and categorical variables between groups, respectively.

Results: The three major phyla in SI microbiota of case/control groups were Proteobacteria (32.8%/47.7%), Bacteroidetes (25.2%/15.3%), and Firmicutes (19.8%/11.2%), and those of stool were Bacteroidetes (41.3%/45.8%), Firmicutes (40.7%/38.2%), and Proteobacteria (15.4%/7.1%). Analysis based on the family level, IBS patients had a higher proportion of Veillonellaceae (mean proportion 6.49% versus 2.68%, p=0.046) in stool than controls. Prevotellaceae was more abundant in IBS patients than in control group (14.27% versus 6.13%, p=0.023), while Mycobacteriaceae (0.06% versus 0.17%, p=0.024) and Neisseriaceae (6.40% versus 8.94%, p=0.038) was less abundant in IBS patients’ jejunal mucosa than those in controls. This less abundant jejunal Neisseriaceae was associated with more severe IBS (p=0.03). The ratio of Firmicutes to Bacteroidetes in the stool of IBS-diarrhea type patients was approximately three-fold higher, and the ratio of Firmicutes to Actinobacter in SI of IBS-mixed type patients was about nine-fold higher than healthy subjects.

Conclusion: Higher abundance of colonic Veillonellaceae and SI Prevotellaceae, and lower amount of oral cavity normal flora in proximal SI were found in IBS patients. We may manipulate these bacteria in IBS patients in future studies.
A single centre experience in managing small bowel bacterial overgrowth in patients with intestinal failure

Jeng Haw Cheng¹, Sue Protheroe¹

¹Birmingham Children’s Hospital, Paediatric Gastroenterology, Birmingham, United Kingdom

Objectives and study: Small bowel bacterial overgrowth (SBBO) and colonic fermentation (CF) are processes that may cause malabsorption and prevent weaning from PN in patients with short bowel syndrome. It presents with non-specific gastrointestinal symptoms. A number of antimicrobial treatments are often given simultaneously. Our approach is to introduce a single antibiotic and monitor clinical response and D-lactic acidosis as a marker of SBBO. A second agent may be cycled according to clinical response. To describe the clinical efficacy of single antibiotic regimens in patients with SBBO/CF in improving symptoms and reducing raised d-lactate.

Methods: Subjects who were treated with oral antibiotics for SBBO/CF were selected from the cohort of patients on home parenteral nutrition (PN) at Birmingham Children’s Hospital. Post prandial D-lactate results were collected from the chemistry system and clinical details were collected from medical records.

Results: 8 out of 40 home PN patients were prescribed antibiotic for clinical suspicion of SBBO/CF. 7 had short bowel syndrome (SBS) secondary to multiple small bowel atresias, gastroschisis, malrotation and volvulus; the majority (6) had no ileocaecal valve. The bowel length ranged from 8cm to 70cm with median of 30cm. One patient had chronic pseudo-obstruction. Criteria for starting a trial of antibiotics were based on symptoms in combination usually with raised DL.

Treatment was initiated based on symptoms in 2 out of 8 who did not have raised DL and 1 improved symptoms. 1 patient with raised DL did not respond to treatment (DL level or symptoms). 5 (63%) of those with raised DL and symptoms improved within 5 months of treatment.

Gentamicin cycled with Rifaximin was the commonest combination (60%) and it reduced DL effectively within 5 months; 20% were on gentamicin only and 20 % on rifaximin cycled with metronidazole.

Table: Symptoms for patients with SBBO before and after antimicrobial treatment.

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>No of Patients (n= 8)</th>
<th>Improved Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting</td>
<td>1</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>3</td>
<td>2 (67%)</td>
</tr>
<tr>
<td>Gaseous Distension</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>3</td>
<td>3 (100%)</td>
</tr>
<tr>
<td>Belching</td>
<td>1</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Flatus</td>
<td>1</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Drowsiness</td>
<td>1</td>
<td>1 (100%)</td>
</tr>
<tr>
<td>Feed Intolerance</td>
<td>2</td>
<td>1 (50%)</td>
</tr>
</tbody>
</table>
Conclusion: We have identified that absence of ICV is a risk factor for developing SBBO/CF in patients with SBS on HPN. Symptoms may improve by reducing carbohydrate load in diet. This approach isn’t always successful and oral antibiotics may be beneficial. We have shown that treatment with single oral antibiotic in a rotating cycle was successful in the majority and monitoring of symptoms and D-lactate has been clinically useful.
Intestinal microbiota and associated inflammation in children with non-IgE mediated cow’s milk protein allergy

Maria Diaz¹, Irene Espinosa², Santiago Jimenez³, Cristina Molinos⁴, David Perez⁵, Juan Miguel Rodriguez², Carlos Bousoño³, Miguel Gueimonde¹, Abelardo Margolles¹, Juan Miguel Rodriguez², Carlos Bousoño³, Miguel Gueimonde¹, Abelardo Margolles¹, Susana Delgado¹

¹Instituto de Productos Lácteos de Asturias (Ipla-CSIC), Department of Microbiology and Biochemistry, Villaviciosa, Spain
²Probisearch S.L, Madrid, Spain
³Hospital Universitario Central de Asturias, Pediatric Gastroenterology and Nutrition, Oviedo, Spain
⁴Hospital de Cabueñes, Pediatrics, Gijon, Spain
⁵Hospital San Agustin, Pediatrics, Aviles, Spain

Objectives and study: Cow’s milk protein allergy (CMPA) is the most common food allergy in infancy. The clinical symptomatology in non-IgE forms is mainly gastrointestinal and diagnosis is based on medical history and a clear positive challenge test. Currently, the only therapeutic option is an elimination diet avoiding milk consumption. A vast majority of infants develop tolerance before the age of three. Standardized oral milk challenges are the only way to evaluate tolerance development in these infants. Although the precise mechanisms leading to no IgE mediated CMPA are unknown, there are data indicating the importance of gut microbiota in both processes, allergy and tolerance. The objective of this study was to analyze the changes in intestinal microbiota and associated inflammatory and immunological parameters in faeces of children with non-IgE mediated CMPA after controlled oral milk challenge tests performed under medical supervision.

Methods: A group of children between 1 and 2 years old, diagnosed with non-IgE CMPA (negative specific IgE determinations and a positive oral challenge) were recruited at different hospitals in Asturias (Spain). Three stool samples were collected for each infant: before the oral challenge test, a week after and a month after. Tolerance acquisition was recorded by the clinicians that documented any signs and symptoms. The intestinal microbiota was determined through high-throughput DNA sequencing of 16S rRNA gene amplicons (Illumina technology), meanwhile microbiota bound to IgA and IgG was analyzed by flow cytometry with specific anti-human immunoglobulins labelled with fluorescein isothiocyanate (FITC). Faecal calprotectin was quantified by a commercial ELISA kit (CALPROLAB™) and different cytokines related with the Th1/Th2 balance by the use of immunoBilex kits (Bio-Rad).

Results: After oral challenge tests the majority of children acquired tolerance and only in one case gastrointestinal symptomatology persisted. Clear differences in the composition of intestinal microbiota were observed for this particular infant with respect to the others, with a marked presence of sequences belonging to the phyla Verrucomicrobia and Proteobacteria. Principal Coordinate Analysis (PCoA) and hierarchical clustering also showed these samples to cluster at an appreciable distance apart from the rest and, additionally, presented a reduced diversity. In relation with the inflammatory and immunological markers, one week after the oral challenge an increase in the concentration of faecal calprotectin was observed, with a decline to basal levels after one month. Moreover, the percentages of intestinal microbiota opsonized by IgG and IgA were enhanced with the introduction of milk. Regarding the cytokine pattern present in faecal samples, despite a great inter-individual variability, a predominant inflammatory response Th1 type was observed.

Conclusion: The findings point to an intestinal inflammatory response of different degree in the intestine of children subjected to oral milk challenges, independently of the tolerance acquisition and gastrointestinal manifestations. A clear microbial dysbiosis was observed in the infant in who the non-IgE-mediated CMA persisted. The colonization by the intestinal microbiota in early life may be playing an essential role in immune non-IgE mediated CMA, at least with respect to response to oral milk challenges and tolerance acquisition.
**GASTROENTEROLOGY: Gastroenterology other**

G-P-119

**The effect of weight loss on dehydration after sports in obese children**

Judith Baert¹, Stephanie Van Biervliet², Johan Vande Walle³, Ann De Guchtenaere⁴

¹Ghent University Hospital, Paediatrics, Ghent, Belgium
²Ghent University Hospital, Paediatric Gastroenterology and Hepatology, Ghent, Belgium
³Ghent University Hospital, Paediatric Nephrology, Ghent, Belgium
⁴Zeepreventorium, Paediatric Nephrology, De Haan, Belgium

**Objectives and study:** Obese adults have a higher dehydration risk after sports than healthy adults. The latter could not yet be confirmed in obese children. The effect of a standardized slimming program on sport-induced dehydration and the renin-aldosterone system (RAA-system) activity in obese children was evaluated in this study.

**Methods:** Sixty-six obese children (BMI z-score 2.52 ± 0.32, aged 15 ± 1 years, blood pressure 135 / 79 (± 16 / ± 9) mmHg) following a 1 year residential slimming program were included. Twenty-eight stopped the program prematurely. At the start and the end of the program urine samples for sodium, chloride, potassium, urea, creatinine, protein and osmolality, weight, blood pressure and pulse were collected before and after a cooper-test.

**Results:** After 1 year, all clinical parameters in rest decreased significantly (BMI z-score 1.52 ± 0.43; blood pressure 121 / 71 (± 13 / ± 10) mmHg). In rest the percentage of urinary potassium over the sum of urinary sodium (Uₖ/(Uₙa+Uₖ) (%)) increased significantly from 40 % ± 11 to 50 % ± 11 at the end of the program.

After the cooper-test only non-obese patients displayed a significant Uₖ/(Uₙa+Uₖ) (%) increase (49 ± 11; 56 ± 12 respectively) (p < 0.01) as well as an increase in Uₙa over urinary creatinine (0.12 ± 0.07; 0.1 ± 0.05 respectively) (p< 0.05).

**Conclusion:** There was a significant weight loss after sports at the 2 test periods, associated with significant dehydration. Normalizing the BMI after the program resulted in a significant higher aldosterone-effect (Uₖ/(Uₙa+Uₖ)), which confirms the re-appearance of a normal functioning RAA-system.
Objectives and study: This study is aimed at assessing condition of intestinal microflora in children with chronic gastritis in different phases of the disease and after a course of probiotic treatment using gas chromatography - mass spectrometry (GC-MS).

Methods: This longitudinal study was conducted among 90 children aged 11-15 years with Helicobacter pylori positive morphologically proven chronic gastritis (CG). 22 healthy children matched by age and gender with the children of the main group were taken as comparison group. Children with CG have been investigated repeatedly in the period of exacerbation, 6 months after the successful eradication of Helicobacter pylori infection. To assess the state of intestinal microbiota we use GC-MS – detecting species-specific fatty acids as genetically determined structural components of the cell wall.

Results: In children with chronic gastritis both in acute and remission phases in 100% of cases were revealed changes in composition of the intestinal microflora affecting not only intraluminal but parietal microflora. In phase of exacerbation, microbiota disorders were expressed by decreased number of obligate bacteria (bifidobacteria, lactobacilli). In phase of remission the revealed changes saved and characterized by decreased number not only bifidobacteria, lactobacilli but propionobacterium and increased number of such opportunistic bacteria as clostridia (Clostridium histolyticum, Clostridium propionicum, and Clostridium ramosum), streptococci, Candida fungi. Excessive proliferation of Candida albicans were found in 16.5% (95% CI 12 – 21.2) children in exacerbation phase and in 30% (95% CI 22.2 – 38.8) in phase of remission (p=0.0412). Intensity of violations of parietal microflora were significantly associated (p<0.05) with morphological changes of gastric mucous.

Conclusion: Chronic gastritis in children is commonly associated with negative changes in parietal microflora in acute phase and in 6 months. Using of gas chromatography - mass spectrometry for studying and evaluating the intestinal microflora in children with chronic gastritis can significantly extend the range of the defined microbiota and its possible changes in different phases in diseases.
Autoinflammatory diseases in differential diagnosis of recurrent abdominal pain in the praxis of paediatric gastroenterologist in Central Europe

Zuzana Havlicekova¹, Zuzana Michnova¹, Katarina Hrubiskova², Peter Banovcin¹, Milos Jesenak¹

¹Martin University Hospital and Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Center for Diagnosis of Primary Immunodeficiencies, Department of Paediatrics, Martin, Slovakia
²Faculty of Medicine, Comenius University in Bratislava, V. Department of Internal Medicine, Bratislava, Slovakia

Objectives and study: Recurrent and chronic abdominal pain represents a frequent problem in the daily praxis of paediatric gastroenterologists. Besides its common causes, there are also several rare conditions which manifest in their clinical presentation also the recurrent abdominal pain, but due to their rare incidence and low general awareness, they are usually misdiagnosed and incorrectly treated. One of the rare diseases associated with abdominal pain is the group of autoinflammatory diseases (so-called periodic fever syndromes), which are considered to be extremely rare in e.g. Central European region.

Methods: We present a case series of monogenic autoinflammatory diseases associated with recurrent abdominal pain accompanied by recurrent fever and increase of non-specific inflammatory markers. All the patients are treated in the Centre for diagnosis and treatment of primary immunodeficiencies in University Hospital in Martin (Slovakia).

Results: Our studied group consists of 11 children and adult patients with the diagnosis of Familiar Mediterranean fever (FMF) and 3 girls with Hyper-IgD syndrome (deficiency of mevalonate-kinase, HIDS) confirmed by genetic testing. In all of the patients, the recurrent abdominal pain was one of the most important clinical symptoms. In 9/11 FMF patients, abdominal pain was accompanied by recurrent fever and increase of C-reactive protein (CRP) and serum amyloid A. During the inter-fever period, in 7/11 FMF patients the serum amyloid A remained increased without the concomitant increase of CRP. All the girls with HIDS suffered from severe abdominal pain during the febrile attack. The average age of the first symptoms was 8.42 years. During the febrile episode with abdominal pain in 6 FMF and 2 HIDS patients we detected peritoneal effusion by ultrasound. The treatment with colchicine and/or IL-1β-blockers significantly decreased the febrile episodes and attenuated the accompanying abdominal pain.

Conclusion: Periodic fever syndromes are rare in Central Europe; however, they should be a part of differential diagnosis algorithms in children and adults with recurrent abdominal pain accompanied by the increase of non-specific inflammatory markers with or without fever. Serositis is another crucial clinical symptom for these diseases. The late diagnosis can lead to the development of organ amyloidosis with poor prognosis.
Wide variation in organization and clinical practice between paediatric intestinal failure teams across Europe

Esther Neelis¹, Barbara de Koning¹, Myriam Van Winckel², Merit Tabbers³, Susan Hill⁴, Jessie Hulst¹

¹Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
²Ghent University Hospital, Paediatric Gastroenterology and Hepatology, Ghent, Belgium
³Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
⁴Great Ormond Street Hospital for Children, Paediatric Gastroenterology, Division of Nutrition, Intestinal Failure and Rehabilitation, London, United Kingdom

Objectives and study: It is recommended to treat children with intestinal failure (IF) receiving home parenteral nutrition (HPN) in multidisciplinary teams (1). However, we hypothesize that, despite an existing parenteral nutrition guideline, the current care for children with IF is heterogeneous. The aim of this study was to assess the similarities and differences in organisation and clinical practice of paediatric IF teams across Europe.

Methods: We conducted a two-part online survey between September and November 2016. Members of the ESPGHAN Network for IF and Transplantation in Europe (NITE), the British Society of Paediatric Gastroenterology, Hepatology and Nutrition and members of European Society for Clinical Nutrition and Metabolism with special interest in paediatric nutrition were invited. Additionally, respondents were asked to forward the survey to other paediatric IF teams. At least 60 teams were invited. The first part concerned general information about the team and patients monitored. Respondents who completed the first part were invited for the second part, concerning specific topics important in the care of children with IF. Testing of clarity and relevance was performed by 4 independent clinicians from 4 centres. If more than one questionnaire was returned from a single team, the answers were weighted.

Results: Sixty-six respondents completed the first part. They represented 53 IF teams in 20 countries. The median number of children on HPN was 15 (range 1-125, most 1-5 y of age). The median number of members of the IF team were as follows: 2 paediatric gastroenterologists (min-max: 1-6), 2 paediatric surgeons (0-5), 1 dietician (0-4), 2 nurses/nurse practitioners (0-8), 1 pharmacist (0-3), 0 physical therapists (0-3), and 0 speech therapists (0-1). The second part of the survey was completed by 60/66 of the respondents (50/53 teams). The HPN prescribed was mostly age/weight specific and customized by the pharmacy. Table 1 shows the use of catheter lock solutions, lipid emulsion and specific medication. To monitor nutritional status, different parameters were used: weight (100%), height (98%), blood parameters (88%), head circumference (82%), BMI (70%), upper arm/calf circumference (48%), and skinfold thickness (32%). To monitor bone health, bone densitometry was used yearly in 32% of the teams, while it was never used in 22% of the teams. In half of the teams, neuropsychological development was standardly assessed. A speech therapist was involved in the introduction of oral feeding in 72% of the teams.

Table: Use of several treatment options for children with IF including catheter lock solutions, medication and lipid emulsion.

<table>
<thead>
<tr>
<th>Use of catheter lock solutions</th>
<th>% of 50 teams</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard use of:*</td>
<td></td>
</tr>
<tr>
<td>Taurolock</td>
<td>92</td>
</tr>
<tr>
<td>Heparin lock</td>
<td>42</td>
</tr>
<tr>
<td>Taurolidine lock</td>
<td>24</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Use of anticoagulation</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>44</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regular use of</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatostatin analogues</td>
<td>12</td>
</tr>
<tr>
<td>Probiotics</td>
<td>40</td>
</tr>
<tr>
<td>Bile acid sequestrant</td>
<td>62</td>
</tr>
</tbody>
</table>
Conclusion: Practices of paediatric IF teams vary widely across Europe. Topics with most variation were strategies for catheter care, medication and monitoring of bone health. Additionally, wide diversity exists between numbers of patients and composition of the IF team. This survey shows the need for evaluation of the existing guideline. Moreover, multicentre trials are needed to develop evidence based protocols for optimizing care.

Graft vs Host disease and gut involvement following paediatric bone marrow transplant: 4 Year experience in Manchester

Adnaan Kala1, Robert Wynn2, Andrew Fagbemi3

1Royal Manchester Childrens Hospital, Paediatric Gastroenterology, Manchester, United Kingdom
2Royal Manchester Childrens Hospital, Paediatric Haematology And Bone Marrow Transplant, Manchester, United Kingdom
3Royal Manchester Childrens Hospital, Department of Paediatric Gastroenterology, Manchester, United Kingdom

Objectives and study: Bone Marrow Transplant has been one of the most exciting medical developments in recent times. The Bone Marrow Transplant programme in Manchester was established in 1985 and is now one of the biggest in the UK. By providing a specialist service covering the North West of England we have developed expertise in providing successful transplantation. The procedure is not without risk and GvHD with involvement of the gut remains a diagnostic and management challenge.

We reviewed all cases of bone marrow transplant over a 4 year period in our tertiary paediatric transplant unit to assess rates of GvHD and Gut GvHD as well as possible trends.

Methods: A retrospective analysis of Bone Marrow Transplants conducted in Royal Manchester Childrens Hospital over a 4 year period between 2010 and 2015. All the patients who received a Bone Marrow Transplant between January 2010 and January 2015 were selected from the local transplant database (143 transplants). The database was analysed and rates of GvHD (72) and Gut GvHD (15) were identified. Those with involvement of the gut were assessed against those without with respect to morbidity and mortality rates as well as the diagnosis, conditioning and matching for the transplant as well as virology results.

Results: Of the 143 patients who had received a transplant in the period, half developed acute GvHD and a quarter developed chronic GvHD. 10 patients required a second transplant and 22 patients in total died following transplant (15%). Matching for transplant was good (69% with 10/10) but 10 out of the 22 that died had a 10/10 HLA Match.

15/72 GvHD patients developed GvHD of the gut and like the rest of the GvHD sample, around half of transplants in this group had a 10/10 match. There were 4 deaths in the gut group (27% of the gut group). Overall rates of chronic GvHD rates were higher in this group (87% vs 20%). There were 2 ICU admissions in the gut group vs 6 in the non gut group (13% vs 4.7%). 7 patients in total were highlighted as having severe GvHD, of these 5 had GvHD of the gut.

There were a wide range of diagnoses as well as conditioning strategies prior to transplant but no differences were found between the 2 groups in this regard. There were no differences in the proportion of patients with CMV and EBV between the 2 groups at 75% and 50% respectively.

Conclusion: 143 patients received a bone marrow transplant in Manchester over a 4 year period. Bone Marrow Transplant does involve risk, however overall levels of GvHD and the need for second transplant were low in our cohort which likely reflects effective matching as well as adequate T-Cell depletion prior to transplant.

Only 10% of patients developed gut involvement, however levels of morbidity and mortality were strikingly higher in those that had gut involvement. Those with involvement of the gut were more likely to develop severe GvHD, Chronic GvHD, be admitted to ICU and die following transplant. We could not find any differences between the groups with regards to diagnosis, virology, matching and conditioning for transplant.
Our results suggest gut involvement in GvHD is a sign of significant GvHD and suspicion of gut involvement should be high. Clinical diagnosis can be difficult and early investigation and management may be merited. We could not attribute any potential cause for our results. Overall numbers are low and we plan on gathering further data to investigate the management of those with gut involvement to provide additional insight on management and highlight areas that can improve outcomes.
Mode of delivery shapes the developing gut microbiota in Korean newborns

Mijin Kim

Chungnam National University Hospital, School of Medicine, Chungnam National University, Pediatrics, Daejeon, Korea, Rep. of South Korea

Objectives and study: Neonates are born sterile, but many parts of their bodies are colonized by various microorganisms thereafter. The neonatal period is important for the colonization of microflora in the intestines, which is influenced by various factors including the type of delivery mode. We investigated the effects of the delivery mode on the temporal dynamics of gut microbiota in healthy Korean newborns.

Methods: One hundred thirty-four healthy term neonates of birth weights which were adequate for gestational age were included in this study (Vaginal delivery=65, Cesarean operation=69). Fecal specimens from newborns were collected at time points of 3 days, 7 days, and 14 days after birth. Microbiological composition was examined by quantitative real-time polymerase chain reaction (RT-qPCR) targeting six species of interest; Lactobacillus, Bifidobacterium, Clostridium, Enterococcus, Bacteriodes, and Staphylococcus. Comparative analysis was performed between the two groups, which were allocated according to different delivery modes of vaginal delivery or cesarean operation.

Results: The fold-differences for Lactobacillus and Bifidobacterium species were both significantly higher in the feces of vaginal-delivered newborns compared to that of cesarean-delivered newborns at time points of 3 days (P=0.0031 and P<0.001, respectively) and 7 days (P<0.001 and P<0.001, respectively) after birth. This significant difference for Lactobacillus and Bifidobacterium species was not detected in feces collected at 14 days from birth. The fold-differences for Enterococcus species were significantly higher in the feces of cesarean-delivered newborns compared to vaginal-delivered newborns that of at time points of 7 days and 14 days after birth (P=0.0042 and P=0.0091, respectively). This difference was not detected in feces collected at 3 days from birth. The fold-differences for Bacteriodes species were significantly higher in the feces of vaginal-delivered newborns compared to that of cesarean-delivered newborns at time points of 3, 7 and 14 days after birth (all <0.001).

Conclusion: The results of this study show that colonization of Lactobacillus, Bifidobacterium and Bacteriodes species after birth occurred earlier in newborns delivered vaginally compared to those delivered by cesarean operation in Korean newborns. Enterococcus species were more abundant in the feces of cesarean-delivered newborns at 7 and 14 days after birth, which may imply the later effect of earlier colonization of Lactobacillus and Bifidobacterium species in vaginal-delivered newborns. This study demonstrated the effect of delivery mode on the dynamics of gut microbiota profiles in healthy Korean newborns.
Pediatric Eosinophilic Esophagitis: results of the retrospective Pediatric Eosinophilic Esophagitis Registry (RetroPEER)

Assaf Hoofien1, Jorge Amil Dias2, Monica Malamisure3, Francesca Rea4, Sonny Chong5, Annemarie Oudshoorn6, Danielle Nijenhuis-Hendriks7, Sebastian Otte8, Alexandra Papadopoulou9, Claudio Romano10, Frédéric Gottrand11, Victor Vila Miravet12, Rok Orel13, Salvatore Oliva14, Carolina Gutierrez Junquera15, Andrzej Załęski16, Vaidotas Urbonas17, Roger Garcia-Puig18, Maria José Martinez19, Gloria Dominguez-Ortega20, Marcus Auth21, Michal Kon22, Amir Ben Tov23, Nicolas Kalach24, Saskia Vande Velde25, Mark Furman26, Erasmo Miele27, Eleftheria Roma28, Noam Zevit29

1Institute of Gastroenterology, Nutrition, and Liver Disease, , Schneider Children’s Medical Center of Israel, Petach Tikva, Israel
2Centro Hospitalar São João, Pediatric Gastroenterology Unit, Porto, Portugal
3Tor Vergata University, Immunology Department, Rome, Italy
4Bambino Gesù Children’s Hospital, , Digestive Disease Unit, Rome , Italy
5Queen Mary’s Hospital for Children, Epsom and St Helier University NHS Trust, Carshalton, United Kingdom
6Gelse Hospitals, Apeldoorn, Netherlands
7Juliana Children’s Hospital, The Hague, Netherlands
8Haunersche Kinderklinik München, LMU, Munich, Germany
9Division of Pediatric Gastroenterology and Hepatology First Department of Pediatrics, University of Athens, Athens Children’s Hospital “agia Sofia”, Athens, Greece
10University of Messina, Pediatrics Department, Messina, Italy
11Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology, Endocrinology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
12Hospital Sant Joan de Déu, Unit for the Comprehensive Care of Pediatric Inflammatory Bowel Disease. Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
13University Children's Hospital Ljubljana, Department of Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia
14Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
15Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
16Warsaw Medical University, 1department of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
17Vilnius University Children's Hospital Vilnius, Lithuania, Santariskiu, Lithuania
18Hospital Universitari Mútua Terrassa, Terrassa, Spain
19Hospital Niño Jesús, Madrid, Spain
20Hospital Infantil Universitario Niño Jesús, Adjunto Servicio de Gastroenterología Y Nutrición, Madrid, Spain
21Alder Hey Children's NHS Foundation Trust, Department of Paediatric Gastroenterology, Hepatology and Nutrition (Ghn), Liverpool, United Kingdom
22Kaplan Medical Center, Rehovot, Israel
23Gastroenterology Unit, Dana-Dewk Children's Hospital Tel Aviv Sourasky Medical Center, Tel Aviv, Israel
24St Vincent de Paul Hospital, Lille, France
25Ghent University Hospital, Pediatric Gastroenterology and Hepatology, Ghent, Belgium
26Royal Free Hospital, London, United Kingdom
27Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
28University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
29Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Petach-Tikva, Israel
Objectives and study: Recommendations for diagnosing and treating eosinophilic esophagitis (EoE) are evolving, however information on clinical practice is lacking. This study aimed to assess the practices of European pediatric gastroenterology centers diagnosing and treating EoE and to identify the allergens reported to trigger EoE.

Methods: Pediatric gastroenterologists from 25 centers in 13 European countries submitted retrospective anonymous patient information to an on-line database. Patient inclusion criteria were: Diagnosis with EoE below the age of 18 (histological criterion ≥15eos/hpf on an esophageal biopsy), completion of the diagnostic work up prescribed by the treating physician, and were on stable medical or dietary interventions. Patients responsive to proton pump inhibitors (PPI) were excluded.

Results: In total, 412 patients (77.3% male, median age at diagnosis 9.1 years (IQR 4.7-13.0)) diagnosed between December 1999 and June 2016 were analyzed. 67% had some form of atopy. The most frequent indications for the diagnostic endoscopy were: Dysphagia (25.4%), gastro-esophageal reflux symptoms (21.3%), foreign body or food impaction (16.3%), and failure to thrive (6.8%). PPI trials were performed in 70.2%, with higher rates of PPI testing noted in more recent cases (p=0.005 for trend) as new consensus guidelines were published. In patients diagnosed between 2014-2016, PPI trials were performed in 81.1%. Clinical characteristics did not differ between patients who had negative PPI trials and those who had not undergone a PPI trial, except for a finding of wheat or meat as triggering food allergens. The most frequently utilized dietary interventions were: Allergy testing based diets, 6 food elimination diets, elimination diets based on clinical history, and milk elimination. In patients who had undergone any form of elimination diet, the allergens reported as causative for EoE were milk (40.1%), egg (20.4%), wheat/gluten (10.3%), and peanut (9.4%). Elimination diets were used exclusively in 156/412 (37.9%), topical steroids without diets in 51/412 (12.4%), both elimination diet and topical steroids in 183/412 (44%), systemic steroids in 22/412 (5.3%), while esophageal dilation was performed in 7/412 (1.7%). For patients using topical steroids, fluticasone was used more often than viscous budesonide gel (71.8% vs. 42.3% respectively p<0.001). Patient refusal, a shortage of endoscopy/anesthetist time, and physician reluctance to perform numerous endoscopies in a single patient were noted as primary factors justifying deviation from guidelines recommending repeat endoscopies following food re-introduction.

Conclusion: In this cohort, milk and egg (and not wheat/gluten as reported in other cohorts) were the most common allergens triggering EoE in children. This may influence future physician recommendations regarding initial elimination diets. While performance of PPI trials has increased, it is still not universal. Measures to overcome barriers faced by patients and physicians and improve the implementation of guidelines are needed.
Pancreatitis series: a fifteen year tertiary paediatric center experience

Anastasia Konidari\(^1\), Jo Puleston\(^2\), Andrew Fagbemi\(^1\)

\(^1\)Royal Manchester Children's Hospital, Department of Paediatric Gastroenterology, Manchester, United Kingdom
\(^2\)Manchester Royal Infirmary, Department of Adult Gastroenterology, Manchester, United Kingdom

**Objectives and study:** Pancreatitis is an increasingly recognized condition in children, with rising incidence and morbidity. The natural history and disease progression in children have not been adequately described to date. There is no clear consensus in managing chronic pancreatitis and experience is largely extrapolated by adult studies. We manage children with pancreatitis from a large catchment area of about 3 million through shared care arrangements with surgical team and adult gastroenterology colleagues, providing joint clinics in chronic cases. This is a retrospective cohort study to describe a single tertiary experience of paediatric patients diagnosed with acute and chronic pancreatitis over the last 15 years with focus on aetiology, patient characteristics, development of chronic disease and management.

**Methods:** Patients diagnosed with one or more episodes of pancreatitis up until the age of 16 were identified through clinical coding. Thirty five children were identified; five were excluded as out of area or insufficient follow up data. Case notes and electronic patient records were reviewed and data on gender, ethnicity, body mass index, number of episodes of pancreatitis, aetiology (lithiasis, idiopathic, drug related or other), lipid and amylase levels, genetic testing (PRSS1, CFTR, SPINK mutations) and family history were collected and analyzed using SPSS 22.

**Results:** Biliary lithiasis and idiopathic cause remain the principal aetiologies of acute, recurrent and chronic pancreatitis accounting for 60% of our cohort. 70% of patients were female, with almost equal split between Asians and Caucasians. Identification of aetiology was important as it significantly correlated with development of chronicity (Spearman’s correlation, \(r=0.369\), \(p=0.045\)). Hyperlipidaemia was not a prominent feature in our cohort, as only two patients had abnormal fasting lipid profile. Mean BMI was 20.01 kg/m\(^2\), standard deviation 4.5; the body mass index was no different across categories of aetiology (Kruskal Wallis, \(p=0.35\)) and same in cases of acute, recurrent and chronic pancreatitis (Mann Whitney U test, \(p=0.66\)). Similarly the distribution of amylase values was not significantly different in patients with disease of various aetiology; mean value was 669.13, standard deviation 619.6 (non-significant Spearman’s correlation \(p=0.45\)). Patients with identified homozygous pathologic genetic mutations (3 out of 30 with SPINK mutation; one out of three patients was also CFTR mutation carrier) all progressed to develop chronic disease. Eleven out of sixteen patients required intervention such as endoscopic retrograde cholangio-pancreatography, endoscopic ultrasound or stent insertion, without adverse events. Chronic patients were followed up in our joint clinic and transition to adult care was therefore facilitated.

**Conclusion:** We would like to emphasise the importance of performing a thorough diagnostic work up, including testing for genetic mutation analysis in patients with more than two episodes of pancreatitis, so as to aid prognostication of chronicity and arrange early follow up in joint clinics. We advocate sharing expertise with adult colleagues, so as to enhance our diagnostic and therapeutic tools and achieve optimal management of chronic cases.
Are children with gallstone disease more overweight than general population? Analysis of 200 children with gallbladder stones

Olga Niewiadomska1, Zbigniew Kulaga2, Irena Jankowska3, Marcin Krawczyk4, Krzysztof Jankowski5, Jolanta Gozdowska6, Dariusz Lebensztejn7, Sabina Wiecek8, Frank Lammert9, Piotr Socha10

1The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutrition Disorders and Pediatrics, Warsaw, Poland
2The Children’s Memorial Health Institute, Public Health, Warsaw, Poland
3The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutrition Disorders and Pediatrics, Warsaw, Poland
4Saarland University Medical Center, Saarland University, Department of Medicine II, Homburg, Germany
5Medical University, Internal Medicine and Cardiology, Warsaw, Poland
6Department of Internal Medicine and Cardiology, Medical University of Warsaw, Warsaw, Poland
7Medical University, Pediatrics, Gastroenterology and Allergology, Bialystok, Poland
8Medical University of Silesia, Department of Paediatrics, Katowice, Poland
9Saarland University Hospital, Homburg, Germany
10Children’s Memorial Health Institute, Departament of Gastroenterology, Hepatology, Nutrition Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Gallstone disease is a multifactorial condition, and we have reported [ESPGAHN 2016] that its incidence in children might be modulated by the presence common genetic variants. Apart from genetic predisposition, increased body weight represents a major risk factor of cholelithiasis. Here we investigate the association of overweight and obesity with gallstones in pediatric patients.

Methods: We measured weight and height, and calculated body mass index (BMI) in 200 Polish children with gallstones (age 1 month - 17 years, 100 males). The presence of gallstones was confirmed by either abdominal sonography or history of cholecystectomy. Body weight status of the study subjects was dichotomized as being overweight or obese, or not being overweight or obese, based on age- and sex-specific International Obesity Task Force BMI cut-offs [Cole TJ, Lobstein T. Pediatr Obes. 2012]. Overweight or obesity rates in the gallstone cohort were compared with current population estimates in preschool-aged children [Kulaga Z et al. Dev Period Med. 2016] and school-aged children and adolescents [Kulaga Z et al. Eur J Pediatr. 2011] with the use of Chi-square tests.

Results: Among the recruited children with gallstones, a total of 75 (38%) were in the pre-school age (i.e. younger than 7 years). In the entire cohort the mean BMI was 19.6 kg/m². Overall, 21.3% of the preschool-aged children with gallstones were overweight or obese. Increased body weight was present in 44.8% of school-aged children and adolescents diagnosed with gallstone disease. As compared to the current population estimates of overweight/obesity, which are 13.6% in preschool-aged and 16.4% in school-aged children, children with gallstones were more frequently overweight or obese in both age groups (P=0.049 and P<0.001, respectively).

Conclusion: We show in a large cohort of children with gallstones that overweight/obesity rates are higher in this group as compared with the population estimates. These results underscore the pivotal role of increased body weight in the stone formation among children and adolescents. Given the epidemics of obesity among youths, we anticipate an increasing prevalence of gallstone disease and its complications.
Incidence of eosinophilic esophagitis (EoE). Seasonal variations and effect of air pollutants and pollen counts

Enrique La Orden Izquierdo1, Carolina Gutierrez Junquera2, Mª Luz Cilleruelo Pascual2, Josefa Barrio3, Sonia Fernández Fernández4, Enrique Medina Benitez5, Carmen Miranda Cid6, Gonzalo Botija Arcos7, Luis Grande Herrero8, Myriam Herrero Álvarez9, Miguel Ángel Carro Rodriguez10, Ignacio Mahillo Fernández11, Patricia Cervigón Morales12, Enriqueta Román Riechmann2

1Hospital Universitario Infanta Elena , Paediatric Gastroenterology Unit, Valdemoro, Madrid, Spain
2Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
3Hospital Universitario de Fuenlabrada, Pediatric Gastroenterology Unit, Madrid, Spain
4Hospital Universitario Severo Ochoa, Paediatric Gastroenterology Unit, Leganés, Madrid, Spain
5Hospital Universitario 12 de Octubre, Paediatric Gastroenterology, Madrid, Spain
6Hospital Universitario Infanta Cristina, Paediatric Gastroenterology Unit, Parla, Madrid, Spain
7Hospital Universitario Fundación de Alcorcón, Paediatric Gastroenterology Unit, Alcorcón, Madrid, Spain
8Hospital Universitario de Getafe, Paediatric Gastroenterology Unit, Getafe, Madrid, Spain
9Hospital Universitario Rey Juan Carlos, Paediatric Gastroenterology Unit, Mostoles, Madrid, Spain
10Hospital U. General de Villalba, Paediatric Gastroenterology Unit, Villalba, Madrid, Spain
11Hospital Universitario Fundación Jiménez Díaz, Epidemiology and Biostatistics, Madrid, Spain
12Área de Vigilancia de Riesgos Ambientales En Salud, Coordinación Red PalinoCAM, Madrid, Spain

Objectives and study: The incidence of eosinophilic esophagitis (EoE) is increasing, although data on paediatric age are scarce. A retrospective study in our area * observed a mean incidence of 8.4 cases/100000 under 15 years old children/year (2008-2013). This study aims to determine the incidence of EoE in southwestern area of the region of Madrid, analysing the relationship between new cases of EoE, the most common pollens measured in monthly absolute counts and major atmospheric pollutants (PM10, PM2.5, O3 and NO2).

Methods: We perform a multi-centre prospective observational descriptive study of the incidence of new cases of EoE diagnosed in children under 15 years in the southwestern area of the region of Madrid between September 2014 and August 2016. We registered the number of gastroscopies, new cases of EoE by month and centre, mean time from onset of symptoms to diagnosis, and the population of the catchment area of each hospital. We estimated the incidence of cases per 100,000 under 15 years old children / year. To test for statistical significance, the relative risk (RR) estimate was performed using regression models to assess the association between monthly incidence, pollen counts and major atmospheric pollutants (data from Red PalinoCAM). All statistical analyses were performed with Stata v.11 software. This study was approved on July 2014 by the Ethics Committee of Fundación Jiménez Díaz.

Results: 148 new cases were included. 97 were male (65.5%), age range 6 months to 15 years old (mean 9.7y, median 10.4y), 32.4% (n=48) under 8 years old. The mean time from onset of symptoms to diagnosis was 11.2±13.8 months. Allergic background: asthma 30%, food allergy 23.6%, and seasonal allergic rhinitis 29% (Table). Mean global incidence vas 15.2. In the whole period (2014-16) mean monthly incidence was 1.4±0.83 in children <8 years and 2.2±1.27 in children ≥8 years (p=0.017).The overall analysis of the relationship between the EoE incidence, absolute counts of pollen types and atmospheric pollutants analysed monthly revealed a RR 2.95; IC 95% (1.45-5.84) for mean pollen count of Artemisia (p=0.003). Air pollutants did not modify this relationship.
Table: Incidence of new cases/100000 under 15 years old children/year:

<table>
<thead>
<tr>
<th></th>
<th>Sept 2014 – August 2015</th>
<th>Sept 2015 – August 2016</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Annual Incidence:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Global</td>
<td>15.6</td>
<td>14.8</td>
</tr>
<tr>
<td>• &lt;8 years</td>
<td>12.2</td>
<td>5.7</td>
</tr>
<tr>
<td>• ≥8 years</td>
<td>19.9</td>
<td>25.7</td>
</tr>
<tr>
<td><strong>Prevalence of EoE diagnosis in children undergoing upper endoscopy</strong></td>
<td>9.9%</td>
<td>12.3%</td>
</tr>
<tr>
<td><strong>Mean and range of monthly incidence by year</strong></td>
<td>1.32 (0.62-2.67)</td>
<td>1.23 (0.41-2.67)</td>
</tr>
</tbody>
</table>

**Conclusion:** The incidence of EoE in children in our area has been duplicated in the last 2 years *(JPGN 2016:62 (Suppl 1):300-301). The incidence in children ≥8 years was significantly higher than in younger children. Although the analysis found out an association with *Artemisia* pollen count, it does not justify the monthly peaks of new cases as it is a perennial allergen.
One-step button percutaneous endoscopic gastrostomy: our experience in pediatric population

avishay lahad¹, Ron Bilik², Dror Shouval¹, Yael Haberman³, Rachel Leshem¹, Daniel Sinhar², Batia Weiss¹

¹Edmond and Lily Safra Children's Hospital, Pediatric Gastroenterology, Ramat Gan, Israel
²Edmond and Lily Safra Children's Hospital, Pediatric Surgery, Ramat Gan, Israel
³Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Pediatric Gastroenterology, Tel-Hashomer, Israel

Objectives and study: The current preferred method for providing long-term enteral nutrition is the pull technique of percutaneous endoscopic gastrostomy (pull-PEG). Replacement by a gastrostomy button is possible 12 weeks after the pull-PEG insertion. Recently, a new method has been designed to perform a button gastrostomy in a one-step (PEG-B) procedure. This technique offers advantages over classical pull-PEG especially in high-risk patients. We describe here our experience with one-step button (PEG-B) procedure.

Methods: A retrospective review of patients in our unit who underwent a PEG-B during 2012-2015. Demographic data, procedure indications, feeding initiation, duration of hospital stay and complications were recorded.

Results: Seventeen patients, aged 6 months to 35 years (mean 15 ±11, median 14) were included. Indications for PEG insertion were partial feeding support in 14 patients and complete need for enteral feeding in 3 patients. Patient diagnosis is summarized in table 1. The patient weight range prior to the procedure was 6.8-56 kg (mean 28.7Kg). The size and length of the buttons were individually adjusted. Feeding through the PEG was started within 12-36 hours after insertion. The average length of hospitalization was 4.4 days (range 2-8). No major procedure-related complications have been recorded within 6 months of follow up. One child died 8 days after the procedure due to an unrelated tracheostomy complication. In one patient the 3 “buttons” – sutures of gastropexy fell one day after the procedure, and the use of the PEG was delayed to 8 days after the insertion, without any complication or difficulties.

Table:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of patients</th>
<th>Average weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ataxia Telangectasia</td>
<td>5</td>
<td>24.4Kg</td>
</tr>
<tr>
<td>Cystic Fibrosis</td>
<td>4</td>
<td>39.25Kg</td>
</tr>
<tr>
<td>Glycogen storage disease</td>
<td>2</td>
<td>12.65Kg</td>
</tr>
<tr>
<td>Malignancy</td>
<td>2</td>
<td>44.5Kg</td>
</tr>
<tr>
<td>Neurologic disease</td>
<td>1</td>
<td>10.5Kg</td>
</tr>
<tr>
<td>Autoimmune dysregulation</td>
<td>1</td>
<td>28Kg</td>
</tr>
<tr>
<td>Pierre Robin syndrome</td>
<td>1</td>
<td>6.8Kg</td>
</tr>
<tr>
<td>Near drowning</td>
<td>1</td>
<td>50Kg</td>
</tr>
</tbody>
</table>
**Conclusion:** The PEG-B procedure was feasible and safe in children in this small series. The results are comparable to published results on the literature. The one-step method involves a single procedure and reduces patient exposure to anesthesia, and is therefore advantageous in high-risk patients.
Eosinophilic gastroenteritis and colitis in children: clinical features, histopathological evidences and response to therapy: a case series

Julie Lemale¹, Hiba Sayah¹, Linda Dainese², Sabah Boudjemaa², Patrick Tounian³

¹Aphp- Trousseau Hospital, Nutrition and Gastroenterology, Department of Pediatrics, Paris, France
²Aphp-Trousseau Hospital, Department of Pathology, Paris, France
³Trousseau Hospital, Nutrition Department, Paris, France

Objectives and study: Eosinophilic Gastroenteritis (EGE) and Eosinophilic Colitis (EC), defined by histological criteria as marked eosinophilia in the gastrointestinal mucosa, are rare diseases and studies in children are lacking. We sought to describe the clinical, endoscopic and histopathological features of EGE and EC, and evaluate response to dietary and pharmacological therapies.

Methods: Pathology files at our medical center were searched for EGE and EC between June 2012 and June 2015. Medical records were reviewed for demographic characteristics, symptoms, endoscopic findings, co morbidities and response to therapy. Standardized criteria defining the histological features of EC and EGE are lacking, and no limits were clearly given to distinguish between normal and pathological number of eosinophils in the gastric and intestinal mucosa. We defined EG by marked; diffuse, eosinophilic infiltrates with $\geq 20$ eosinophils per HPF in the antrum and/or fundus, either diffusely or multifocally. Hypereosinophilic infiltrates were defined as $\geq 50$ eosinophils per HPF in the duodenum and the colon, as past studies have reported an upper limit of normal eosinophil. The presence of cryptitis, cluster of eosinophils and/or eosinophilic abcesses was necessary to provide the diagnosis.

Results: Ten children (5 boys/5 girls) with eosinophilic gastrointestinal disorders were identified, median age was 5.2 years, 7 of whom had EC and 3 had EGE. Forty percent of the patients (4/10) were young children below 2 years of age. Two patients had associated Eosinophilic Esophagitis (EoE). Symptoms were highly variable and no specific. For all EGE, asthenia, failure to thrive, abdominal pain, episodes of vomiting were observed. One patient presented with diffuse edema. For EC, abdominal pain and rectal bleeding were noted in all patients. Two children had chronic diarrhea. Biologically, 50% of patients had peripheral eosinophilia, 50% had anemia (3 EGE et 2 EC) and 30% presented hypoalbuminemia (3 EGE). Four out of the ten patients had a family history of atopy, only 30% had positive prick tests (milk protein for one and multiple antigens for the other). Endoscopic features of the digestive mucosa were highly variable and included normal appearance, nonspecific gastritis or colitis, ulcers, white plaques, and nodular lesions. Histologically, in all of the patients, eosinophilia was diffuse or multifocal. Associated lymphoid follicular hyperplasia was identified in 70% of the patients. Clusters of polymuclear eosinophils were seen in 100% of the patients and were predominantly infiltrating the full depth of the lamina propria. When present in the biopsies, the muscularis mucosa was also involved by eosinophils (3 patients). Half of the patients (4/8) who had dietary restriction (elemental diet or specific allergens elimination) therapy responded clinically and histologically. The other responded partially to corticosteroids and/or mesalazine.

Conclusion: EGE and EC affect children as well as adults. Symptoms and endoscopic findings vary, highlighting the importance of biopsies and the importance of the high index of suspicion for the diagnosis. The treatment is empirical but the disease is responsive to dietary restriction therapies preventing the potential adverse effects of steroids in children. Food reintroductions are complex with frequent relapses.
Infantile eczema may be associated with the presence of low-abundant bacterial species in neonatal stool samples

Ting Fan Leung¹, Kam Lun Hon¹, Man Fung Tang¹, Wing Hung Tam², Stephen Tsui³

¹The Chinese University of Hong Kong, Department of Paediatrics, Hong Kong, Hong Kong
²The Chinese University of Hong Kong, Department of Obstetrics and Gynaecology, Hong Kong, Hong Kong
³The Chinese University of Hong Kong, School of Biomedical Science, Hong Kong, Hong Kong

Objectives and study: Gut microbiota is increasingly recognised to play crucial roles in the pathogenesis of asthma, obesity and autoimmune diseases. Faecal microbiome is likely ethnic and diet-specific, but such data is lacking in Asians. This study characterised faecal microbial compositions of Hong Kong Chinese neonates and investigated if such might be associated with eczema development during infancy.

Methods: Random stool samples were obtained from 4-week-old infants with eczema (n = 15) and without any allergy (n = 15) at 9 months. Genomic DNA extracted by PowerSoil DNA Isolation Kit (MO BIO Laboratories) was sequenced using Ion PGM Sequencing 200 Kit v2, Ion 318 TM Chip v2 on Ion PGM System (Ion Torrent). Reads from each patient were filtered for low quality (Phred < 20). Microbial diversity was evaluated using Shannon-Weaver diversity index in Swedish (J Allergy Clin Immunol 2012; 129: 434-40). The taxonomic classification of the reads was assigned by BLASTn.

Results: 5 controls had insufficient DNA for sequencing. No significant association was detected between eczema and any bacteria with ≥ 1% relative abundance, including Bacteroides, Escherichia, Klebsiella, Bifidobacterium, Streptococcus and Lactobacillus. Among the less abundant genera (relative abundance < 1%), Campylobacter was more abundant in cases (median 0.008%, IQR 0.003 - 0.022%) than controls (median 0.001%, IQR 0.001 - 0.004%) while Roseburia was less abundant in eczema (median 0%, IQR 0 - 0.063%) than controls (median 0.055%, IQR 0.002 - 0.270%). Nonetheless, Shannon-Weaver diversity index of stool microbiota at 4 weeks was similar between infants with eczema and non-allergic controls at 9 months (median [IQR]: 1.28 [0.94 - 1.93] versus 1.47 [1.31 - 1.80]; P = 0.698). Comparing microbial compositions in our newborns and Swedish, Escherichia coli was found among top 5 genera only in both our cases and controls whereas enterobacter only in Swedish newborns. Clostridium, parabacteroides and lactobacillus were found only in Chinese eczema and healthy Swedish newborns.

Conclusions: The low-abundant bacteria Campylobacter and Roseburia appear to be less frequently detected in stool of 4-week-old Chinese infants who subsequently develop eczema. Microbial diversity is not associated with eczema susceptibility. This study reveals ethnic-specific early-life faecal microbial compositions, and larger prospective studies are needed to confirm our findings.

Funding: Research Committee’s One-off Strategic Fund for Research (3132910) and Direct Grant for Research (4054292), CUHK
GASTROENTEROLOGY: Gastroenterology other

G-P-133

Symptoms beyond the gastrointestinal tract that need to be taken into account in children with suspected food protein induced gastrointestinal allergies

Adriana Lozinsky¹, Rosan Meyer², Heather Godwin³, Kate Reeve³, Robert Dziubak⁴, Ru-Xin Fone⁵, Neil Shah⁶

¹Great Ormond Street Hospital for Children Foundation Trust, London, United Kingdom
²Great Ormond Street Hospital for Children Foundation Trust, Gastroenterology, London, United Kingdom
³Great Ormons Street Hospital, London, United Kingdom
⁴Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom
⁵Guys and St Tomas Hospital, London, United Kingdom
⁶Great Ormond Street Hospital for Children Foundation Trust, Dept of Gastroenterology, London, United Kingdom

Objectives and study: An allergy focused history remains the cornerstone for the diagnosis of non-Immunoglobulin E (non-IgE) mediated food allergy. We aimed to assess the prevalence of atopic co-morbidities, family history of allergies and prevalence of extraintestinal manifestations (EIM) in children with suspected non-IgE mediated gastrointestinal food allergies to aid the diagnosis and inclusion in a allergy focused history for non-IgE mediated allergies.

Methods: A prospective observational study was performed on patients aged 4 weeks – 16 years with symptoms of non-IgE mediated gastrointestinal food allergies, who improved after a 4-8 week elimination diet. Atopic family history was established at baseline and patients also had a questionnaire on atopic co-morbidities and EIM before and after the elimination diet to establish symptoms improvement not only on gastrointestinal symptoms, but co-morbidities and EIM.

Results: Data from 131 patients was analysed including 90 boys with a median age of 21 months [IQR: 7 to 66]. Based on the questionnaire 83 (63.3%) children had atopic co-morbidities, including 68 (51.9%) with eczema, 38 with asthma, and 27 with allergic rhinitis. Nasal congestion was reported in 70% (91) of children. After the elimination diet 55% of parents reported improvement on eczema. The median number of EIM per patient was 2 [IQR: 1 to 4]. The most commonly reported symptoms were poor sleep (74.3%) and atopic shiners (51.4%). After 4 weeks of elimination diet there were a significant decrease in percentage of children with presenting with poor sleep, fatigue, night sweats and atopic shiners were less prominent.

Conclusion: This study showed that atopic co-morbidities and EIM are important features in patients with non-IgE gastrointestinal food allergies. The elimination diet contributes not only for improvement of gastrointestinal symptoms, but also decreases the percentage of patients with eczema and EIM.
Vascular access devices (VADs) localization by trans thoracic echocardiography (TTE) in children receiving total parenteral nutrition (TPN)

Claudia Mandato1, Ugo Graziano2, Pasquale Esposito3, Ferdinando Spagnuolo5, Salvatore Ferraiuolo2, Rodolfo Paladini4, Vittorio Serio5, Maria Immacolata Spagnuolo6, Paolo Siani1

1Aorn Santobono-Pausilipon, Pediatrics, Naples, Italy
2Aorn Santobono-Pausilipon, Pediatric Surgery, Naples, Italy
3Aorn Santobono-Pausilipon, Neonatal Intensive Care Unit, Naples, Italy
4Aorn Santobono-Pausilipon, Pediatric Cardiology, Naples, Italy
5Aorn Santobono-Pausilipon, Pediatric Nephrology, Naples, Italy
6University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy

Objectives and study: Total parenteral nutrition (TPN), administered by central catheter, permits normal growth and development in children unable to follow oral feeding. Catheter tip positioning at cavo-atrial junction is mandatory for monitoring correct implantation/functioning of the Vascular Access Device (VAD) and to minimize related complications, which may occur even after a long time after positioning. Intra-cavitary ECG is nowadays considered the most effective method in terms of benefit-cost ratio although no specific recommendation can be given due to the low level of available evidences. Trans Thoracic Echocardiography (TTE) is an advantageous potential alternative technique in children, but it needs specific equipment and adequate staff training.

Here we report our experience in a prospective observational study on intra/post procedural VAD location monitoring by TTE, in infants and children.

Methods: 22 consecutive children on TPN (mean age of 3.7±3.1 yo) were evaluated for intra-procedural catheter tip positioning by TTE, for 3 months. TPN indications were: short bowel syndrome, abdominal surgery, caustic ingestion, severe pancreatitis, anorexia nervosa. Ultrasound scans were: 2° intercostal space-left sternal border, short axis; subcostal scan for long bicaval view. Both techniques were enriched by CEUS (Contrast Enhanced Ultrasound). Patient were revalued at 6 months follow-up.

Results: In 19 (86.4%) children tip device was correctly visualized at cavo-atrial junction. In 3 (13.6%) patients tip was not visible at TTE. In 2 of them catheter was displaced into left anonymous vein and into superior vena cava respectively, at X-Ray control. In one patient (11 yo, obese) poor echogenicity led to the ultrasound examination being abandoned. At 6 months follow up, TTE did not evidence any catheter dislocation in patients population.

Conclusion: In pediatrics, tip detection by TTE warrants consideration for identifying catheter positioning and misplacement in addition to intracavitary ECG. TTE avoids catheter manipulation and suggests dislocation. It can also show evidence of right atrium thrombosis, during follow-up.
Atopic dermatitis, digestive disease symptoms, and intestinal microflora metabolic activity

Natalia Narinskaya¹, Sergey Belmer²

¹Pirogov Russian National Research Medical University, Dermatology, Moscow, Russian Federation
²Pirogov Russian National Research Medical University, Pediatrics, Moscow, Russian Federation

Objectives and study: In recent years, there was a significant increase in the prevalence of atopic dermatitis (AD) in children. AD in most cases is accompanied by digestive system disorders. Intestinal motility disorders often, in turn, characterized by disturbances of the intestinal microbiota with changing of bacterial metabolic activity and changes in the short-chain fatty acids (SCFA) synthesis. The aim of this study was to examine the metabolic activity of the intestinal microflora in children with AD.

Methods: We examined 41 children with AD (20 boys and 21 girls) aged 5-16 years (mean age - 10.95±0.50 years). We analyzed the clinical data and disease history, including the assessment of the severity of skin process by SCORAD scale. The intestinal microflora metabolic activity was evaluated by the definition of short chain fatty acids (SCFA) in the stool using gas-liquid chromatography. Also, we evaluated the intestinal motility by electrogastroenterography (EGEG).

Results: The average value of SCORAD scale was 62.50±1.61 (45.50-82.00). In 26 children it was identified severe AD, in 15 - moderate severity. Clinical signs of the digestive system disorders were identified in AD children: abdominal pain - in 68%, nausea - 51%, vomiting - 32%, heartburn - 22%, diarrhea - 32%, constipation - 20%, flatulence - 63%. The study of SCFA in the stool as markers of metabolic activity of the intestinal microflora showed an increase in the overall level of their production with a predominance of acetic acid (1.910±0.183mg/l vs 0.634±0.004 mg/l as ref. value, p<0.05) and reduction in butyric acid (0.189±0.001 mg/l vs 0.710±0.06 mg/l as ref. value, p<0.05). Moreover, the degree of SCFA changes correlated with the severity of the skin process by SCORAD (Pearson correlation for acetic acid/SCORAD - R=+0.389, p<0.05). In EGEG the gastric accommodation to the food and colon motility were impaired. We found also a direct association of the skin process severity (according to the SCORAD values) with the duodenum and colon pacemakers activity. We found in AD children increased duodenal motility and decreased colonic motility.

Conclusion: Thus, it can be considered a well-defined relationship between the main skin process and intestinal microflora, probably indirectly through changes in the bowel motility. Moreover, these changes can increase the main disease symptoms. Our results indicate the possibility of prokinetics, probiotics and prebiotics using in AD, but further studies are needed. We can conclude that 1. Children with atopic dermatitis have symptoms of digestive system disorders: abdominal pain, constipation, nausea, diarrhea flatulence. 2. The main pathological process in AD is leading to changes in intestinal microflora metabolic activity, probably through intestinal motility disorders.
GASTROENTEROLOGY: Gastroenterology other

G-P-136

Diagnostic clinical exome sequencing for the diagnosis of pediatric gastroenterology

Sujin Cho¹, Insook Jeong¹, Seak Hee Oh¹, Kyung Mo Kim¹

¹Asan Medical Center, Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Exome sequencing (ES) is becoming one of the promising diagnostic modalities to identify genetic factors in children with various gastrointestinal and hepatic problems, such as infantile colitis and acute liver failure (ALF). The aim of this interim study is to evaluate practicability of WES in pediatric gastroenterology.

Methods: DNA samples were used for ES from 50 pediatric patients with various etiologies: ALF (N=7), liver cirrhosis (LC) (N=4), inflammatory bowel disease (IBD) (N=34), and neonatal cholestasis (NC) (N=5). Ten children had ‘Diagnostic ES’ by Green Cross Genome Inc. (sequencing exons of 4,813 genes using TruSight One panel, Illumina MiSeq platform), while 38 had whole ES by Macrogen Inc. (Illumina HiSeq2000 platform). Rare variants (minor allele frequency < 0.01) were identified by comparison with SNPs from the 1000 genomes, ExAc, and 397 Korean ES data. Additional custom filtering using primary immunodeficiency panel for children with IBD and cholestasis panel for children with cholestasis. A family-based analysis was conducted in children (N=15).

Results: Among 50 children, 15 (30%) children carried known pathogenic mutations (N=9, 18%) that confirmed their own diseases and deleterious homozygote variants (N=6, 12%) that provided the possibility of genetic diseases. Two patient with ALF carried a known homozygote mutation in ABCG5 (sitosterolemia). Among children with LC, two children with LC carried deleterious homozygote variants in ABCB11 (progressive familial intrahepatic cholestasis type II). One with NC carried known homozygote mutations in VPS33B (syndrome of Arthrogryposis, renal dysfunction, and cholestasis), while two with NC carried deleterious homozygote variants in VPS33B and one had a possibly pathogenic variant in CLDN1 (syndrome of Ichthyosis, leukocyte vacuoles, alopecia, and sclerosing cholangitis). Four and two children with IBD carried known mutations in IL10RA and XIAP, respectively, and one had deleterious homozygote mutation in CD207 (Birbeck granule deficiency). Functional validations were conducted only in two children with sitosterolemia (measurement of sitosterol) and four with IL10RA deficiency (STAT3 phosphorylation).

Conclusion: The diagnostic rate of ES to identify known mutations among children with gastrointestinal problems was relatively acceptable. However, functional studies to validate the pathogenicity of deleterious variants were challenging.
Association of cow milk protein allergy and transcobalamin II deficiency

Catalina Ortiz¹, Sandra Catalina Mesa-Restrepo¹, Susana Molina¹, Feliza Restrepo¹, Ana Marverin Correa-Varela¹, Sandra Isabel Alzate-Vanegas¹, Paula Andrea Cañaveral-Londoño¹, Ana Carolina Sierra-Montoya¹, María Elsy Sepúlveda-Hincapié¹, Beatriz Helena Aristizabal¹, Carolina Baquero Montoya¹

¹Hospital Pablo Tobón Uribe, Medellín, Colombia

Objectives and study: The prevalence of food allergy including enterocolitis induced by proteins in the diet, is raising. In infants, the principal manifestations are vomiting, diarrhea, cough, rhinitis, pruritus and anaemia associated or not with atopic eczema, which is solved by amino acids formula. In a patient in whom the cutaneous manifestations persist despite good adherence to restriction of the allergen, deficiency of trace elements or the coexistence of other disorders should be suspected. Here, we report on a patient with Allergic Proctocolitis associated to Transcobalamin II deficiency.

Methods: The proband is 1-year-old, who from the first month of life presented vomiting, diarrhea, rhinorrhea, abdominal distension and atopic dermatitis. A rectosigmoidoscopy was performed and the respective biopsies were taken for histopathological analysis. IgE levels specific for casein and cow milk were assessed, as well as serum levels of folic acid, vitamin B12, plasma amino acids, acylcarnitins and organic acids. At the molecular level whole exome sequencing was carried out.

Results: The rectosigmoidoscopy showed aphthae, recent bleeding, and edema. At the histopathological level, a count of eosinophils of up to 45 per field of high power with distortion of the crypts was reported. Specific IgE by ImmunoCAP-Phadia were negative. The acylcarnitine profile showed an increase in C2 levels with normal organic acids and serum amino acids. Whole exome sequencing demonstrated a de novo homozygous nonsense mutation in TCN2.

Conclusion: In the case of a patient with Allergic Proctocolitis and refractory cutaneous manifestations, the presence of additional nutritional disorders should be considered.
Assessment of the diagnostic process of cow's milk allergy (CMA) in young children using amino acid formula or extensively hydrolysed formula in a public healthcare centre

Cristina Palmer Barros¹, Ana Luiza Bonfim¹, Ana Paola Lunguinho¹, Anna Luiza Ribeiro¹, Dayana Resende¹, Erica Rezende², Giovana Fatureto¹, Marina Rosa¹

¹Federal University of Uberlandia, Uberlandia, Brazil
²Uberlandia Federal University, Uberlandia, Brazil

Objectives and study: This is an observation cross-section study that aim to assess and compare the diagnostic process of CMA in young children using amino acid formula (AAF) or extensively hydrolysed formula (eHF) as the elimination diet in a tertiary Healthcare Centre.

Methods: This was a retrospective analysis that assessed the data records of patients (≤36 months) who were evaluated in the gastroenterology and allergy out-patient clinic of a Brazilian Public University Hospital, between January 2013 and December 2014. In this institution, there was a Public Healthcare Programme that supports the diagnostic and therapeutic elimination diet of all infants and toddlers with suspected and diagnosed CMA. Only diagnostic data was collected.

Results: 647 medical registers were analyzed and the diagnostic protocol of CMA was applied in 149 (23%) patients based on the presence of suspected symptoms. The median of age was 6 months (4-12). 59 (39.6%) and 31 (20.8%) children used AAF and eHF, respectively, as the first elimination diet. The principal initial related symptoms were vomiting and regurgitation (42.2%), diarrhea (36.2%), excessive crying and fussing (21.4%), bloody stools (19.4%), dermatitis (19.4%), abdominal pain (16.1%), urticaria and angio-edema (9.3%). The remission of symptoms was observed in 42 (71.1%) patients with AAF and 20 (64.5%) with eHF. The oral food challenge test could be done in 39 (66.1%) patients with AAF and 20 (64.5%) with eHF. In 16 (17.7%) patients who were using eHF as the first elimination diet there was the necessity of changing for AAF to permit the thorough diagnosis. The median of days spent during the diagnostic process was 31 days in the AAF group and 58.5 days in the eHF group, showing significant statistic difference (p=0.02).

Conclusion: The frequency of unspecific and delayed symptoms in young children with suspected CMA is high. There is some clinic and economic evidence of advantages in the use of AAF instead eHF in the CMA diagnostic process in a Public Healthcare Centre.
Gastrointestinal and nutritional aspects in patients with ataxia telangiectasia: a longitudinal study

Alexander Krauthammer1, Avishay Lahad1 Avishay Lahad1, Yifat Saruk2, Raz Somech3, Andrea Nissenkorn3, Dalit Modan-Moses3, Hila Levi-Kidron3, Tal Sadeh Kon2, Batia Weiss4

1Edmond and Lily Safra Children's Hospital, Pediatric Gastroenterology, Ramat Gan, Israel
2Edmond and Lily Safra Children's Hospital, Tel-Hashomer, Ramat-Gan, Israel
3Edmond and Lily Safra Children's Hospital, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Israel
4Edmond & Lily Safra Children's Hospital, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Pediatric Gastroenterology and Nutrition, Ramat Gan, Israel

Objectives and study: Ataxia telangiectasia (A-T) is a rare genetic disease involving multiple organs. Data regarding long-term gastrointestinal involvement and nutritional state of A-T patients is scarce. We aimed to study the gastrointestinal (GI) and nutritional complications in a large national cohort of patients with A-T.

Methods: A retrospective chart review of A-T patients, followed from January 1986 to January 2015 at a national center. Patients followed at the national A-T center are evaluated at least every 6 month by a multi-disciplinary team. Clinical data including demographic, laboratory and nutritional data were retrieved. BMI values were converted to BMI-Z score (BMIZ) according to the age, height, weight and gender. Mild malnutrition was defined as BMI Z-score of (-1.0) – (-1.9), moderate malnutrition as BMI Z-score of (-2) – (-2.9), and severe malnutrition was defined as BMI Z-score ≤ (-3.0). The age specific caloric intake of A-T patients was compared to the expected energy requirement (EER) of a healthy population with light physical activity - physical activity level (PAL) 1.5..

Results: Fifty three patients, 28 (53%) males, aged 14.6±5.2 years, followed for 7.6±4.3 years, were included. BMI-Z score was inversely correlated with age (r=0.48, Spearman's p<0.004). During early childhood, BMI-Z scores spanned the normal range (i.e BMI ranged between 3rd-95th percentiles). However a marked decline in BMI percentiles was observed after the age of 4 years in males and 7 years in females. The percentage of caloric intake compared to EER of healthy population with PAL 1.5 decreased with age (r=-0.5, Spearman's p<0.002). There was a positive correlation between the percentage of caloric intake of expected EER and BMI-Z-score (r=0.35, Spearman's p<0.05).

Gastrostomy tubes were inserted in 12 patients, leading to improvement in BMI-Z score from -5.1±2.4 to -4±2.9 (Spearman's, p=0.05). Only one gastrointestinal malignancy, a lethal sigmoid denocarcinoma, at age 16.5 years was found.

Conclusion: There is a progressive growth failure and low nutritional intake with age in A-T patients, starting in early childhood in males and at school-aged females. A pro-active approach and earlier PEG insertion as soon as the BMI Z-score start decreasing should be considered.
Objectives and study: A diagnostic dilemma presenting as pediatric gastrointestinal (GI) bleeding is a devastating scenario for any medical team. Knowing the presenting characteristics associated with a specific diagnosis and common causes of upper gastrointestinal bleeding (UGIB) locally, will allow for a systematic approach to diagnosis leading to prompt management and proper allocation of medical resources. This study was undertaken to determine associations between presenting clinical characteristics and etiologic diagnosis of pediatric patients presenting with UGIB.

Methods: All patients admitted for UGIB in a tertiary hospital from January 2002 to December 2012 were identified through records review. Patients with previously diagnosed causes of UGIB were excluded. The data gathered was analyzed to test for associations between the clinical characteristics and diagnosis as well as to test for accuracy of the presenting symptom in determining the cause of UGIB.

Results: There were 87 patients admitted for UGIB with an incidence rate of 0.08%. Mean age of the subjects was 6 years old, with 56% being males and 35% having malnutrition. The most common presenting symptoms were hematemesis (53%) and melena (30%). Thirty four percent of the subjects had endoscopically verified etiologic diagnoses, the most common being upper GI varices (41%), gastritis (16%) and ulcers (11%). The factors significantly associated with diagnosis of varices and gastritis were previous hospitalization and concomitant morbidity, with the presenting manifestation of hematemesis being sensitive and specific for the diagnosis of gastritis.

Conclusion: Previous hospitalization and concomitant morbidity are associated with varices and gastritis with hematemesis being sensitive and specific to gastritis. Although the incidence of UGIB can be as small as 0.08% this can significantly contribute to hospital mortality and morbidity and affect utilization of hospital resources. Therefore, the factors identified in this study could be useful in establishing a clinical pathway or approach to diagnosis for pediatric patients presenting with UGIB.
Esophageal eosinophilia in children undergoing esophagogastroduodenal endoscopy: a retroperspective analysis

Kleoniki Roka1, Daphne Margoni1, Paraskevi Papadogeorgou1, Amalia Patereli2, Kalliopi Stefanaki2, Ioanna Panayotou3, Alexandra Papadopoulou4, Eleftheria Roma5, George Chouliaras1

1University of Athens, First Department of Paediatrics, Athens, Greece
2Aghia Sophia Children’s Hospital, Pathology Department, Athens, Greece
3Iaso Children’s Hospital, Athens, Greece
4Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece
5University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece

Objectives and study: Esophageal eosinophilia (EE) is becoming increasingly common. We aimed to study the prevalence of EE in children who underwent first esophagogastroduodenal endoscopy (EGD) for different gastrointestinal symptoms.

Methods: Clinical, endoscopic and histological findings were assessed retrospectively using the patient’s medical records as well as the endoscopy and pathology reports. Subjects with ingestion of caustic substances were excluded. EE was defined by the presence of at least 15 eosinophils per HPF in esophageal biopsy. H.Pylori gastritis was defined by positive culture of gastric biopsy tissue or by positive histology and CLO-test or by positive one biopsy based test (either CLO or histology) and positive 13C-urea breath test.

Results: 2167 patients (median age 7.5 years, range 1 mo-18 y, 1076 boys) were included in the study. Celiac disease, H. Pylori gastritis and inflammatory bowel disease (IBD) were diagnosed in 206 (16.5%), 369 (9.5%) and 189 (8.7%) patients respectively. The remaining 1415 (65.3%) patients were used as control group.

EE was found in 129 children (5.9%, 85 boys). Male gender was associated with higher prevalence of EE (p<0.001). Celiac disease, H. Pylori gastritis and IBD coexisted with EE in 15.5%, 8.5% and 2.3% of the patients respectively. A 24 hour esophageal pH monitoring was performed in 30 patients with EE and acid reflux was found in 21 (70%) subjects.

With regards to clinical symptoms, children with retrosternal pain and/or dysphagia were 1.85 times more likely to have EE compared to those without (OR=1.85, 95% CI: 3.95, p=0.1) while, children with epigastric pain were 4.3 times less likely to have EE compared to those without (OR=4.3, 95% CI: 2.24-8.28, p<0.001).

With regards to macroscopic findings at endoscopy, children with the presence of esophageal rings were 9.99 times more likely to have EE compared to those without (OR=9.99, 95% CI: 4.47-22.29, p<0.0001) while, children with the presence of nodules in their esophagus were 1.89 times more likely to have EE compared to those without (OR=1.89, 95% CI: 1.15-3.08, p=0.01).

The prevalence of EE in children with celiac disease was comparable to controls (5.4% vs 6.7% respectively, p=0.36).

Conclusion: Retrosternal pain and/or dysphagia and endoscopic presence of rings or nodules in esophagus enhance the suspicion of esophageal eosinophilia in paediatric patients.
Refilling time in the triage: why not?

Silvia Salvatore¹, Samuele Caruggi¹, Martina Rossi¹, Chiara Armano¹, Elisa Rota¹, Alessandro Salvatoni¹

¹University of Insubria, Varese, Italy

Objectives and study: Severe dehydration represents a clinical emergency. A proper assessment is necessary to start urgent treatment. No specific parameter of dehydration is currently present in the triage line-up. The aim of the study was to evaluate the reliability and validity of Capillary Refill Time (RT) evaluated by the Triage nurse.

Methods: We prospectively enrolled children who presented to our Pediatric Emergency Department from July 2015 to June 2016, with symptoms of acute diarrhoea and vomiting. Acute diarrhoea was defined as more than 3 liquid stools in the last 24 hours and started in the last 72 hours. Vomiting was considered if more than 3 episodes were reported in the last 24 hours. Reliability of RT was assessed by comparing the measurements obtained by the triage nurse with those obtained by the clinicians during the physical examination. Each triage nurse was trained by one doctor for approximately 5 minutes about the correct way to elicit the RT at the beginning of the study. Similarly, the CDS scale was also explained. Validity of RT was demonstrated by using parameters suggestive of dehydration: difference in weight percentage whenever a previous recent (within 48 hours) weight was recorded in a health chart or emergency visit, number of episodes of diarrhoea and vomiting, oral rehydration therapy duration, cardiac and respiratory frequency and need for intravenous rehydration treatment. Comparison between RT and CDS-scale score was also considered. The scale’s discriminative ability was evaluated for the outcome of starting intravenous rehydration therapy. For statistical analysis, we used Cohen’s kappa to measure the inter-rater agreement and Pearson’s ρ to measure the linear dependence, considering p<0.05 as significant for both. We also used the area under Roc curve (AUC) to assess the RT and CDS discriminative ability.

Results: Participants were 172 children (range 9 months - 17 years). All nurses found easy to elicit the RT with the trained method whilst difficult, time consuming and less objective the CDS scale. Hence, the CDS scale was completed only by the clinicians during the physical examination. We found a fair inter-observer reliability, with a K Cohen of 0.30 (95% confidence interval [CI] 0.07, 0.53). Yet, it is likely related to a “kappa paradox” issue due to an imbalance in the frequency of the system variables, with a great excess of non-dehydrated children (84%) in our population. There was a significant correlation between RT and weight loss percentage (ρ = 0.4, 95% CI 0.08, 0.65), but only 32 children (18.6%) had a recent previous weight to accurately estimate the dehydration rate, determining a possible defective estimate. The scale’s discriminative ability yielded an area under the receiver operating characteristic curve (AUC) of 0.61 (95% CI 0.53, 0.68), with a similarity between RT and CDS-scale, matching the two ROC curves, with an AUC difference of 0.0181.

Conclusions: RT represents a fast and an handy tool to recognize dehydrated children who need a prompt rehydration and may be introduced in the triage line-up. A large study with dehydrated children is necessary to prove a good nurse-doctor inter-observer reliability.
Microbiota indicators of infants with infantile colic treated with Lactobacillus reuteri DSM 17938 for one month

Francesco Savino¹, Maria Garro², Simone Ceratto², Ilaria Galliano³, Paola Montanari³, Massimiliano Bergallo³

¹Città Della Salute e Della Scienza Di Torino, S.A.P.I. Chidren Hospital Regina Margherita, Turin, Italy
²Regina Margherita Children’s Hospital – Città Della Salute e Della Scienza, Department of Public Health and Pediatrics, Turin, Italy
³University of Turin, Department of Public Health and Pediatrics, Torino, Italy

Objectives and study: Infantile colic is defined as episodes of inconsolable crying in a healthy infant in the first three months of life and occurring at least three hours per day, at least three days per week, at least three weeks per month in a healthy infant.

The etiology, probably multifactorial, it is still not entirely clear. The immaturity of the digestive system, meteorism and abdominal distension would cause pain and inconsolable crying, but there are growing evidences in literature about gut microbiota composition and the employment of probiotics. In particular, some clinical trials have shown that Lactobacillus reuteri is able to significantly reduce crying time compared to simethicone, but its mechanism of action remains partially unknown.

We have analyzed some microbiota indicators in colicky infants compared to a control group made of non-colicky subjects, and we investigated whether there is a change of these indicators, in children with colic, after the use of L. reuteri DSM 17938.

Methods: We enrolled 59 infants, 32 colicky subjects (according to Rome Criteria III) (average age 42.3±19.1 days) and 27 non colicky ones (average age 45.4±22.3 days). We collected a faecal sample for each enrolled subject. Using a Real-Time PCR Taqman we have analyzed the absolute number and percentage of Escherichia coli, Lactobacillus and Bifidobacterium and the relationship Lacto/Coli, Bifido/Coli and Bifido/Lacto.

For the total bacterial counts we used the Broad-range PCR All-bact.

In the colic group, 32 infants received supplementation with 5 drops/day of L. reuteri DSM17938 for 1 month, after which we collected again a fecal sample and analyzed the gut microbiota indicators.

Comparisons between data were performed with Mann-Whitney U-Test. The statistical significance was set at p<0.05.

Results: Among all the analyzed indicators, we observed in colicky group (before probiotic treatment) a higher absolute number (p=0.0193) and percentage (p=0.0085) of Escherichia coli than in healthy controls. After administration of L. reuteri for 1 month, in infants with colic, we observed a significant increase of percentage of lactobacillus (p=0.048).

<table>
<thead>
<tr>
<th>Indicators</th>
<th>Colicky Day 0</th>
<th>Colicky Day 30</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of E. coli</td>
<td>1.689 (19.23)</td>
<td>7.29 (26.42)</td>
<td>0.236</td>
</tr>
<tr>
<td>% of Lactobacillus</td>
<td>9.51 (15.29)</td>
<td>23.13 (33.32)</td>
<td>0.048</td>
</tr>
<tr>
<td>% of Bifidobacteria</td>
<td>0.95 (12.85)</td>
<td>3.16 (8.32)</td>
<td>0.841</td>
</tr>
</tbody>
</table>
Data reported as median (IR) of genome/mg feces. * Mann-Whitney t-test.

**Conclusion:** In this study, we observed, in colicky infants, an alteration of the gut microbiota compared to controls, as highlighted by significantly higher concentrations of *E. coli*, a gas-producing bacteria. It is also noted that the probiotic *L. reuteri* DSM17938, administered for one month, is able to colonize the intestine and influence the microbiota, resulting in an increased percentage of *Lactobacillus* compared to total bacterial count.
Long-term gastrointestinal outcomes in children after necrotizing enterocolitis

Laura Schipper, A. Holvast, EMW Kooi, JBF Hulscher

1Beatrix Children's Hospital, University Medical Center Groningen, Paediatric Surgery, Groningen, Netherlands
2Beatrix Children's Hospital, University Medical Center Groningen, Paediatric Gastroenterology, Groningen, Netherlands
3Beatrix Children's Hospital, University Medical Center Groningen, Neonatology, Groningen, Netherlands

Objectives and study: Necrotizing Enterocolitis is a devastating condition, with high mortality and considerable morbidity among survivors. Data on long-term gastrointestinal outcome are rarely described. We performed this study to evaluate long-term gastrointestinal sequelae in children after being treated either conservatively or surgically for NEC.

Methods: A retrospective observational cohort study was performed in patients treated for NEC (Bell’s stage II-IIIb) in a tertiary neonatology unit in the Netherlands between 2000 and 2014. Patients who died during follow-up and patients with abdominal wall defects or intestinal atresia were excluded. Primary outcome measures were hospital readmission and surgical (re-)intervention because of gastrointestinal problems. Secondary outcome measure was growth restriction, defined as Z-scores below -2SD for height or weight, at age 1, 5 and 10.

Results: We included 120 patients (52% boys). Median gestational age was 30 weeks (range 25-41), median birth weight was 1327 g (range 535-4320). Median postmenstrual age at onset of NEC was 32 weeks (range 26-42). Seventy-three (61%) patients had NEC II, 47 NEC III. Sixty-nine (58%) patients were primarily treated conservatively for NEC and 51 surgically. Median follow-up was 48 months (range 3-180). Gastrointestinal symptoms occurred in 74/120 (62%) patients; 41 (34%) presented with obstipation, 32 (27%) with gastroenteritis and 27 (23%) with feeding problems. We found a post-discharge readmission rate of 35% (42/120 patients) due to gastrointestinal symptoms. Main reasons for readmission were ileus (22/120; 18%), gastroenteritis (15/120; 13%) and feeding problems (9/120; 8%). Previous surgical treatment was an independent risk factor (OR 4.8, 95% 2.1-10.7, p < 0.001) for readmission. Elective surgery for restoration of bowel continuity was performed in 38/120 (32%) patients. Additional non-elective surgical intervention was required in 25/120 (21%) patients, mainly because of ileus (18/120; 15%) and stenosis (13/120; 11%). Significantly more interventions were performed in primarily surgically treated patients compared to conservatively treated patients (15/51; 29% versus 10/69; 14%, p = 0.047). However, primary surgical treatment was not an independent risk factor for non-elective reoperations. Growth restriction in height or weight was seen in 8/112 (7%) patients at age 1, in 8/72 (11%) patients at age 5 and in 2/16 (13%) patients at age 10, with no significant difference between surgically and conservatively treated patients (4 vs. 4; p = 0.724 and 1 vs. 1; p = 1.000 respectively).

Conclusion: Long-term gastrointestinal sequelae after NEC leading to hospital admission and surgical intervention are significantly more common in patients treated surgically for NEC when compared to those treated conservatively. Growth retardation seems limited (13%). These outcomes may suggest the need for a gastrointestinal follow-up program for patients treated surgically for NEC.
A retrospective study looking at diagnostic tests used for lactose intolerance

Jennifer Shallop\textsuperscript{1}, Vinod Kolimarala\textsuperscript{2}, Hany Banoub\textsuperscript{3}, Mashhood Ayaz\textsuperscript{3}, Sonny Chong\textsuperscript{4}

\textsuperscript{1}Queen Mary's Hospital for Children, St. Helier Hospital, Gastroenterology Department, Carshalton, Surrey, United Kingdom
\textsuperscript{2}Epsom and St Heliers Hospital NHS Trust, Carshalton, United Kingdom
\textsuperscript{3}Queen Mary's Hospital for Children, St. Helier Hospital, Paediatrics, Carshalton, Surrey, United Kingdom
\textsuperscript{4}Queen Mary’s Hospital for Children, Epsom and St Helier University NHS Trust,, Carshalton, United Kingdom

Objectives and study: In patients with suspected symptoms of lactose malabsorption or intolerance, we looked at:

1) Common clinical symptoms that presented to St. Helier gastroenterology clinic
2) The different diagnostic tests used
3) Comparison of lactose hydrogen breath test versus quick mucosal lactase test in patients that had both
4) The outcome following a lactose free diet with or without lactase supplements
5) Finally, we aim to calculate the sensitivity, specificity, positive predictive and negative predictive value of varying tests used to diagnose lactose malabsorption.

Methods: A retrospective analysis of all patients referred to Queen Mary’s Hospital for children at St. Heliers hospital between 2009-2016. The data was collected using patient notes from an online database. Breath tests were carried out using hydrogen breath desktop gastrolyzer (Bedfont Scientific) following a challenge with oral lactose solution. The symptoms patients presented with were grouped into; chronic abdominal pain, chronic diarrhoea, a combination of both and others (flatulence, vomiting, failure to thrive).

Results: Of 84 patient collected, 43 had positive hydrogen breath desktop gastrolyzer test (Bedfont Scientific) gastrolyzer for lactose intolerance. 44 had quick lactase biopsies, of those 42 were positive and 2 were normolactasia. 23 were tested for both hydrogen breath test and quick mucosal lactase. Out of those 23, 16 had positive results. 63 out of 84 patients improved on lactase supplement/lactose free diet.

H2-breath test had a 78% sensitivity and 43% specificity. PPV of 81% and NPV of 37%.

Quick mucosal lactase test (Biohit) had a 100% sensitivity but 22% specificity. PPV of 83% and NPV of 100%.

Table:

<table>
<thead>
<tr>
<th>Lactose malabsorption</th>
<th>No lactose malabsorption</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Hydrogen breath test</td>
<td>A=35</td>
</tr>
<tr>
<td>Negative Hydrogen breath test</td>
<td>C=10</td>
</tr>
<tr>
<td>Positive Mucosal lactase test</td>
<td>A=35</td>
</tr>
<tr>
<td>Negative Mucosal lactase test</td>
<td>C=0</td>
</tr>
</tbody>
</table>
Conclusion: Although hydrogen breath test is less sensitive than the quick mucosal lactase test, it is more specific and easier to perform as the quick mucosal lactase test is an invasive endoscopic procedure. It is possible that the children who were symptomatic with mild hypolactasia, had an alternative diagnosis such as irritable bowel syndrome. The mainstay of management is having a lactose free diet with lactase supplementation tablets or lactase drops to which 75% of our patients responded.
Perceived prevalence and practice in the diagnosis and management of lactose intolerance in 1-5 year old children among healthcare professionals in South East Asia

Michelle Li Nien Tan¹, Seksit Osatakul², Badriul Hegar³, Leilani Muhardi⁴, Thomas Ludwig⁴, Jacques Bindels⁴, Eline Van Der Beek⁵, Seng Hock Quak¹

¹National University Health System, Paediatrics, Singapore, Singapore
²Prince of Songkla University, Faculty of Medicine, Paediatrics, Hat Yai, Thailand
³University of Indonesia, Faculty of Medicine, Paediatrics, Indonesia,
⁴Nutricia Research, Singapore, Singapore
⁵Nutricia Research, Utrecht, Netherlands

Objectives and study: Little is known about the prevalence of lactose intolerance (LI) in early childhood and there is a perceived heterogeneity in its diagnosis and management. We aim to gather information amongst healthcare professionals on the incidence and diagnosis of LI in children aged one to five years old in Southeast Asia (SEA).

Methods: An anonymous electronic survey using SurveyMonkey was sent to healthcare professionals registered in the database of the paediatric societies in Thailand, Indonesia and Singapore from June 2016 to October 2016. The survey received ethics approval from Singapore Ethics Board.

Results: In total, 283 healthcare professionals responded. 94.0% were paediatricians, 2.5% general practitioners and 3.5% others; of which 38.8% were in private practice and 36.3% from tertiary referral government hospitals, 25% were either from referral hospitals or others. 46.3% of responders were from Thailand, 36.4% from Indonesia and 17.3% from Singapore. 62.0% of responders had at least five years of clinical practice.

Almost 60 percent of participants who responded to the question on primary LI estimated its prevalence to be less than 5%. For secondary LI, 64.4% of respondents estimated the prevalence to be less than 15%. Rotavirus gastroenteritis was ranked as the top cause for secondary LI. Clinical diagnosis, milk challenge and stool pH were the three most commonly used methods for diagnosis. At least three-quarter of responders would recommend lactose-free milk for managing primary and secondary LI, while 5% of respondents would recommend total milk avoidance in primary LI.

Conclusion: In this survey with paediatricians as the majority of responders, primary LI was considered to be uncommon in SEA children in early childhood which is in contrast with the general belief. The diagnosis and management of LI is currently empirical rather than evidence-based. Further epidemiological studies with comparable methodology are required.
Effect of dietary elimination on psychosocial functioning status in breastfeeding mothers of infants with food allergy

Anil Safak Kacar, Tuba Mutluer, Nuray Uslu Kızılkan, Ali Sarper Taskiran, Cansin Sackesen

Koc University, Faculty of Medicine, Istanbul, Turkey
Koc University, Child and Adolescent Psychiatry, Istanbul, Turkey
Koc University, Paediatric Gastroenterology, Istanbul, Turkey
Koc University, Medical School, Paediatric Allergy, Istanbul, Turkey

Objectives and study: Childhood food allergies (FA) lead to a general decline in quality of life in connection with social, psychological and family functioning. The studies predominantly include adolescent and young adult age groups and IgE-mediated food allergies. However, the evaluation of the psychosocial functioning status of infants-children and their families with food allergies so early has not been considered to date. We aimed to define the psychosocial functioning status of nursing mothers whom are on an elimination diet for nursing infants with FA.

Methods: Nursing mothers of babies (1-12 months) who were diagnosed with FA were included. “Symptom Checklist 90” (SCL-90-R) screening test was performed to measure psychosocial symptoms. The optimal cut off score of “1” for SCL-90 subscales (Somatization, Obsessive-compulsive, Interpersonal sensitivity, Depression, Anxiety, Hostility, Phobic anxiety, Paranoid Ideation, Psychoticism) was evaluated and frequently used in previous research as a screening test. During the outpatient visit the participants filled the test and a questionnaire listing the numbers of the foods, which were eliminated from the diet of nursing mothers.

Results: Fifty-six mothers were included in the study. The mean age of the mothers and children were 31.2±3.2 years and 5.6±2.7 months respectively. Twenty (35.7%) mothers had an atopy history. Most of the mothers did not have a history of psychiatric disease (82.1%), but 4 had a history of depression, 3 general anxiety disorder, 2 postpartum depression and 1 sleep disorder. The mean duration of elimination diet was 99.1±78.7 days. Food elimination rates among nursing mothers were reported as following (n:49) : 2 (4.1%) eliminated 3-5 different foods, 9 (18.3%) eliminated 6-10 foods, 17 (34.6%) eliminated 11-20 foods and 17 (34.6%) took off more than 20 foods from diet. The results of SCL-90-R scale is shown at Table 1. The mean score for Somatization, Obsessive-compulsive, Interpersonal sensitivity and Depression were higher than the cut-off score “1” among participants. In the study group 66% and 71% of the participant mothers had a mean score higher than the cut-off level “1” for the subscales of obsessive-compulsive and depression, respectively. The depression and anxiety score of the mothers who eliminate more than 20 different foods from the diet was significantly higher than that of the ones who eliminate less (<20) foods, respectively (p = 0.02, p = 0.019).
Conclusion: The increase in the number of children with FA leads to a fear about foods in nursing mothers and this fear about the risk of foods lead mothers to stop eating many essential foods. The significant association between the degree of the food elimination and maternal psychiatric symptomatology brings a new aspect to the follow-up of mothers of infants with FA. These mothers may benefit from psychiatric evaluation and psychosocial support or encouraging attitude of the physicians to open the diet.

Table:

<table>
<thead>
<tr>
<th>Symptom name</th>
<th>Mean score</th>
<th>Minimum-maximum score</th>
<th>n/% (score&gt;1)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Somatization</td>
<td>1.05± 0.76</td>
<td>0-3.42</td>
<td>24/42.8</td>
</tr>
<tr>
<td>Obsessive-compulsive</td>
<td>1.42 ±0.88</td>
<td>0-3.34</td>
<td>37/66.1</td>
</tr>
<tr>
<td>Interpersonal sensitivity</td>
<td>1.46 ±0.76</td>
<td>0-3.34</td>
<td>20/35.7</td>
</tr>
<tr>
<td>Depression</td>
<td>1.46 ±0.77</td>
<td>0-3.38</td>
<td>40/71.4</td>
</tr>
<tr>
<td>Anxiety</td>
<td>0.84 ±0.74</td>
<td>0-3.2</td>
<td>15/26.8</td>
</tr>
<tr>
<td>Hostility</td>
<td>0.98 ±0.83</td>
<td>0-3.17</td>
<td>20/35.7</td>
</tr>
<tr>
<td>Phobic anxiety</td>
<td>0.54 ±0.70</td>
<td>0-3</td>
<td>11/19.6</td>
</tr>
<tr>
<td>Paranoid Ideation</td>
<td>0.83 ±0.84</td>
<td>0-3.1</td>
<td>16/28.5</td>
</tr>
<tr>
<td>Psychoticism</td>
<td>0.52 ±0.66</td>
<td>0-2.4</td>
<td>10/17.8</td>
</tr>
</tbody>
</table>
The attitude of the paediatricians towards a big number of food elimination among food allergic children and their nursing mothers

Efnan Melek, Tekin Nacaroglu, Mustafa Erkoçoğlu, Raziye Dut, Ebru Arik Yılmaz, Betül Büyüktiryaki, Ozge Uysal Soyer, Umit Sahiner, Deniz Akkaya, Nuray Uslu Kızılkan, Cansin Sackesen

Objectives and study: The prevalence of food allergy (FA) has increased in recent decades. Food allergy has different clinical presentations based on the immunological mechanisms. In this study, we aimed to determine the clinical approach of the pediatricians for the diagnosis and management of the FA.

Methods: One hundred and seventy pediatricians from different cities of Turkey fulfilled a questionnaire with 24 multiple choice and void filling questions.

Results: Sixty-nine percent of the participants were paediatricians, 17% were paediatric allergists, and 13% were paediatric gastroenterologists. Ninety percent of participants claimed that they took care of FA patients. Among the participants 83% said that they offer diet elimination for children with FA and 82% for their breastfeeding mothers. The most frequently eliminated foods are as follows for children and mothers respectively:

- Cow’s milk (79%-86%), egg (51%-50%), peanut (48%-43%), hazelnut (44%-36%), shellfish (27%-28%), food with additives (21%-26%), walnuts (29%-25%), almonds (28%-25%), soy (17%-23%), fish (23%-21%), strawberry (22%-21%), tomato (20%-18%), sesame (16%-17%), cacao (17%-14%), cow’s meat (10%-14%), kiwi (17%-14%), orange (8%-12%), blackberry (11%-9%), sheep meat (4%-8%), grapefruit (7%-7%), mango (7%-7%), bananas (7%-6%), mandarin (8%-6%), goat meat (3%-6%), chicken meat (3%-5%), gluten (8%-7%), lentil (6%-5%), lemon (4%-5%). The number of foods and percent of participants who offer to eliminate from breastfeeding mothers and children’s diet are as following respectively: 1 food (21-19%), 1-5 foods (51-48.5%), 5-10 foods (21-26%), more than 10 foods (28-35%).

Eighty-three of participants offer calcium supplement for the mother during breastfeeding with dairy elimination and 60% consult them with a dietitian.

Twenty-four percent of respondents postpone starting of complementary feeding over 6 months.

The questions including the symptoms of IgE and non-IgE mediated food allergy showed that 50% of the participants reported blood in stool as an IgE-mediated FA symptom and 19% reported anaphylactoid reactions as a presentation of non-IgE-mediated FA.

Conclusion: Elimination diets are suggested by a great majority of the paediatricians for both children and breastfeeding mothers including a large number of food groups even the ones known to be nonallergic for most of the time. It is noteworthy that participants did not differentiate IgE-mediated and
non-IgE-mediated BA findings with 100% accuracy. The introduction of interdisciplinary education programs can be proposed.
Objectives and study: The Bristol Stool Scale (BSS) is used worldwide to describe stool composition. However, this scale is not adapted for non-toilet-trained infants and young children. The goal was to replace the original drawings of the BSS with photos from infant defecations in diapers.

Methods: A core-set of 7 photos of infant defecations representing original descriptions of stools on the BSS was selected by a group of 11 experts, all experienced paediatric gastroenterologists. These photos were shown to 308 paediatricians, 290 nurses and 422 parents, who were asked to assign each photo to the best fitting description of stool on the BSS.

Results: BSS types 1 and 2 describe hard stools, and the photos were correctly assigned by 86 % of the paediatricians, 81 % of the nurses, and 72 % of the parents. BSS types 3 and 4 describe normal stool composition, and the photos were correctly assigned by 86 % of the paediatricians, 80 % of the nurses, and 67 % of the parents. Type 5 describes loose stools, and the photos were correctly assigned by 78 % of the paediatricians, 75 % of the nurses, and 65 % of the parents. Types 6-7 describe diarrhoea, and the photos were correctly assigned by 93 % of the paediatricians and nurses and 90 % of the parents. Fleiss’ kappa value (above 0.60: substantial agreement; 0.41 to 0.60: moderate agreement) overall for all data was 0.55. This value fluctuated also in function of the country, ranging from 0.45 to 0.59. The Fleiss’ kappa value for the paediatricians was 0.69, for the nurses 0.58 and for the parents 0.48.

Conclusion: We developed and validated a paediatric BSS based on photos of infant stools. Healthcare professionals describe stool composition better than parents. "Diarrhoea" was best scored by the 3 groups. .
Clinical characteristics of Thai infants experiencing minor gastrointestinal discomfort

Boosba Vivatvakin 1, Sheri Volger 2, Palittiya Sintusek 1, Wimol Leewiboonsilp 3, Jowena Lebumfacil 4, Robert Northington 2

1 Chulalongkorn University, Department of Pediatrics, Faculty of Medicine, Bangkok, Thailand
2 Nestlé Nutrition, R & D, King of Prussia, United States
3 Nestle (Thai) Ltd., Wyeth Nutrition, Bangkok, Thailand
4 Wyeth Nutrition Philippines, Makati City, Philippines

Objectives and study: Many otherwise healthy infants exhibit symptoms of gastrointestinal (GI) discomfort during the first 12 months of life. The objective of this study is to describe the clinical characteristics of Thai infants considered by their parents as being fussy and/or crying frequently and experiencing GI discomfort.

Methods: Thai infants enrolled in this study were part of a larger multicounty, randomized controlled trial examining the effect of a new infant formula on GI intolerance. Children enrolled in this study were full-term, formula-fed infants with parent-reported infant crying or fussing for 2 to 3 hours daily and at least one symptom of GI discomfort (i.e., a stooling difficulties or moderate to severe gassiness), identified using a brief screening questionnaire. As part of the baseline assessment, parents completed validated infants’ cry and fuss behavior diaries (the Baby’s Day Diary) and also completed a GI symptom diary. Stool consistency was assessed with a validated 5-point scale (1=watery; 2=runny; 3=mushy-soft; 4=formed; 5=hard). In addition, infant anthropometrics were measured and GI tolerance was assessed with the parent-reported Infant GI Symptom Questionnaire (IGSQ), which includes 13 items in 5 symptom domains (stooling, spitting-up/vomiting, crying, fussiness, flatulence) that are summed to generate an index score that ranges from 13-65 (lower scores indicate better parent-perceived GI tolerance). Baseline breath hydrogen was measured following a 4-hour fast at 30-minute intervals for 180 minutes after ingestion of lactose (dissolved in water) 2gm/kg body weight to evaluate lactose malabsorption.

Results: A total of 63 infants (male, n=32) with a mean±SD age of 50.6±9.1 days were enrolled in the study. Mean z-scores for weight and length at enrollment for males and females were -0.44 ±.79, -0.38±0.99 and -0.62±0.72, -0.41 ±0.76 respectively. Parental-reported infant crying or fussiness time was 135±93 minutes/day, and caregivers held the infants an average of 422±132 minutes daily. Mean stool consistency score was 2.80±0.46, with the majority (>60%) of infants’ stools reported as mushy. Infant IGSQ scores were generally high 32.8±8.3, compared to mean IGSQ scores for healthy infants without GI intolerance (range 14.0-23.0), suggesting notable GI symptom burden. Of the 63 infants examined, 39 (61.9%) were found to have time zero breath hydrogen values >20 ppm, raising the suspicion of small intestinal bacterial overgrowth (SIBO). 25 (39.7%) infants had a positive hydrogen breath test indicating lactose malabsorption.

Conclusion: Thai infants identified by their parents as being fussy and/or crying frequently and having GI discomfort were shown to have notable levels of GI symptom burden and a high percentage of positive hydrogen breath test results. These clinical findings underscore the importance of the clinical assessment of minor GI discomfort in infants and the role of SIBO and lactose malabsorption as contributors to GI intolerance in this population.

Disclosure of interest: This research study was funded by Nestlé Nutrition. Sheri Volger and Robert Northington are Nestlé employees. Wimol Leewiboonsilp is an employee of Wyeth Nutrition Thailand and Jowena Lebumfacil is an employee of Wyeth Nutrition Philippines.
Common variants in GAL, GAP43 and NRSN1 and interaction networks contribute to the risk of Hirschsprung disease

Yang Wang¹, Jun Wang¹, Wei Cai²

¹Shanghai Jiao Tong University, Department of Pediatric Surgery, Xin Hua Hospital, School of Medicine, Shanghai, China
²Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Pediatric Surgery, Shanghai, China

Objectives and study: Hirschsprung disease (HSCR) is a severe multifactorial genetic disorder, caused by the absence of enteric neurons along a variable region of the gastrointestinal tract. Genome-wide studies indicated GAL (galanin and GMAP prepropeptide), GAP43 (growth associated protein 43) and NRSN1 (neurensin 1) might contribute to the altered risk in Hirschsprung disease. In the present study, we aimed to interrogate genetic variations in GAL, GAP43 and NRSN1, and assess gene-gene interactions, which might be involved in HSCR susceptibility in Han Chinese.

Methods: Genotype distributions of the 18 polymorphisms showed no significant deviations from Hardy-Weinberg equilibrium in either cases or controls (P > 0.05). We observed statistically significant differences between 104 HSCR subjects and 151 normal controls at five genetic variants (GAL: rs1042577, allele, P = 0.0004, genotype, P = 0.003; GAP43: rs283367, allele, P = 0.002, genotype, P = 0.004, rs14360, allele, P = 0.002, genotype, P = 0.004; NRSN1, rs10946675, allele, P = 0.004, genotype, P = 0.01, rs3829810, allele, P = 0.005, genotype, P = 0.02). For each of the three genes, the haplotypes combining all markers were the most significant (GAL: global P = 6.78 × 10⁻⁸; GAP43: global P = 4.16 × 10⁻¹²; NRSN1: global P = 9.51 × 10⁻³). By using SNPsyn, GO enrichment and MDR analyses, we further explored the interactions among GAL, GAP43, NRSN1 and our previous identified RELN, GABRG2 and PTCH1 gene. Significant gene-gene interactions were observed among these six genes (Figure 1).

Results: Genotype distributions of the 18 polymorphisms showed no significant deviations from Hardy-Weinberg equilibrium in either cases or controls (P > 0.05). We observed statistically significant differences between 104 HSCR subjects and 151 normal controls at five genetic variants (GAL: rs1042577, allele, P = 0.0004, genotype, P = 0.003; GAP43: rs283367, allele, P = 0.002, genotype, P = 0.004, rs14360, allele, P = 0.002, genotype, P = 0.004; NRSN1, rs10946675, allele, P = 0.004, genotype, P = 0.01, rs3829810, allele, P = 0.005, genotype, P = 0.02). For each of the three genes, the haplotypes combining all markers were the most significant (GAL: global P = 6.78 × 10⁻⁸; GAP43: global P = 4.16 × 10⁻¹²; NRSN1: global P = 9.51 × 10⁻³). By using SNPsyn, GO enrichment and MDR analyses, we further explored the interactions among GAL, GAP43, NRSN1 and our previous identified RELN, GABRG2 and PTCH1 gene. Significant gene-gene interactions were observed among these six genes (Figure 1).
Figure 1. Gene-Gene interaction networks among GAL, GAP43, NRSN1 and our previous identified RELN, GABRG2 and PTCH1 gene. (A) (B) Distribution of SNP pair synergy (Syn) and information gain (I). The scores for SNP pairs on true data are plotted in a I versus Syn scatterplot (blue dots) with the superimposed null-distribution (red dots). The selection criteria for SNP pairs are: synergy ratio (Syn/I) ≥ 0.5 and FDR ≤ 0.05, by which the region defined is highlighted in blue. Distributions of Syn and I are plotted in histograms on the sides of the scatterplot. (C) (D) Gene-Gene interactions. Genes shown in the interaction network are connected if the SNP pair meets the selection criteria (i.e. synergy ratio (Syn/I) ≥ 0.5 and FDR ≤ 0.05). (A) (C) The interactions among GAL, GAP43 and NRSN1. (B) (D) The interactions among GAL, GAP43, NRSN1, RELN, GABRG2 and PTCH1.
Conclusion: Our study for the first time indicates that genetic variants within GAL, GAP43 and NRSN1 and related gene-gene interaction networks might be involved in the altered susceptibility to HSCR in the Han Chinese population, which might shed more light on HSCR pathogenesis.
The short and long-term outcome of children with lactose intolerance

Anat Yerushalmy Feler, Hagai Soback, Ronit Lubetzky, Dror Weiner, Margalit Dali-Levy, Shlomi Cohen

1 Tel Aviv Sourasky Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
2 "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatric Department, Tel Aviv, Israel
3 "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatrics, Tel Aviv, Israel
4 "Dana-Dwek" Children's Hospital, Tel Aviv Sourasky Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
5 "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology Unit, Tel Aviv, Israel
6 "Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel

Objectives and study: Lactose intolerance is a frequent gastrointestinal diagnosis in children. Although common, data regarding the natural history of lactose intolerance in children is lacking. Our aims were to define the short and long-term outcome of children with lactose intolerance.

Methods: All children who performed the hydrogen breath test in the pediatric gastroenterology unit, "Dana-Dwek" Children's Hospital, during the years 2012-2013 were included. Patients with positive test results (rise of > 20 PPM) were assigned to the study group, while patients with negative results served as controls. We collected data regarding the dietary instructions that were given to the patients by their local physicians, improvement in symptoms and attempts for re-introduction of lactose. The current quality of life of the study group compared to controls was assessed by the Pediatric Quality of Life Inventory (PedsQL): gastrointestinal symptoms scale and quality of life questionnaire, at least three years after the diagnosis. The scores are presented in a 0-100 scale (0-higly symptomatic/lowest quality of life, 100-free of symptoms/highest quality of life).

Results: Two hundred and three children were included, 154 (75.8%) in the positive test group and 49 (24.2%) in the control group. The average age during the test was 10.27±2.73 years. One hundred twenty-one patients (78.6%) in the study group were guided to start lactose free/reduced diet while only 11 patients (7.2%) were advised to enrich their diet with calcium. Under the recommended diet, 24 (15.7%) patients indicated no improvement of their symptoms. Most of patients (119, 77.8%) attempted to re-introduce lactose, with 65 (42.8%) indicated deterioration in their symptoms. Nowadays, 96 patients (62.3%) are still under lactose free/reduced diet. The current quality of life was assessed after a median of 3.3 (interquartile range (IQR) 3.3-3.5) years. The total gastrointestinal and quality of life scores are described in Table 1.
Table: Total gastrointestinal and quality of life scores

<table>
<thead>
<tr>
<th>Currently treated</th>
<th>Study group</th>
<th>Control group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N=154</td>
<td>N=49</td>
</tr>
<tr>
<td>Currently treated</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>N=58</td>
<td></td>
<td></td>
</tr>
<tr>
<td>P</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total N=96</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total gastrointestinal scores [median (IQR)]</td>
<td>87.93 (80.17-93.1)</td>
<td>92.24 (82.75-95.04)</td>
</tr>
<tr>
<td>Total quality of life scores [median (IQR)]</td>
<td>75 (65.86-80.76)</td>
<td>75 (65.38-82.69)</td>
</tr>
</tbody>
</table>

Conclusion: Children with a positive hydrogen breath test under long-term lactose free/reduced diet have significantly more gastrointestinal symptoms, compared to patients who are no longer under restrictive diet or controls. Further studies are merited to better characterize this group in terms of diagnosis and treatment.
Cow’s milk protein allergy awareness and practice among Turkish paediatricians: a questionnaire-survey

Objectives and study: This cross-sectional questionnaire-survey was designed to evaluate cow’s milk protein allergy (CMPA) awareness and practice among paediatricians in Turkey.

Methods: A total of 410 paediatricians (56.3% general paediatricians (P), 23.7% paediatric gastroenterologists (PG), 12.2% paediatric allergists (PA), 7.8% other subspecialties) were included. The questionnaire elicited diagnostic symptoms, tests for diagnosis, use of therapeutic formulas with respect to clinical presentations and feeding patterns and timing for re-challenge. Data were also evaluated with respect to sub-specialties of participants.

Results: Atopic dermatitis (91.5%), diarrhoea (88.0%), blood in stool (87.8%) and colic (83.7%) were overall the most common symptoms considered suggestive of CMPA by P. Continuation of breast feeding via elimination of cow’s milk protein and products from maternal diet was the selected therapeutic option (82.7%, 85.6%, 62.0% by P, PG and PA, respectively) in exclusively breast-fed infants diagnosed with CMPA while amino acid-based formula (AAF) (46.8%, 48.5%, 60.0% by P, PG and PA, respectively) and extensively hydrolysed formula (eHF) (20.8%, 32%, 26% by P, PG and PA, respectively) was selected in formula-fed infants. Overall, AAF was the most commonly selected formula for infants presenting with anaphylaxis (58.8%), enterocolitis (40.7%) or multiple food allergies (52.0%) by P. None of other types of mammalian milk was considered to be appropriate in infants with CMPA (57.1%, 80.4%, 66.0% by P, PG and PA, respectively). Earliest time to re-challenge after a therapeutic diet was identified as 6 months (54.1%, 43.3%, 54.0% by P, PG and PA, respectively). In at-risk infants with no chance of exclusive breastfeeding, AAF was the most commonly (39.8%, 35.1%, 48.0%) selected formula followed by eHF (21.2%, 16.5%, 18.0%) and pHF (19.5%, 25.8%, 18.0%) by P, PG and PA, respectively for CMPA prophylaxis. Significant difference was noted between paediatric sub-specialties with respect to selection of first-line treatment among infants with or without exclusive breast-feeding, appropriateness of using other types of mammalian milk, earliest time to re-challenge in CMPA and formula recommendation for at-risk infants with no chance of exclusive breast feeding.

Conclusion: Our findings revealed high awareness of CMPA among Turkish paediatricians in terms of clinical presentation and appropriate management of CMPA among exclusively breast-fed infants in accordance with guidelines. However, CMPA practice among Turkish paediatricians, non-gastroenterologists in particular, needs to be improved in terms of selection of therapeutic formulas among formula-fed infants and at-risk infants, avoidance of other mammalian milks and optimal time to re-challenge consistent with guideline-based indications.

Disclosure of interest: Aysugul Alptekin Sarioglu, M.D. is an Abbott employee. Other authors declare that they have no conflict of interest.
Laryngeal cleft as anatomical cause of oropharyngeal dysphagia in paediatric age

Johanna Martínez Osorio¹, José Vicente Arcos¹, Mariela Mercedes de Los Santos¹, Raquel García Ezquerra¹, Oliver Heinz², Javier Martin de Carpi³, Sergio Pinillos Píson³

¹Sant Joan de Déu Hospital, Barcelona, Paediatric Gastroenterology, Hepatology and Nutrition Unit, Barcelona, Spain
²Sant Joan de Déu Hospital, Barcelona, Department of Otolaryngology, Barcelona, Spain
³Sant Joan de Deu Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain

Objectives and study: Oropharyngeal dysphagia (OD) in children is manifested with multiple symptoms, being the cough with the feeding the main. Within the anatomical causes of OD, the laryngeal cleft (LC) is a rare cause (less than 0.3% of laryngeal congenital malformations) that can be classified in four types based on the caudal extension from the interarytenoid area towards the carina. Type I and II are both supraglottic and types III and IV extend through the cricoid lamina to the cervical and intrathoracic trachea. Symptoms are non-specific and the delay in diagnosis leads to multiple complications. The objective of our study is to describe the clinical course, management and outcomes of children with OD produced by type I laryngeal clefts.

Methods: we selected patients with OD secondary to type I LC diagnosed between 2015-2016 in a tertiary-teaching hospital. Data from baseline characteristics, clinical presentation, analysis of feeding function, treatment and prognosis were collected.

Results: Ten children were identified with type I LC in our Dysphagia Unit, six boys and four girls with a median age of diagnosis of 5 years (range 1-12 years). We identified significant comorbidities in eight: three with Down’s Syndrome, two extremely premature infant, one with left vocal cord paralysis after patent ductus arteriosus surgery, one with esophageal atresia type III and the last one with laryngotracheomalacia and congenital subglottic stenosis. All patients presented with cough/choking after liquid ingestion, with chronic pulmonary infections. The functional tests performed were: feeding observation (100% of cases), videofluoroscopic swallowing study (VFSS) (80% of cases, in three of them anatomical defect was suggested with later aspirations) and videoendoscopic swallowing study (VEES) (50% of cases, in four of them LC was suggested). LC confirmation was performed in all patients with direct laryngoscopy (DL) under sedation. Four patients with suspected LC are awaiting confirmation with DL.

In eight patients, cleft repair was performed with injection laryngoplasty without complication. Before the repair four patients received nasogastric tube feeding and four were with adapted feeding. The evolution after surgery has been remarkable and all patients are feeding by mouth with a significant reduction in respiratory infections.

Two patients are on an adapted diet (liquids with thickening and volume control) with improvement of symptoms.

Conclusion: The LC should be taken into account in the differential diagnosis of children with OD, since delayed diagnosis can lead to chronic aspiration disease. It should be suspected especially in neurologically healthy patients with persistent symptoms and liquid dysphagia with or without anatomical abnormalities of the airway. Although VFSS and VEES help in the diagnosis process, the definitive diagnosis should be made by DL. Cleft repair surgery is the procedure of choice as it is safe and effective.
Efficacy of low fodmap diet in children with functional abdominal pain and the role of the breath test as predictor of response

María Luisa Baranguan1, Ignacio Ros1, Ruth García Romero1, Eduardo Ubalde Sainz1, Jose Miguel Martinez de Zabarte1, Monica López Campos1

1Miguel Servet Children's Hospital, Pediatric Gastroenterology and Nutrition Unit, Zaragoza, Spain

Objectives and study: Functional abdominal pain is a common disorder in childhood, and many treatments have been suggested, including dietary interventions. One of them is the low FODMAP (fermentable oligosaccharides, monosaccharides, disaccharides and polyols) diet, which has been shown to be a good treatment for irritable bowel syndrome in adults. This diet is based on the restriction of these poorly absorbed, short-chain carbohydrates, which are osmotically active and rapidly fermented by colonic bacteria, increasing gas production and producing luminal distension, leading to abdominal pain and bloating.

The aim of this study is to investigate the efficacy of a low FODMAP diet in the treatment of functional abdominal pain in children, and also to evaluate the relationship between small intestinal bacterial overgrowth and the improvement after following the diet.

Methods: We performed a prospective trial involving children with functional abdominal pain from our Paediatric Gastroenterology Unit. Information about abdominal pain features was collected during 3 days, a hydrogen and methane breath test was performed to rule out small intestinal bacterial overgrowth and later on patients followed a two-week low FODMAP diet. Afterwards, information about abdominal pain features was collected again, and breath test was repeated in those with initially positive results. We classified as responders those with a ≥ 50% decrease in abdominal pain frequency.

Results: Fourteen children with functional abdominal pain undertook this trial, and after that, they showed fewer daily abdominal pain episodes compared to baseline (2.2 versus 4.2 daily episodes), less pain severity compared to baseline (measured by 10 cm visual analogue scale, 2.7 versus 4.9 cm), and less gastrointestinal symptoms, as abdominal bloating and flatulence.

Finally, 50% of them were classified as responders, and these responders showed a longer story of abdominal pain than non-responders (66.8 months versus 35.8 months on average).

Initially, breath test was positive in 5 patients, and even though the average of hydrogen production was reduced after following the diet (21.4ppm versus 31.2ppm at the beginning), we found that only 3 of them were finally classified as responders.

At the end of the trial, 64% of families indicated they found it easy to follow the diet, and also 64% were satisfied with the low FODMAP diet.

Conclusion: The low FODMAP diet for 2 weeks was effective in the treatment of functional abdominal pain in half of our patients.

Breath test results don’t seem to be a good predictor of response to a FODMAP diet.

This diet might be a useful tool in the treatment of functional abdominal pain in children.
The role of some hormones and fractions of hydroxyproline in the pathogenesis of gastroesophageal reflux disease in children

Natalia Butorina¹, Galina Volynets ²

¹Izhevsk State Medical Academy, Izhevsk, Russian Federation
²Scientific Center of Children Health, Moscow, Russian Federation

Objectives and study: metabolism of collagen, secretion of hormones and an estimation of conjugation of their changes in GERD in children were studied.

Methods: 62 children with GERD were examined. Group of control patients consisted of 32 children. Concentration of insulin and cortisol by the methods of electrohemoluminescent immunoanalysis «ECLIA», gastrin and somatostatin in the blood by the methods of immunofermental analysis were determined. Fractions of hydroxyproline in the stomach juice by the method of P.N. Sharaev and et al (1998) were studied.

Results: Different stage of the esophageal mucosa lesion was found out in children with GERD: 40 children (58%) had I stage of esophagitis, 24 children (38,8%), - II stage, 2 children (3,2%) - III stage. It was revealed that children with GERD demonstrated increased decay of collagen level in the mucous membrane of the esophagus and the stomach. High level of free hydroxyproline (29,6±3,2 mkm/L; p<0,05) and peptin-connected hydroxyproline (25,5±2,1 mkm/L; p<0,01) testify to it. High level of cortisol (389±15,5 nmol/L; p<0,05) in children with GERD is the cause of collagen decay. Insulin level increase in GERD (28,5±3,2 µU/ml; p<0,05) is the compensatory reaction to catabolic processes. We revealed changes of gastrointestinal hormones. Children with GERD at the age of 9-12 years old had an increased level of somatostatin but low index of gastrin. But children older of 12 years demonstrated gastrinemia and low index of somatostatin.

Conclusion: Increased concentration of cortisol in the blood influences on mucosa and results in disturbance of dynamic equilibrium of aggressive-protective factors of gastro-duodenal zone. Decomposition of collagen takes place. Increase of insulin level testifies to stimulation of the protective and adaptation mechanisms in children with GERD.
Clinical findings in children with functional constipation, evaluation of life quality, psychosocial status of patients and parents

Yeliz Cagan Appak1, Şermin Yalın Sapmaz2, Güzide Doğan3, Ahmet Herdem2, Beyhan Cengiz Özyurt4, Erhun Kasırga3

1Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, İzmir, Turkey
2Celal Bayar University School of Medicine, Department of Child and Adolescent Psychiatry, Manisa, Turkey
3Celal Bayar University School of Medicine, Department of Paediatric Gastroenterology, Manisa, Turkey
4Celal Bayar University School of Medicine, Department of Public Health, Manisa, Turkey

Objectives and study: In this study, clinical and sociodemographic findings of patients with functional constipation (FC), quality of life and evaluation of psychological states of children and parents is aimed.

Methods: According to Roma III diagnosis criteria, 32 patients with FC and 31 healthy controls were included. Patients’ clinical and sociodemographic data set associated with constipation was determined and the life quality was evaluated by the Paediatric Quality of Life Scale for Children. For the screening of emotional and behavioral problems in children, Strengths and Difficulties Questionnaire was used. To evaluate the parents and family Beck Depression Inventory, State-Trait Anxiety Inventory, Family Assessment Device, Parental Attitude Research Instrument was used.

Results: 56.2% patients with FC were female and average age of FC patients was 8.6±2.9 years. In 21.9% of the patients and in 16.7% of healthy controls force in toilet training was found and no significant difference was observed (p=0.7). Consumption of fiber-rich fruits and vegetables was found to be similar in patients and healthy controls. Our study revealed 29.6% of the patients attending to school were not using school toilet however no statistically significant difference was observed between healthy controls and patients (p=0.7). In our study, constipation history in families were detected higher in patients (p=0.016). 43.8% of the patient had enuresis and statistically significant difference was found (p=0.001). %28.1 of the patient had encopresis too. Our study revealed decrease in constipation rate with increasing education level of parents, higher rate of constipation in families with less income than expenses and lower rate of working mother in patients with constipation. Life quality scores of patients and their families were found to be statistically significantly lower than of healthy controls (Table). Emotional problems (p=0.0001) and peer problems (p=0.001) were found to be statistically significantly higher than of healthy controls. Parental concerns (p=0.005) and as well as attitude of over-parenting (p=0.014) was found significantly higher in patients. Statistically significant difference was also observed between the groups in terms of mean score of authoritarian attitude dimensions (p=0.0001). Attitude of hostility and rejection (p=0.036) and marital discordance (p=0.016) was found significantly high in patient families.
Table. Pediatric Quality of Life Scale, Strengths and Difficulties Questionnaire Findings in Parents

<table>
<thead>
<tr>
<th>Paediatric Life Quality Scale</th>
<th>Child Notification</th>
<th>Parental Notification</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td><strong>FC</strong></td>
<td><strong>Control</strong></td>
</tr>
<tr>
<td></td>
<td>Mean±SD</td>
<td>Mean±SD</td>
</tr>
<tr>
<td>Physical health total score</td>
<td>69.82±17.49</td>
<td>78.83±17.59</td>
</tr>
<tr>
<td>Emotional functioning total score</td>
<td>58.43±22.66</td>
<td>79.19±17.61</td>
</tr>
<tr>
<td>Social functioning total score</td>
<td>74.84±22.48</td>
<td>91.77±13.26</td>
</tr>
<tr>
<td>School functioning total score</td>
<td>62.77±21.45</td>
<td>82.90±13.83</td>
</tr>
<tr>
<td>Psychosocial health total score</td>
<td>65.49±16.90</td>
<td>84.13±13.19</td>
</tr>
<tr>
<td>Scale total score</td>
<td>67.12±15.86</td>
<td>82.29±13.45</td>
</tr>
</tbody>
</table>

Conclusion: FC affect children’s social and functional functions, may cause to deterioration in the psychology of the patient and family and impaired life quality.
Prevalence of functional gastrointestinal disorders in Russian children

Natalya Ilenkova¹, Vladimir Chikunov¹

¹Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation

Objectives and study: Functional gastrointestinal disorders (FGIDs) are a group of disorders of the digestive system in which the chronic or recurrent symptoms cannot be explained by the presence of structural or tissue abnormality. Pediatric functional gastrointestinal disorders are a common problem worldwide. So far, epidemiologic data about FGIDs with respect to infants and younger children in Russia is limited. In this prospective study we aim to determine the prevalence of functional gastrointestinal disorders in young children in single Russian center.

Methods: We have enrolled infants and children aged between 0 and 4 years, who attended in University clinic, Krasnoyarsk, Russia, for a regular check-up. Two separate study questionnaires have been developed: one for children aged between 0 and 6 months, and the other one for children aged between 7 months and 4 years. Each questionnaire consisted of 3 parts evaluating: 1) clinical history 2) symptoms 3) socio-demographic information on the family and exposure to stressful life events. FGIDs were defined according to the Rome criteria IV (2016).

Results: A total of 300 children has been included: Group 1 consisted of 180 children (male 110 (61.1%), female 70 (38.9%)) aged between 0 and 6 months, whilst Group 2 consisted of 120 children (male 50 (41.7%), female 70 (58.3%) aged between 7 months and 4 years of age. According to the Rome IV (2016) criteria, the prevalence of FGIDs in children between 0 and 6 months of age was 23%, while in children aged between 7 months and 4 years the prevalence of FGIDs was 18.33%. Specifically, the most common FGIDs in children from Group 1 were infant regurgitation (5.55%) and infant colic (19.44%), whereas in children from Group 2 the most common FGID was functional constipation (31.66%). Data regarding the prevalence of all FGIDs in each age group are summarized in the Table.

Table: Prevalence of functional gastrointestinal disorders in Russian children

<table>
<thead>
<tr>
<th>FGIDs</th>
<th>0 – 6 months</th>
<th>7 months – 4 years</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n = 180</td>
<td>n = 120</td>
</tr>
<tr>
<td>G1. Infant regurgitation</td>
<td>10 (5.55%)</td>
<td>1 (0.83%)</td>
</tr>
<tr>
<td>G2. Rumination syndrome</td>
<td>2 (1.11%)</td>
<td>1 (0.83%)</td>
</tr>
<tr>
<td>G3. Cyclic vomiting syndrome</td>
<td>1 (0.55%)</td>
<td>4 (3.33%)</td>
</tr>
<tr>
<td>G4. Infant colic</td>
<td>35 (19.44%)</td>
<td>3 (1.65%)</td>
</tr>
<tr>
<td>G5. Functional diarrhea</td>
<td>4 (2.22%)</td>
<td>8 (6.67%)</td>
</tr>
<tr>
<td>G6. Infant dyschezia</td>
<td>10 (5.55%)</td>
<td>1 (0.83%)</td>
</tr>
<tr>
<td>G7. Functional constipation</td>
<td>7 (3.88%)</td>
<td>38 (31.66%)</td>
</tr>
<tr>
<td>Any FGIDs</td>
<td>69 (23%)</td>
<td>55 (18.33%)</td>
</tr>
</tbody>
</table>

FGIDs: functional gastrointestinal disorder

Conclusion: This community sample, collected in Russian clinical center, demonstrated that FGIDs are common in young children. Prevalence of FGIDs tends to be higher in the first months of life.
**Association of vitamin D level and the quality of life in adolescents with irritable bowel syndrome**

YoungSun CHO¹, sujin Jeong²

¹Cha Medical University, Pediatrics, Seoul, Korea, Rep. of South  
²Cha Medical University, Pediatric Gastroenterology, Seoul, Korea, Rep. of South

**Objectives and study:** There was a recent report on the successful treatment of diarrhea-predominant irritable bowel syndrome (IBS) with high dose of oral vitamin D supplement. Vitamin D could improve various symptoms of IBS through its beneficial effect on inflammation and psychological factors. So, the object of this study is to determine the relationship between vitamin D level and the severity of IBS symptoms that may affect the patients’ quality of life.

**Methods:** 129 adolescents aged 10-17 years old (70 boys and 59 girls, mean age 16.3±6.6 years old) were included in this study from 2014 to 2016. IBS patients were diagnosed by ROME III criteria and classified to three types by clinical manifestation: IBS with constipation (IBS-C, n=30), IBS with diarrhea (IBS-D, n=66), and IBS with mixing constipation and diarrhea (IBS-M, n=33). Severity of IBS symptoms and school performance were evaluated by a questionnaire. Demographic information such as age, gender, and body measurement was collected through medical record review. Vitamin D levels were measured by serum 25-hydroxyvitamin D.

**Results:** The average vitamin D level of IBS patients is 12.3±1.9ng/mL. This study shows that vitamin D level is significantly lower in winter than summer and autumn. There was no statistically significant difference in the average vitamin D level, as well as baseline demographic data, according to the types of IBS. Association of the severity of abdominal pain with vitamin D level shows negative correlation (p=0.001). Also, there was a statistically significant difference in the mean vitamin D level (p<0.001) between the good and bad school performance groups.

**Conclusion:** This study shows that the average vitamin D level is low in IBS adolescents. There is no difference of the average vitamin D level according to the types of IBS. Based on the result of this study, the severity of abdominal pain and school performance in IBS patients are related to vitamin D level. Therefore, vitamin D supplement could be considered as a choice of therapeutic methods to Korean IBS adolescent patients.
The predictive value of colon transit time and anorectal manometry in the approach of faecal continence in children with spina bifida

Charlotte Daeze, Saskia Van de Velde, Ann De Guchtenaere, Stephanie Vanbiervliet, Myriam Van Winckel, De Bruyne Ruth

1University Hospital Ghent, Paediatrics, Ghent, Belgium
2University Hospital Ghent, Paediatric Gastroenterology and Hepatology, Ghent, Belgium
3Zeepreventorium, Paediatric Nephrology, De Haan, Belgium

Objectives and study: Only a minority of children with spina bifida (SB) achieve spontaneously faecal continence. Despite adequate bowel management, a substantial part of them still suffers from faecal incontinence, which is associated with major psychological problems. At the present, there is no standard protocol to predict whether these children will achieve continence spontaneously, nor what the designated treatment is for bowel management.

The aim of the current study is to analyze colon transit time (CTT) and anorectal manometry (ARM) in children with SB as a predictor of spontaneous faecal continence.

Methods: SB patients (2.5-7 years old), who underwent a CTT study and/or ARM before starting bowel management, were asked to participate in this retrospective study. A questionnaire about the presence of constipation or faecal incontinence was completed. Constipation was present if ≥2 of the Rome III criteria for paediatric functional constipation were fulfilled. Faecal incontinence was defined as faecal loss more than once a month in children >4 years old. Normal values for CTT were based on the results of a study by Vande Velde. Sixteen age and sex-matched controls were selected from this population. Normal values for ARM were based on the results of a study by Kumar et al.

Total and segmental CTT was measured using a 6-day method, as described by Abrahamsson. ARM was performed in non-sedated children with a water-perfused latex-free catheter. Ethical approval was obtained (2016/0841).

Results: Twenty-two patients were studied. They all had a CTT study, and seventeen had agreed to ARM. 10/22 patients (45.5%) suffered from constipation, according to Rome III criteria. 5/22 patients (22.7%) became spontaneously continent, 10/22 (45.5%) became pseudo continent with bowel management, and 7/22 (31.8%) remained incontinent.

SB patients had a significant longer CTT compared to healthy controls (p=0.001), which was mainly due to difference in the left CTT (p=0.037) and the rectosigmoidal CTT (p=0.007). As expected, constipated SB patients had a significant longer CTT in comparison to non-constipated SB patients (p=0.000). There was also a significant difference in CTT according to continence status (p=0.001). In the group with an abnormal CTT study, 10 patients had undergone ARM, which was abnormal in 6 cases and normal in 4 cases. None of these patients developed continence spontaneously. In case of a normal CTT study (10 patients), 7 had undergone ARM. Four children had a normal resting pressure, they all gained continence spontaneously. The three children with abnormal resting pressure rested incontinent. Comparing the resting pressure in the spontaneous continence group with the incontinent patients, there was no significant difference (p=0.156), but this could be due to the small group number of spontaneous continent children.

Conclusion: This study confirms that, in case of a normal CTT and normal resting pressure, spontaneous continence is to be expected. If CTT is abnormal, independent of the result of ARM, there will be need for bowel management in order to develop pseudo-continence. In these cases, ARM is not a designated examination.
Concordance between indication and formulation of proton pump inhibitors and H2 antagonist in children with gastroesophageal reflux and gastroesophageal reflux disease

Wilson Daza1, Silvana Dadan1, Tatiana Guerrero1, Emilia Prieto1, Michelle Huguera1, Juliana Garcia1

1Gastronutriped, Bogota, Colombia

Objectives and study: This study compared prescription indications, by general physicians or Paediatricians, of proton pump inhibitors (PPI) or histamine H2 antagonists (antiH2) in paediatric patients diagnosed with gastroesophageal reflux (GER) or gastroesophageal reflux disease (GERD), with indications of the clinical practice guides (CPG) by the British National Institute for Health and Clinical Excellence (NICE) and by the North American Society for Paediatric Gastroenterology, Hepatology and Nutrition - European Society for Paediatric Gastroenterology Hepatology and Nutrition (NASPGHAN - ESPGHAN).

Methods: Retrospective descriptive and concordance study with patients between 0 and 17 years of age, receiving pharmacological management with PPI or antiH2 prior to consultation. The study reviewed the clinical charts of paediatric patients evaluated during paediatric gastroenterology consultation for the first time between Jan/2009 and Dec/2014 in a Gastroenterology Unit. Descriptive and inferential statistics was used for analysis. Description of continuous variables was done through medium or median central tendency measures, with their respective dispersion measurement (standard deviation and interquartile range), according to their distribution. Normality of continuous variables was evaluated via the Shapiro-Wilk test. Discrete variables were expressed through percentages. The Kappa coefficient evaluated concordance.

Results: Of 1459 paediatric patients seen during the study period, 197 were diagnosed with GER or GERD. Most patients were <2 years of age; 68.53% were neonates and infants; 62% had adequate nutritional state; 73% were diagnosed with GERD and 27% with GER. Most frequent symptoms were vomit (55.3%) and regurgitation (47.7%). In 71.1%, some type of pharmacological management was received; of these, 72.8% received only one medication; PPI use was at 25.38% and antiH2 at 34.52%; use of both medications in the same patient corresponded to 5.8%. As noted, 91 of the 197 patients had indication of PPI use according to the application of the NICE and NASPGHAN – ESPGHAN CPGs. Of these, 59.34% did not receive it in spite of having the indication. Inter-observer concordance between the PPI formulation and the indications of the CPG selected had a Kappa of 0.293 (acceptable degree). With respect to antiH2, 47.72% had indication for use, however, 42.55% did not receive it. Inter-observer concordance between the antiH2 formulation and indications of the CPG selected reported a Kappa of 0.444 (moderate degree). Regarding the indication of PPI or antiH2 and their prescription, a Kappa of 0.5303 was reported.

Conclusion: Prescription of PPI and antiH2 by Paediatricians and general physicians was inadequate in this study, probably due to lack of knowledge of the CPG and because confusion still exists to differentiate GER from GERD.
G-P-162

Methodological quality of clinical practice guidelines to management and/or treatment gastroesophageal reflux disease in paediatrics

Wilson Daza¹, Silvana Dadan¹, Michelle Huguera¹, Emilia Prieto¹, Juliana Garcia¹, Tatiana Guerrero¹

¹Gastronutriped, Bogota, Colombia

Objectives and study: The study selected the best clinical practice guidelines (CPG) on managing and/or treating gastroesophageal reflux (GER) or gastroesophageal reflux disease (GERD) in paediatric population.

Methods: Systematic search in MEDLINE, EMBASE, OVIDSP, LILACS, PUBMED, and SCOPUS databases identified CPG aimed at managing and/or treating GER or GERD in paediatric population. Keywords used in “MESH” terms were: “Gastroesophageal Reflux”, “Gastroesophageal Reflux Disease”, “Proton Pump Inhibitors”, “Histamine H2 Antagonists”, “guidelines”, and “Paediatrics”. “DECS” terms were: “Guidelines” and “gastroesophageal reflux”. In addition, a manual search broadened the search to CPG developers, scientific societies, or related entities. The search was restricted to CPG published in the last 15 years in Spanish or English, age limited between 0 days and 17 years. Guide quality was assessed via AGREE II methodology in Spanish version. “High quality” means the score is ≥60% in four domains. To compare quality among the guidelines evaluated, the “methodological rigor” domain was used. Upon identifying two guidelines with the best scores, these were critically read, extracting recommendations on formulating proton pump inhibitors (PPI) and histamine H2 antagonists (antiH2). After the reading, the guidelines were independently reviewed by two paediatric residents, an epidemiologist, two gastroenterology Paediatricians, and a gastroenterology paediatrics fellow via AGREE II methodology

Results: The initial search yielded 17 CPG; titles and abstracts were reviewed, discarding those corresponding to topic reviews, updates of existing guidelines, or surgical management guidelines. Finally, 14 guidelines were subjected to the AGREE II methodology. The better-quality guidelines were the British National Institute for Health and Clinical Excellence (NICE) and the North American Society for Paediatric Gastroenterology, Hepatology and Nutrition - European Society for Paediatric Gastroenterology Hepatology and Nutrition (NASPGHAN – ESPGHAN) guidelines; hence, recommendations were extracted on the use and indications to manage GERD with PPI and antiH2 in Paediatrics.

Conclusion: The NICE and NASPGHAN – ESPGHAN guidelines have the best methodological quality, according to the AGREE II classification, and establish the following recommendations: 1. Reserve pharmacological treatment for patients with persistent symptoms and associated to some comorbidity that worsens GER or with alteration of the esophageal mucosa. 2. The PPI can have more benefits than the antiH2. 3. When deciding on PPI or antiH2, consider presentation, costs, and availability and not only their effectiveness. 4. Prokinetics or antacids are not suggested with GER or GERD. 5. Polypharmacy is not recommended, unless prescribed by a gastroenterology Paediatrist.
Quality of life in children with Hirschsprung disease

Lucile Espeso¹, Frederic Lavrand², Thierry Lamireau¹, Raphael Enaud¹

¹University Hospital, Paediatric Gastroenterology, Bordeaux, France
²University Hospital, Paediatric Surgery, Bordeaux, France

Objectives and study: Few studies have been carried out on quality of life (QoL) of children with Hirschsprung disease (HD), although it is a useful tool to evaluate the efficacy of surgical interventions. The aim of this study was to assess the QoL of the children with HD using a specific questionnaire (Hirschsprung disease and Anorectal malformations Quality of Life, HAQL), and its correlations with the initial characteristics of the disease, the functional score, and the nutritional status.

Methods: 71 children operated on for HD and aged above 8 years were asked to participate to the study via mailed questionnaires: QoL using the HAQL questionnaire, functional scores using the Krickenbeck classification and the Ann Arbor score. Disease characteristics, initial management and growth were also collected.

Results: 45 (63%) children and their families answered the questionnaires. Soiling and voluntary bowel movements improved with age, but constipation remained a problem in half of them. The overall HAQL score averaged 554/700 in 17 children aged 8 to 11, and 533/700 in 7 adolescents aged 12 to 17. A good correlation was observed between the scores of children and parents (r = 0.88), and between the HAQL and Ann Arbor scores (r = -0.73). Age at surgery, length of resected bowel, and nutritional status had no influence on QoL.

Conclusion: Soiling improves with age in patients operated for HD but constipation often persists. QoL remains fairly good, although there were large disparities between patients.
Need of antireflux surgery after percutaneous endoscopic gastrostomy in children

Pablo Ercoli, Carlos Ruiz Hernández, Belinda Garcia Cuerva, Ecaterina Julio, Marcela Alarcon, Javier Martín de Carpi, Sergio Pinillos Pisón

1Sant Joan de Deu Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain

Objectives and study: Percutaneous Endoscopic Gastrostomy (PEG) tube placement is becoming more frequent in children whose underlying pathology requires maintaining an adequate nutritional status and to decrease morbidity and mortality.

Many conditions associated with the need for gastrostomy, particularly neurologic impairment, are also associated with gastroesophageal reflux (GER). In addition, it is believed that PEG could cause or worsen GER symptoms. It is unclear what type of patients will require antireflux surgery after PEG placement, neither what conditions increase the risk of needing it.

The objective is to describe our experience and characteristics of patients who required antireflux surgery after a PEG was placed.

Methods: A retrospective descriptive study of clinical records review of patients who underwent percutaneous endoscopic gastrostomy for 15 years (period 2000 - 2014 both included) in a third level Paediatric Hospital. As inclusion criteria, patients under 18 years of age were selected with gastrostomy performed exclusively by the endoscopic way.

The following variables were analyzed: the need for Nissen-type anti-reflux surgery after PEG placement and as secondary variable: age at PEG time, sex, primary disease, indication of PEG disease, nasogastric tube (NGT) use before PEG, GER symptoms at baseline and after PEG, endoscopic findings, as well as feeding route after PEG placement.

For statistical analysis SPSS 15.0 was used, with Pearson test for correlation between main and secondary variables.

Results: A total of 224 PEG were performed. The mean age at time of PEG placement was 6.1 years (range 0.2-18). 57% (n = 128) were male. In total, 12% (n = 27) required antireflux surgery at some time after PEG placement. Of these 52% (n = 14) had symptoms of GER before PEG placement and 44.5% (n = 12) started GER symptoms only after PEG placement. The majority of the patients with primary neurological disease, whereas the main indication was oropharyngeal dysphagia with 77.7% (n = 21), followed by height failure 15% (n = 4). 63% (n = 17) used SNG as nutritional support prior to PEG for an average time of 5.5 months. Only 7.5% (n = 2) presented findings of esophagitis at the time of PEG placement. 66.7% (n = 18) received exclusive feeding by gastrostomy.

When correlating the different variables, only patients who started GER symptoms only after PEG placement were at increased risk of needing antireflux surgery (see table).

Table:

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Need of antireflux surgery</th>
<th>Correlation</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary disease</td>
<td>-0.087</td>
<td>0.193</td>
<td></td>
</tr>
<tr>
<td>Indication of PEG disease</td>
<td>-0.07</td>
<td>0.918</td>
<td></td>
</tr>
<tr>
<td>NGT use before PEG</td>
<td>0.016</td>
<td>0.811</td>
<td></td>
</tr>
<tr>
<td>GER symptoms at baseline</td>
<td>0.100</td>
<td>0.137</td>
<td></td>
</tr>
<tr>
<td>GER symptoms after PEG</td>
<td>0.308</td>
<td>0.001*</td>
<td></td>
</tr>
<tr>
<td>Endoscopic findings</td>
<td>0.014</td>
<td>0.836</td>
<td></td>
</tr>
</tbody>
</table>

*P<0.05 (statistical significance)
**Conclusion:** Although the need for antireflux surgery following PEG placement may be considered low, it is more frequent in children who initiate GER symptoms only after gastrostomy.
What pH-impedance parameters are predictive endoscopic and histological esophagitis?

junko fujino¹, Grace Seiboth², Rammy Abu-Assi², Paul Hammond², Richard Couper², David Moore²

¹Dokkyo Medical University, Pediatric Surgery, Saitama, Japan
²Women's and Children's Hospital, Gastroenterology, Adelaide, Australia

Objectives and study: Multichannel intraluminal impedance (MII) study in the esophagus is predominantly used for patients with reflux symptoms recently. Some papers show MII could play an important role in predicting endoscopic and oesophagitis. However, interpretation of these data is still controversial. We would like to further investigate the correlation between reflux oesophagitis proven by endoscopy/histopathology and parameters in pH-MII study in this study.

Methods: A retrospective review of patients undergoing both MII studies and esophagogastroduodenoscopy (EGD) performed between August 2013 and November 2016 at Women’s and Children’s Hospital in Adelaide was conducted, and the following data were collected: demographics (age, gender), medical history, pH-MII data (acid exposure (pH): reflux index, mean acid clearance time, longest episode of acid exposure). Impedance data included: number of acid and non-acid reflux events, percent acid exposure, median bolus clearance time, frequency of proximal reflux events. Findings of EGD examination and histopathology recorded. The relationship of pH-MII data to endoscopic findings (Study 1), and to histological findings (Study 2) was examined. In Study 1, patients were divided into two groups; Group N with normal findings, and Group A with reflux oesophagitis greater than grade A according with Los Angeles classification. In Study 2, patients were divided into two groups: Group Nh with normal findings, and Group Ah with histological oesophagitis.

Results: One hundred and thirty seven patients (69 boys, 50%) were enrolled with a mean age of 8.3 years (range: 6 months to 18 years).

1. Correlation between endoscopic esophagitis and pH-MII data.
   One hundred twenty nine patients (94%) were enrolled to Group N, while Group A was eight patients (6%). Statistical differences were observed in five parameters: reflux index, acid longest episode in pH study, and acid percent time, median bolus clearance time, number of proximal extent in MII study.

2. Correlation between histological esophagitis and pH-MII data.
   Eighty nine patients (65%) were allocated to Group Nh, and 48 (35%) to Group Ah. There were statistically significant differences in three impedance parameters: acid percent time, median bolus clearance time, and number of proximal reflux events.

Conclusion: Predicting endoscopic oesophagitis, some pH and Impedance parameters were helpful. However, in patients with histological oesophagitis, three impedance parameters were predictive including acid percent time, bolus clearance time, and number of proximal extent events.
Use of complementary studies in functional constipation

Etna Masip 1, Esther Donat 2, Begona Polo Miquel 3, Sandra Martinez Barona 4, Carmen Ribes Koninckx 2

1Hospital La Fe, Valencia, Spain
2La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
3Hospital Universitari La Fe, Valencia, Spain
4Instituo Investigacion La Fe, Valencia, Spain

Objectives and study: The Rome IV criteria indicate the clinical characteristics of functional constipation in pediatric patients for both the elderly and children fewer than 4 years. When patients don’t have signs of alarm and fulfill the criteria, it is not necessary to perform other explorations for the diagnosis and treatment. The objective of this study is to assess the relevance of complementary tests in pediatric patients who have the criteria for functional constipation in a tertiary hospital.

Methods: Retrospective study of pediatric patients who consult for constipation as first time in a third-level hospital during two years period (2014-2015). Demographic variables, functional criteria, complementary tests requested, diagnosis and treatment have been reviewed. Patients were divided into 2 groups according to Rome IV criteria: Group A (<4 years) and group B (≥4 years).

Results: A total of 93 patients have been included, representing 5.9% of the first visits referred to our unit in the last 2 years.

Group A: we found 40 patients, mean age 28 months (range 3m-47m), 55% men. The mean number of months of symptoms evolving before going to the clinic was 13.67. In the physical exploration or medical file: 37.5% of the patients had alarm signs, such as growth failure and constipation from birth, with this subgroup being the most prevalent diagnosis of non-IgE mediated cow’s milk protein (CMP) allergy. The remaining A group patients (62.5%) were diagnosed as having infant dyschezia (infants <9 months of age) or functional constipation, and in these subgroup, up to 68% was performed at least one blood test, including anti-transglutaminase antibodies and CMP study. Among the imaging tests, the abdominal x-ray is the most frequent 17.6%, with ultrasound being performed only in 5.8%.

Group B: a total of 52 patients were included, mean age 7.27 years (range 4-13 years), 57.7% women. The mean number of months of clinical evolution was 24.2. Only 15% presented red flag signs, all of them presenting neurological disabilities. The remaining 85% had functional constipation: 66% of them had been performed blood test including celiac disease study, and imaging tests: abdominal ultrasound in 11.4% and abdominal x-ray 9%. We did not find any case of IgE-mediated CMP allergy, or any case of celiac disease. Neither organic / structural pathology has been found in the imaging tests performed.

The most frequent treatment has been polyethylene glycol with dietary changes, except in the A group where the patients diagnosed with CMP allergy (17.5%) have performed CMP free diet. In both groups there are no statistically significant differences in treatment, prognosis and number of visits between patients in whom complementary tests were performed and those in which they did not.

Conclusion: Constipation is a frequent pathology of consultation. The imaging tests performed, as well as the analysis most frequently requested – serologic markers of celiac disease, IgE antibodies specific to CMP - have not been helpful to the diagnostic. These results reinforce the poor utility of complementary tests in the patient with functional constipation criteria.
Intestinal permeability is increased in children with irritable bowel syndrome: a case control study

Valentina Giorgio1, Consuelo Russo2, Arcangelo Schiattarella2, Franco Scaldaferr2, Anna Galimberti1, Valentina Tesori2, Gaia Margiotta2, Fabio Lecci2, Giacomo Giarrusso2, Ilaria Venezia2, Silvia Persichilli2, Jacopo Gervasoni2, Antonio Gasbarrini2

1Fondazione Policlinico Gemelli, University of Sacred Heart of Rome, Pediatric Department, Rome, Italy
2Fondazione Policlinico Gemelli, University of Sacred Heart of Rome, Rome, Italy

Objectives and Study: Intestinal permeability (IP) seems to play a pivotal role in Irritable Bowel Syndrome (IBS) pathogenesis. Aim of this work was to assess IP in a pediatric population with IBS.

Methods: We recruited a prospective consecutive cohort of children diagnosed with IBS according to Rome IV Criteria, and a cohort of healthy controls. All patients performed L/M ratio test to assess IP, and underwent Lactulose Breath Test (LBT) for the diagnosis of Small Intestinal Bacterial Overgrowth (SIBO).

Results: 30 children (19 males, age range 7-16) were enrolled. 41 healthy children (29 males, age range 8-14) constituted the control group. IP was significantly increased in IBS compared to controls (IBS 0.03±0.03 vs controls: 0.77±0.95; p=0.002). Among IBS children, 16 (53%) had a diarrhea predominant subtype; these showed a significantly higher IP (IBS-D: 1.19±1.01 vs IBS-Other 0.48±0.40; p=0.04). IP did not differ between SIBO positive (66%) and SIBO negative (34%) children (p=0.8), neither among patients who followed different therapies in the 3 months prior to the visit (No therapy L/M 1.04±1.22; VSL#3 L/M: 0.46±0.43; Rifaximin L/M: 0.79±1.06. No therapy vs VSL#3 p=0.4; No therapy vs Rifaximin p=0.8; VSL#3 vs Rifaximin p=0.6).

Conclusions: IP is increased in children with IBS, especially if diarrhea predominant. In our series, IP did not seem to differ if antibiotics or probiotics are used, suggesting a background role in IBS pathogenesis. Further studies on larger series are needed to clarify how IP can act in the pathogenesis of functional gastrointestinal disorders.
Prevalence of acid gastro esophageal reflux after the age of 18 months in infants with esophageal atresia

Marion Lebreton¹, Frédéric Gottrand¹, Delphine Ley¹, Stephanie Coopman¹, Rony Sfeir², Dominique Turck³, Laurent Michaud¹

¹Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
²Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
³Chru, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France

Objectives and study: The high prevalence of gastro esophageal reflux disease (GERD) in children operated for esophageal atresia (EA) led to the very recent recommendation for a systematic treatment by proton-pump inhibitor (PPI) for all the EA infants up to the age of 1 year. The aims of our study were to assess the prevalence of GERD after the age of 18 months in children who were operated for EA and to identify associated risk factors.

Methods: All patients with EA type III or IV who were born between January 2007 and December 2012 were prospectively included in the study. Patients were a priori classified into 3 groups: 1) Clinical reflux: digestive or respiratory symptoms compatible with GERD after PPI discontinuation which resolved or improved when PPI was started again; 2) Definite GERD: positive pH-monitoring after discontinuation of PPI and/or esophagitis and/or anti-reflux surgery; 3) No acidic GERD (normal 24h pH-monitoring). Patients who still had GERD at the age of 18-30 months were re-evaluated at follow-up. Potential factors (ie prematurity birth weight…. ) associated with the persistence of GERD were recorded.

Results: 57 patients were followed in our center for EA type III and IV during the study period among whom 82% could be evaluated for GERD (median age: 24 months (18-30)): 82% had GERD (27% clinical reflux, 40% positive pH-monitoring, 9% esophagitis, 6% anti-reflux surgery); only 18% had no GERD. At last follow-up (median age: 3.7 years (3.0-6.5)), 27 patients who previously had GERD were re-evaluated: 48% still presented GERD including 4% clinical GERD, 18% positive pH-monitoring and 26% anti-reflux surgery. No significant association was found between GERD after the age of 18 months and prematurity, associated malformation, undernutrition, or tension of the esophageal anastomosis.

Conclusion: The prevalence of acidic GERD after 18 months of age is high in patients with EA, and decreased to 50% after the age of 3 years. This supports the recommendation of systematic PPI treatment up to the age of 18 months and pH-monitoring thereafter (ESPGHAN-NASPGHAN Guidelines for the Evaluation and Treatment of gastrointestinal and nutritional complications in children with esophageal atresia-tracheoesophageal fistula. J Pediatr Gastroenterol Nutr. 2016).
Multicenter study evaluating the efficacy of polyethylene glycol (PEG) 3350 (Dicopeg Junior) in comparison with lactulose for the treatment of functional constipation in children aged 6 months to 6 years. A prospective, randomized study - preliminary report

Dorota Jarzebicka¹, Joanna Sieczkowska², Jaroslaw Kierkus², Maciej Dadalski², Piotr Socha³, Dariusz Lebensztejn⁴, Monika Kowalczyk-Kryston⁵, Bartosz Korczowski⁶, Grzegorz Oracz¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
²The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology and Nutrition Disorders Pediatrics, Warsaw, Poland
³Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
⁴Medical University, Pediatrics, Gastroenterology and Allergology, Bialystok, Poland
⁵Medical University of Bialystok, Department of Pediatrics, Gastroenterology and Allergology, Bialystok, Poland
⁶State Hospital No 2, University of Rzeszow, Department of Pediatrics and Pediatric Gastroenterology, Rzeszow, Poland

Objectives and study: Constipation is one of the most common problems in pediatric gastroenterology. According to ESPGHAN/NASPGHAN guidelines, as first-line drugs are recommended polyethylene glycols (PEG) - 3350 or 4000 and in case of unavailability or in children under 1 year of age recommends use of lactulose. There is a lack of prospective, randomised trials estimating efficacy of PEG 3350 in young children. The aim of the study is to evaluate the efficacy of polyethylene glycol (PEG) 3350 (Dicopeg Junior) in comparison with lactulose for the treatment of functional constipation in children aged 6 months to 6 years. Secondary endpoint of the study is the presence of adverse drug reactions.

Methods: Children with functional constipation aged 6 months to 6 years, from three academic hospitals in Poland, fulfilling the inclusion criteria were enrolled into the study. For diagnostic criteria of functional constipation were adopted Rome III Criteria. Data collection started from November 2015. The study covers 12 weeks of treatment and 4 weeks follow-up. During the first visit patients were randomized into two groups – treated with Dicopeg Junior (maximum 4 sachets) or lactulose (Lactulose MIP) 2ml/kg. Patients were asked to fulfill the diary, making the defecation training and the use of proper diet. Telephone consultation was made after 4 weeks from enrolling. In the case of intolerance or lack of efficacy of lactulose, treatment with Dicopeg Junior was proposed. On the final visit at week 12 the effectiveness of treatment, summary of recommendations and assessment of adverse events were recorded. At week 16 state of the child, was checked during call visit. The results were statistically analyzed.

Results: 82 patients (M 46, F 36) were enrolled to the study. 71 patients have already finished the study, and they were assessed in this preliminary report. Three patients terminated study after one month–2 due to good clinical response, 1 because of adverse events (abdominal pain, bloating). Four patients resigned from the study after 2 weeks, by parent’s decision. Mean age of the patients was 3.55 y (median 3.43). 35 patients were randomized to the group treated with Dicopeg Junior, 36 patients to the group with lactulose. After 4 weeks of treatment 2 patients change the course of treatment, because of lack of effect of lactulose. The mean time of disease course was similar in both groups (20.2 vs. 19.3 months). PEG 3350 significantly increase bowel movement in comparison to lactulose from 1.8 to 7.8 vs. 5.5, respectively. Results of treatment PEG 3350 vs. lactulose are presented in the Table 1.
Table:

<table>
<thead>
<tr>
<th></th>
<th><strong>Dicopeg Junior</strong> (number of patients; total n = 37)</th>
<th><strong>Lactulose</strong> (number of patients; total n = 34)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Day 0</td>
<td>Week 16</td>
</tr>
<tr>
<td>Painful defecation</td>
<td>31 (84%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Stool retention</td>
<td>30 (81%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Defecation with effort</td>
<td>30 (81%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Defecation with blood</td>
<td>2 (5%)</td>
<td>0</td>
</tr>
<tr>
<td>Stool consistency according to the Bristol scale (mean)</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Hard stool consistency</td>
<td>35 (95%)</td>
<td>3 (8%)</td>
</tr>
<tr>
<td>Encopresis</td>
<td>15 (41%)</td>
<td>7 (19%)</td>
</tr>
<tr>
<td>Fecal mases during abdominal palpation</td>
<td>25 (68%)</td>
<td>2 (5%)</td>
</tr>
<tr>
<td>Bowel movements (mean)</td>
<td>1.8</td>
<td>7.8</td>
</tr>
<tr>
<td>Adverse events (abdominal pain, bloating)</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Polyethylene glycol (PEG) 3350 (Dicopeg Junior) is an effective and safe treatment option of functional constipation in infants and young children with similar effectiveness to lactulose and less number of adverse events.
Efficiency of medical procedures most frequently requested in paediatric chronic abdominal pain

M. Isabel Jiménez-Candel1, Tatiana Salvador-Pinto2, Elena Crehuá-Gaudiza3, Carmen Jovani-Casano4, Monica García-Peris5, Maria Antonia Moreno-Ruiz6, Ester Largo-Blanco7, Tomás Hernández-Berti8, Cecilia Martínez-Costa9

1Hospital Virgen del Castillo, Pediatrics, Yecla, Murcia, Spain
2Hospital Marina Baixa, Pediatrics, Villajoyosa, Alicante, Spain
3Hospital Clínico Universitario, Pediatrics, Valencia, Spain
4Hospital General, Pediatrics, Castellón, Valencia, Spain
5Hospital Luis Alcanyís, Pediatrics, Xàtiva, Valencia, Spain
6Hospital de Manises, Pediatrics, Valencia, Spain
7Hospital General, Pediatrics, Valencia, Spain
8Hospital General, Pediatrics, Albacete, Spain
9University of Valencia, Pediatrics, Valencia, Spain

Objectives and study: Chronic Abdominal Pain (CAP) in scholar and adolescents is a common cause of consultation in primary care and in specialized assistance. Most of them are categorized as functional disorder. The role of numerous requested tests is still unclear. Our objective was to determine the efficiency of diagnosis tests most frequently requested in assessment of CAP.

Methods: A prospective observational multicentre (8 hospitals) study was conducted in children with CAP according Roma III criteria. Patients older than 4 years were recruited during the first visit in the paediatric gastroenterology and nutrition department of each hospital. All the diagnostic tests were collected and analysed.

Results: The study included 238 children, 59% girls, mean age 9.7 years. More than 85% were sent from primary care. All the children included in the study had undergone at least one investigation. Abdominal ultrasound was done in 87% of patients; 17 of them detected abnormalities (1 renal microlithiasis, 2 cholecystolithiasis, 1 ileitis and 13 mesenteric adenitis). Blood analysis was the most common investigation (88%); abnormalities in 5 of complete blood cell count (4 anaemia and 1 eosinophilia) and 7 in the biochemical testing (3 patients with hypercholesterolemia, 2 with iron deficiency and 2 exhibited elevated transaminases). Two out of the 171 patients who were screened for coeliac disease had positive anti-tissue transglutaminase antibodies. There were no significant abnormalities into inflammatory markers (only 6 cases exhibited slight elevation without obvious cause). Thirty three percent of children were organised urinalysis with abnormalty results in 2 cases (urinary infection and microscopic haematuria). Stool testing were sent in 67% of the children, intestinal parasites were detected in 7 of them and 1 stool culture was positive. 50% had faecal calprotectin testing (11 of them lower than 200mcg/kg and 2 higher that after were normal; none had faecal occult blood.

Conclusion: In childrens with CAP, diagnosis tests are commonly used either by general pediatricians or paediatric gastroenterologist. The diagnosis tests are heterogeneous and yield of it is minimal. Only 6% of the children had an organic cause, similar to literature. According to our study, abdominal ultrasonography and intestinal parasites determination are efficient tests for evaluate CAP in children. Diagnostic test should be individualized according to clinical presentation as proposed in the new Rome IV criteria.
Rumination syndrome in children documented by using High Resolution Manometry

Paraskevi Karanika¹, Thrasyvoulos Podas², Maria Fotoulaki³

¹Department of Paediatric Gastroenterology Papageorgiou Hospital, Thessaloniki, Greece
²Adrianio Gi and Metabolic Diseases Center, Thessaloniki, Greece
³Aristotle University of Thessaloniki, 4th Department of Paediatrics, Papageorgiou Hospital, Thessaloniki, Greece

Objectives and study: Rumination is an eating disorder that is clinically suspected when chronic, effortless regurgitation of recently ingested food occurs, followed by re-mastication, re-swallowing or expulsion. The diagnosis of rumination syndrome in adults is based on the ROME IV criterion. The diagnostic criterion is similar in children except that rumination should not occur during sleep and should not respond to standard to medical therapy for reflux. The clinical presentation of the rumination syndrome shows many similarities with other conditions and is often mistaken for more common diseases such as GERD.

Our aims were to improve diagnosis of rumination syndrome using high-resolution manometry.

Methods: Eight patients (five males) with a mean age of 11 years (range: 9–16) with clinically suspected rumination syndrome underwent manometry monitoring after a solid liquid meal. Water perfused HRM system with 22 circumferential pressure sensors with an outer diameter of 4.2 cm was used to produce oesophageal pressure topography plots. Subjects were studied in sitting position. After an accommodation period (30 min) manometry recordings were obtained.

Results: The postprandial manometry recording showed an oesophageal pressure pattern compatible with rumination in 6/8 referred patients (75%). 2/8 patients had ‘reflux-related’ events (25%). End-expiratory resting pressure of the LES in the patients with rumination was 6 (4–10) mm Hg and all patients exhibited complete relaxation of the LES during wet swallows. Furthermore, all rumination patients demonstrated abdominal pressure peaks exceeding 20 mm Hg. In adults the diagnosis of the rumination syndrome can be made when reflux events extending to the proximal esophagus that are closely associated with an abdominal pressure increase > 30 mm Hg.

Conclusion: Manometry monitoring improves diagnosis of rumination because it allows distinction between rumination and postprandial belching and regurgitation. The diagnosis of the rumination syndrome is based on demonstration of reflux events extending to the proximal esophagus that are closely associated with an abdominal pressure increase.
Polyethylene glycol maintenance treatment in childhood functional constipation: a double-blind, randomized, placebo-controlled trial

Line Modin\textsuperscript{1}, Marianne Jakobsen\textsuperscript{1}

\textsuperscript{1}Hospital Lillebaelt, Department of Paediatrics, Kolding, Denmark

**Objectives and study:** Our aim was to investigate the long-term efficacy of polyethylene glycol (PEG) in a placebo-controlled, randomized trial during maintenance treatment of childhood functional constipation (FC). At present, laxative treatment is recommended for both disimpaction and maintenance treatment. However, only short-term placebo-controlled studies have been performed to establish efficacy of PEG in the treatment of FC in children. Furthermore, new evidence is revealing significant consequences of parental factors on development and treatment of FC, mounting the need for evidence for a beneficial effect of the current recommended treatment regime.

**Methods:** Children with FC according to the Rome III criteria underwent disimpaction with PEG and were afterwards randomly assigned to maintenance treatment with either PEG or placebo for 24 weeks in a regional pediatric outpatient clinic. Effect of treatment between the two groups was compared in a survival model. Relapse of FC was defined as occurrence of previously successfully treated Rome III criteria without effect of dose escalation of study medication within one week or if the dose of study medication exceeded 1.5 g/kg/day. When relapse was confirmed the child was switched to rescue medication with open labeled PEG. Treatment effect ratios were compared using Cox proportional hazard regression model. If relapse were confirmed the child was censored at the time of switch to rescue medication. If the child was lost to follow-up before 24 weeks treatment, status was ascertained at the date of last visit. Children were considered successfully treated with absence of any Rome III criteria with or without use of medication after 24 weeks. Intention-to-treat analysis was used and safety evaluated by registration of clinical adverse events.

**Results:** Overall, 102 children were included in the intention-to-treat population with 49 children (median age 6.2 years, range 2.5-12.3) and 53 children in the placebo group (median age 6.1 years, range 2.0-15.1). Duration of symptoms of constipation at inclusion was median 7 months (range 2-60) in the PEG group and median 12 months (range 2-72) in the placebo group. Of 86 children, fecal incontinence was present in 21 children (51\%) in the PEG group at inclusion and 20 children (44\%) in the placebo group, while 8 children in each group were using diaper and had never been trained for toilet at time of inclusion. Significantly more children switched to rescue medication in the placebo group (56.6\%, 30/53) compared to the PEG group (4.1\%, 2/49) (P<0.001). Median time to rescue medication was initiated was 27 days (range 12-70 days). Furthermore, we found significantly more well treated children in the PEG group 67.3\% (33/49) compared to the placebo group (35.8\% (19/53)) (Hz= 3.21 (1.73-5.94) P=0.024). We found a significant larger number of children still using study medication at 24 weeks in the PEG group (55.1\%, 27/49) compared to the placebo group (13.2\%, 7/53) (P<0.001). No serious adverse events related to the study medication were registered during the study period.

**Conclusion:** PEG is significantly more effective than placebo in preventing relapse of constipation symptoms during long-term maintenance treatment of childhood FC. We recommend that maintenance treatment with PEG should be continued for at least eight weeks after disimpaction to prevent relapse and secure treatment success.
Objectives and study: Gastric emptying study (GES) is the standard for the measurement of gastric motility. However, gastric emptying values are dependent on multiple factors such as meal composition and consistency, body position, age, gender, phase of menstrual cycle, and time of the day the study is performed. Therefore, study protocol standardization and established normal values for such protocols are needed for accurate interpretation of the test.

We aimed to evaluate the adult gastric emptying normal ranges in a paediatric population. Adult normal ranges based on joint consensus recommendations by the Society of Nuclear Medicine and American Neurogastroenterology and Motility Society 2009 (SNM)

Methods: We correlated the GES study results and the final clinical diagnosis in order to estimate the sensitivity and specificity in the paediatric population.

GES technique: Patients were fasted for minimum of 6 hours before the test and medications that could affect gastric motility such as prokinetics were stopped 2 days prior to the test. The study was performed using an omelette meal (2 eggs) with 15mls milk mixed with technetium 99m nano-colloid radiotracer, which was ingested within 10 minutes. This differs from the SNM consensus technique because, in our experience, most children could not tolerate the large meal of toast with jam and scrambled eggs that is recommended. The rate of gastric emptying was measured at 1, 2 and 4 hours respectively. Diagnosis of delayed gastric emptying was confirmed by one of two consultant radiologists using the following normal rates of gastric emptying; 1 hour >10%, 2 hours >40% and 4 hours >90%, as recommended by the 2009 consensus paper.

Results: 65 children with a median age of 14 years (range: 1-18 years) were referred for GES between 2009-2016 due to suspected gastroparesis. 23/65 (35%) of patients had a delayed GES. 14/65 (22%) of patients were given a final diagnosis of gastroparesis. 12/14 patients with a final diagnosis of GP had an abnormal GES (sensitivity of 86%). GES was negative in 40/51 patients with other diagnoses (specificity of 78%). Negative predictive value of GES was 40/42 (95%).

Conclusion: Our results demonstrate rates of GES mentioned in adult consensus criteria can be used in the paediatric population along with clinical correlation for diagnosis of gastroparesis. High (95%) negative predictive value as demonstrated when gastric emptying normal might exclude gastroparesis. Multi-institutional study is required to further validate our findings.
Misdiagnoses of cyclical pattern of vomiting as cyclical vomiting syndrome; A case series

Vinod Kolimarala¹, Hany banoub¹, Mashhood Ayaz², Sonny Chong²

¹Epsom and St Heliers Hospital NHS Trust, Carshalton, United Kingdom
²Queen Mary's Hospital for Children, St. Helier Hospital, Paediatrics, Carshalton, Surrey, United Kingdom

Objectives and study: We present a series of cases referred to our unit with cyclical pattern of vomiting that were misdiagnosed as Cyclical Vomiting syndrome (CVS).


Results: We had 30 cases of misdiagnoses of CVS and included patients with GERD, malrotation, Sinusitis, PUJ obstruction, intracranial tumors, metabolic defects, EoE, Addison’s disease. A series of 4 cases are presented below

Case 1: Diagnosis- Malrotation

5 year old girl with multiple episodes of vomiting which started at the age of 3 months initially perceived to be GERD. Subsequently the episodes of vomiting continued lasting 3-5 days, every 3-4 weeks with occasional biliary emesis. She had investigations including OGD, CT scan of head, metabolic screen and barium studies done at various hospitals was normal. She was diagnosed with cyclical vomiting syndrome and commenced on Prophylactic treatment. Since there was no improvement she was referred to us for further review.

Following her review she has investigations including USS of abdomen and Barium study which showed malrotation. Following her surgery she improved and has remained well.

Case 2: Diagnosis- PUJ obstruction

6 years old with episodes of vomiting every 2-4 weeks with abdominal pain and cramps. She had multiple hospital admissions requiring IV fluid rehydration and was well between episodes. Investigations including metabolic screen, barium study, OGD were normal. She was diagnosed with cyclical vomiting syndrome and prophylactic treatment which was ineffective and was then referred to us.

She underwent further investigations including USS of abdomen and Barium study which showed malrotation. Following her surgery she improved and has remained well.

Case 3: Diagnosis- L-carnitine dependent CVS

6 year old boy with symptoms of intermittent vomiting, began at 2 years of age was diagnosed with CVS. He had stereotypical episodes lasting 5 days with numerous hospital admissions requiring IV rehydration. investigations including metabolic screen, ultrasound of his abdomen, OGD was normal. A trial of L-carnitine was started in spite of a normal carnitine level following which he made a dramatic improvement with cessation of vomiting.

He was started on L-cartinine following which he improved and remains well.

Case 4: Diagnosis- Intracranial teratoma

7 week old baby with history of difficulty feeding with recurrent vomiting was referred with possible diagnosis of cyclical vomiting. He had been vomiting intermittently since birth with multiple presentations to GP and A&E. He was diagnosed initially with GERD and managed accordingly. At
birth he was noted to have unilateral swollen eye and was referred to Ophthalmology who diagnosed him with congenital squint and left rectus palsy.

On review he had swollen left orbit with dilated pupil. Pressure to the orbit reduced crying.

He underwent cranial ultrasound and MRI which showed an intracranial teratoma. He underwent surgical resection of his tumour.

**Conclusion:** Patients with cyclical pattern of vomiting interspersed with normal health can be wrongly diagnosed with cyclical vomiting syndrome. Investigations of these patients should include Urine MC&S, FBC, LFT’s, lipase, amylase, metabolic screen, USS, barium study, sinus x-ray, CT/MRI if raised ICP is suspected and EEG before diagnosing them with cyclical vomiting syndrome.
How physicians approach functional defecation disorders in children; a survey study on guideline adherence in the Netherlands and the United States

Ilan Koppen¹, Mana Vriesman¹, Merit Tabbers², Carlo Di Lorenzo³, Marc Benninga⁴

¹Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands
²Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
³Nationwide Children's Hospital, Pediatric Gastroenterology, Columbus, United States
⁴Academic Medical Center/Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Functional constipation is a common disorder among children. In 2014, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) and the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition (NASPGHAN) published the ESPGHAN/NASPGHAN guidelines for functional constipation. Studies on physicians’ adherence to this guideline have not yet been performed. The aim of this study was to examine how physicians approach children with defecation disorders and if their practices adhere to the ESPGHAN/NASPGHAN guidelines.

Methods: We invited attendees to a pediatric gastroenterology symposium in the Netherlands and a general pediatrics meeting in the USA to participate in this anonymous survey. We administered a self-developed questionnaire containing 19 multiple-choice questions. The frequency of implementation of items of the medical history and physical examination was scored on a 5-point Likert scale (never-rarely-sometimes-often-always).

Results: We received 200 completed questionnaires (response rate 65%). The majority of US responders (88%) worked in private practices whereas most Dutch responders (98%) were based in a hospital setting. A total of 47% of responders were not familiar with the guideline, 15% of Dutch vs. 71% of US physicians (p=0.000). Anal inspection was frequently (often or always on the 5-point Likert scale) conducted by 69% of responders and digital rectal examination was frequently done by 27%. Inquiry about sexual abuse was frequently made by 20%. Significantly more Dutch than US physicians reported performing these three items in their diagnostic workup (table 1). A commonly reported reason for omitting these items was perceived patient discomfort.

Polyethylene glycol was the most commonly prescribed medication for disimpaction (68%) and maintenance treatment (73% for infants, 99% for children ≥1 year of age). The primary reason for choosing polyethylene glycol over enemas for disimpaction was patient comfort (70%). Most commonly implemented initial non-pharmacological interventions included: optimizing fluid and fiber intake (91% and 88%), establishing a toilet training program (88%), keeping a defecation diary (65%) and implementing a reward system (54%). Seven Dutch (8%) and 43 US physicians (38%) advised taking any pre- or probiotics (p=0.00).

Table: Number of responders who reported to frequently implement inquiry about sexual abuse, perianal inspection and digital rectal examination in the diagnostic workup for children with functional constipation.

<table>
<thead>
<tr>
<th></th>
<th>Netherlands, n (%)</th>
<th>USA, n (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inquiry about sexual abuse</td>
<td>25 (29)</td>
<td>14 (12)</td>
<td>0.004*</td>
</tr>
<tr>
<td>Perianal inspection</td>
<td>78 (90)</td>
<td>60 (53)</td>
<td>0.000*</td>
</tr>
<tr>
<td>Digital rectal exam</td>
<td>30 (35)</td>
<td>24 (21)</td>
<td>0.028*</td>
</tr>
</tbody>
</table>

Conclusion: Many responders were not familiar with the ESPGHAN/NASPGHAN guideline on childhood functional constipation. Nonetheless, therapeutic decisions correlated fairly well with recommendations from the guideline. Future research should focus on guideline adherence in other countries and aim to develop methods to improve guideline awareness and adherence.
Analysis of eosinophils of the gastrointestinal tract in children with abdominal pain-related functional gastrointestinal disorders and those with inflammatory bowel disease

Eun Hye Lee¹, Hye Ran Yang²

¹Seoul National University Bundang Hospital, Pediatrics, Seongnam-Si, Gyeonggi-Do, Korea, Rep. of South
²Seoul National University Bundang Hospital, Seoul National University College of Medicine, Pediatrics, Seongnam-Si, Gyeonggi-Do, Korea, Rep. of South

Objectives and study: Abdominal pain-related functional gastrointestinal disorder (AP-FGID) is common in children and adults. However, the mechanism of AP-FGID is not clearly known. Recently, micro-inflammation, especially eosinophilia in the gastrointestinal tract, was suggested in the pathophysiology of AP-FGID in adults. The aim of this study was to evaluate eosinophil infiltration in the entire gastrointestinal tract in children with AP-FGID, compared to those with inflammatory bowel disease (IBD).

Methods: In total, 56 paediatric patients with AP-FGID, 52 children with Crohn’s disease (CD), and 23 children with ulcerative colitis (UC) were recruited. All subjects underwent esophagogastroduodenoscopy, colonoscopy, and endoscopic biopsies in the same day. Tissue eosinophil counts were assessed in 10 regions of the entire gastrointestinal tract from the stomach to the rectum. Tissue eosinophil counts were compared between AP-FGID and IBD. To minimize effects of IBD itself inflammation, after eliminating pathology slides of local parts confirmed as severe inflammation by endoscopy exam, eosinophil counts were analyzed as well.

Results: Before excluding local anatomic regions with active inflammation of IBD, analysis between AP-FGID and IBD revealed that the stomach and the entire colon tract of paediatric IBD patients had significantly higher eosinophils than those with AP-FGID (2.6 ± 2.5 vs. 6.4 ± 8.9/high power field (HPF), p = 0.001 in the stomach; 15.7 ± 9.5 vs. 22.7 ± 17.4/HPF, p = 0.011 in the A colon; 13.1 ± 9.1 vs. 24.6 ± 20.5/HPF, p < 0.001 in the T colon; 12.7 ± 8.8 vs. 23.4 ± 17.0/HPF, p < 0.001 in the D colon; 11.9 ± 12.8 vs. 22.0 ± 18.6/HPF, p = 0.001 in the S colon; 3.3 ± 3.0 vs. 13.1 ± 18.1/HPF, p < 0.001 in the rectum). Eosinophil counts of the duodenum and the terminal ileum were also higher in children with IBD, but not significantly when compared with AP-FGID. Even after deducting biopsy slides from active mucosal lesions, children with IBD showed significantly higher tissue eosinophils in the stomach, cecum, ascending colon, sigmoid colon, and rectum than those with AP-FGID (all p < 0.05). In comparing CD with UC, UC had significantly higher eosinophils in the ascending colon, descending colon, sigmoid colon, and rectum than CD (all p < 0.05). However, after excluding the tissue specimens from active ulcerative lesions, there were no differences in tissues eosinophil counts between the 2 groups excepting for the ascending colon (17.1 ± 12.6 vs. 28.1 ± 16.4/HPF, p = 0.043).

Conclusion: The present study reveals tissue eosinophils infiltration is related to gastrointestinal inflammation. Particularly, eosinophils infiltration in the stomach and the colon seem to be more associated with intrinsic pathogenesis of both AP-FGID and IBD, regardless of local inflammation. This suggests some contribution of gastrointestinal eosinophils in the development of paediatric IBD as well as AP-FGID.
Long-term outcome of total colonic aganglionosis extended to the small bowel: retrospective analysis over 16 years

Elise Payen1, Cécile Talbote2, Virginie Colomb3, Christophe Chardot4, Sabine Sarnacki5, Naziha Khen-Dunlop5, Cécile Lambe6, Florence Lacaille6, Olivier Goulet2

1Hôpital Necker-Enfants Malades, Peadiatric Resident, Paris, France
2Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
3Hôpital Necker-Enfants Malades, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
4Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Chirurgie Viscérale Pédiatrique, Paris, France
5Hôpital Necker-Enfants Malades, Pediatric Surgery, Paris, France
6Necker-Enfants Malades, Gastroenterology-Hepatology- Nutrition , Paris, France

Objectives and study: Total colonic aganglionosis (TCA) extended to the small bowel (SB) is a rare and severe form of Hirschsprung disease (HD). Our aim is to analyze its long-term outcome, especially digestive autonomy and complications, including enterocolitis, in order to give guidelines for the management.

Methods: All patients born between 2000 and 2015 and treated at Necker-Enfants malades were retrospectively included in the study. The data analyzed were growth, digestive autonomy: duration of parenteral nutrition (PN), length of aganglionosis, and the main complications: enterocolitis, liver disease, bowel transplantation, and death. The genetic data were also analyzed.

Results: Twenty patients (8 girls) were included and followed for a median of 9 years (y) 4 months (m) (5 m to 15 y 6 m). The mean age at last follow-up was 8 y 10 m. The first symptom was a neonatal occlusion in all patients. The mean age at diagnosis was 19 days. Ten patients had less than 80 cm of healthy SB. The mean PN duration was 2 y 7 m (4 m to 12 y 6 m, median: 20 m). It was significantly shorter for patients with more than 80 cm of healthy SB: mean 11 m (4 m to 2 y 2 m, median: 8 m) compared to 4 y 9 m (8 m to 12 y 6 m, median: 4 y 3 m) for patients with less than 80 cm of healthy SB (p < 0.0001). All patients with more than 80 cm of healthy SB were weaned off PN (half of the group). Eleven patients suffered from enterocolitis at a mean age of 20 months, leading in eight cases to ileostomy or emergency colectomy. Liver disease was more frequent in patients with less than 80 cm of healthy SB (7 versus 0, p=0.01), severe in one only. Two patients needed a transplantation, one isolated small bowel and one multivisceral. Genetic analysis showed one Down syndrome and five (25%) identified mutations (3 RET, 1 SOX10, 1 EDNIII).

Conclusion: Digestive autonomy was acquired in patients with extensive HD and more than 80 cm of healthy SB length. The more severe complication was enterocolitis. It should be prevented with nursing and the early performance of colectomy. Liver disease should carefully controlled but was not severe in most children.
The use of combined oesophageal impedance-pH recording in the evaluation of gastro-oesophageal reflux in patients with respiratory illness

Huey Miin Lee¹, Sarah Allen¹, Caroline Pao², Chinedu Nwokoro², Sarah Brown², Ahmed Kadir¹, Daniel Sifrim³, David Rawat¹

¹The Royal London Hospital, Paediatric Gastroenterology, London, United Kingdom
²The Royal London Hospital, Paediatric Respiratory, London, United Kingdom
³Queen Mary University of London, Wingate Institute of Neurogastroenterology, London, United Kingdom

Objectives and study: Combined oesophageal multichannel intraluminal impedance-pH recording (MII-pH) has been increasingly used in patients with chronic respiratory illnesses including cystic fibrosis and recurrent chest infections to assess whether gastro-oesophageal reflux (GOR) could be a contributing factor to their respiratory symptoms and illnesses. Our aim is to review our single centre’s use of MII-pH in the evaluation of GOR in patients with respiratory illness and to assess the value of the test on the therapeutic implications in respiratory patients.

Methods: Data of all patients in a tertiary paediatric unit referred by the respiratory team to our gastroenterology team for MII-pH from July 2015 to October 2016 were retrospectively reviewed. Information including patients’ clinical condition, anti-reflux treatment, results of MII-pH and subsequent management was collected.

Results: Over the 16-month period, there were 94 referrals from the respiratory team to our gastroenterology team for MII-pH. Median age was 6 years old (range 6 months – 16 years old). Of the 94 referrals, 38 referrals (41%) did not have the study carried out due to non-attendance (15 referrals), technical failure (7), and intolerance to intubation of impedance catheter (16). 41 of the 94 referrals were for MII-pH off anti-reflux treatment, and 53 referrals were for MII-pH on anti-reflux treatment. Of the 94 referrals, 15 patients were referred twice for MII-pH. Taking repeated referrals into consideration, there were 79 individual respiratory patients referred for MII-pH. Of these, 28 (35%) patients had diagnosis of cystic fibrosis, 24 (30%) had background of recurrent chest infections and 7 (9%) had asthma. Of the 56 referrals that successfully had the MII-pH, 24 had the MII-pH off anti-reflux treatment: 8 were anti-reflux treatment-naïve whereas 16 were on anti-reflux treatment but had the treatment stopped for the purpose of the MII-pH. 32 of the 56 referrals that had the MII-pH on anti-reflux treatment: 3 referrals were on ranitidine and not proton-pump inhibitor (PPI), 7 were on single agent PPI, 7 were on combined PPI and prokinetic, 7 were on combination of three anti-reflux treatments and 6 referrals were on quadruple anti-reflux treatment. Of the 56 referrals that had the MII-pH, 20 had abnormal results ranging from mildly elevated oesophageal acid exposure in recumbent position to pathological GOR. Of these, 12 had a change of their anti-reflux medications on follow-up, either with the addition of anti-reflux treatments or change of medications, 4 continued on the same medications, and 1 had fundoplication and percutaneous endoscopic gastro-jejunostomy inserted. Of the 36 referrals with normal study or with no evidence of pathological GOR: 15 had no change in their anti-reflux regimen, 4 had their anti-reflux regimen weaned or stopped, 3 had their anti-reflux medication dose increased, 6 remained on no anti-reflux treatment and 2 had a change of their anti-reflux medications.

Conclusion: MII-pH remains one of the useful diagnostic modalities that may help guide respiratory physicians in managing their patients. However, there is no consensus about pathways of referral for diagnosis of GOR in children presenting with chronic respiratory symptoms. Further multicentre prospective studies and better collaboration with our respiratory and Ear, Nose and Throat colleagues is necessary to more rationally utilize MII-pH to diagnose supra-oesophageal manifestations of GOR.
Systematic review: interventions and costs associated with functional gastrointestinal disorders in infants

Thomas Ludwig1, Julie Glanville2, James Mahon2, Anita Fitzgerald6, Nikhil Thapar3, Mohammad Miqdady4, Miguel Saps5, Seng Hock Quak6, Irene Lenoir-Wijnkoop7, Mary Edwards2, Hannah Wood3, Carlos Lifschitz8, Hania Szajewska9

1Nutricia Research, Singapore, Singapore
2University of York, York Health Economics Consortium, York, United Kingdom
3Great Ormond Street Hospital, London, United Kingdom
4Sheikh Khalifa Medical City, Pediatric Gastroenterology, Hepatology & Nutrition Division, Abu Dhabi, United Arab Emirates
5Nationwide Childrens Hospital, Columbus, United States
6National University Health System, Paediatrics, Singapore, Singapore
7University of Utrecht, Utrecht, Netherlands
8Hospital Italiano, Buenos Aires, Argentina
9The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland

Objectives and study: The objectives of this systematic review were to investigate in relation to functional gastrointestinal disorders (FGIDs) in infants: i) the costs they cause to third party payers and parents and ii) treatment options.

Methods: A systematic literature review with a registered protocol was conducted. The review followed rigorous methods, including an extensive search, with study selection, data extraction and quality assessment conducted by two independent reviewers. To ensure currency, the review was focused on studies published since 2005. The population of interest was healthy term infants under 12 months of age with colic, regurgitation and/or functional constipation, and related signs and symptoms provided that these were thought to be linked to FGIDs. Outcomes of interest were the reported treatments including their frequency and volume; the cost to third party payers and parents for prescribed or over the counter treatments, visits to healthcare professionals, and the loss of income through time taken off work and out of pocket costs.

Results: In total, 12364 records were identified from database searching and 78 from additional searches of which 34 studies were included that contributed data about treatments of FGIDs and related signs and symptoms in infants. Twenty-six were randomized controlled trials and five were case series studies. Regardless of the considerable spectrum of reported interventions for the management of FGIDs, studies on the associated costs are scarce. Only three articles provided partial information on the cost of FGIDs in infants, however there were no studies identified that contributed data about parental or caregiver costs.

Conclusion: Despite the reportedly high incidence of FGIDs and related signs and symptoms in infancy, there is a gap in the knowledge on their economic impact. Those interventions reported in the systematic review may represent only a fraction of the remedies that are being used on a daily basis. The multitude of different treatments and approaches in managing infant FGIDs suggested there are discrepancies between published guidelines for the diagnosis and treatment of FGIDs, what physicians routinely recommend, and the steps that parents take to address signs and symptoms of FGIDs.

Disclosure of interest: T. Ludwig is an employee of Nutricia Research.
Gastro-oesophageal reflux and cow's milk allergy: finding the culprit

Saverio Mallardo¹, Paolo Rossi¹, Sara Isoldi¹, Danilo Rossetti¹, Anna Dilillo², Francesca Carlacci³, Giulia Biscione², Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
²Sapienza University of Rome, Pediatric Gastroenterology and Liver Unit, Rome, Italy
³Sapienza University of Rome, Pediatrics and Childhood Neuropsichiatry, Rome, Italy

Objectives and study: Cow's milk (CM) proteins allergy (CMPA) and gastro-oesophageal reflux disease (GORD) are very common in children and presenting symptoms are not uncommonly similar. GORD is usually viewed as a primary disorder or secondary to an underlying entity. CMPA has been considered the most common cause of secondary paediatric GORD.

We aimed at evaluating the usefulness of 24-hours pH impedance monitoring (MII-pH) study in characterizing patients with primary GORD and those with CMPA-secondary GORD. We also evaluated the role of a CM protein-free diet in patients with both positive MII-pH study, non-responding to antisecretory drugs, and in symptomatic patients with normal MII-pH test.

Methods: From January 2015 and February 2016, 117 children aged 0-6 years (median age: 2.7) with suspected symptomatic GORD were enrolled into the study. All underwent MII-pH study to detect the abnormal GOR and define the reflux pattern (acidic/non acidic/weakly alkaline). Children with abnormal MII-pH started an antisecretory drug (proton pump inhibitors = PPI). Patients unresponsive to PPI or with a normal MII-pH underwent a dairy free diet. All subjects were followed up at 3 and 6 months.

Results: A) MII-pH study was abnormal in 94: 61 of them (65%) responded to PPI therapy (age: 3.1±1.8 years) and were diagnosed as a primary GORD, while 33 (35%) were unresponsive to PPI. Of the latter group, 24 (72%) (age: 1.2±1.7 years) had symptom disappearance following CM protein free diet, 3 had eosinophilic oesophagitis, 6 were affected by chronic upper respiratory tract infections. Primary GORD patients were older than CMPA-related GORD (p<0.01)

B) MII-pH study was normal in 23: 19 (83%) responded to a CM protein free diet, while 4 were affected by functional intestinal disorders.

The response to a CM protein-free diet was faster in those with a normal MII-pH study (7.2±3.5 days) than in those with GORD (12.3±9.5 days) by the beginning of CM protein-free diet. Patients with primary GORD has significantly higher acid exposure time than CMPA-GORD (p<.001) while the latter has a markedly higher number of non-acid and weakly acid GOR episodes than primary GORD (p< 0.01)

Conclusion: In small children investigated for GORD, the MII-pH can be very useful in distinguishing primary GORD from CMPA-related GORD, thus avoiding an inappropriate PPI therapy. In patients with suspected GORD and normal MII-pH test a CMPA diet is strongly warranted, since the latter is effective in resolving symptoms and signs in the majority of patients.
Management of gastroesophageal reflux in children with neurological impairment: an audit of practices

Régine Maximilien-Francois¹, Delphine Ley¹, Guimber Dominique², Laurent Michaud¹, Stephanie Coopman¹, Primael Dautel³, Dominique Turck⁴, Frédéric Gottrand¹

¹Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
²Chu Lille, Reference Center for Congenital and Malformative Esophageal Disease (Cracmo), Division of Gastroenterology, Hepatology and Nutrition, Lille, France
³Centre de Soins Antoine de Saint-Exupéry, Vendin-Le-Vieil, France
⁴Chru, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France

Objectives and study: Children with neurological impairment (NI) are at high risk for prolonged and severe gastroesophageal reflux disease (GERD). GERD diagnosis is difficult in this vulnerable population because of impaired oral communication, non-specificity of GERD associated symptoms (e.g. seizures, hypertonia), and difficulty for performing investigations.

The objective of our study was to describe the management of GERD in children with NI living in an institution.

Methods: This single center, retrospective study, included all 46 patients (median age: 8.5 years [range: 5 - 13]), living in a specialized institution for children with NI (Gross motor function grade IV: n=3; and grade V: n=43).

Data collection was conducted from June 2014 to January 2015, using a standardized survey, which defined GERD symptoms (recurrent regurgitation, vomiting…) or suggestive symptoms (weight loss, irritability, seizures…) and complications (esophagitis, recurrent pneumonia…).

Results: All 46 had at least one symptom of GERD or suggestive of GERD; 57% of them had at least one complication related to GERD (esophagitis: n=7; recurrent pneumonia: n=17; anemia: n=6; esophageal stricture: n=1; weight loss: n=9).

At least one investigation (upper gastrointestinal series, endoscopy, pH-metry) was performed in 33 patients. GERD was confirmed by a positive investigation for 75% of them.

Patients who had a confirmed GERD had more symptoms of GERD (n=4 [3 - 5] vs n=2 [1 - 3], p = 0.0006), in particular more digestive GERD symptoms (n=2 [1 -3] vs n =1 [0 - 2], p = 0.01) than patients who did not undergo any investigation to confirm GERD.

The cumulative duration of antireflux treatment was higher in patients who had proven GERD compared to the others (3.5 years [1.9-6] vs 1.8 years [0.4-2.5], p = 0.003).

At the time of the study, 83% of patients were receiving a medical treatment for GERD (prokinetics alone: n=1; prokinetics + proton pump inhibitors (PPI): n=14; PPI alone n=23).

Twenty-eight of the 44 children (64%) who received PPI presented between 1 and 3 adverse events potentially related to PPI (pneumonia (41%); iron and vitamin deficiencies (33%); bone fractures (17%).

Antireflux surgery was performed in 41% of patients who had all received PPI therapy before. They had more extradigestive GERD symptoms (p=0.02), and more GERD complications (p <0.0001), compared to patients who did not undergo surgery.

68% of patients who underwent a fundoplication were still receiving PPI at the time of the study.
**Conclusion:** Severely children with NI living in institution are at very high risk of GERD. Most of them are on long term PPI treatment even if GERD is not confirmed and if a fundoplication has been performed.
Indistinguishable gastric functional abnormalities reported among children with both functional and organic dyspepsia

Ahmed Megahed1, Ahmed Abdalla1, Khaled Zalata2, Suzy Abd El-Mabood3

1Mansoura University Children’s Hospital, Mansoura University, Pediatrics; Gastroenterology, Hepatology and Nutrition, Mansoura, Egypt
2Mansoura University, Pathology, Mansoura, Egypt
3Mansoura University Children’s Hospital, Mansoura University, Pediatrics, Mansoura, Egypt

Objectives and study: Functional gastric abnormalities had been demonstrated among children with functional dyspepsia (FD). Moreover some studies documented such functional abnormalities to be present in organic causes as a consequence of inflammation or a mere association. The current study was conducted to quantify electrogastrographic (EGG) as well as gastric emptying (GE) time abnormalities in children with dyspepsia (functional and organic), and also to evaluate their possible relation to symptoms profile and histopathology severity.

Methods: A prospective non randomized observational study was conducted on 53 children (male/female = 27/26; age = 9.9±2.6 ys) with dyspepsia; another group of 16 age and sex matched children were included as a control for GE & multichannel EGG testing. Clinico-epidemiologic data including presence of alarming symptoms and signs; symptoms severity and frequency scoring; upper GI endoscopy with routine mucosal biopsy and rapid urease test were applied. In addition Four-channel EGG was performed in preprandial and postprandial states; and 13C acetate (liquid meal) breath test was used to assess GE.

Results: The most bothersome symptom(s) was (were) pain alone in 15 (28%) patients; pain and vomiting in 21 (40%) patients; pain and upper GI bleeding in 5 (9%) patients; and pain, vomiting and upper GI bleeding in the remaining 12 (23%) patients. The symptoms severity as measured on 5-points scale was reported as 3- moderate; 4- severe; 5-very severe in 15 (28.3%); 26 (49.1%); and 12 (22.6%) patients, respectively. While the symptoms frequency was reported as 2- ≤ 2 times /week: in 12 (22.6%) patients; 3- ≥ 3 times /week, not daily: in 17 (32.1%) patients; 4- daily, intermittent: in 15 (28.3%) patients; and 5- daily, almost continuous: in the remaining 9 (17%) patients. Based on Endoscopic findings FD; H. pylori Gastritis, other organic causes of dyspepsia were diagnosed in 11 (20.8%); 29 (54.7&); 13 (24.5%) children respectively. Twenty seven children reported gastric functional abnormalities, 19 (35.8%) with abnormal both EGG and GE test results; 4 (7.5%) with abnormal EGG; and another 4 (7.5%) children reported delayed GE. Gastric emptying test parameters significantly correlated with EGG parameters. Seven (63.6%) patients with FD; H. pylori gastritis and 6 (43.1%) with non H. pylori organic dyspepsia reported functional abnormalities. Significantly lower percentage EGG classification normogastria in both preprandial and postprandial states, as well as failure of postprandial EGG power augmentation were universal among dyspeptic children with FD; H. pylori gastritis; non H. pylori organic dyspepsia as compared with controls. In addition GE was also significantly slower among different dyspepsia subgroups versus controls. Patients' symptom profile, severity, frequency, histopathology topography and severity were not different among patients with functional abnormalities versus those without.

Conclusion: Children with both functional and organic dyspepsia have a significant slowing of GE as well as gastric arrhythmias and failure of postprandial EGG power augmentation. Clinical relevance and the influence of both EGG and GE abnormalities on patients’ symptoms are questionable.

Disclosure of interest: None of the authors has any conflict of interest to declare.
Gastroenterology: GI motility, GERD and functional GI disorders

G-P-183

Association between extra-oesophageal symptoms and gastro-oesophageal reflux in children

Paolo Rossi¹, Saverio Mallardo¹, Giulia Biscione², Anna Dilillo², Elena Cavalli², Alessandra Micalizzi², Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
²Sapienza University of Rome, Pediatric Gastroenterology and Liver Unit, Rome, Italy

Objectives and study: Gastro-oesophageal reflux may present with both oesophageal and extra-oesophageal atypical features. The latter usually include either signs frequently related to GORD (apnoea, chronic cough, bronchial asthma, laryngitis, dental erosions) or less commonly to GORD (pharyngitis, sinusitis, idiopathic pulmonary fibrosis and recurrent otitis media).

The study aims at evaluating the relationship between GOR and atypical signs.

Methods: From October 2014 to September 2016 we evaluated 510 patients with symptoms suggestive of GORD. 135 patients, who presented with atypical features, were enrolled in the study. All underwent oesophageal 24-hour pH impedance monitoring (MII-pH), in order to establish the presence of abnormal GOR.

Results: Predominant features were symptoms such as sinusitis, pharyngitis and/or recurrent otitis media in 9 (7%); 32 patients (24%) presented laryngitis and/or stridor, hoarseness, dysphonia; 22 patients (16%) had asthma, bronchospasm or dyspnoea; 72 patients (53%) presented with cough as main feature. All had a previous specific diagnostic algorithm prior to MII-pH.

The MII-pH was abnormal in 59 patients (44%), while normal in 76 (56%). In particular, the study was abnormal in 3 patients presenting with sinusitis/pharyngitis/otitis (5%), 19 patients presenting with laryngitis/hoarseness (32%), 16 with asthma (27%) and 21 patients with cough (36%).

An abnormal MII-pH was detected significantly more frequently in children complaining of extra-oesophageal signs frequently related to GORD than in those with features less commonly GORD related (p< 0.001)

Conclusion: 24-hours MII-pH is required in order to correctly diagnose GORD in paediatric patients presenting with atypical extra-oesophageal signs. However, GORD is not commonly detected in this patient population as traditionally believed. Performing MII-pH in patients with extra-oesophageal signs may avoid unnecessary antisecretory therapy in children with suspected atypical GORD.
Assessment of the neurohumoral reculation in children with gastroesophageal reflux disease

Inna Nesina¹, Olha Tkachenko¹, Tetyana Kryuchko¹

¹Higher Educational Institution of Ukraine "Ukrainian Medical Dental Academy", Paediatric # 2, Poltava, Ukraine

Objectives and study: We observed 48 children aged 7-15 years with exacerbation of chronic gastroduodenal pathology who were treated in paediatric department of the Poltava Regional Clinical Hospital. Verification of the diagnosis was based on clinical, laboratory and instrumental examination of sick children according to regional guidelines.

Methods: fibrogastroscopy, esophageal pH monitoring, determination of melatonin and gastrin.

Results: Using endoscopy in 32 children (group 1) with gastroesophageal reflux disease (GERD) reflux esophagitis (RE) was found and in 17 children (group 2) had endoscopic negative form of GERD (nGERD), which made the comparison group. The control group consisted of 20 healthy children of similar age and gender. Studying of pH in the esophagus in children with RE significantly more frequently diagnosed pathological acid gastroesophageal reflux (GER) (41.8% against 9.4%, p≤0.001). In the group of children from GERD physiological GER (78.1% against 34.4%, r≤0.05) and alkaline abnormal GER (12.5% against 8.63%) were detected more significantly. Results of the study melatonin showed that the concentration of the peptide in children with RE was 4.3 times higher (p<0.05) than the same mark of the control group (5.75 ± 0.94 mmol/L) and 1.7 times more in children from GERD (p <0.05). The study of gastrin in patients with gastroesophageal reflux disease showed significant reduction of this neurotransmitter (1.89 ± 0.48 mmol/l) compared with healthy children (14.82 ± 4.12 mmol/l (p <0.001). Analyzing concentrations of gastrin, depending on the variant of GERD, we found that in patients with nGERD level of gastrin was slightly increased but in case of erosive esophagus process presence in children the level of gastrin decreased (1.71 ± 0,49 mmol/l (p<0.05)). It is important to emphasize that such changes in the content of neuropeptides have the opposite direction. The peculiarity of the neurohormonal violation shows significant differences of pathogenic inflammatory and erosive processes in children with GERD depending on of certain opportunities of compensatory possibilities.

Conclusion: Thus, the severity of morphological changes of esophageal mucosa depends on the peculiarities of neurohumoral of child’s reactivity. In children with gastroesophageal reflux disease we detected the dependence between indicators of gastrin, melatonin and clinical form of this disease. Multidirectional neurotransmitters depend on the predominance of acid or alkali reflexes which must be considered by the doctor when he prescribes the treatment.
The association between maternal intrapartum antibiotic administration and the development of infant colic

Anna Pärty, Marko Kalliomäki, Elli Leppälehto, Eliisa Löyttyniemi, Erika Isolauri, Samuli Rautava

1Turku University Hospital, Department of Paediatrics, Turku, Finland
2University of Turku, Department of Paediatrics, Turku, Finland
3Faculty of Medicine, Department of Biostatistics, Turku, Finland

Objectives and study: Evidence is persuasively pointing to aberrant gut microbiota composition in colic infants. The objective of this study was to establish the interconnection between perinatal factors potentially affecting gut microbiota colonization and thus development of infant colic.

Methods: The study population consists of 51 full-term children with infant colic and 34 healthy full-term controls. Parents kept Baby Day Diary to record their infant’s daily crying time. Colic infants cried more than 180 minutes a day whereas the control infants cried less than 90 minutes a day. In these, we assessed the duration of pregnancy, maternal smoking during pregnancy, delivery mode, birth weight, Apgar-scores, intrapartum and neonatal antibiotic use, and breastfeeding at two months of age.

Results: The background characteristics were similar between the infants with and without colic (Table 1). Altogether 24% of infants with infantile colic and 3% of healthy controls were exposed to intrapartum antibiotics (p=0.013). This difference remained statistically significant after adjusting for potential confounding factors (OR (95% CI) 12.43(2.00-244.20); p=0.0044).
Table: Background characteristics of infants with and without colic.

<table>
<thead>
<tr>
<th>Exposure</th>
<th>Colic</th>
<th>Healthy control</th>
<th>P-score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal smoking during pregnancy</td>
<td>5/51 (10%)</td>
<td>3/32 (9%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Antibiotic exposure during pregnancy</td>
<td>12/51 (24%)</td>
<td>5/32 (16%)</td>
<td>0.42</td>
</tr>
<tr>
<td>Intrapartum antibiotic exposure</td>
<td>12/51 (24%)</td>
<td>1/32 (3%)</td>
<td>0.013</td>
</tr>
<tr>
<td>Duration of pregnancy</td>
<td>40 (38 - 43)</td>
<td>40 (35 – 42)</td>
<td>0.40</td>
</tr>
<tr>
<td>Caesarean section delivery</td>
<td>11/51 (22%)</td>
<td>5/32 (16%)</td>
<td>0.58</td>
</tr>
<tr>
<td>Birth weight</td>
<td>3515g (2370g-4700g)</td>
<td>3668g (2490g-4800g)</td>
<td>0.19</td>
</tr>
<tr>
<td>5 minute apgar score</td>
<td>9 (7-10)</td>
<td>9 (8-10)</td>
<td>0.47</td>
</tr>
<tr>
<td>Neonatal antibiotic exposure</td>
<td>5/51 (10%)</td>
<td>3/32 (9%)</td>
<td>1.00</td>
</tr>
<tr>
<td>Exclusively breastfed at two months age</td>
<td>18/49 (37%)</td>
<td>23/32 (72%)</td>
<td>0.003</td>
</tr>
</tbody>
</table>

Conclusion: Administration of antibiotics during labor increases the risk of the development of infant colic. This association may be of high clinical significance since more than a third of all neonates are exposed to maternal antibiotics during delivery. If this novel finding is confirmed in larger cohorts, it should be taken into consideration when practice guidelines on intrapartum antibiotic prophylaxis are devised.
Quality of life in children post-fundoplication for the treatment of gastroesophageal reflux disease

Shravya Pilli¹, Ashish Jiwane², Usha Krishnan³

¹University of New South Wales, Sydney, Australia
²Sydney Children’s Hospital, Paediatric Surgery, Sydney, Australia
³Sydney Children’s Hospital, Paediatric Gastroenterology, Sydney, Australia

Objectives and study: Evidence on quality of life (QOL) outcomes in children post-fundoplication surgery is limited. Previous studies lack the use of paediatric-specific instruments and fail to provide a child’s perspective when possible. This study aims to explore and understand QOL outcomes in children who have had a fundoplication surgery for the treatment of gastroesophageal reflux disease (GORD) using post-operative results of GORD-specific and paediatric-specific questionnaires.

Methods: In this monocentric exploratory study, 115 patients who underwent fundoplication between 2006 and 2013 were contacted for recruitment and provided with parent and child reports of three questionnaires – GERD-HRQL, PEDS-QL Gastrointestinal Symptoms Module and PEDS-QL Generic Core Scales. Data analysis on QOL outcomes were based on these responses.

Results: A total of 29 patients responded. The mean age was 11.26 years, 55.2% were male and 20.7% were neurologically impaired (NI). Males, neurologically normal children, children who had a concurrent gastrostomy insertion and those who are currently not on any anti-reflux medications have significantly better QOL outcomes than their counterparts (p<0.05). Significant positive correlation (p<0.05) was found between symptom-based QOL and general QOL. While there was trend towards QOL being better in the medium-term group compared to the short-term group and in accordance to child perception compared to parental perception, statistical significance was not found.

Conclusion: Post-fundoplication QOL outcomes have multiple influential factors. Developing research models which will permit assessment of QOL by comparing not only pre-surgical and post-surgical patients, but also QOL in children who are being treated with only anti-reflux medications and lifestyle modification in both the short- and long-term, are needed before the current high trend in paediatric fundoplication surgeries can be justified.
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-P-187

Rectoanal inhibitory reflex in children with functional constipation and large diameter of the rectum

Daniela Pop\(^1\), Otilia Fufezan\(^2\), Dorin Farcau\(^3\)

\(^1\)University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania
\(^2\)Children Emergency Hospital, 3rd Pediatric Clinic, Cluj-Napoca, Romania
\(^3\)University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, 3rd Pediatric Clinic, Cluj-Napoca, Romania

**Objectives and study:** The aim of the study was to evaluate the volume of air necessary to induce the rectoanal inhibitory reflex in children with functional constipation and large diameter of the rectum.

**Methods:** The diagnosis of constipation was based on the Rome III criteria for functional constipation in children. We collected retrospectively the data of the patients with functional constipation, evaluated in our unit between January 2013 and January 2016. The transverse rectal diameter of the rectum was measured using transabdominal ultrasound and the rectoanal inhibitory reflex was evaluated using water-perfusion anorectal manometry.

**Results:** A total of 50 children entered the study. Twenty five children (16 boys, mean age±SD=6.67±3.97 years) were diagnosed with functional constipation. Twenty five children (11 boys, mean age±SD=4.54±4.04) were with normal bowel movements and the rectal diameter was evaluated in them using transabdominal ultrasound. There was no statistically significant difference between the age of the patients included in the two groups (p=0.06). The mean value±SD of the transverse rectal diameter was 41.44±14.02 mm in children with functional constipation and 24.32±6.14 mm in children without constipation. There was a statistically significant difference between these two groups regarding this parameter (p<0.0001). The mean value of the volume of air necessary to induce the rectoanal inhibitory reflex ±SD in children with functional constipation was 20.4±13.98 cm\(^3\) air. We found no correlation between higher transverse diameter of the rectum and higher volumes of air necessary to induce the rectoanal inhibitory reflex (r=0.06).

**Conclusion:** A large diameter of the rectum does not mean that a high volume of air will be necessary to induce the rectoanal inhibitory reflex in children with functional constipation.
Gastric emptying time, esophageal pH-impedance parameters, quality of life and gastrointestinal comorbidity in obese children and adolescents

Paolo Quitadamo¹, Letizia Zenzeri², Roberta Schiano di Cola¹, Enza Mozzillo¹, Irene Cuccurullo¹, Alba Rocco³, Adriana Franzese³, Gerardo Nardone³, Annamaria Staiano¹

¹Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
²University of Perugia, Department of Pediatrics, Perugia, Italy
³Federico II University, Department of Gastroenterology, Naples, Italy

Objectives and study: Gastroesophageal reflux disease (GERD) and obesity are currently two of the most common disorders in Western populations. Rates of overweight and obesity among children have more than doubled in the past decades, with the most recent estimates indicating that about 30% of children are overweight or obese. Although there are many studies about the association between GERD and obesity in adults, very few data are available for pediatric age. A few years ago, we've reported that both total and abdominal obesity are independent risk factors for reflux symptoms in children. The present study was drawn in order to provide further evidence about the relationship between obesity and GERD in children, through the use of instrumental testing such as 13C-octanoic acid breath test (13C-OABT) and multichannel intraluminal impedance pH-testing (MII-pH).

Methods: Children and adolescents aged 2-17 years, followed-up at the outpatient clinic for Pediatric Obesity from March 2016 to September 2016, were asked to fulfill 3 different questionnaires, investigating the presence of reflux symptoms, possible associated functional gastrointestinal disorders and both parent- and patient- reported quality of life (QoL). 20 randomly selected obese patients reporting GERD symptoms and 20 obese patients without GERD symptoms were asked to undergo 13C-OABT, in order to evaluate gastric emptying time (GET). Symptomatic patients were also required to undergo MII-pH. Age- and sex- matched asymptomatic non-obese children were enrolled in order to obtain comparative data for non-invasive procedures, such as 13C-OABT and study questionnaires.

Results: 113 obese patients (M/F: 60/53; mean age ± SD: 123 ± 7.3 months; range: 48-204 months) were enrolled in the study. Of these, 44/113 (38.9%) reported reflux symptoms. 22/44 underwent MII-pH: the mean reflux index was 14.6% and the mean number of daily reflux episodes was 51.8. 20/44 underwent 13C-OABT: the mean T½ GET was 107.6 min. Among the remaining 69/113 (61.1%) obese asymptomatic patients, 20 underwent 13C-OABT: the mean T½ GET was 116.5 min. 15 healthy non-obese children (M/F: 8/7; mean age ± SD: 115 ± 6.5 months; range: 55-191 months) were enrolled as comparison group. Their mean T½ GET was 100.1 min. Both symptomatic and asymptomatic obese patients had a worse quality of life than non-obese (p:0.003 and p:0.0002, respectively); the percentage of excess body weight was directly related with QoL score (p:0.01); the narrow waist circumference was directly related to GET (p:0.01); chronic functional constipation (FC) and irritable bowel syndrome (IBS) were more prevalent among obese patients with reflux symptoms than obese asymptomatic patients (p:0.03 and p:0.007, respectively).

Conclusion: The present study confirms that a high percentage of obese children and adolescents experience gastro-esophageal reflux symptoms. GET was found to be directly related to the narrow waist circumference, though it did not differ significantly between obese and non obese patient groups. Neither subjective nor objective reflux scores were related to GET. Obese patients suffering from reflux symptoms had a higher GI comorbidity than asymptomatic obese patients, reporting more frequently FC and IBS. Finally, as expected, both symptomatic and asymptomatic obese patients had a worse QoL compared to non obese healthy patients.
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-P-189

**PPI treatment in children with oesophageal atresia: predictive factors for long term treatment; data from a prospective cohort**

Franziska Righini-Grunder¹, Laetitia Marie Petit², Prevost Jantchou¹, Jessica Ezri³, Martine Pomerleau¹, Ann Aspirot⁴, Christophe Faure¹

¹Chu Ste Justine, Paediatric Gastroenterology, Hepatology and Nutrition, Montreal, Canada
²Hopitaux Universitaires de Geneve, Pediatrics, Geneva, Switzerland
³Centre Hospitalier Universitaire Vaudois, Unité de Gastro-Entérologie Pédiatrique, Lausanne, Switzerland
⁴Chu Ste Justine, Paediatric Surgery, Montreal, Canada

**Objectives and study:** Clinical course in oesophageal atresia (EA) may be complicated by gastroesophageal reflux and formation of anastomotic strictures. After EA repair, new-borns should be treated systematically with proton pump blockers (PPI) according to recent recommendations.

The objective of this study is the evaluation of PPI treatment in a prospectively followed cohort of EA patients at a tertiary centre with determination of predictive factors for discontinuation of PPI treatment.

**Methods:** Children born with EA from September 2005 to December 2014 were included. Evaluation of the current PPI treatment was made at time of last follow-up.

Statistical analysis was performed by using SAS® University edition program. Chi-square, Fisher’s exact were used to compare qualitative variables and unpaired Wilcoxon test to compare continuous variables. Cox regression model was used for multivariate analysis. P value <0.05 is considered as statistically significant.

**Results:** 77 patients (44 boys) were included, 8 type A, 66 type C, 3 type D (16 long gap). All 77 patients but 4 were treated with PPI. 3 of the 4 remaining patients were treated with H2RA. Median FU was 4.4y (range 1-10.9). Median duration of PPI treatment was 1.7y (range 0.01-10). At time of last FU PPI treatment was stopped in 36 patients (49%). 29 of the 36 patients had a pH-study (normal in 21, 72%). Among the 8 with abnormal pH-study, 8 had at least one EGD (4 with peptic esophagitis).

38 patients (51%) had still ongoing treatment with PPI at time of follow up (11 long gap). In this group, 35 patients (92%) had at least one EGD during FU. 14 patients presented with recurrent anastomotic strictures (8 long gap) and 22 patients with histologic complications (peptic oesophagitis, eosinophilic oesophagitis, and gastric metaplasia). 16 pH-studies were performed in this group, 7 showed an elevated reflux index.

On univariate analysis, tracheomalacia at diagnosis of atresia (OR 0.18, p=0.0016), hospitalization >30days (OR 0.18, p=0.0009), complications after surgery (anastomotic leak and re-fistula) (OR 0.28, p=0.04), recurrent anastomotic stricture (OR 0.15, p=0.005) are negatively associated with stopping of PPI treatment. Multivariate analysis was adjusted for weight at birth, hospitalization >30d and anastomotic leak. Tracheomalacia (HR 0.21, p=0.004) and recurrent anastomotic stricture (HR 0.16, p=0.005) are negatively associated with discontinuation of PPI treatment.

**Conclusion:** PPI treatment could be stopped in almost 50% of EA patients. Tracheomalacia and recurrent anastomotic stricture are risk factors for long term PPI treatment.
Adequate determination of the transition zone in Hirschsprung disease and the role of calretinin staining in clinical practice

Franziska Righini-Grunder¹, Dorothée Dal Soglio², Christophe Faure¹, Natalie Patey²

¹Chu Ste Justine, Paediatric Gastroenterology, Hepatology and Nutrition, Montreal, Canada
²Chu Ste Justine, Paediatric Pathology, Montreal, Canada

Objectives and study: The transition zone (TZ) in intestinal aganglionosis, also called Hirschsprung’s disease (HD), is a heterogenous zone and the histopathological morphology is not yet fully understood. Nevertheless, an accurate determination of TZ is mandatory for avoiding inadequate surgical intestinal resection in HD.

The objective of this study is to describe the TZ with determination of the length of TZ in HD and evaluation of the clinical value of calretinin immunohistochemistry staining in TZ.

Methods: TZ of HD patients were analyzed on HPS specimen by studying the expression of the neuronal markers calretinin and PGP9.5. We determined the order of appearance of neurites in mucosa and ganglion cells in submucosal and myenteric plexuses in direction from aganglionic to ganglionic zone. We measured the distance between calretinin positive neurites in the mucosa and calretinin and/or PGP9.5 positive ganglion cells in the submucosal and myenteric plexuses.

Results: Tissue samples from intestinal pull-through surgery between 2006 and 2016 were reviewed in 29 HD patients (23 males). The median age at pull-through surgery was 2.6 months (0.4-34.8). 26 (90%) presented with a short form of HD (rectosigmoid).

In 27 out of 29 TZ, Calretinin positive mucosal neurites appeared prior to submucosal plexus calretinin or PGP9.5 positive ganglion cells (median distance 4mm, range 2-12mm) and prior to calretinin or PGP9.5 positive myenteric plexus ganglion cells (median distance 10mm, range 10- >30mm). In 2 specimens, Calretinin positive neurites, submucosal and myenteric ganglion cells were expressed at the same level.

Calretinin positive ganglion cells in submucosal plexus appeared in 48% of TZ prior to ganglion cells in myenteric plexus (14 cases) with a median distance between calretinin positive ganglion cells in the submucosal and myenteric plexus of 6 mm (3-12mm) in 10 patients and a distance >25mm in 4 patients.

In 5 cases calretinin positive ganglion cells of myenteric plexus were expressed prior to ganglion cells in submucosal plexus. In 8 cases, calretinin positive ganglion cells in myenteric plexus and submucosal plexus appeared at the same level 3 mm after the calretinin positive mucosal neurites (2-5mm).

In all cases at 30 mm proximal to the zone of first appearance of calretinin positive cells, ganglionic cells were present in both plexuses.

Conclusion: There is a high heterogenicity in the order of appearance of ganglionic cells in the intestinal wall of TZ. Immunohistochemistry staining with calretinin and PGP9.5 allows adequate determination of length of TZ. Within a 30mm length distance after the first appearance of calretinin positive neurites, the surgical resection could be performed in ganglionic healthy tissue in all individuals.
The role of manometry in the post-operative assessment of children born with anorectal malformations: a systematic review

Todd Matthews¹, Mark Safe², Sebastian King³

¹University of Melbourne, General Practice, Melbourne, Australia  
²Royal Children's Hospital, Gastroenterology and Clinical Nutrition, Melbourne, Australia  
³Royal Children's Hospital, Murdoch Children's Research Institute & University of Melbourne, Paediatric Surgery, Clinical Nutrition, Surgical Research & Paediatrics, Melbourne, Australia

**Objectives and study:** Anorectal malformations (ARM) are relatively common congenital abnormalities of the terminal hindgut. They exist on a wide spectrum, ranging from a simple perineal fistula to a complex cloacal exstrophy. The incidence of ARM ranges from 1:2000 –1:5000 live births. There has been significant variability in classification of ARM, and the classification system has undergone a number of alterations over the last three decades. Prior to 2005, ARM were classified as high, intermediate or low malformations. However, the detail lacking in this classification system has led to significant variations in management internationally.

Similarly, there is a lack of standardization in post-operative assessment and, for many children with ARM, the post-operative outcomes remain poor. It is unknown whether the resultant constipation and/or faecal incontinence is related to abnormal motility within the remaining colon. Post-operative assessment is hampered by the relative inaccessibility of the colon, and a lack of diagnostic tools that may accurately record colonic contractions along its length, in real time. There is limited understanding of normal paediatric colorectal physiology and, therefore, colorectal dysfunction treatment is based upon the adult literature.

The present systematic review was performed to evaluate the use of manometry in the post-operative assessment of children with ARM.

**Methods:** Using PRISMA protocols, we performed a systematic review of the literature pertaining to anorectal and colonic manometry in children with ARM. Eligible studies were identified by searching relevant databases, including PubMed, Embase, MEDLINE and the Cochrane Library. Articles and data were reviewed independently by two people, with any discrepancies and conflicts discussed with a third reviewer.

**Results:** Forty studies were identified, with 1379 paediatric ARM patients. The study types included 16 prospective studies, 22 retrospective studies, and 2 case studies. Manometry had been completed in 1139/1379 (82.6%) children. There was lack of standardization in manometry, with variable reporting of equipment and technique, and frequent use of outdated terminology and equipment. All 40 studies performed anorectal manometry, with one study performing colonic manometry. There was similar lack of standardization in clinical scoring systems used, with many systems modified by study authors.

**Conclusion:** Although reported frequently in the literature, manometry for post-operative assessment of ARM lacks consistency and has been hampered by outdated terminology and equipment. New high-resolution manometry and standardized protocols for assessment will dramatically advance the understanding of paediatric colonic and anorectal motility, thus guiding future treatments.
Clinical and psychological coping strategies can predict pain subtypes and evolution in paediatric chronic abdominal pain

Tatiana Salvador-Pinto¹, Caterina Calderón², Elena Crehuá-Gaudiza³, Cecilia Martinez Costa⁴

¹Hospital Marina Baixa, Pediatrics, Villajoyosa, Alicante, Spain
²University of Barcelona, Department of Personality, Assessment and Psychological Treatment Faculty of Psychology, Barcelona, Spain
³Hospital Clínico Universitario, Pediatrics, Valencia, Spain
⁴Hospital Clínico Universitario, Pediatric Gastroenterology Unit, Valencia, Spain

Objectives and study:
Functional Abdominal Pain (FAP) in children is a set of recurrent pain conditions with no demonstrable organic cause. Greater impairment has been associated with the child’s use of poor psychological coping strategies such as catastrophic thinking about pain and maladaptive coping strategies.

Objectives: Firstly, to identify, through a person-centred analysis, homogeneous groups of children with FAD who have similar patterns of pain intensity. Secondly, to assess whether clinical characteristics and psychological coping strategies are predictive of profile membership.

Methods: 44 children (aged 5 to 15 years) with FAP according Roma III criteria were recruited. Latent profile analysis (LPA) was applied to identify pain intensity subgroups based on similar responses to the Abdominal Pain Index (API). Demographic factors, clinical characteristics, responses to the Pain Catastrophizing Scales (PCS), Pain Beliefs Questionnaire (PBQ), and Anxiety and Depression Symptoms (RCADS) were employed as predictors of profile membership. The study was approved by the Ethics Committee of the Hospital.

Results: Mean age was 9.7 years, with a lifetime history of pain of 3.75 years. LPA identified 3 subtypes: Profile-1 (low pain, 37.5%) had low-grade pain catastrophizing, and highest mean score in children’s coping strategies (problem-focused pain coping efficacy and emotion-focused pain coping efficacy); Profile-2 (mild pain, 25%), had medium pain intensity, with highest mean score in pain catastrophizing (e.g. helplessness) and highest mean score in children’s coping strategies; and Profile-3 (high pain, 37.5%) had the highest rates of reported pain catastrophizing and maladaptive coping strategies.

Conclusion: Evidence was found for 3 pain profiles in children with FAP. Our study determined that patients with highest rates of pain catastrophizing and maladaptive coping strategies comprised 37.5% of our cohort, and evidenced the worst evolution. These findings may be used to design subgroup-specific interventions for pain in children with FAP.

The authors declare no conflicts of interest.
Efficacy of alginate in infants with gastroesophageal reflux by esophageal impedance

Silvia Salvatore1, Antonio Ripepi1, Koen Huysentruyt2, Kris Van de Maele3, Alessandro Salvatoni4, Yvan Vandenplas3

1University of Insubria, Varese, Italy
2Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
3Uz Brussel, Paediatrics, Brussels, Belgium
4Insubria University, Varese, Italy

Objectives and study: Alginate is considered by NICE guidelines the first pharmacological treatment of gastroesophageal reflux (GER), but the evidence of its efficacy is currently limited.

Objectives: To assess the efficacy of alginate on GER in infants.

Methods: We conducted a prospective study (January - November 2016) consecutively including infants submitted to multichannel intraluminal esophageal impedance (MII) (Sleuth®, Sandhill Highland Ranch, CO, USA) for suspected GER-disease. All infants had symptoms of GER including apnoea, Apparent Life Threatening Episodes, persisting crying or cough and did not respond to behaviour and diet modifications. A 48-hour pH-MII was performed and, during the second 24-hours, treatment with alginate formulation (1 ml/kg per day divided into the number of meals) was started. No other changes were allowed during the investigation. Sodium alginate (Gaviscon) or magnesium alginate (Gastrotuss baby) was used depending on the location of the patient (neonatal or pediatric ward, different hospital). The pH-MII was analyzed according to ESPGHAN consensus using a dedicated software (Bioview) and manual revision. We compared GER parameters of the first 24-hour pH-MII (drug-free, DF) with the second 24-hour (drug-given, DG) using Wilcoxon signed rank test. We defined improvement a reduction of at least 10% in ≥1 of the following: total and proximal number of bolus reflux episodes, percentage of acid (RI%) or non-acid exposure time. The median values and number of symptoms during the investigation (DF and DG) were also compared. The Ethical Committee of the Hospital approved the study and parents gave informed consent.

Results: We have currently included 43 infants (median age 68 days, range 16-306 days; 21 males). All well tolerated the 48-hour recording; we excluded 3 pH-MII tracings because of prolonged artefacts. Gaviscon was used in 17 and Gastrotuss baby in 23 infants. Our data showed an overall improvement of GER pH-MII parameters, during the 24-hour on treatment, in 75% of infants (30 out of 40): 70% of the patient treated with magnesium alginate and 82% treated with sodium alginate. Alginate significantly reduced the total number of GER episodes (DF vs DG: median 76 vs 69; P<0.001), the number of acid (DF vs DG: median 19 vs 14.5; P<0.04) and non-acid GER episodes (DF vs DG: median 52 vs 49.5; P<0.004) and the number of proximal episodes (DF vs DG: median 46 vs 41.5; P<0.007). We observed a no significant reduction in the duration of the longest episode of GER (DF vs DG: median 6.8 min vs 5.4 min; P=0.12) and in RI% (DF vs DG: median 2.7 vs 2.2; P=0.24). Treatment with alginates also reduced the number of symptoms of crying and fussiness in our infants (DF vs DG: median 14 vs 9).

Conclusions: This is the first study to demonstrate that alginate treatment for infant GER may significantly improve number and extension of both acid and non-acid reflux episodes.
Alginate efficacy on laryngeal inflammation in children

Elisa Rota¹, Francesca Macchi¹, Antonio Ripepi¹, Patrizia Latorre², Silvia Salvatore¹

¹University of Insubria, Varese, Italy
²Ent Dept, Varese, Italy

Objectives and study: Laryngeal edema and erythema and laryngopharyngeal reflux (LPR) are increasingly reported in children. No specific symptom or sign exists but proton pump inhibitors are frequently prescribed without a clear diagnosis of gastroesophageal reflux (GER) disease. The aim of our study was to assess the efficacy of alginate on laryngeal inflammation.

Methods: All infants and children referring to our hospital for laryngoscopy because of symptoms suggestive of LPR were prospectively and consecutively recruited since January 2015. A flexible laryngoscopy was performed, without sedation, because of persistent noisy breathing or apneas, cough, dysphonia, globus pharyngeus, and swallowing problems. Exclusion criteria were as follows: patients on treatment for GER at first laryngoscopy or with previous respiratory or gastrointestinal surgery, or with severe neurological disorders. Only patients with abnormal laryngoscopy requiring two laryngeal investigations, at diagnosis and subsequently as control, and performed by the same ENT specialist were analyzed. Abnormal laryngeal findings were defined by the ENT specialist as the presence of posterior or vocal cord erythema or edema or nodules. Patients who also presented gastrointestinal symptoms were referred to our pediatric gastroenterology clinic and submitted to 24 hour multichannel intraluminal esophageal pH impedance (pH-MII) (Sleuth®, Sandhill Highland Ranch, CO, USA). The pH-MII was analyzed according to ESPGHAN consensus using a dedicated software (Bioview) and manual revision by one author. Fisher test and Pearson correlation were used for statistical analysis.

Results: We have currently analysed 44 patients (median age 9 months, range 2-54 months, 29 male). At presentation the most common laryngeal and gastrointestinal symptoms were: recurrent apneas (66% of patients) and regurgitations (63% of patients). The most common laryngeal finding was represented by posterior laryngeal inflammation (hyperemia and/or edema of the arytenoids) in 76% of patients. The ENT specialists gave recommendations to all patients regarding feeding, position and the use of voice and started alginate treatment (sodium or magnesium alginate formulation, 1 ml/kg per day) in 36 patients (82%). MII-pH was performed in 12 patients and 6/36 patients (14%) added ranitidine (10 mg/kg per day) because of pathological GER. At second laryngoscopy median age and duration of treatment were 12 and 9 months, respectively. Symptoms improved or resolved in 0/8 and 1/8 without drug treatment, in 14/30 (47%) and 13/30 (43%) on alginate, and in 5/6 on added ranitidine. Laryngeal findings were unchanged in 86% without treatment, improved in 27% and resolved in 63% on alginate, and in 83% and 17% on ranitidine, respectively. Alginate was significantly superior to non pharmacological treatment for symptoms and laryngeal findings (P=0.00007). No significant difference was found when added ranitidine.

Conclusions: Alginate is effective for laryngeal inflammation and LPR in children. A specific pediatric laryngeal score is needed to tailor GER investigations and treatment.
Can symptoms and questionnaire predict the result of esophageal PH-impedance in infants?

Alex Moretti¹, Chiara Armano¹, Letizia Fumagalli¹, Francesca Macchi¹, Antonio Ripepi¹, Silvia Salvatore¹

¹University of Insubria, Varese, Italy

Objectives and study: Symptoms of gastroesophageal reflux (GER) are common in infants but discrimination between physiological and pathological GER is challenging. Empirical use of acid inhibitors is still frequent despite lack of evidence of efficacy and guidelines recommendations. The aim of this study was to evaluate the predictive value of a validated questionnaire for the results of esophageal pH-impedance (MII-pH) in infants.

Methods: We conducted a prospective study (from March 2010 to May 2016) consecutively enrolling infants submitted to esophageal multichannel intraluminal pH-impedance (MII-pH) (Sleuth®, Sandhill Highland Ranch, CO, USA) for suspected GER-disease. Respiratory abnormalities including recurrent apneas/desaturations, apparent life threatening episodes, chronic cough or noisy breathing, simill- epileptic episodes or persisting crying not improving with behavior and diet modifications were the presenting symptoms. All parents completed the I-GERQ-R (with normal value <16) questionnaire and a symptom diary during the investigation. MII-pH was analysed according to a previous ESPGHAN consensus and considered as pathological when one of the following results was present: acid exposure index >7%, total number of GER episodes >100/24 hour, symptom index >50% or symptom association probability ≥95%. Comparison between the I-GERQ-R score and MII-pH results was analyzed; sensitivity, specificity, positive (PPV) and negative predictive values (NPV) were calculated.

Results: We included 104 MII-pH infants (median age 4 months, range 0.5-16 months, 46 males). MII-pH was pathological in 88 (85%) infants. Clinical presentations were not associated with different MII-pH results. I-GERQ-R was positive in 48/104 (46%) but failed to identify 45 pathologic MII-pH tracings whilst the score was positive in 6/16 infants with a normal MII-pH. The sensitivity of I-GERQ-R was 48% (CI 0.48 ± 0.10) and the specificity was 65% (CI 0.650 ± 0.09) with a PPV of 88% (CI 0.88±0.08) and an NPV of 20% (CI 0.20±0.05). Acid exposure was pathologic in 34/104 patients (33%) but the I-GERQ-R was negative in 17 of these infants (50%). In 13/104 (12.5%) infants the RI was >3% but <7%, and 5 (38.5%) had a positive I-GERQ-R. The PPV for acid exposure was 48% (CI 0.477 ± 0.08) and the NPV was 56% (CI 0.561 ± 0.08).

Conclusions: In infants and toddlers the result of MII-pH monitoring cannot be predicted by clinical presentation or questionnaire. A normal I-GERQ-R score does not exclude a pathologic MII-pH study or the presence of pathological acid exposure.
G-P-196

Gatorade is no good substitute for liquid saline in pediatric High Resolution (Impedance) Manometry (HR(I)M) measurement

Rolando Sanabria Mongelos1, Maartje Singendonk1, Rachel Rosen2, Marc Benninga1, Taher Omari3, Sam Nurko2, Michiel van Wijk1

1Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Children’s Hospital Boston, Center for Motility and Functional Gastrointestinal Disorders, Boston, United States
3Flinders University, School of Medicine, Bedford Park, Australia

Objectives and study: Gatorade® is often used as a substitute for liquid saline as a challenge medium in pediatric High Resolution (Impedance) Manometry (HR(I)M) measurement due to its richness in electrolytes and more palatable taste. Its influence on HR(I)M characteristics and Chicago Classification (CC) diagnosis in children has not yet been investigated. The aim of this study was therefore to compare HR(I)M characteristics of Gatorade® vs. saline in children.

Methods: Baseline impedance bench testing was performed for Gatorade® and liquid saline (NaCl 0.9%). Twenty children (6M, 14.1±3.4Y) without evidence of achalasia, anatomical and/or neurological abnormalities underwent diagnostic HRIM for gastroesophageal reflux and/or dysphagia symptoms. Patients were administered 10 saline and 10 Gatorade® boluses (each 5ml) and were studied in the supine position. HRM analysis was performed by software-dedicated analysis software (ManoView 3.0). Integrated Relaxation Pressure (IRP4s), Contractile Front Velocity (CFV), Distal Latency (DL) and Distal Contractile Integral (DCI) were extracted, allowing a manometric diagnosis according to the CC algorithm (V3.0). Matlab-based analysis software was used for HRIM analysis. Parameters of interest included Pressure Flow Index (PFI), Impedance Ratio (IR), Bolus Pressure Time (BPT) and Bolus Flow Time (BFT). Effects of bolus consistency were assessed by Paired Samples T-Test and Wilcoxon-Signed-Rank Test.

Results: Baseline impedance for Gatorade® was higher than for saline liquid (1000Ω vs 170Ω). 198 saline and 193 Gatorade® swallows were analyzed. IRP4s was significantly higher for saline when compared to Gatorade® (8.3±0.95mmHg vs. 6.7±0.71mmHg; p=0.025). No differences were found for the other HRM metrics (CFV: p=0.242, DL: p=0.672 and DCI: p=0.765). In 4 (20%) patients, the CC diagnosis altered (from EGJ outflow obstruction, distal esophageal spasm and ineffective motility to normal and from normal to ineffective motility) when the algorithm was applied to Gatorade® swallows. HRIM analysis showed statistically significant differences in all impedance-driven metrics (PFI: 2.8±29 vs. 4.2±10; p=0.033, IR: 0.2±0.2 vs. 0.4±0.2, BPT: 6.3±0.3s vs 4.3±0.3s, and BFT: 5.2±0.3s vs. 3.9±0.3s; all p <0.001), whilst no differences were identified in the pressure-driven metrics.

Conclusion: Gatorade® and saline differ largely with regards to baseline impedance. Based on the results of this study, Gatorade® may not be suitable as an alternative to saline neither for conventional HRM nor for HRIM analysis, as it might impact the IRP4s value and CC classification, as well as impedance-driven HRIM metrics.
Reducing PPI and H2RA prescriptions in paediatrics

Nina Steutel¹, Minke Jansen², Miranda Langendam³, Marc Benninga¹, Merit Tabbers¹

¹Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Academic Medical Centre, Pharmacology, Amsterdam, Netherlands
³Academic Medical Centre, Department of Clinical Epidemiology, Bioinformatics and Biostatistics, Amsterdam, Netherlands

Objectives and study: Prescribing acid-suppressant medication for children has increased substantially over the past two decades, despite (inter)national guideline recommendations to prescribe prudently. This medication is often not effective in reducing symptoms of gastro-oesophageal reflux disease and can lead to side effects. Therefore, a national campaign was launched (Choosing Wisely) to reduce unnecessary prescriptions. The aim of our study was to reduce the number of prescriptions of acid-suppressant medication for gastro-oesophageal reflux disease in children aged 0 – 18 years through active implementation of the Dutch guideline recommendations (Wise Choices).

Methods: Active implementation consisted of two parts: paediatricians and residents of the Emma Children’s Hospital (ECH), Amsterdam, The Netherlands, received information on appropriate prescribing of acid-suppressant medication. They received a link to an app and a pocket-sized summary card with evidence-based recommendations (Wise Choices). Additionally, clinicians who prescribed acid-suppressant medication were contacted by e-mail/telephone to provide individual feedback which consisted of discussing the indication for prescribing and their knowledge of the national guideline and Wise Choices. Data on prescriptions of acid-suppressant medication in the ECH were collected electronically before (January 2014–August 2015), during (September 2015–February 2016) and after the intervention (March–April 2016). Interrupted time series analysis was used to assess the effect of the intervention on the number of prescriptions for acid-suppressant medication.

Results: In total 4053 prescriptions for PPI (93.1%, n = 3776) and H2RA (6.9%, n = 279) were registered between January 2014 and April 2016. The number of prescriptions ranged from 99 to 195 per month (mean 145, SD 20.0). Of the 78 clinicians that were contacted in the intervention period, 76 (97%) responded. Upon first contact 61.5% of the respondents was familiar with the guideline and 43.6% was familiar with the Wise Choices (see table). Two months post-intervention, a decrease of 43.6 prescriptions per month was measured (95% CI 1.2 to 86.1).

Table:

<table>
<thead>
<tr>
<th>First contact (n = 78)</th>
<th>Knowledge of guideline</th>
<th>Knowledge of Wise Choices</th>
</tr>
</thead>
<tbody>
<tr>
<td>Unaware</td>
<td>12.8% (n = 10)</td>
<td>29.4% (n = 23)</td>
</tr>
<tr>
<td>Heard of it, unfamiliar with content</td>
<td>23.1% (n = 18)</td>
<td>24.4% (n = 19)</td>
</tr>
<tr>
<td>Familiar with content</td>
<td>61.5 % (n = 48)</td>
<td>43.6% (n = 34)</td>
</tr>
<tr>
<td>No response</td>
<td>2.6% (n = 2)</td>
<td>2.6% (n = 2)</td>
</tr>
<tr>
<td>Total</td>
<td>78</td>
<td>78</td>
</tr>
</tbody>
</table>

Conclusion: This study shows that the majority of the clinicians was familiar with the national guideline, less than half of the clinicians were familiar with the Wise Choices. A non-significant reduction of acid-suppressant medication prescriptions on the short term was observed. Since this was measured after a very short follow-up period, repeated measurements after a longer follow-up period are necessary in order to evaluate the implementation effect on the longer term.
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-P-198

**Gastro-oesophageal reflux symptoms in relation to psychiatric disorders evaluated by development and well-being assessment (DAWBA) diagnostic tool in urban Siberian adolescents**

Sergey Tereshchenko¹, Margarita Shubina¹, Nina Gorbacheva¹

¹Scientific Research Institute of Medical Problems of the North, Department of Child's Physical Health, Krasnoyarsk, Russian Federation

**Objectives and study:** Psychiatric comorbidity has a well-established effect on functional gastrointestinal disorders such as functional dyspepsia and irritable bowel syndrome in children and adolescents but relationship between psychiatric disorders and GERD in these age groups is not studied well. The Development and Well-Being Assessment (DAWBA) diagnostic tool was developed by R. Goodman et al. [J Child Psychol Psychiatry. 2000; 41: 645-655] as comprehensive semistructured interview for the diagnosis of psychiatric disorders and has been found to been an effective diagnostic tool in clinical and epidemiological settings. We aimed to investigate the DAWBA estimated psychiatric disorders in urban adolescents with GERD-related symptoms and its impact on daily life.

**Methods:** We performed a questionnaire-based survey of 173 urban Siberian (Krasnoyarsk, Russia) adolescents aged 12-18 using the Russian version of Gastroesophageal Reflux Disease Questionnaire (GerdQ) and computer-assisted DAWBA package of interviews. The sum of the scores for the six GerdQ questions ranged from 0 to 18 and was defined as the GerdQ score, with a score ≥ 8 indicative of high probability for GERD. The sleep disturbance and use of medication are also used for assessment of the impact of GERD on daily life, giving a separate ‘impact score’ (IS) ranging from 0 to 6. GerdQ positive adolescents were divided into two groups, with low (IS≤3) and high (IS>3) impact of GERD on daily life. Each of psychiatric disorders was coded on a computer-generated 5-point probability scale. Data are shown as Mean (Mean–SE-Mean+SE) of computer-predicted probability. The Kruskal-Wallis test (KW) was used to determine differences between groups.

**Results:** Significant positive associations were detected between GERD presence and depressive disorder (Table 1). Notably, the probability of a depressive disorder increased with impact of GERD on daily life. No associations were revealed between GERD-related symptoms and anxiety, phobias, posttraumatic stress disorder and obsessive-compulsive disorder.
Table: Computer-predicted probability of psychiatric disorders, generated by the DAWBA, in adolescents with GERD

<table>
<thead>
<tr>
<th>PSYCHIATRIC DISORDERS</th>
<th>No GERD (n=121)</th>
<th>GERD with low impact (n=40)</th>
<th>GERD with high impact (n=12)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>KW</td>
</tr>
<tr>
<td>Specific phobia</td>
<td>0.50 (0.45-0.56)</td>
<td>0.40 (0.32-0.48)</td>
<td>0.92 (0.60-1.23)</td>
<td>0.186</td>
</tr>
<tr>
<td>Social phobia</td>
<td>0.24 (0.19-0.29)</td>
<td>0.53 (0.38-0.67)</td>
<td>0.25 (0.12-0.38)</td>
<td>0.126</td>
</tr>
<tr>
<td>Posttraumatic stress disorder</td>
<td>0.25 (0.20-0.31)</td>
<td>0.30 (0.20-0.40)</td>
<td>0.17 (0.05-0.28)</td>
<td>0.807</td>
</tr>
<tr>
<td>Obsessive-compulsive disorder</td>
<td>0.37 (0.32-0.42)</td>
<td>0.35 (0.26-0.44)</td>
<td>0.42 (0.22-0.61)</td>
<td>0.963</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>1.29 (1.24-1.35)</td>
<td>1.40 (1.28-1.52)</td>
<td>1.33 (1.15-1.52)</td>
<td>0.862</td>
</tr>
<tr>
<td>Depressive disorder</td>
<td>0.98 (0.87-1.10)</td>
<td>1.45 (1.23-1.67)</td>
<td>1.75 (1.42-2.08)</td>
<td>0.014</td>
</tr>
</tbody>
</table>

Conclusion: These results indicate that some psychological symptomatologies, such as depressive disorder, are positively associated with GERD-related symptoms in urban adolescents. We suggest that chronic stress may lead to acid overproduction and violation of gastrointestinal motility and visceral sensitivity. High probability of depressive disorder should be taken into account when evaluating the adolescents with GERD. The reported study was funded by Russian Foundation for Basic Research, Government of Krasnoyarsk Territory, Krasnoyarsk Region Science and Technology Support Fund to the research project № 16-44-240668.
Reporting on outcome measures in pediatric gastroesophageal reflux disease (GERD): a systematic review

Maartje Singendonk¹, Anna Brink¹, Faridi Van Etten - Lamaludin², Miranda Langendam³, Nina Steutel¹, Michiel van Wijk¹, Marc Benninga¹, Merit Tabbers⁴

¹Academic Medical Center/Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Academic Medical Center, Medical Library, Amsterdam, Netherlands
³Academic Medical Centre, Department of Clinical Epidemiology, Bioinformatics and Biostatistics, Amsterdam, Netherlands
⁴Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Gastroesophageal reflux (GER) is defined as GER disease (GERD) when it leads to troublesome symptoms and/or complications. No gold standard test for its diagnosis exists, which hampers uniform evidence based clinical management. We hypothesized that definitions and outcome measures in randomized controlled trials (RCTs) on pediatric GER(D) would also be heterogeneous. Therefore, our aim was to systematically assess definitions and outcome measures in RCTs on children with GER(D).

Methods: Embase, MEDLINE and Pubmed were searched from inception to November 2015. A study was included if it was an English-written therapeutic RCT concerning GER(D) in children 0-18 years old. Data were tabulated and presented descriptively. Quality was assessed using the Delphi score.

Results: A total of 1105 unique articles were found; 46 articles were included. Twenty-six (57%) studies defined GER, using 25 different definitions, and investigated 25 different interventions. GERD was defined in 21 (46%) studies, all using a unique definition and investigating a total of 23 interventions. Respectively 87 and 61 different primary outcome measures were reported by the studies in GER and GERD. Eight (17%) studies did not report on side-effects. Of the remaining studies, eighteen (47%) included side-effects as predefined outcome measure and 4 (11%) as a primary outcome measure. Sixteen studies (35%) were of good methodological quality.

Conclusion: Inconsistency and heterogeneity exist in definitions and outcome measures used in RCTs on pediatric GER and GERD. To improve comparison between future studies, we recommend the development of a minimum core outcome set (COS) for clinical research in children with GER and GERD.
Two-way stratification of pediatric achalasia patients by using novel pressure-impedance parameters

Maartje Singendonk¹, Taher Omari², Nathalie Rommel³, Michiel van Wijk¹, Marc Benninga¹, Rachel Rosen⁴, Sam Nurko⁴

¹Academic Medical Center/Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Flinders University, School of Medicine, Bedford Park, Australia
³University of Leuven, Translational Research Center for Gastrointestinal Diseases, Leuven, Belgium
⁴Children’s Hospital Boston, Center for Motility and Functional Gastrointestinal Disorders, Boston, United States

Objectives and study: In achalasia, absent peristalsis and reduced esophagogastric junction (EGJ) relaxation and compliance underlie dysphagia symptoms. Novel high-resolution impedance manometry (HRIM) variables, i.e. bolus presence time (BPT) and trans-EGJ-bolus flow time (BFT) have been developed to estimate the duration of EGJ opening and trans-EGJ bolus flow. The aim of this study was to evaluate esophageal motor function and bolus flow by BPT and BFT in children with achalasia.

Methods: HRIM recordings from 20 children who fulfilled the Chicago Classification (V3.0) criteria for achalasia (seven treated achalasia patients with persisting symptoms studied post-treatment) were compared with recordings of 15 children with normal esophageal HRM findings and no other evidence suggestive of achalasia. Matlab-based analysis software was used to calculate BPT and BFT. The BFT/BPT ratio was used to estimate the effectiveness of trans-EGJ emptying relative to the period of bolus presence (i.e. BFT/BPT=1: unrestricted trans-EGJ flow; BFT/BPT=0.5: flow during only half the period of bolus presence).

Results: Integrated relaxation pressure (IRP4s) was significantly higher in untreated achalasia patients (Figure 1; adjusted p<0.001 vs normal motility and p=0.014 vs treated achalasia), but did not differ between treated achalasia patients and patients with normal motility (adjusted p=0.892). Patients with normal motility had significantly higher BFT and BPT compared to both untreated and treated achalasia patients (BFT: adjusted p<0.001 and p=0.020; BPT: adjusted p=0.001 and p=0.020 respectively), but there was no difference between treated and untreated achalasia patients (adjusted p=0.662 and p=1.000 respectively). BPT and BFT correlated significantly in patients with normal motility (r=0.961, p<0.001), but not in (un)treated achalasia patients (p=0.078 and p=0.027 respectively). There was a two-way stratification of achalasia patients; those in whom the BPT and BFT were proportional (i.e. BFT/BPT ≥0.5), but significantly lower than in patients with normal motility, and those in whom BFT was disproportionately lower than BPT (i.e. BFT/BPT <0.5).
**Table:**

**Figure 1 – EGJ related parameters in achalasia patients and patients with normal motility**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Normal Motility</th>
<th>Untreated Achalasia</th>
<th>Treated Achalasia</th>
</tr>
</thead>
<tbody>
<tr>
<td>IRP4s</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>BFT</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
<tr>
<td>BPT</td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
<td><img src="image" alt="Graph" /></td>
</tr>
</tbody>
</table>

*a* vs. Normal, *b* vs. Untreated Achalasia type II, *c* vs. Treated Achalasia type II (\(^{a,b,c}p<0.05\), \(^{aa,bb,cc}p<0.01\), \(^{aaa,bbb,ccc}p<0.001\))

**Conclusion:** Unlike IRP4s, BPT and BFT were significantly different between treated symptomatic achalasia patients and normal patients. Stratifying pediatric achalasia patients based on BPT and BFT may help determine whether esophageal bolus transport to the EGJ and/or esophageal emptying through the EGJ are aberrant and may help to better understand the pathophysiology of postoperative problems.
Paediatric functional dyspepsia in adulthood: what’s up?

Justo Valverde-Fernandez¹, Alejandro Rodriguez-Martinez², Maria Rubio-Murillo¹, Jose Carlos Salazar Quero¹, Beatriz Espin-Jaime¹

¹Hospital Virgen del Rocio, Gastroenterology, Hepatology and Nutrition Unit, Seville, Spain

Objectives and study: There is a clear knowledge of the evolution of many pediatric diseases in adulthood. This is not the case of functional dyspepsia, a lot of questions about its transition in adult remains unknown. Our goal is to introduce the evolution of functional dyspepsia in our sample, and try to identify potential prognostic factors that may influence in the persistence of dyspepsia.

Methods: It is a retrospective longitudinal study, with patients over 18 years, who were diagnosed of functional dyspepsia with less than 14 years old in our hospital (from 2006 to 2011). Organic disease was excluded in all patients, including normal upper endoscopy. They were contacted by telephone, informed consent was obtained before conducting the interview. First of all, we confirmed the pediatric functional dyspepsia and then this diagnosis was reviewed in adulthood, following the Rome III diagnostic criteria. We analyzed in each patient: other diseases, extra-intestinal symptoms, treatment administrated and functional gastrointestinal disorders in first-degree. All these variables were analyzed using contingency tables.

Results: Initially 58 adults were recruited. 12 patients did not answer the call or were not interested in the study. Another 16 were excluded after reviewing the medical history. Finally 32 adults were included (10 men and 22 women) and fifteen of them met the Rome III criteria of dyspepsia (59.4%), 6 are now worse than before (31.5%). 23 children with functional dyspepsia did treatment with proton-pump inhibitor (71.8%), adults had a similar percentage (73.7%). 18 children with functional dyspepsia had a first-degree relative with functional gastrointestinal disorder (56.2%). When we analyzed the possible prognostic factors, we found a statistically significant relationship: the existence of a first-degree familiar with functional gastrointestinal disorders (with Fisher's Exact Test. P<0,05). The other analyzed variables have not shown statistical significance.

Conclusion: A high percentage of children with dyspepsia keep this disorder in adulthood. Family background of functional gastrointestinal disorders appears to be associated with persistent of dyspepsia. Sex, other diseases, extra-intestinal symptoms or treatment have not acted as prognostic factors in our group. Prospective studies to confirm these conclusions are needed.
FLACC scale to assess pain in crying infants

Kris Van de Maele¹, Koen Huysentruyt², Silvia Salvatore³, Yvan Vandenplas⁴

¹Uz Brussel, Paediatrics, Brussels, Belgium
²Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
³Clinica Pediatrica, Università Dell’insubria, Varese, Italy
⁴Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives. According to World Health Organization pain assessment should be integrated into all clinical care. Optimal pain management begins with accurate and thorough assessment that enables health-care providers to treat pain and alleviate needless suffering. Parents are often very anxious and worried about their crying infant and often interpret this as pain. The "Face, Legs, Activity, Cry, Consolability (FLACC)" scale is a validated measurement used to assess pain for children. The main objective of this study was to educate parents to observe their child and to discriminate normal from painful crying. A secondary aim was to assess the usefulness for parents to use the FLACC scale to quantify pain during crying episodes.

Methods. We conducted a prospective study (from January to September 2016) consecutively including infants submitted to oesophageal multichannel intraluminal impedance (MII) for suspected gastro-oesophageal reflux disease. The FLACC scale and scoring system were explained to the parents by a trained nurse. The parents were instructed to fill in a symptom diary and the FLACC scale whenever their infant cried. The scale uses scores in a range from 0 to 10, with 0 representing no pain and 2 the maximum pain expression for any of the five categories (face, legs, activity, cry, consolability).

Results: The explanation of the FLACC scale took a mean of 10 minutes. We recruited 44 subjects (age 20 days - 23 months). 40/44 (90%) of the parents understood the method of scoring and the importance of closely observing their child during crying episodes and of using the FLACC scale. During the investigation they properly filled in the diary and they tried to complete the score whenever crying episodes occurred. 233 episodes of crying (range 1-14/infant) were reported with complete FLACC assessment. According to the diaries of the impedance tracing, there are over 50 episodes of crying that were not registered with the FLACC score. The parents explained that this was not related to the difficulty of the scale but to the simultaneous impedance investigations requiring other activities such as filling in the detailed diary for the impedance interpretation and caring for the child.

Conclusion: We demonstrated that the FLACC scoring system is an easy and reliable tool for parents to detect and quantify pain in crying infants. Parents cooperated very well and learned to better observe, to realize that most crying episodes are accompanied by normal behavior and not necessarily manifestations of pain. The FLACC scale could be recommended before invasive tests to better identify infants with pain related crying. The FLACC scoring system may also be useful for parents to evaluate the benefit of treatment.
Patient control cross-over study between two different colon enema systems (colotip and peristeen) in children, preliminary results

Katrien Van Renterghem¹, Stephanie Van Biervliet², De Bruyne Ruth², Myriam Van Winckel², Saskia Vande Velde²

¹Ghent University Hospital, Pediatric Surgery, Ghent, Belgium
²Ghent University Hospital, Paediatric Gastroenterology and Hepatology, Ghent, Belgium

Objectives and study: Colon enemas is used especially in children with spina bifida, anorectal malformations and Hirschsprung’s disease for the treatment of constipation and/or fecal incontinence. In Belgium there are 2 different systems available: colotip ® (CT) or peristeen ® (PT). CT is a much cheaper system for colon enemas, but it is not clear if this system is less efficient or less tolerated in children then PT.

The aim of the study is a patient-control cross-over study for 2 different colon enema systems.

Methods: Children using colotip® for colon enemas were asked to participate after informed consent. A questionnaire and 2 week diary was filled with CT. Patients switched to peristeen® and filled a questionnaire and 2 week diary. Non parametric statistics by spss statistics 24® were used.

Results: 7 patients are enrolled (median 9 years, 3 girls) with consent. 3 patients had spina bifida, 2 had Hirschsprung’s and 2 had anorectal malformations. Timing and frequency during the week of the enema did not change between CT and PT. There was no statistical difference found between CT and PT for continence, time on toilet, quantity of water used, being self-reliable and Visual Analog Scale (VAS). Patients scored the 2 systems by a VAS score, where 1 means completely unsatisfied with the system and 10 means completely satisfied with the colon enema system. The results not being significant can be due to the small sample group. After using PT system: 1 patient became continent who was not with CT, 1 patient used 0.5L less water, 2 patients spent 10 minutes less time on the toilet and 1 patients became self-reliant and 4 patients can perform the colon enema with help, compared to not self-reliant with CT. The median VAS score for CT is 6, the median VAS score for PT is 8. Statistical there was a positive trend for a better VAS score and better self-reliance for PT compared to CT. All patients and parents preferred using PT, compared to CT.

Conclusion: Comparing colotip enema system to peristeen in children, peristeen is preferred. There is yet no statistical difference for various of parameters, probably due to the small group. A positive trend was found for a better VAS score and better self-reliance with PT, compared to CT. Enrollment will continue.
Children with functional gastrointestinal disorders report an abnormal response to family stress: a case-control study

Peter Lu¹, Puck Blom², Marc Benninga³, Carlos Alberto Velasco-Benitez⁴, Miguel Saps⁵

¹Nationwide Children's Hospital, Pediatric Gastroenterology, Columbus, United States
²Academisch Medisch Centrum, Amsterdam, Netherlands
³Academic Medical Center/Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
⁴Universidad del Valle, Cali, Colombia
⁵Nationwide Children's Hospital, Columbus, United States

Objectives and study: Exposure to psychological stress is an established risk factor for the development of functional gastrointestinal disorders (FGIDs). However, only a proportion of children exposed to stress develop a FGID. Our objective was to compare stress responses, coping methods, and resilience in children with and without FGIDs. We hypothesized that children with FGIDs respond to stress differently than healthy children.

Methods: We performed a case-control study. Schoolchildren meeting Rome III criteria for FGIDs and controls matched for age and sex completed validated measures of response to various types of stress (Peer Stress, Family Stress, Academic Problems, and Recurrent Abdominal Pain versions of the Response to Stress Questionnaire [RSQ]) and resilience (Connor-Davidson Resilience Scale 10 [CD-RISC-10]). Each 57-item RSQ measures 3 categories of coping methods and 2 categories of involuntary stress responses: Primary Control (e.g. problem solving), Secondary Control (e.g. positive thinking), Disengagement (e.g. avoidance), Involuntary Engagement (e.g. rumination), and Involuntary Disengagement (e.g. emotional numbing). One-way ANOVA and z-test for proportions were used to compare age and sex. Linear regression was used to compare scores while controlling for age and sex.

Results: We included 134 children with a FGID (63% F, mean age 13.4) and 135 healthy controls (62% F, mean age 13.5). Among cases, 57 had functional constipation (FC; 47% F, mean age 12.3) and 74 had an abdominal pain-predominant FGID (AP-FGID; 76% F, mean age 14.4). Children with FGIDs responded to family stress differently than controls. Children with FGIDs were more likely to take action and less likely to remain involuntarily engaged in response to family stress (p<0.001). Differences remained when comparing children with FC or AP-FGIDs to controls. Children with AP-FGIDs were also more likely to respond with involuntary disengagement through emotional numbing or wanting to escape (p=0.002). In response to abdominal pain-related stress, children with FGIDs reported using coping methods like positive thinking and acceptance less than controls (p=0.033). Response to peer and academic stress was similar between FGID groups and controls. Children with FC had lower resilience scores than controls (p=0.056), but scores were similar between children with AP-FGIDs and controls.

Conclusion: Although children with FGIDs and healthy children respond to peer and school stress in a similar manner, we found important differences in how children with FGIDs respond to family stress. These differences suggest that family stress may play a more important role in the pathophysiology of pediatric FGIDs than peer or school stress. Early recognition and management of family stressors may be a key component of the effective care of children with FGIDs.
The role of puberty in the development of pediatric functional gastrointestinal disorders: a population-based case-control study

Puck Blom¹, Peter Lu², Marc Benninga³, Carlos Alberto Velasco-Benitez⁴, Miguel Saps⁵

¹Academisch Medisch Centrum, Amsterdam, Netherlands
²Nationwide Children's Hospital, Pediatric Gastroenterology, Columbus, United States
³Academic Medical Center/Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
⁴Universidad del Valle, Cali, Colombia
⁵Nationwide Childrens Hospital, Columbus, United States

Objectives and study: Although a female predominance has been established among adults with functional gastrointestinal disorders (FGIDs), this has not been consistently shown in children. Therefore, the age at which FGIDs become more common in females remains unclear. Hormonal differences are thought to contribute to the female predominance in adults with FGIDs. We therefore hypothesized that FGIDs become more common in females after the hormonal changes that occur during puberty. Our objective was to evaluate for an association between menarchal status and physical development as assessed by Tanner stage and FGID diagnosis.

Methods: We performed a case-control study. Schoolchildren meeting Rome III criteria for FGIDs and controls matched for age and sex were asked to report their Tanner stage and females were asked to report whether they had reached menarche and if so, age at menarche and date of last menstrual cycle. Pearson’s chi-squared test and Fisher’s exact test were used for comparison as appropriate.

Results: We included 134 children with a FGID (63% female, mean age 13.4) and 135 healthy controls (62% female, mean age 13.5). Mean age of menarche was 11.8 years (SD 1.5 years). The proportion of females who were postmenarchal did not differ between children with FGIDs (63/85, 74.1%) and controls (66/85, 77.6%; p=0.59). The prevalence of FGIDs did not differ between females who reported menarche <5 years prior and ≥5 years prior. Children were placed into three developmental categories based on Tanner stage: Prepubertal (Stage I), Pubertal (Stages II-IV), and Mature (Stage V). Mature status was associated with a lower likelihood of FGID diagnosis (p=0.04), while Prepubertal and Pubertal statuses were not associated with FGID diagnosis. Developmental category was not associated with FGID diagnosis when children were divided by gender.

Conclusion: FGID diagnosis was not associated with menarchal status or physical development as assessed by Tanner stage in female participants. This suggests that pubertal hormonal changes do not play a major role in the development of FGIDs in female children and adolescents. However, participants who had reached pubertal maturation were less likely to have an FGID. This is consistent with earlier studies demonstrating lower FGID prevalence in adolescents compared to younger children.
An epidemiological study exploring the prevalence of functional gastrointestinal disorders in South American infants

Ashish Chogle¹, Carlos Alberto Velas-Benitez², Ricardo Chanis³, Milton Mejia⁴, Edgar Jativa⁵, Miguel Saps⁶

¹Children’s Hospital of Orange County, Orange, United States
²Universidad del Valle, Cali, Colombia
³Hospital del Niño, Panama City, Panama
⁴Hospital Nacional de Niños de Nicaragua, Managua, Nicaragua
⁵Universidad Central del Ecuador, Quito, Ecuador
⁶Nationwide Childrens Hospital, Columbus, United States

Objectives and study: Our aim is to perform a population-based study using Rome III criteria to describe the prevalence of FGIDs in infants in 4 countries in South America.

Methods: We conducted a multi-country cross-sectional study to investigate the epidemiology of FGIDs in children 0 to 12 months of age, using the Rome III criteria, in Colombia, Panama, Nicaragua and Ecuador. Children with organic medical diseases were excluded. Parents provided demographic information and completed the Spanish version of the Questionnaire on Pediatric Gastrointestinal Symptoms for Infants & Toddlers (QPGS III IT- Spanish).

Results: Parents of 455 infants completed the questionnaires. Eighty-six infants were excluded due to presence of organic diseases and being more than 12 months of age. One hundred and seventy four infants (38.2%) were diagnosed with at least one FGID according to the Rome III diagnostic criteria (47% female, median 5.2 months). Thirty-three infants (7.2%) had more than one FGID diagnosis. Functional constipation and regurgitation were the most commonly diagnosed disorders in infants (9.2% and 9% respectively) followed by rumination and colic (5.9% and 5.7% respectively). Analysis revealed that being the only child in the family, the first born child, having divorced or separated parents, family history of FGIDs or prior history of diarrhea did not result in a higher FGID prevalence in these infants.

Conclusion: Current findings suggest that FGIDs are common in infants from South America. Functional constipation and regurgitation were the most common FGIDs in infants.
Lactobacillus casei rhamnosus Lcr35 in the management of functional constipation in children: a randomized trial

Katarzyna Wojtyniak1, Andrea Horvath1, Piotr Dziechciarz1, Hania Szajewska1

1The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland

Objectives and study: Although not currently recommended, probiotics are commonly used to treat functional constipation in children. We assessed the effectiveness of Lactobacillus casei rhamnosus Lcr35 (Lcr35) in the management of functional constipation in children.

Methods: A randomized, double-blind, placebo-controlled trial was conducted in 94 children aged <5 years with functional constipation according to the Rome III criteria. Children were assigned to receive Lcr35 (8 x 10^8 colony-forming units, n=46) or placebo (n=48), twice daily, for 4 weeks. The primary outcome measure was treatment success, defined as 3 or more spontaneous stools per week, without episodes of fecal soiling, in the last week of the intervention. Analyses were by intention to treat.

Results: Eighty-one (86%) children completed the study. There was no significant difference in treatment success between the placebo and the Lcr35 group (28/40 versus 24/41, respectively; relative risk, 0.6, 95% confidence interval, CI, 0.24 to 1.5, p=0.4). With one exception, there were no statistically significant differences between groups in the stool consistency, frequency of fecal soiling, frequency of pain during defecation, frequency of abdominal pain or flatulence, need for additional laxative treatment, and adverse events. Compared with the placebo group, in the Lcr35 group there was a significantly reduced defecation frequency throughout the study, including at intervention end (week 4) [median (IQR) 6 (4.0, 9.0) versus 4 (3.0, 5.0); median difference, MD, 2, 95% CI 0.5 to 4, p=0.005].

Conclusion: Lcr35 as a sole treatment was not effective in the management of functional constipation in children younger than 5 years. This study adds to current recommendations that do not support the use of probiotics in the treatment of childhood constipation.
Effects of metabolites from different probiotic strains on RV infection in an in-vitro model of RV diarrhea

Vittoria Buccigrossi¹, Maiara Brusco de Freitas², Eugenia Bruzzese³, Antonella Marano⁴, Noemi Iannuzzi⁵, Alfredo Guarino⁴

¹University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
²Federal University of Santa Catarina, Brazil, Department of Nutrition, Graduate Program in Nutrition, Florianopolis, Brazil
³University of Naples Federico II, Naples, Italy
⁴University of Naples Federico II, Dept.of Translational Medical Science, Section of Pediatrics, Naples, Italy

Objectives and study: Rotavirus (RV) causes diarrhea through a sequence of ion secretion and epithelial damage induced by its enterotoxin NSP4 or directly, respectively. Probiotics are recommended for active therapy of gastroenteritis. Postbiotics are non-viable bacterial products or metabolites from probiotic microorganisms that have biological activity in the host. We investigated the effects of secreted molecules by three different probiotic strains in an in-vitro model of RV diarrhea in human enterocytes.

Methods: Caco-2 cell monolayers were preincubated with conditioned media from S. boulardii (SB), L. reuteri (LR) and L. paraceasei (LP) and then exposed to NSP4 or infected with RV. Short circuit current (Isc) and transepithelial resistance (TER) were measured in Ussing chambers as parameters of fluid secretion and epithelial damage, respectively.

Results: Ion secretion: All 3 postbiotics significantly inhibited the NSP4-induced ion secretion measured in Ussing chambers (Table).

Epithelial damage: All postbiotics inhibited RV epithelial damage with a maximal effect by SB and LR (Table).

Table: Effects of conditioned media by three probiotics strains on the cytotoxic effects induced by RV

<table>
<thead>
<tr>
<th></th>
<th>Enterotoxic effect: Isc (µA/cm²)</th>
<th>Cytotoxic effect: TER (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Controls</td>
<td>+0,4±0,5</td>
<td>Controls 100</td>
</tr>
<tr>
<td>NSP4</td>
<td>+9,24±0,3³</td>
<td>RV 33,5⁶</td>
</tr>
<tr>
<td>SB + NSP4</td>
<td>-4,55±0,73 -149,2%</td>
<td>SB + RV 92,2</td>
</tr>
<tr>
<td>LR + NSP4</td>
<td>-0,70±0,49 -107,6%</td>
<td>LR + RV 96,3</td>
</tr>
<tr>
<td>LP + NSP4</td>
<td>-2,46±0,29 -126,6%</td>
<td>LP + RV 79,6</td>
</tr>
</tbody>
</table>

³p<0,005 vs controls; ⁶p<0,005 vs RV; ⁵% of TER decrease at 48 hours post-infection compared with initial value of transepithelial resistance

Conclusion: The three postbiotics limited chloride secretion and cytotoxic damage induced by RV with different potency. SB exerts the maximal effect in terms of both ion secretion and epithelial integrity acting in the short and long-term. These results open for new study to identify specific and effective moieties representing a new option for treatment of acute gastroenteritis.
Evaluation of gelatine tannate against symptoms of acute diarrhoea in paediatric patients

Eren Çağan¹, Saime Ceylan², Şenay Mengi², Havva Hasret Çağan²

¹University of Medical Sciences Bursa Yüksek İhtisas Teaching Hospital, Department of Pediatrics Division of Pediatric Infectious Diseases, Bursa, Turkey
²University of Medical Sciences Bursa Yüksek İhtisas Teaching Hospital, Bursa, Turkey

Objectives and study: Acute diarrhoea, with or without vomiting, is a frequent problem in childhood. Mucoprotective agents such as gelatin tannate and xyloglucan help to reestablish normal intestinal function. Besides its mucoprotective activity, additional evidence suggests that gelatin tannate reduce inflammation, prevents growth of some bacterial species, and preserves the intestinal mucous layer. Thus, in line with the need for additional assessment of mucoprotectors, the current single-centre, randomised, controlled, double-blind trial was designed to assess the efficacy and safety of gelatin tannate in paediatric patients with acute diarrhoea.

Methods: This randomised, controlled, double-blind, parallel-group, single-centre clinical trial was conducted to determine the efficacy and safety of gelatin tannate plus ORS, compared with ORS plus placebo, in paediatric patients (aged 3 months to 12 years) with infectious or noninfectious acute diarrhoea.

Results: A total of 251 eligible patients were enrolled in the trial. 203 patients completed the study (gelatin tannate plus ORS, n=103; ORS alone, n=100). As shown in Figure 1, at all study assessment timepoints from 24 hours onwards, the incidence of nausea was significantly lower in the gelatin tannate-plus-ORS group than the ORS group alone (p=0.01). The same was true for abdominal pain (at 24 hours: p=0.02). From 12 hours onwards, the incidence of watery stools was significantly lower in the gelatin tannate than ORS group (p=0.01). Significantly more patients in the combination than ORS-alone group had dehydration at baseline (p<0.01). Subsequently, no significant difference in the occurrence of dehydration was noted between the two groups, since all patients in both groups were treated with ORS. Nonetheless, from 36 hours onwards, a nonsignificant trend (p=0.05) was evident towards a lower incidence of dehydration in the combination than ORS-alone group. After 36 and 72 hours’ hospitalisation, fever was recorded in significantly fewer patients treated with gelatin tannate plus ORS rather than in the ORS-alone group (p<0.01).

Effects on stool frequency
As shown in Figure 2, from 12 hours onwards, stool frequency was significantly lower in the gelatin tannate-plus-ORS group than in the ORS-alone group (at 12 hours: p<0.01). At all timepoints during the study, the proportion of patients with SDI improvement, indicating resolution of diarrhoea, was significantly greater (p<0.01) in the gelatin tannate-plus-ORS group than in the ORS-alone group (at 12 hours: p<0.01; Figure 3).

No adverse events occurred during the trial.

Vol. 64, Supplement 1, April 2017 416
FIGURE LEGENDS

Figure 1. Effects of gelatin tannate (GT) plus oral rehydration solution (ORS), versus ORS alone, on symptoms of acute diarrhoea during hospitalisation. Statistical significance: § p=0.05; # p=0.02; * p≤0.01.

![Nausea Graph](image1)

![Abdominal pain Graph](image2)
Figure 2. Effects of gelatin tannate (GT) plus oral rehydration solution (ORS), versus ORS alone, on stool frequency in patients hospitalised with acute diarrhoea. 
Statistical significance: $p<0.01$ at all timepoints, including baseline.
**Figure 3.** Effects of gelatin tannate (GT) plus oral rehydration solution (ORS), versus ORS alone, on Stool Decrease Index (SDI) in patients hospitalised with acute diarrhoea. *Statistical significance:* p<0.01 for GT + ORS vs ORS alone at all timepoints.

**Conclusion:** administration of gelatin tannate in combination with ORS is an effective and safe option for the treatment of acute diarrhoea in the paediatric population.
Infectious esophagitis in a secondary level hospital in the south of Madrid

Josefa Barrio Torres¹, Beatriz Martínez Escribano¹, Cristina Pérez-Fernández¹, Lorena Costal¹, Carlos Grasa Lozano¹, Arantxa Vidal Esteban¹

¹Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Madrid, Spain

Objectives and study: Infectious esophagitis (IE) appears to be rare in childhood and is a disorder commonly associated with immunosuppression, although it has also been diagnosed in immunocompetent patients. The most common infectious agents are Candida Albicans, Herpes simplex type I virus and Cytomegalovirus.

Our aim is to describe the clinical, epidemiological and laboratory findings in pediatric patients with IE represented in a secondary level hospital.

Methods: Retrospective descriptive study in children aged 16 and below diagnosed with infectious esophagitis over a period of 8 years (2007-2015) in a hospital in the South of Madrid. We identify children with IE based on endoscopic, anatomopathological and microbiological findings. Description of demographics, clinical data and management of these patients was carried out.

Results: During the period of study, 1040 endoscopic procedures were performed: ten of those patients reported being suspicious of herpetic esophagitis, but only seven actually received laboratory confirmation (70%). The mean age was eight years old (SD 3.56), predominantly boys (80%). The more frequent symptoms were fever and dysphagia, presented in the emergency department in 90% of those patients. One patient was receiving oral treatment with fluticasone because of Eosinophilic Esophagitis (EoE) when the symptoms began, but no alteration in immune system was detected in any patient. Nine out of 10 children were admitted and managed with intravenous acyclovir. They all improved making a complete recovery from the symptoms. A follow-up endoscopy was performed, and an underlying condition in the gastrointestinal tract was detected in all children. An EoE, previously unknown, was diagnosed in seven of them, reflux esophagitis in two of them, and celiac disease in one.

Four patients out of 1040 were diagnosed with Esophageal Candidiasis. In three of them, an endoscopy was performed as a review for previous pathology (two reflux esophagitis and one EoE). The fourth patient claimed abdominal pain and reflux. All of them were males, and the mean age was 12 years old (SD 2.3). All were treated with fluconazole, and just two months later, they had made a complete recovery based on endoscopic and histopathological findings. All of them were immunocompetent patients.

Conclusion: None of the patients with infectious esophagitis had alteration in immune system but most of them had a previous esophageal pathology.

In patients with Infectious Esophagitis, a follow-up endoscopy after resolution will help rule out an underlying esophageal disease. In our short series, most Herpetic Esophagitis patients came down with an Eosinophilic Esophagitis.
Probiotics for gastrointestinal disorders: proposed recommendations for children of Asia-Pacific region

Donald Cameron¹, Quak Seng Hock², Musal Kadim³, Neelam Mohan⁴, Eell Ryoo⁵, Bhupinder Sandhu⁶, Yuichiro Yamashiro⁷, Chen Jie⁸, Hans Hoekstra⁹, Alfredo Guarino¹⁰

¹Monash University, Monash Children’s Hospital, Royal Children’s Hospital, Melbourne, Australia
²National University of Singapore, Yong Loo Lin School of Medicine, Singapore, Singapore
³University of Indonesia, Child Health Department, Cipto Mangunkusumo Hospital, Jakarta, Indonesia
⁴Medanta The Medicity, Gurgaon, Department of Pediatric Gastroenterology, Hepatology And Liver Transplantation, Haryana, India
⁵Gachon University and Gachon Children’s Hospital, Department of Pediatrics, Incheon, Korea, Rep. of South Korea
⁶Royal Hospital for Children, Department of Paediatric Gastroenterology, Bristol, United Kingdom
⁷Juntendo University Graduate School of Medicine, Probiotics Research Laboratory, Bunkyo-Ku, Japan
⁸Juntendo University Graduate School of Medicine, 7probiotics Research Laboratory, Tokyo, Japan
⁹Hieronymus Bosch Hospital, Department of Pediatrics, ’s-Hertogenbosch, Netherlands
¹⁰University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Napoli, Italy

Objectives and study: Recommendations for probiotic use for treatment or prevention in of pediatric intestinal diseases have been produced by scientific societies in several continents, but not in Asia-Pacific region. This paper proposes recommendations for probiotic use for prevention and treatment of gastrointestinal diseases for children living in Asia-Pacific region. Recommendations are based on existing guidelines and on trials conducted in Asia-Pacific countries as well as on considerations of local conditions.

Methods: Target intestinal diseases were identified and their epidemiological and clinical pattern in Asia-Pacific countries were discussed by a panel of experts. Current evidence-based recommendations and guidelines and randomized-controlled trials in the region were revised. Cultural aspects, health management issues, and economic factors were also taken into consideration to formulate recommendations. The strength of each recommendation was rated using the GRADE system.

Results: The probiotic strains *Saccharomyces boulardii* CNCM I-745 (Sb) and *Lactobacillus rhamnosus* GG (LGG) were strongly recommended as active treatment of gastroenteritis in adjunct to oral rehydration. Also *Lactobacillus reuteri* can be considered. Probiotics may be considered based on evaluation of candidate patients and local setting for the following indications (with the indicated strains): prevention of antibiotic associated diarrhea (LGG or Sb); prevention of *Clostridium difficile*-induced diarrhea (Sb); prevention of nosocomial diarrhea (LGG); prevention of infantile colics (*L. reuteri*); adjunctive treatment of *Helicobacter pylori* (Sb and others). Finally probiotics may be considered in infants for prevention of necrotizing enterocolitis but the decision should be left to the physician and discussed with the parents of candidate preterm babies in the light of individual conditions. There is insufficient evidence to formulate recommendations for other gastrointestinal diseases.

Conclusion: Despite a diversity of epidemiological, socioeconomical and health system conditions, common recommendations for Asia-Pacific may be applicable. However these need to be validated with local randomized-controlled trials.
The association between hepcidin and iron deficiency in children with Helicobacter pylori infection

Szu-Ta Chen¹, Chuan-Chun Li², Shing-Hwa Liu³, Yen-Hsuan Ni⁴
¹National Taiwan University Hospital Yun-Lin Branch, Dept. of Pediatrics, Dou-Liu City, Taiwan
²National Taiwan University Hospital Yun-Lin Branch, Dept. of Laboratory Medicine, Yun-Lin County, Taiwan
³Institute of Toxicology, National Taiwan University, Taipei, Taiwan
⁴National Taiwan University, Dept. of Paediatrics, Taipei, Taiwan

Objectives and study: Helicobacter pylori infection could result in chronic antral gastritis, peptic ulcer disease, and gastric cancer. Chronic inflammation and various cytokines reactions are thought to influence different consequences of H. pylori infection. Iron deficiency (ID) and iron deficiency anemia (IDA) are major complications in some children with H. pylori infection. Interfering iron absorption and increased iron consumption by bacteria are reported to contribute to iron deficiency. Hepcidin is known as an important regulator in iron homeostasis and could be induced by chronic inflammation. The role of hepcidin in H. pylori-infected children remains unclear. In this study, we aim to analyze the serum hepcidin, cytokines levels and the iron profiles in children with H. pylori infection.

Methods: Subjects (n = 43) aged between 10 to 18 years were enrolled, based on a positive serology testing for anti-H. pylori IgG. Serum hepcidin level and iron profiles, including iron, ferritin, and total iron binding capacity, were measured. ID is defined as iron saturation below 15%. Subjects were divided into two groups: (1) low hepcidin (n = 21); (2) high hepcidin (n = 22). Serum levels of IL-1 beta, IL-6 and IL-8 were analyzed and compared between two groups.

Results: Among 43 cases, the serum hepcidin levels were ranged 0.09 – 30.37 ng/mL (median, 6.38 ng/mL). The serum iron, ferritin levels, and iron saturation in subjects with low and high hepcidin groups were 94.1 ± 42.8 µg/dL and 127.1 ± 44.0 µg/dL, 42.3 ± 23.2 µg/mL and 98.1 ± 53.8 µg/mL, and 22.5 ± 10.8 % and 35.9 ± 14.0 %, respectively. Serum iron, ferritin levels, and iron saturation were significantly lower in low hepcidin group than in high hepcidin group (P = 0.0150, 0.0001, and 0.0006, respectively). The prevalence of ID was significantly higher in low hepcidin group than in high hepcidin group (33.3% v.s. 4.5%, P = 0.015). The serum levels of cytokines IL-1 beta, IL-6, and IL-8 were 3.96 ± 4.28 pg/mL, 2.58 ± 2.65 pg/mL, and 16.77 ± 13.07 pg/mL in low hepcidin group and 8.39 ± 3.34 pg/mL, 5.55 ± 2.60 pg/mL, and 16.56 ± 9.49 pg/mL in high hepcidin group. The serum levels of IL-1 beta and IL-6 were significantly decreased in low hepcidin group (P = 0.0065 and 0.0021).

Table:

<table>
<thead>
<tr>
<th></th>
<th>Low Hepcidin (n = 21)</th>
<th>High Hepcidin (n = 22)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Iron (µg/dL)</td>
<td>94.1 ± 42.8</td>
<td>127.1 ± 44.0</td>
<td>0.0150</td>
</tr>
<tr>
<td>TIBC (µg/dL)</td>
<td>421.7 ± 59.1</td>
<td>362.0 ± 67.3</td>
<td>0.0003</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>42.3 ± 23.2</td>
<td>42.3 ± 23.2</td>
<td>0.0001</td>
</tr>
<tr>
<td>Iron Saturation (%)</td>
<td>22.5 ± 10.8</td>
<td>35.9 ± 14.0</td>
<td>0.0006</td>
</tr>
<tr>
<td>IL-1 beta (pg/mL)</td>
<td>3.96 ± 4.28</td>
<td>8.39 ± 3.34</td>
<td>0.0065</td>
</tr>
<tr>
<td>IL-6 (pg/mL)</td>
<td>2.58 ± 2.65</td>
<td>5.55 ± 2.60</td>
<td>0.0021</td>
</tr>
<tr>
<td>IL-8 (pg/mL)</td>
<td>16.77 ± 13.07</td>
<td>16.56 ± 9.49</td>
<td>0.7337</td>
</tr>
</tbody>
</table>
**Conclusion:** Among children with positive anti-*H. pylori* antibody, low serum hepcidin was associated with lower serum iron level and higher ID prevalence. Increased IL-1 beta and IL-6 levels were associated with high serum hepcidin. Instead of the cause of ID, hepcidin expression might be the consequence of inflammatory cytokines in children with *H. pylori* infection.
Resolution of symptoms in pediatric patients with Clostridium difficile infection following administration of a bioactive polyphenol supplement: results of an open-label study

Anders Dahlstrom¹, Helen Pavis², Thomas Lawson³

¹Stanford University, Monterey, United States
²Pediatric Gastroenterology of Monterey, Monterey, United States
³Lawson & Associates, Clinical Research, Berkeley, United States

Objectives and study: Presentation of Clostridium difficile-associated diarrhea following administration of antibiotics is a health concern for patients of all ages. The objectives of this pilot study were to determine whether a bioactive polyphenol supplement has a clinical benefit by reducing frequency and severity of diarrhea and other symptoms and if the supplement can eliminate C. difficile toxin A from the stool of pediatric patients.

Methods: With parental consent, a prospective open-label study was conducted in a pediatric gastroenterology outpatient clinic on patients with chronic diarrhea who had not responded to standard treatment. Those who were still C. difficile enterotoxin A positive were given the polyphenol-based supplement (LiveLeaf, Inc., San Carlos, CA, USA) daily in serving sizes based upon their weight. Symptoms were monitored for up to 21 days and stools retested for toxin A one week after the treatment period.

Results: A total of 15 patients, ranging in age from 1 month to 16 years, with chronic diarrhea and additional symptoms of abdominal pain, rectal bleeding, and growth failure, were monitored and treated. Following consumption of the supplement, diarrhea resolved completely in 9 (60%) of the patients, with the median time to resolution within 14 days, and was reduced in volume and frequency in another 3 (20%). Twelve (80%) of the patients without IBD were found to be C. difficile toxin A negative in post-treatment stool sampling. Of the three patients who remained toxin A positive, one had complete symptom resolution, one had reduction in diarrhea, and one with comorbidity of Crohn's disease had no improvement in diarrhea or abdominal pain. No adverse events were reported.

Conclusion: In patients with C. difficile infection, resolution of diarrhea without antibiotics is the goal. Use of this bioactive polyphenol supplement resulted in resolution of diarrhea and elimination of C. difficile toxin A from stool cultures in the majority of pediatric patients, with no side effects. Resolution of diarrhea in the majority (80%) of non-IBD patients with no side effects using this supplement makes it an attractive alternative to repeated antibiotic treatments.

Disclosure of interest: Thomas Lawson, PhD, Consultant to LiveLeaf, inc.
Resolution of chronic diarrhea in pediatric patients following administration of a bioactive polyphenol supplement

Anders Dahlstrom¹, Helen Pavis², Thomas Lawson³

¹Stanford University, Monterey, United States
²Pediatric Gastroenterology of Monterey, Monterey, United States
³Lawson & Associates, Clinical Research, Berkeley, United States

Objectives and study: Multiple infectious agents, food proteins, and inflammatory bowel disease (IBD) are primary causes of chronic diarrhea (> 3 weeks), a major cause of morbidity in children. Treatment with antibiotics is not recommended for the majority of bacterial gastrointestinal infections and can exacerbate the condition, which is why alternative treatments are needed. The objective of this study was to assess the capability of a bioactive polyphenol supplement to attenuate chronic diarrhea in children caused by multiple intestinal infections and other conditions.

Methods: With parental consent, a prospective open-label pilot study was conducted in a pediatric gastroenterology outpatient setting on patients with chronic diarrhea who had not responded to standard treatment. These patients were given a polyphenol-based supplement (LiveLeaf Bioscience, San Carlos, CA) daily for three weeks, in serving sizes based upon their weight. Positive clinical response was measured as resolution of diarrhea and/or negative bacterial cultures and stool inflammatory markers after 3 weeks' use of the supplement. Adverse events were recorded as to type and treatment given, if needed.

Results: A total of 40 patients, ranging in age from 1 month to 18 years, were followed for up to four weeks. The primary symptom for all patients was chronic diarrhea, with etiologies of Clostridium difficile (40%), Salmonella (12%), Shigella (5%), Campylobacter (3%), and intolerance to cow's milk and other proteins causing enterocolitis (22%). IBD was the sole diagnosis or a comorbidity in 30% of the patients. Diarrhea resolved completely in 65% of all patients in the study, in 67% of those with cow's milk protein enterocolitis, and in 90% of all non-IBD patients following consumption of the supplement. Of those with a response, 85% of the diarrheal episodes resolved within 14 days after starting use of the supplement; 42% resolved within the first week. After administration of the supplement, 13/16 C. difficile, 3/5 Salmonella, and 2/2 Shigella cultures were negative in subsequent testing. Those whose diarrhea did not resolve had comorbidities of ulcerative colitis (10%) and Crohn's disease (10%). No adverse events were reported in any child.

Conclusion: Polyphenols have both anti-inflammatory and anti-infective effects. We evaluated a bioactive polyphenol supplement in a pediatric population with chronic diarrhea and demonstrated that its consumption was an effective treatment alternative, with no side effects. This supplement warrants a randomized, controlled clinical study.

Disclosure of interest: Thomas Lawson, PhD Consultant to LiveLeaf, Inc.
Lower prevalence of pathogenic E.coli in stools from children with allergy compared to healthy children

Ilva Daugule¹, Daiga Karklina¹, Silvija Remberga¹, Dmitrijs Perminovs², Mikus Gavars², Ingrida Rumba-Rozenfelde¹

¹University of Latvia, Faculty of Medicine, Riga, Latvia
²University of Latvia, Riga, Latvia

Objectives and study: Although Escherichia coli (E.coli) is a part of the normal gastrointestinal microflora, pathogenic variants could cause diarrheal diseases, although asymptomatic carriage of pathogenic E.coli in children has been described. However, studies show that gastrointestinal microflora is an important player also in the development of allergy.

The aim of the study was to identify the presence of different pathogenic E.coli in stool samples of allergic and healthy children, in addition, to analyze factors associated with the presence of pathogenic E.coli.

Methods: Parents of children at primary health care centres/ kindergartens and allergologist consultation were asked to bring a stool sample and answer a questionnaire (breast feeding, parental education, family, allergy in family, previous treatment with antibiotics). DNA was extracted from stool samples and analysed for the presence of pathogenic E.coli - enterotoxigenic(ETEC), enteroaggregative(EAEC), enteropathogenic(EPEC), enterohemorrhagic (EHEC) and type O157 - by PCR.

Results: The final patient sample contained 209 children (median of age - 5.5 years, range 1-6 years; boys 45%): out of them 114 were healthy children, 95 – had allergy (food allergy, asthma, allergic rhinitis). Among healthy children 22 had marked the presence of allergy in the questionnaire.

In the total sample 14% (30/209) of isolates were positive for pathogenic E.coli: 18 individuals were positive for EPEC; six – for EAEC, one - for ETEC and one – for O157. Two children carried simultaneously two types of pathogenic E.coli: EPEC/O157 and EHEC/O157; two other children carried simultaneously three types of pathogenic E.coli: EPEC/ EHEC/ETEC and EHEC/ EPEC/O157.

The prevalence of pathogenic E.coli was significantly lower among children with allergy (reported by parents and/or diagnosed at the allergologist consultation) compared to children without allergy (8.5%(10/117) vs. 21%(20/92); p=0.007) and among children with no siblings compared to those with at least one sibling (8%(7/88) vs. 20%(23/117); p=0.02).

Children positive for pathogenic E.coli compared to negative ones had slightly less duration of exclusive breast feeding (4.8 mo (±SD3.7) vs. 4.4 mo (±SD2.27), p=0.05).

Prevalence of pathogenic E.coli did not differ significantly in respect to delivery type (vaginal vs. C-section), allergy in family, parental education and antibacterial therapy (received during the previous month, previous year or during the 1st year of life).

Conclusion: In the represented population high proportion of children without gastrointestinal symptoms may carry potentially pathogenic E.coli.

Lower prevalence of pathogenic E.coli among allergic children could indirectly point to the role of hygienic conditions and sterile environment in the development of allergy.

Higher prevalence of pathogenic E.coli in children with siblings suggest more frequent infection from other children, while previous antibacterial therapy did not have an impact to the presence of pathogenic E.coli.
**GASTROENTEROLOGY: GI-infections**

**G-P-219**

**PROBAGE Study: Final report of the largest clinical trial with probiotic/synbiotics in children with acute infectious gastroenteritis in Turkey**

Ener Cagri Dinleyici, Ates Kara, Metehan Özen, Nazan Dalgic, Sirin Guven, Zafer Kurugol, Ozge Metin Akcan, Olcay Yasa, Adem Karbuz, Ahmet Sami Yazar, Ozden Turel, Burcin Nalbantoglu, Vefik Arica, Ibrahim Silfeler, Gonul Tanir, Mesut Sancar, Makkule Eren, Yvan Vandenplas

1 Eskişehir Osmangazi University Faculty of Medicine, Department of Pediatrics, Eskişehir, Turkey
2 Hacettepe University Faculty of Medicine, Department of Pediatric Infectious Diseases, Ankara, Turkey
3 Acıbadem University Faculty of Medicine, Pediatric Infectious Diseases, Istanbul, Turkey
4 Sisli Etfal Training Hospital, Pediatric Infectious Disease Unit, Istanbul, Turkey
5 Ege University Faculty of Medicine, Pediatric Infectious Disease Unit, Izmir, Turkey
6 Okmeydani Research/Training Hospital, Department of Pediatrics, Istanbul, Turkey
7 Medeniyet University, Department of Pediatrics, Istanbul, Turkey
8 Okmeydani Reserach and Teaching Hospital, Pediatric Infectious Disease Unit, Istanbul, Turkey
9 Umraniey Research/Training Hospital, Department of Pediatrics, Istanbul, Turkey
10 Bezmialem University Faculty of Medicine, Pediatric Infectious Disease Unit, Istanbul, Turkey
11 Namik Kemal University Faculty of Medicine, Department of Pediatrics, Tekirdag, Turkey
12 Yeni Yuzylı University Faculty of Medicine, Department of Pediatrics, Istanbul, Turkey
13 Mustafa Kemal University Faculty of Medicine, Department of Pediatrics, Hatay, Turkey
14 Or. Sami Ulus Children Hospital, Pediatric Infectious Disease Unit, Ankara, Turkey
15 Marmara University, Faculty of Pharmacy, Istanbul, Turkey
16 Eskişehir Osmangazi University, Pediatric Gastroenterology and Hepatology, Eskişehir, Turkey
17 Uz Brussel, Department of Pediatrics, Brussels, Belgium

**Objectives and study:** Acute gastroenteritis (AGE) continues to be a leading cause of morbidity and hospitalisation, with a huge economic burden.

**Methods:** We performed a large multicenter, randomized trial to evaluate and compare the efficacy of different probiotic strains with or without prebiotics (with 5 different study arms: see Table for the different study groups) in 1168 children with AGE. Children with AGE lasting >24 but <72 hours with clinical signs of mild to moderate dehydration were eligible for inclusion. All children received conventional oral rehydration solution (ORS) with or without probiotic/synbiotics for 5 days. All study arms were singled blind, except for the study arm Bifidobacterium lactis which was double blind. The primary endpoint was duration of diarrhoea (in hours), defined as the first normal stool according to Bristol stool score (score <5). Secondary outcome measures were duration of hospitalization (days) and percentage of children without diarrhoea 72 hours after the start of the intervention, percentage of children without diarrhoea during intervention. Adverse events were also recorded.

**Results:** In total, the duration of diarrhoea was significantly shorter in all probiotic and symbiotic study arms in comparison to placebo (Table 1). The length of hospitalisation was significantly reduced in all probiotic/synbiotic study arms, except for the group *Lactobacillus GG plus BB12*. The efficacy is already detectable after 24 hours, but increases after 48 hours and is largest after 72 hours. The efficacy of the probiotics is also related with the severity of the diarrhoea as efficacy starts more rapid and is larger in outpatients than in children requiring hospitalization. All investigated products are safe and well-tolerated in in- and outpatients.
### Table 1: Duration of diarrhoea in children with acute infectious gastroenteritis related to different probiotics or synbiotics

<table>
<thead>
<tr>
<th>Investigated Products plus ORS</th>
<th>ORS plus placebo</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>Lactobacillus acidophilus, L. rhamnosus, Bifidobacterium bifidum, B. longum, Enterococcus faecium</em> plus fructooligosaccharide <strong>Hospitalized</strong></td>
<td><em>Hospitalized</em> 77.9 ± 30.5 hours (n=113)</td>
<td>114.6 ± 37.4 hours (n=96)</td>
</tr>
<tr>
<td><em>Saccharomyces boulardii CNCM I745</em> <strong>Hospitalized</strong></td>
<td>75.4 ± 33.1 hours (n=220)</td>
<td>99.8 ± 32.5 hours (n=143)</td>
</tr>
<tr>
<td><em>Hospitalized</em> 83.1 ± 36.3 hours (n=148)</td>
<td>114.8 ± 35.4 hours (n=72)</td>
<td></td>
</tr>
<tr>
<td><em>Emergency care unit</em> 60.4 ± 23.1 hours (n=25)</td>
<td>78.4 ± 20.9 hours (n=26)</td>
<td></td>
</tr>
<tr>
<td><em>Outpatient</em> 58.9 ± 15.3 hours (n=47)</td>
<td>88.90 ± 19.1 hours (n=45)</td>
<td></td>
</tr>
<tr>
<td><em>Lactobacillus reuteri DSM 17938 Hospitalized</em> 70.7 ± 26.1 hours (n=64)</td>
<td>103.8 ± 28.4 hours (n=63)</td>
<td></td>
</tr>
<tr>
<td><em>Lactobacillus reuteri DSM 17938 Outpatient</em> 60.4 ± 24.5 hours (n=29)</td>
<td>74.3 ± 15.3 hours (n=31)</td>
<td></td>
</tr>
<tr>
<td><em>Bifidobacterium lactis Hospitalized</em> 67.1 ± 25.7 hours (n=64)</td>
<td>94.1 ± 22.9 hours (n=64)</td>
<td></td>
</tr>
<tr>
<td><em>Bifidobacterium lactis plus inulin Hospitalized</em> 66.5 ± 26.7 hours (n=63)</td>
<td>94.1 ± 22.9 hours (n=64)</td>
<td></td>
</tr>
<tr>
<td><em>LGG plus BB12 Hospitalized</em> 74.5 ± 40.8 hours (n=150)</td>
<td>98.4 ± 22.9 hours (n=68)</td>
<td></td>
</tr>
<tr>
<td><strong>TOTAL</strong></td>
<td>N=703</td>
<td>N=465</td>
</tr>
</tbody>
</table>

**Conclusion:** This is the largest clinical trial evaluation the efficacy of probiotics/synbiotics on AGE in children. All evaluated probiotics/synbiotics reduced the duration of AGE, both in out and inpatients.

**Disclosure of interest:** Ener Cagri Dinleyici is Advisory Board Member and speaker of Biocodex, Ates Kara is speaker of Nobel Ilac and Sanofi and has received research grant from Biocodex, Metehan Ozen is a speaker for Sandoz and Sanofi, Yvan Vandenplas is a consultant for United Pharmaceuticals and Biocodex. Other authors have no conflict of interest.
Gastroenterology: GI-infections

G-P-220

Capillary blood potassium measurements are unreliable in children with acute gastroenteritis

Jan Nowak¹, Hanna Wielinska¹, Michal Dabrowski¹, Paula Szydlowska¹, Mariusz Szczepanik¹, Patrycja Krzyzanowska¹, Jaroslaw Walkowiak¹

¹Poznan University of Medical Sciences, Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland

Objectives and study: Potassium concentration assessment in the capillary blood is prone to pseudohyperkalemia. However, the data on the accuracy of potassium level determination in the capillary blood in clinical settings are lacking. We aimed to quantify the precision of this measurement, which by the common pediatric knowledge is not entirely reliable.

Methods: This retrospective cross-sectional study concerned children with acute gastroenteritis (AGE) in whom potassium concentration was measured: (1) in the capillary blood in the emergency department and (2) in the serum soon afterwards, on admission to a pediatric ward, where intravenous access was established without delay. Time differences were calculated between receiving the results of capillary blood (almost instantaneous) and serum measurements (up to 4 hours after sampling in the ward).

Results: Out of 1080 electronic health records screened (years 2006-2015; ICD-10 codes A09, A08.0, and A08.2) 249 met the inclusion criterion of time difference between obtaining both results < 4 hours. The mean patients’ age was 2.7 ± 2.6 years, the average mass was 15 ± 8 kg; 131 of the children were male (52.6%). Hyperkalemia – as measured in the serum – occurred in 6 children (2.4%) and hypokalemia in 3 (1.2%). Poor agreement between potassium concentration in the capillary blood and in the serum was found using modified Bland-Altman plots and the intraclass correlation coefficient (ICC = 0.37). Spearman’s ρ correlation coefficient was moderate (0.54, p ≤ 10^-6). The mean absolute error was (mean ± SD) 0.51 ± 0.69 mmol/L (greater capillary concentrations; 95%CI: -0.84–1.86). Positive and negative predictive values for hyperkalemia and hypokalemia were 9.4% and 98.6%, respectively, with the area under the curve for identifying hyperkalemia of 0.69 (95%CI: 0.44–0.94). The positive predictive value for hyperkalemia was 9.4% (3 out of 32); curiously, it fell to 0% (20 false-positive cases) after increasing the hyperkalemia threshold by 0.35 mmol/L (the difference between venous and capillary potassium levels’ 3rd quartiles). The three hypokalemia cases (serum) were not detected by capillary measurements. The mean time between receiving results of potassium concentration assessment in the capillary blood and in the serum was 130 ± 46 min. The findings of the study were replicated in a subgroup of 90 patients with the shortest time differences (85 ± 21 min; ICC = 0.32; p = 0.50, p ≤ 10^-6). A comparison of capillary and venous potassium measurements grouped biannually (2006-2007, 2008-2009, 2010-2011, 2012-2013, 2014-2015) did not attribute their variability to capillary or venous blood analysis equipment (Kruskal-Wallis H test p = 0.99 and 0.27, respectively).

Conclusion: Measurements of potassium in capillary blood of children with AGE are unreliable. Just as their value in diagnosing hyperkalemia is null, their accuracy in excluding hyperkalemia is excellent.
Cost analysis of Lactobacillus reuteri DSM 17938 in children with acute infectious gastroenteritis (PROBAGE Study)

Ener Cagri Dinleyici, Metehan Özen, Ates Kara, Nazan Dalgic, Zafer Kurugol, Sirin Guven, Ozge Metin Akcan, Gonul Tanir, Adem Karbuz, Ahmet Sami Yazar, Ozden Turel, Olcay Yasa, Mesut Sancar, Makbule Eren, Yvan Vandenplas

1Eskisehir Osmangazi University Faculty of Medicine, Department of Pediatrics, Eskisehir, Turkey
2Acibadem University Faculty of Medicine, Pediatric Infectious Diseases, Istanbul, Turkey
3Hacettepe University Faculty of Medicine, Department of Pediatric Infectious Diseases, Ankara, Turkey
4Sisli Etfal Training Hospital, Pediatric Infectious Disease Unit, Istanbul, Turkey
5Ege University Faculty of Medicine, Pediatric Infectious Disease Unit, Izmir, Turkey
6Osmangazi University Research/Training Hospital, Department of Pediatrics, Istanbul, Turkey
7Konya Training and Research Hospital, Pediatric Infectious Disease Unit, Konya, Turkey
8Dr. Sami Ulus Children Hospital, Pediatric Infectious Disease Unit, Ankara, Turkey
9Okmeydani Research and Teaching Hospital, Pediatric Infectious Disease Unit, Istanbul, Turkey
10Istanbul University Research Hospital, Department of Pediatrics, Istanbul, Turkey
11Bezmialem University Faculty of Medicine, Pediatric Infectious Disease Unit, Istanbul, Turkey
12Medeniyet University, Department of Pediatrics, Istanbul, Turkey
13Marmara University, Faculty of Pharmacy, Istanbul, Turkey
14Eskisehir Osmangazi University, Pediatric Gastroenterology and Hepatology, Eskisehir, Turkey
15Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives and study: Lactobacillus reuteri DSM 17938 (1 × 10^8 CFU of L. reuteri DSM 17938 for 5 days) was shown in our multicenter, randomized, prospective, controlled, single blind clinical trial in children with acute gastroenteritis (AGE) to reduce the duration of watery diarrhea and length of hospitalization. The pharmaco-economic impact of the administration of L. reuteri DSM 17938 in children with AGE was evaluated.

Methods: The direct cost related to AGE in inpatient and outpatient settings was evaluated. Indirect costs related to parental loss of working days and costs related intensive care unit were excluded. These data have been extrapolated to the number of all cases of rotavirus AGE during a one year period for Turkey.

Results: The cost of add-on L. reuteri DSM 17938 was significantly lower than conventional treatment (203 ± 65 US$ vs. 254 ±68 US$, p<0.001 and 53.4 ± 17.8 US$ vs. 79.6 ±20+ US$, p<0.01) in hospitalized children and children visiting the emergency care. In the outpatient group, the direct cost was higher in the probiotic than in the control group (31.2 ± 8.8 US$ vs. 24.4 ±9.2 US$, p<0.05). When this direct cost was extrapolated to the yearly number of rotavirus GE in Turkey, the total cost related with hospitalization and emergency care unit visits was reduced with 28.4% or 29.7 US$ per patient. Over a one year perspective, the total cost would be reduced with 14.7% or 9.5 US$ if L. reuteri DSM 17038 would be administered in all rotavirus GE cases in all children under 5 years of age.

Conclusion: L. reuteri DSM 17938 reduces the direct cost of AGE along with a reduction of hospital and emergency care unit stay. Further analysis considering of the impact of a reduced indirect cost including the socio-economic impact of AGE would help to evaluate the economic benefit of probiotics.

References:
Disclosure of interest: This is an investigational initiated study and all authors have no conflict of interest with the study product.
Menetrier’s disease as a GI manifestation of active CMV infection in an 22 month-old boy: a case report with a review of literature of Korean pediatric cases

Jeana Hong1, Seungkoo Lee2

1Kangwon National University, Pediatrics, Chuncheon, Korea, Rep. of South
2Kangwon National University, Anatomic Pathology, Chuncheon, Korea, Rep. of South

Objectives and study: Menetrier’s disease (MD) is a rare disease characterized by hypertropic gastric folds and marked protein loss through the gastric mucosa. Pediatric MD has different clinical course compared with adult cases and has been often reported to be associated with cytomegalovirus (CMV) infection. While CMV infection in gastrointestinal (GI) tract most afflicts immunocompromised hosts, there have been several reports describing the CMV infection-associated MD in previously healthy children. However, CMV was hardly identified in the gastric tissue for the confirmation of CMV as the etiologic agent in the pediatric MD.

Methods: We describe the youngest case ever reported in Korea. In addition, we present a review of literature of Korean pediatric cases of MD to better understand its presenting clinical characteristics, treatment, and outcome.

Results: A previously healthy 22-months-old boy presented to ER with a 6 days history of emesis and poor oral intake. Approximately 1 week before presentation, he developed cough and rhinorrhea with 1 day of fever. While his symptoms seem to be resolved with 2 days of medication, he developed 2 or 4 episodes of vomiting per day. One day before presentation, the mother noticed progressive swelling of the boy’s eyelids and scrotum. Initial laboratory findings were significant for leukocytosis with eosinophilia and hypoalbuminemia. Under the initial impression of protein losing enteropathy (PLE) associated with eosinophilic GI disorder, we decided to perform endoscopy for tissue confirmation. By detection of CMV DNA in gastric biopsy sample by PCR, he was finally diagnosed to have MD associated with active and primary CMV infection. With supportive treatments with albumin replacement for two consecutive days and proton pump inhibitors for 3 weeks, his hypoalbuminemia and edema gradually resolved and repeated esophagogastroduodenoscopy performed on 4 weeks later showed nearly healed mucosa.
### Table: 5 reported cases of Korean children with MD

<table>
<thead>
<tr>
<th>Case</th>
<th>Age (yr)</th>
<th>Gender</th>
<th>Symptoms at presentation</th>
<th>Albumin (g/dL)</th>
<th>Eosinophil count (/mm3)</th>
<th>Serum CMV IgM</th>
<th>CMV PCR</th>
<th>CMV in tissue</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cho JR et al. 2001</td>
<td>4</td>
<td>M</td>
<td>Vomiting, Generalized edema</td>
<td>2.4</td>
<td>not reported</td>
<td>+</td>
<td>not done</td>
<td>not done</td>
<td>Supportive</td>
</tr>
<tr>
<td>Choi WJ et al. 2004</td>
<td>5</td>
<td>M</td>
<td>Abdominal pain, Vomiting Generalized edema</td>
<td>2.2</td>
<td>1050</td>
<td>+</td>
<td>Urine</td>
<td>Inclusion body (-)</td>
<td>Omeprazole, albumin</td>
</tr>
<tr>
<td>Son KH et al. 2012</td>
<td>9</td>
<td>M</td>
<td>Abdominal pain/distension Decreased urine output</td>
<td>1.3</td>
<td>840</td>
<td>-</td>
<td>not done</td>
<td>Inclusion body (-)</td>
<td>Fluid restriction, albumin and diuretics avoidance of milk and bread</td>
</tr>
<tr>
<td>Yoo Y et al. 2013</td>
<td>3</td>
<td>M</td>
<td>Anorexia, vomiting Generalized edema</td>
<td>1.9</td>
<td>NR</td>
<td>+</td>
<td>Blood</td>
<td>Inclusion body (+)</td>
<td>Fluid restriction, albumin and diuretics high-protein diet</td>
</tr>
<tr>
<td>Present case</td>
<td>22 mo</td>
<td>M</td>
<td>Vomiting, Poor oral intake</td>
<td>1.9</td>
<td>1130</td>
<td>+</td>
<td>Urine</td>
<td>CMV PCR (+) Inclusion body (-)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** We reported the youngest Korean child with MD associated with active CMV infection, which was confirmed by detection of CMV DNA in gastric tissue by PCR. MD is the most common non-erosive GI condition causing PLE, which should be differentiated from eosinophilic GI disorder showing peripheral eosinophilia. Peripheral eosinophilia most observed in the reviewed literature as well represents a hypersensitivity reaction induced by CMV infection.
GASTROENTEROLOGY: GI-infections

G-P-223

Risk factors analysis of recurrent enterocolitis associated Hirschsprung’s disease

Li Hong¹, Yuqing Li², Yi Feng¹

¹Shanghai Children’s Medical Center, Clinic Nutrition, Shanghai, China
²Shanghai Children’s Medical Center, Shanghai, China

Objectives and study: To investigate the non-surgical risk factors of recurrent episodes of Hirschsprung-associated enterocolitis (HAEC).

Methods: A retrospective analysis was conducted on 67 cases of Hirschsprung’s Disease (HD) treated by radical operation between January 2007 and January 2014 in Shanghai Children’s Medical Center. Patients suffered 3 times or more episodes of enterocolitis were enrolled into the recurrent HAEC group (HAEC-R group). Patients with 1 or 2 times episodes were enrolled into the HAEC group. Patients without enterocolitis were enrolled into the control group. The clinical data were collected and analyzed by SPSS Statistics.

Results: Gender and age at surgery had no statistical differences among the three groups (P > 0.05); Clinical types of HD and the incidence of hypoalbuminemia had no statistical differences between the HAEC-R and the HAEC group (P > 0.05), but had significant statistical differences between the HAEC-R and the control group (P < 0.05). The incidences of preoperative malnutrition, enterocolitis, upper respiratory tract infection and pneumonia in the HAEC-R group were significantly higher than that in the HAEC group (P < 0.05), and no statistical differences between the HAEC group and the control group (P > 0.05). The multivariate logistic regression analysis showed that the incidences of preoperative malnutrition and enterocolitis were independent risk factors of recurrent HAEC (OR = 9.000, 95%CI = 1.355-59.783; OR = 8.667, 95%CI = 1.526-49.220).

Conclusion: The incidences of preoperative malnutrition and enterocolitis were the risk factors for recurrent HAEC.
Economic and health burden of rotavirus gastroenteritis in Egyptian children

Hatem Hussein¹, Ashgan A. Elghobashy¹, Hosam F. Elsaadany¹

¹Zagazig Faculty of Medicine, Pediatrics, Zagazig, Egypt

Objectives and study: Rotavirus is the leading cause for severe gastroenteritis (RVGE) in under-five age group and the most important cause of childhood mortality and poses a major economic burden. Affordable rotavirus vaccine gave promises but challenges policy makers to study its feasibility in view of the health and economic burden of the infection. The aim of this study was to highlight the burden of RVGE in our community and to check the cost-benefit of the vaccine.

Methods: 148 patients with clinical picture suggestive of RVGE presenting to the ER at Zagazig university hospital –Egypt were included. History taking including detailed social and medical background of the family, followed by medical examination using Vesikari scoring system. Rota antigen in stool was tested using rapid ELISA test. After detailed interview with parents, utilizing the data from the Hospital statistics office for the medical cost through a specially adapted schedule, the total cost of the individual illness was calculated.

Results: Rotavirus prevalence in our cohort was 60.8%( 90 out of 148). Rotavirus induced severe dehydration in 52.2% of the positive. RV possible GE needed admission in 46.5% (78 out of 148) with a mean ±SD of 3.6±2.47 hospital stay days. Complications in admitted Rota positive patients were metabolic acidosis in 10%, hypernatremia in 10 % and URTI in 7.8%. There were no statistical difference between patterns of feeding and severity of illness. We reported zero mortality reflecting early presentation, prompt attention and success of anti-diarrhea TV campaign. The cost of the single RV patient in our cohort was 287-860 LE (one US dollar≈20 LE) and the total economic cost of the Rota positive admissions was 182,448LE compared to average cost of 45,000LE for the vaccination program.

Conclusion: Including Rotavirus vaccine in the compulsory vaccination program in Egypt is a cost-beneficial valuable step.
Increased transaminase in Rotavirus infection: can we use it as a prognostic factor for the evolution of gastroenteritis?

Kinga Cristina Slavescu¹, Radu Razvan Slavescu², Laura But³, Mihaela Spirchez⁴

¹University of Medicine and Pharmacy “Iuliu Hatieganu”, Second Pediatric Clinic, Cluj-Napoca, Romania
²Technical University of Cluj-Napoca, Computer Science, Cluj-Napoca, Romania
³University of Medicine and Pharmacy “Iuliu Hatieganu”, Cluj-Napoca, Romania
⁴University Of Medicine and Pharmacy "Iuliu Hatieganu", Second Pediatric Clinic, Cluj-Napoca, Romania

Objectives and study: Rotavirus infections are the most common causes of gastroenteritis in infants and toddlers worldwide. Children infected with Rotavirus often show increased levels of transaminase. There are a small number of studies which investigate this correlation, but no study assessing the relation between elevated transaminase and duration of gastroenteritis. The aim of this study was to assess the correlation between elevated liver enzymes and the evolution of Rotavirus gastroenteritis.

Methods: 104 children with acute gastroenteritis were evaluated. They were divided into two groups: 50 children with Rotavirus gastroenteritis (27 boys) and 54 (32 boys) having gastroenteritis with other etiology (Adenovirus, Campylobacter, EPEC, Salmonella) or with no etiological agent identified. Clinical symptoms and results of liver function tests, mainly the elevation of transaminase, were evaluated.

Results: The mean age of patients with Rotavirus gastroenteritis was 29 months compared to 39 months of the patients with gastroenteritis due to other etiologies. 39 children (78%) with rotavirus gastroenteritis presented elevated liver enzymes compared to only 28 cases (51%) of the second group (OR=3.292; 95%CI=1.39-7.748, p<0.05). The average length of stay in hospital for the entire group was 4 days (5 days for those with Rotavirus infection and 3 days for the gastroenteritis due to other etiology). Twenty-one (20.2%) patients with elevated transaminase and Rotavirus infection were hospitalized for more than 4 days, while only 8 (7.7%) patients with gastroenteritis due to other etiology and high levels of transaminase were hospitalized for more than 4 days (OR = 3.0625; 95%CI 1.09 – 8.57; p<0.05).

Conclusion: The mild increase of transaminase is specific to Rotavirus gastroenteritis, compared to other etiology gastroenteritis. Rotavirus gastroenteritis associated with mild elevations of transaminase requires longer hospitalization compared to gastroenteritis due to other etiologies, therefore elevated transaminase in Rotavirus gastroenteritis can be used as a prognostic factor regarding the duration of hospitalization.
GASTROENTEROLOGY: GI-infections

G-P-226

Blastocystis and colitis, unknown association

Mirjana Stojsic

Institute for Child and Youth Health Care, Gastroenterology, Novi Sad, Serbia

Objectives and study: Blastocystis hominis (Bh) is the most outspread protist on our planet, but also the most controversial. The disease caused by Bh on humans is called blastocystisis. The subject of research is to establish the connection between the presence of the infection Bh and the existence of mucosal inflammation of the colon in children with gastrointestinal complaints, as well as to establish the group of the children with a special form of colitis, inflammatory bowel disease and the ones infected by Bh, which would ensure better understanding of the blastocystosis in children.

Methods: The prospective study included pediatric patients with abdominal pain and/or diarrhea, and stool positive on Bh, that have been hospitalised and standard testing methods were used: anamnasesis, physical examination, laboratory analysis of blood and stool, ultrasound examination of the abdomen, colonoscopy and histopathological examination of the biopsy of the colon.

Results: The study included 102 patients, which are divided into three groups: 1. group (patients that have no colitis, included 4 patients (4.4%)), 2. group (patients with unspecified colitis, included 56 patients (56.55%)) and 3. group (patients with inflammatory bowel disease, included 42 patients (42.41%)). Among them, there was an equal number of children that were male and female, 51 boys and 51 girls. Age of respondents who have Bh infection ranged from 11 months to 17 years and 7 months. The median is 12.54 years, and the average age of 11.25 years. Children with blastocystosis had anthropometric parameters within normal limits. Respondents most frequently been admitted to hospital under diagnosis gastroenteritis due to diarrhea and abdominal pain, and that the presence of gastrointestinal symptoms and general signs of infection are not a significant clinical signs of infection Bh. Based on laboratory findings, clinical and endoscopic activity score for IBD most patients had moderate activity of disease. Children with Bh infection usually have normal C-reactive protein in terms of value, unless if have IBD. Elevated erythrocyte sedimentation rate is characteristic of patients with IBD. Children with blastocystosis usually have normal level of Immunoglobulin A, leukocytes, neutrophils and eosinophils. Serum iron indicate that most subject were anemic, especially children who have had an infection with the Bh and IBD. Mesenterial lymphadenitis and splenomegaly are non-specific ultrasound findings in infected with Bh, although they were usually described pathological changes in abdominal ultrasound.

Conclusion: Children infected with Bh colitis usually have pathological changes in the large intestine, with no significant difference between the non-specific colitis and inflammatory bowel disease. Significantly less infected with Bh has a normal colonoscopy findings. Confirmed the importance of Bh in the development of chronic colitis and inflammatory bowel disease in children, increase public acceptance Blastocistisa hominis as pathogens and points to the necessity of treatment.
**Clinical manifestation and predictive index of Campylobacter enteritis in children**

Jung Min Yoon¹, Joon Yeol Bae¹, Jeongseob Lee²

¹Konyang University Hospital, Pediatrics, Daejeon, Korea, Rep. of South Korea
²Gongju National Hospital, Internal Medicine, Gongju, Korea, Rep. of South Korea

**Objectives and study:** In bacterial enteritis, these symptoms are similar and cannot be distinguished. Timely antibiotics therapy in select cases of diarrhea related to bacterial infections can reduce the duration and severity of illness and prevent complications. If we have predictive index before we identify the causative bacteria, it will help us choose a therapeutic agent.

**Methods:** Patients who were admitted to the pediatrics unit at Konyang University Hospital for acute and inflammatory diarrhea between Aug 1, 2015, to July 31, 2016, and received Multiplex polymerase chain reaction tests were examined. Of the total 248 patients, 83 patients were positive. We analyzed the clinical symptoms and blood test results in 61 patients with frequent Campylobacter sp. (25 patients), Salmonella sp. (18 patients) and Clostridium perfringens (18 patients). The mean age of 61 patients (M:F=31:30) was 84.0 ± 54.8 months and the mean hospital stay was 4.6 ± 1.7 days.

**Results:** There were no statistical differences in sex, age, hospital stay, gastrointestinal and extra-gastrointestinal symptoms, fever severity, pattern of diarrhea and the findings of abdominal ultrasonography or computed tomography. The onset age were 122.0 ± 45.4 months in Campylobacter sp. infected group, 64.1 ± 36.8 months in Salmonella sp. infected group and 51.3 ± 51.6 months in Clostridium perfringens infected group. The age of Campylobacter sp. infected group was significantly higher (p=0.00). CRP was detected 9.6 ± 6.1mg / dl in Campylobacter sp. infected group, Salmonella sp. 6.0 ± 5.0 mg / dl in the infected group and 1.5 ± 2.5 mg / dl in the Clostridium perfringens-infected group (p=0.00). The results of the receiver-operating characteristic (ROC) analysis showed that the cut off value of age is ≥103.5 months (sensitivity 96%, specificity 59%) and the cut off value of CRP is ≥4.55 mg/dl (sensitivity 80%, specificity 69%).

**Conclusion:** The age (≥103.5 months) and higher CRP (≥4.55 mg/dl) were good predictors of Campylobacter enterocolitis. If both of the criteria are not satisfied, it is not likely to be Campylobacter enterocolitis (Negative predictive value 97.2%). When two criteria were fulfilled, Campylobacter enterocolitis was highly suspected. It will be helpful in the choice of therapeutic agents.
Clinical and laboratory variables that predict clinical and endoscopic remission in children with Crohn’s disease treated with infliximab

Giulia D’Arcangelo¹, Salvatore Oliva², Francesca Tarani¹, Franca Viola², Fortunata Civitelli², Salvatore Cucchiara², Marina Aloi²

¹Sapienza University of Rome, Rome, Italy
²Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy

Objectives and study: We aimed to identify early clinical and laboratory predictors of sustained clinical and endoscopic remission in children with Crohn’s disease (CD) under infliximab (IFX).

Methods: Prospective study conducted in children with moderate-to-severe CD starting IFX treatment. All patients underwent endoscopy, weighted pediatric CD activity index (wPCDAI) assessment, C-reactive protein (CRP) at week 0 and 52. wPCDAI and CRP were also evaluated at 14 weeks. Primary outcomes were to determine the ability of 14-week wPCDAI and CRP to predict steroid-free sustained remission and mucosal healing after 1 year. As a secondary outcome we sought to evaluate the concordance between wPCDAI and SES-CD at week 52.

Results: Forty-one children were enrolled (median age 13.5±2.7, females 41.5%). At 1 year, 21 (51%) and 16 (39%) were in clinical (wPCDAI <12.5) and endoscopic (SES-CD<3) remission respectively. Fourteen-week wPCDAI didn’t differ between patients who achieved both clinical and endoscopic remission at 1 year (p=0.21 and p=0.35 respectively). By using a multivariable logistic regression model, week-14 wPCDAI and CRP were not predictors of 1 year clinical (p=0.83 and p=0.30, respectively) and endoscopic remission (p=0.22 and p=0.48). wPCDAI resulted significantly correlated with 1-year SES-CD (r=0.38, p=0.01). The concordance between wPCDAI and SES-CD was excellent and good for severe and moderate disease (k cohen 0.87 and 0.76), moderate and absent for mild and moderate disease, respectively.

Conclusion: Based on our results, 14-week post induction wPCDAI and CRP are not predictors of 1-year sustained steroid-free clinical and endoscopic remission in children with CD under biologic therapy. Continuous wPCDAI shows a good correlation with SES-CD, particularly for patients in remission and with severe disease.
Efficacy and safety of adalimumab after infliximab failure in paediatric ulcerative colitis

Marina Aloi, Matteo Bramuzzo, Serena Arrigo, Claudio Romano, Patrizia Alvisi, Simona Gatti, Maria Teresa Illiceto, Francesca Zucconi, Dario Diillo, Giovanna Zuin, Daniela Knafelz, Alberto Ravelli, Franca Viola

1 Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
2 IRCCS Burlo Garofalo of Trieste, Pediatric, Trieste, Italy
3 I. G. Gaslini, Pediatric Gastroenterology and Endoscopy Unit, Genoa, Italy
4 University of Messina, Pediatrics Department, Messina, Italy
5 Ospedale Maggiore, Paediatric Department, Bologna, Italy
6 Universita Politecnica Delle Marche, Department of Pediatrics, Ancona, Italy
7 Spirito Santo Hospital of Pescara, Pediatric Gastroenterology and Endoscopy Unit, Pescara, Italy
8 Sapienza University of Rome, Rome, Italy
9 Buzzi Children Hospital, Pediatric Gastroenterology Unit, Milan, Italy
10 V. Buzzi Children's Hospital, University of Milan, Department of Paediatrics, Milan, Italy
11 Bambino Gesù Children Hospital, Hepatogastroenterology and Nutrition, Rome, Italy
12 Spedali Civili Hospital, Pediatric Gastroenterology Unit, Brescia, Italy

Objectives and study: The objective of the present study was to evaluate the effectiveness and safety of adalimumab (ADA) in children with ulcerative colitis (UC) who experienced previous infliximab (IFX) failure or intolerance.

Methods: This retrospective study included all children with UC from a national pediatric registry who received ADA therapy. The primary endpoint was the rate of corticosteroid (CS) free remission (PUCAI<10) at week 52. Secondary outcomes were: the rate of continuous clinical response and remission, primary non-response and loss of response at Weeks 12, 30, and 52 and rate of mucosal healing at week 52.

Results: A total of 32 children of 514 patients with UC (65) received ADA (median age 10±4 years). Median disease duration before ADA therapy was 27 months. All patients received previous IFX therapy (43% intolerant, 50% not-responders, 6.7% positive anti-IFX antibodies). Fifty-two weeks after ADA initiation 13 patients (41%) were in CS-free remission. MH occurred in 9 patients (28%) at 52 week. The cumulative probability of clinical relapse-free course was 69%, 59% and 53% at 12, 30 and 52 weeks, respectively. Ten patients (31%) had a primary failure and 5 (15%) loss of response to ADA. No significant differences in terms of efficacy were reported between not-responders and intolerant to IFX to (p=1.0). Overall, nineteen patient (59%) maintained ADA therapy during 52-week follow-up. Seven patients (22%) experienced a adverse event. No serious side effects were observed and none resulted in ADA discontinuation.

Conclusion: In this cohort of children with UC ADA had a favorable short- and long-term efficacy, allowing to recover a significant percentage of patients intolerant or not-responding to IFX. The safety profile was acceptable.
Management and outcomes of children with localised ileo-caecal Crohn’s disease: survey from a tertiary-level centre

Tommaso Alterio¹, Franco Torrente¹, Mary Brennan¹, Matthias Zilbauer¹, Robert Heuschkel¹, Marco Gasparetto¹

¹Cambridge University Hospitals, Addenbrooke’s, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Cambridge, United Kingdom

Objectives and study: The management of children with Crohn’s Disease (CD) is complex and up to 70% of these patients will require surgical intervention. We analysed the cohort of children with localised Ileo-caecal Crohn’s (IC-CD, i.e. Paris Classification L1) in our paediatric gastroenterology unit, aiming to investigate the type of treatment provided, i.e. biologics versus IC resection, and to determine whether the use of biologics delayed / prevented the need for surgery. Our secondary outcome was to compare children with localised IC-CD to children with more extensive disease, identifying differences in presentation and disease course.

Methods: The Department of Paediatric Gastroenterology at Addenbrooke’s Hospital in Cambridge (UK) is currently looking after 237 patients with Inflammatory Bowel Disease, 121 with CD and 116 ulcerative colitis.

Children with IC-CD in our cohort were classified into 3 groups based on treatment and disease outcomes: Group A (patients who received IFX but had no surgery; n=8), Group B (patients who had surgery +/- IFX; n=8) and Group C (patients who did not require either IFX or surgical treatment; n=21).

The statistical analysis included t student test, Welch’s adaptation and Mann-Whitney U test for continuous variables, and square test and Fisher exact test for categorical variables.

Results: Of the 121 patients on our database with CD, 37 (31%) had localised ileo-caecal disease, 36 (30%) colonic distribution and 48 (40%) ileo-colonic. The mean duration of follow up was 31.1 months (range 1-149, median 24.5). All children with CD showed a similar age at diagnosis across subgroups with different disease distribution (P=0.122 for L1 vs L2; P=0.101 for L1 vs L3). Gender distribution was comparable (P=0.634 for L1 vs L2; P=0.364 for L1 vs L3). The age at diagnosis of the 37 children with localised IC-CD was comparable between Groups A and B (i.e. severe outcomes) and those in Group C (milder disease course)(P=0.69). Gender distribution was also similar in Groups A and B (P=0.464), and in Group C (P=0.257). Within the cohort with IC-CD, children in Groups A and B (severe outcomes) were treated with Thiopurines more frequently than those in Group C (P=0.0003). The time-delay between diagnosis and start of IFX was significantly shorter in Group A (IFX only) vs Group B (IFX + surgery)(P=0.0003).

Conclusion: According to our survey, there are no significant differences in age at diagnosis and gender between children with localised IC-CD and those with more extensive disease distribution (L2 and L3). This survey was an initial step to investigate a specific group of children with localised, thiopurine-resistant IC-CD, and to assess how the use of biologics impacts on their disease course and potential surgery. Interestingly, the children who needed surgery were escalated to IFX later than those who responded to biologics only; this may suggest that an earlier start with biological treatment has the potential to delay/rescue children with severe disease course from surgical intervention. The power of our analysis was limited by the small group size. Given the limited cohort size and the relatively short follow-up time, we have submitted a research/data request to the US paediatric IBD ImproveCareNow network that we joined within the last 12 months.
Phenotypic features and clinical outcomes of pediatric perianal Crohn’s disease

Yonathan Herman¹, Firas Rinawi¹, Raanan Shamir², Assa Amit¹

¹Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach - Tikva, Israel
²Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel

Objectives and study: Data on the outcomes of children with perianal Crohn’s disease are limited, although its presence is often used for justifying early use of biologics. We aimed to assess whether perianal disease in children is associated with more severe outcomes as found in adults.

Methods: The medical records of 296 pediatric onset Crohn’s disease patients diagnosed from 2002 to 2015 were reviewed retrospectively. Baseline characteristics included age at onset, gender, severity indices, laboratory data, extra-intestinal manifestations, endoscopic findings and anthropometric measurements. Main outcome measures included time to first flare, hospitalization, surgery and biologic therapy.

Results: Of the 296 included patients [mean age 13.6 ±2.8 years; 125 (42%) females], 70 (24%) had non-fistulizing perianal findings while only 40 (13.5%) had fistulizing perianal disease at diagnosis. There were no significant differences in either demographic, clinical, laboratory or anthropometric measures between groups at diagnosis. Time to first hospitalization was significantly shorter for both non-fistulizing and fistulizing perianal disease (HR 4, 95% CI 1.6-6.4; HR 5.5, 95% CI 1.2-9.9, respectively, p=0.027) as well as time to biologic therapy (HR 3.3, 95% CI 1.4-5.5; HR 2.5, 95% CI 0.4-4.6, respectively, p=0.002). There were no differences in time to first flare or time to surgery. During follow-up, 50 patients (17%) developed fistulizing perianal disease after a median time of 7 years (IQR 5-9 years). The presence of non-fistulizing disease at diagnosis was a significant risk-factor for the development of fistulizing perianal disease (p=0.02).

Conclusion: Pediatric perianal Crohn’s disease does not present with distinct phenotypic features, however patients with both non-fistulizing and fistulizing disease have worse specific clinical outcomes. Non-fistulizing disease is a risk factor for the development of fistulizing disease over time.
Anti-TNF treatment following surgical resection for Crohn’s disease is effective despite previous pharmacodynamic failure

Assa Amit¹, Jiri Bronsky², Kaija Leena Kolho³, Kristyna Zarubova⁴, Tim de Meij⁵, Oren Ledder⁶, Margaret Sladek⁷, Stephanie Vanbiervliet⁸, Caterina Strisciuglio⁹, Raanan Shamir¹⁰

¹Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel
²Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic
³Helsinky University, Department of Pediatric Gastroenterology, Helsinky, Finland
⁴University Hospital Motol, Department of Paediatrics, Prague, Czech Republic
⁵VU University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
⁶Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
⁷Polish-American Children’s Hospital, Krakow, Poland
⁸Ghent University Hospital, Paediatric Gastroenterology and Hepatology, Ghent, Belgium
⁹Second University of Naples, Department of Woman, Child and General and Specialistic Surgery, Naples, Italy
¹⁰Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach -Tikva, Israel

Objectives and study: The outcome of crohn’s disease (CD) patients who failed anti-TNFα therapy despite adequate serum drug levels (pharmacodynamic failure) is unclear. We aimed to assess such pediatric patients who underwent intestinal resection and were re-treated with the same anti-TNFα agent post operatively.

Methods: Pediatric CD patients who underwent intestinal resection and were treated with anti-TNFα agents post-operatively were assessed retrospectively. Patients were stratified to those with pre-operative anti-TNFα pharmacodynamic failure and those with no pre-operative anti-TNFα treatment.

Results: A total of 61 children were included, 21 with pharmacodynamic failure and 40 controls. Median age at intestinal resection was 15 years with 28 (46%) females. The median time from intestinal resection to anti-TNFα initiation was 7 months (IQR 4-13 months). At the time of post-operative anti-TNFα initiation there were no differences in clinical, laboratory and anthropometric measures between groups. Similar proportions of patients from both groups were in clinical remission on anti-TNFα treatment after 12 months and at the end of follow-up (1.7 years, IQR 1-2.9 years): 90.5% vs. 87.5% and 85.7% vs. 82.5% for pharmacodynamic failure patients and controls, respectively; p=0.8. No significant differences were observed at 14 weeks and 12 months of post-operative anti-TNFα treatment including endoscopic remission rate and fecal calprotectin. Both groups significantly improved all measures during post-operative anti-TNFα treatment.

Conclusion: Pediatric CD patients who failed anti-TNFα therapy despite adequate drug levels and underwent intestinal resection can be re-treated with the same agent for post-operative recurrence with high success rate similar to anti-TNFα naïve patients.
**Infliximab therapy in very early onset inflammatory bowel disease: experience in a Japanese children's hospital**

Katsuhiro Arai¹, Ichiro Takeuchi¹, Yuichiro Kaburaki², Hirotaka Shimizu¹, Itsuhiro Oka¹, Satoru Nagata²

¹National Center for Child Health and Development, Division of Gastroenterology, Tokyo, Japan
²Tokyo Women's Medical University, Paediatrics Medicine, Shinjuku, Japan

**Objectives and study:** Very early onset inflammatory bowel disease (VEO-IBD), defined as chronic inflammation of gastrointestinal tract confirmed by endoscopy and histopathology before 6 years of age, is an emerging field of challenge for pediatric gastroenterologists with its difficulty in diagnosis and treatment. Some VEO-IBD has very active disease with poor response to conventional treatment for IBD, and require high dose corticosteroids (CS) to induce and maintain remission. Infliximab (IFX) is known to be effective for pediatric IBD for both Crohn’s disease and ulcerative colitis (UC), however; very few information is available about the use of IFX for VEO-IBD. The objective of this study is to evaluate for the effectiveness and safety of IFX in VEO-IBD.

**Methods:** Retrospective review of medical record of VEO-IBD patients who had received IFX in order to control their IBD in a tertiary pediatric hospital. With the uncertainty of diagnosis in VEO-IBD, subjects were categorized into 3 groups, UC type (UC-T), non-UC-T with perianal disease (NUC-PD), and non-UC-T without perianal disease (NUC-NPD).

**Results:** Among the 34 VEO-IBD (UC-T(10), NUC-PD(6), NUC-NPD(9), primary immunodeficiency associated enterocolitis (9)), 13 has received the IFX as their first biologics for their active disease (UC-T(5), NUC-PD(3), NUC-NPD(5)). For the UC-T, all of them remained CS resistance/dependent. 2 had surgical colectomy, one on waiting list for colectomy for CS dependency with complication, and one with severe neurological deficit has been on prolonged moderate dose of CS(0.8-1.5mg/kg/day) with total parenteral nutrition (TPN) for parental refusal to surgery. A UC-T with primary sclerosing cholangitis is in remission but with CS(0.1mg/kg/day) and scheduled IFX(10mg/kg/day). All 5 had infusion reaction (IR), but IFX was discontinued only in one with severe neurological deficit. Other 4 tolerated to IFX with premedication and slow infusion. For the NUC-PD, 2 had remarkable improvement in colitis and PD. Although IFX improved the colitis and PD in other one, PD recurs in 4-5 weeks after infusion. This patient had eventually developed recto-vaginal fistula, and colostomy placement is being considered. For the NUC-NPD, all but 1 responded to IFX. However, 1 still require TPN and 1 had colonic resection for the stenotic lesion. wPCDAI improved with use of IFX in Non-UC-T. Although mild IR occurred in 3 of 8 Non-UC-T, all the 8 remained on scheduled IFX (for 27.8±19.6 months).

**Conclusion:** IFX appeared effective for VEO-IBD with NUC-PD and NUC-NPD, however; its efficacy appeared limited in UC-T in this small size retrospective review. IR was common in this population, but premedication and slow infusion enabled the continuation of IFX in majority of cases.

**Disclosure of interest:** Katsuhiro Arai Conflict with Mitsubishi Tanebe Coorporation for Lecturer Fee.
Awareness of smoking in adolescents with inflammatory bowel disease: preliminary results

Aleksandra Banaszkiewicz1, Kinga Kowalska-Duplaga2, Marta Baranowska1, Magdalena Nescioruk1, Stefan Kuzniarski3, Marcin Banasiuk3, Iza Łazowska1

1The Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
2Department of Pediatrics, Gastroenterology and Nutrition Jagiellonian University Kraków, Kraków, Poland
3Medical University of Warsaw, Department of Pediatric Gastroenterology and Nutrition, Warsaw, Poland

Objectives and study: There is a limited data on the awareness of patients suffering from Crohn’s disease (CD) and ulcerative colitis (UC) about the impact of smoking on the course of inflammatory bowel disease (IBD). The aim of this study was the assessment of such awareness among children and adolescents with IBD in Poland.

Methods: The study was conducted in two university-affiliated children’s hospitals in Poland (cities of Warsaw and Cracow) between April and November 2016. Children and adolescents with IBD diagnosed according to Porto criteria were asked to complete a questionnaire consisting of 20 items. The questionnaire included, apart questions about age, sex, smoking status, diagnosis and current treatment, the set of items inquiring about the influence of smoking on IBD severity, course and occurrence of extraintestinal symptoms. The group of healthy children was treated as a control for frequency of smoking.

Results: In total, 208 patients (103 IBD patients and 105 controls) were enrolled into the study. IBD group consisted of 68 patients suffering from CD and 35 patients from UC. Smoking was confirmed by 6.7% (14) of IBD patients; among CD patients there were 8.8% (6) and among UC patients 22.9% (8) smokers. The frequency of smoking in the control group was 17.1% (18). There were no significant difference about knowledge on the impact of smoking on the course of diseases and the risk of extraintestinal symptoms between patients with CD and UC (p=0.39 and p=0.55, respectively). Both groups did not differ in relation to opinion about the risk of surgical interventions related to smoking (p=0.25).

Conclusion: We found no differences in awareness of the influence of smoking on IBD between children and adolescents with CD and UC.
The availability of laboratory investigations for paediatric inflammatory bowel disease; findings of a nationwide survey

Dharam Basude¹, Lucy Bates², Gemma Sheldon³, Siba Prosad Paul⁴

¹Bristol Royal Hospital for Children, University of Bristol, Department of Paediatric Gastroenterology, Bristol, United Kingdom
²University of Bristol, Department of Paediatric Gastroenterology, Bristol, United Kingdom
³Bristol Royal Hospital for Children, Bristol, United Kingdom
⁴Bristol Royal Hospital for Children, Department of Paediatric Gastroenterology, Bristol, United Kingdom

Objectives and study: To investigate the availability of IBD related laboratory investigations in National Health Service (NHS) laboratories in England with Paediatric services and to discern any regional variations which may effect the health care standard.

Methods: A structured telephone survey was conducted in July 2016 by a single interviewer who contacted all the clinical Laboratories in Acute NHS trusts across England with paediatric services. The available online handbooks for each laboratory were also accessed and where appropriate scientists were unavailable, the survey questions were sent by email. The data was collected on a database and analysed using Microsoft excel.

No ethical approval was required for this study.

Results: A response was obtained from 136 out of 139 laboratories (97.8%).

- Inflammatory markers (other than CRP): ESR is widely available at 98%, followed by Plasma viscosity (PV) at 71% and Orosomucoid (ORM) at 48%. Regional variations are significant with East of England and London having least access to PV and ORM.
- Faecal calprotectin was available in 89% of labs although only 51% offer in house testing. 84% allow any clinician to request the test whereas the rest allow only a few clinician groups to request.
- ANCA can be tested in 94% of labs but ASCA is available only in 29%.
- TPMT activity was available in 96% of labs with only 29% testing this on site.
- 6-Thioguanine metabolites was offered only by 58% of labs with 89% outsourcing it. This was most widely accessible in the south east.
- Infliximab serology is offered in only 61% of labs with only 14% able to test this on site. This is least accessible in the East Midlands.

Conclusion: There is extensive regional heterogeneity in the availability of laboratory investigations for PIBD in England. There is also a low level of on-site testing for a number of investigations which is likely to significantly add to the time lag in obtaining results. More research is needed to confirm the utility of the laboratory investigations in PIBD and establish their use. National and European guidelines should include standards for the investigations required for PIBD and provide information on cost effectiveness. This is will support the units diagnosing and treating PIBD to access the tests promptly and standarise the care of these children throughout the nation.
Inflammatory bowel disease in children - clinical, phenotypic, immunological and genetic aspects of diagnosis and treatment

Sonja Bojadzieva¹, Aco Kostovski²

¹University Children's Hospital, Gastroenterohepatology, Skopje, Macedonia
²University Children's Hospital, Pediatric Gastroenterohepatology, Skopje, Macedonia

Objectives and study: Inflammatory bowel disease (IBD), including ulcerative colitis (UC) and Crohn’s disease (CD) are idiopathic chronic diseases of the gastrointestinal tract. The etiology and pathogenesis of IBD is still unknown, but the abundant research indicates simultaneous influence of the immunological, genetic and environmental factors. The aim of the study was to present clinical, phenotypic and immunological characteristics of disease, diagnostic and therapeutic aspects of pediatric patients with IBD.

Methods: In total 46 children were diagnosed with IBD (25 with CD and 21 with UC), at the University Children’s Hospital in Skopje, in the period of fifteen years (2001-2015 y). In terms of gender distribution, 19 children were female and 21 male. The age of patients ranged from 4-19 years, main age was 10.4. Diagnosis was confirmed after the realisation of all diagnostic protocols provided by the European Society for Pediatric Gastroenterohepatology and Nutrition (ESPGHAN), including clinical and laboratory investigations, upper gastrointestinal endoscopy, flexible colonoscopic procedure and histological analysis. Immunological investigations include, proinflammatory cytokines (Il-1, IL-6 and TNF-α), ASCA (Anti Saccharomyces cerevisiae antibodies), and p-ANCA (Perinuclear Anti Neutrophil Cytoplasmic Antibodies) with ELISA (Enzyme-linked immunosorbent assay). For genetic investigation we used PCR-SSP (polymerase chain reaction-sequence specific primers).

Results: From clinical aspect, the intestinal manifestation of the disease was dominant, in the 65% of examined patients. Classic triad for CD (abdominal pain, diarrhea and weight loss) manifested 30% of patients. The abdominal pain was the most frequent clinical symptom at patients with CD, while prolonged diarrhea at the patients with UC. Extra-intestinal manifestations had 35% of patients with IBD. Terminal ileitis was the most common phenotypic manifestation in children with CD, while stenosis and fistulas were diagnosed in 20% of the children. Pancolitis was the most frequent phenotypic characteristic of UC. The Post Hoc test of multiple comparison showed that IL-1, IL-6 and TNF-α values were statistically significant (p<0.01) increased in patients with CD. There was correlation between the increased values of ASCA and cytokines profile and the structural and fistulous phenotypic manifestations in children with CD. The sensitivities of ASCA in CD were high (89.4% for ASCA IgA and 73.6% for ASCA IgG). Average values of p-ANCA were increased in children with UC. Standard treatment for IBD were administered to all patients, while 5 patients were treated with infliximab and one patient with adalimumab. The mutation frequency of the gene complex CAR15/NOD2, including the allele Ley1007fsinsC and Arg702Trp present in examined patients with CD were very low.

Conclusion: As a whole, the genotypic, phenotypic and immunological characteristics represent the key parameters and have a major role in the diagnostic, clinical, and therapeutic aspects of the pediatric patients with IBD.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-237

Inflammatory bowel disease in chronic granulomatous disease: a paediatric tertiary care center experience

Giulia Angelino1, Paola De Angelis1, Simona Faraci1, Francesca Rea1, Erminia Romeo1, Filippo Torroni2, Renato Tambucci2, Paola Francelanci3, Maria Chiriaco4, Gigliola Di Matteo4, Alessia Claps4, Caterina Cancrini4, Paolo Palma4, Patrizia D'Argenio4, Luigi Dall'Oglio5, Paolo Rossi4, Andrea Finocchi4

1Bambino Gesù Children's Hospital, Irccs, Digestive Surgery and Endoscopy Unit, Rome, Italy
2Bambino Gesù Children's Hospital, Irccs, Unit of Digestive Surgery and Endoscopy, Inflammatory Bowel Disease Group, Rome, Italy
3Bambino Gesù Children's Hospital, Irccs, Department of Pathology and Molecular Histopathology, Rome, Italy
4Bambino Gesù Children's Hospital, Irccs, University Department of Pediatrics, Unit of Immune and Infectious Diseases, Rome, Italy
5Bambino Gesù Children's Hospital, Digestive Surgery and Endoscopy Unit, Rome, Italy

Objectives and study: Chronic Granulomatous Disease (CGD) is a primary immunodeficiency of phagocytes, characterized by life-threatening infections and dysregulated inflammatory responses. Overall survival has changed remarkably over the last two decades, and gastrointestinal involvement, presenting as Inflammatory Bowel Disease (IBD), is becoming a relevant issue. A better knowledge of CGD-associated IBD (CGD-IBD) is mandatory for a long term correct management of the disease and for the improvement of patients' quality of life. In this study, we aimed to evaluate the clinic, endoscopic and histologic features of CGD-IBD patients referred to Bambino Gesù Children’s Hospital of Rome, Italy, together with diagnostic and therapeutic implications.

Methods: Among a total population of 20 CGD patients, 9 presented CGD-IBD at diagnosis and/or during follow up. These patients constitute the study cohort. A retrospective data analysis was performed on clinical reports for clinical and laboratory data, endoscopic and histologic features, and treatments.

Results: The onset of IBD symptoms was observed at a mean age of 16 years old, with an overall delay of one year between clinical onset and endoscopic diagnosis. The majority of patients complained nonspecific recurrent/chronic diarrhea, with a frequent discrepancy between paucity of symptoms and severity of endoscopic appearance. Colonic involvement was the most frequent macroscopic picture, either as pancolitis or proctosigmoiditis. Histology revealed characteristic features, such as epithelioid granulomas, pigmented macrophages, and increased eosinophils. Serologic markers and fecal calprotectin did not correlate with the gastrointestinal phenotype. All patients except one received oral mesalamine and half required systemic steroids. A short-term antibiotic therapy was often administered at onset and during flares. Only one patient required azathioprine due to steroid dependence and severe disease. No patient required biological therapy, neither surgery. Clinical remission was obtained in all patients after the first course of treatment, but the majority complained occasional symptoms relapse, well controlled with topical therapy. Two episodes of severe infection occurred early after initiating steroid therapy.

Conclusion: IBD should be considered as a part of the natural course of CGD, with variable penetrance due to genetic and environmental factors. Gut inflammation may be the onset symptom of CGD and may occur early in life or in adolescence and young adults. Clinical manifestations may be subtle, thus delaying endoscopic diagnosis. Treatment with NSAIDs and/or steroids usually achieves a good response, not requiring second level therapies, but relapse usually occur during follow up. Infections surveillance is mandatory during treatment, as well as proper prophylaxis, in order to prevent opportunistic infections. CGD patients should be followed up at highly specialized centers. A close collaboration between paediatric immunologists and gastroenterologists is pivotal, including focused anamnesis for early diagnosis, endoscopic evaluation by expert endoscopists, and periodic combined follow up. Future directions include the individuation of diagnostic/prognostic biomarkers, tissue studies on immune response, analysis of the possible role of intestinal microbiota, as well as implementation of treatment strategies and improvement of patients' quality of life.
Body composition analysis using bioelectrical impedance in paediatric patients with Crohn's disease

Kriszta Katinka Boros¹, Katalin Eszter Müller¹, Fanni Orova¹, Nóra Judit Béres¹, Áron Cseh¹, Zoltán Kiss¹, András Arato¹, Attila Szabo¹, Gábor Veres¹

¹Semmelweis University; First Department of Pediatrics, Budapest, Hungary

Objectives and study: Paediatric Crohn's Disease (CD) is associated with malnutrition, weight loss, osteopenia and failure to thrive. These deficits could result an altered body composition. The reduction of protein related compartments (lean body mass, fat free mass) are well described in adult patients with CD, but less is known about this topic in paediatric patients. Our aim was to compare the body composition in children suffering in CD and an age matched control group, and to follow the changes in the body composition in CD patients getting exclusive enteral nutrition (EEN) and using biologics (anti-TNFα).

Methods: Body composition was measured in CD patients (n=15, mean age: 15,4 years) using bioelectrical impedance at the beginning of the therapy they received, and 6-8 weeks later. Six patients were treated with EEN, eight patients received anti-TNFα therapy. One patient was measured before and after hemicolectomy. Healthy (n=9, mean age: 15,21) and CD patients (n=7, mean age: 13,11) in remission as controls were enrolled in the study. In parallel, we followed the alterations in the body composition in the treated children through their therapy. We calculated the z-scores using Joubert-method.

Results: Patients in active phase had lower values compared to the patients in remission phase and healthy controls (HC): weight z-score (-0,8 vs. 0,4 and 0,3), fat mass index (FMI: 3 vs. 5,2 and 4,6) and fat free mass index (FFMI: 14,2 vs. 16,3 and 14,5). During the EEN therapy the weight z-score (from -0,9 to -0,7), the FMI with 0,07% and the FFMI with 2,76% increased. In patients who react to biologics the z-score increased with 0,12, the FMI 3,66% and the FFMI with 2,33%. The values in therapy resistance group decreased: weight z-score: with 0,5, FMI with 11,5%, and FFMI with 9,9%. The hemicolectomised child weight z-score increased from -1,98 to -0,48, the FMI 75,8% and FFMI with 27,8%.

Conclusion: Our findings suggest, that the weight z-score, FMI and FFMI of the patients in active phase were lower compared to the patients in remission phase and HCs. During the EEN the parameters did not change significantly. Through the induction of anti-TNFα therapy clear difference between patients who responded and non-responded were detected. In conclusion, the induction of biologics and the EEN may have an effect on body composition.
**GASTROENTEROLOGY: Inflammatory bowel disease**

G-P-239

**IBD in children: the safety and efficacy of an on-demand balloon catheter in disease diagnosis and assessment**

Efrat Broide

1The Kamila Gonczarowski Institute of Gastroenterology and Liver Diseases, Assaf Harofeh Medical Center, Tzrifin, Israel

**Objectives and study:** In 15%-25% of diagnosed inflammatory bowel disease (IBD) cases, including Crohn's disease (CD) and ulcerative colitis (UC), disease manifestation begins before the age of 18. Early and accurate diagnosis and extension of IBD is important for correct prognosis, therapeutic decisions, and follow-up. Therefore, proper diagnosis of IBD is extremely important in pediatric patients. The NaviAid™ AB device (Smart Medical Systems Ltd., Ra'anana, Israel) is an on-demand through-the-scope balloon system for small bowel evaluation which can be utilized for both antegrade and retrograde approaches (Figure 1). The safety and efficacy of the NaviAid™ AB has been evaluated in adult patients and was found to be both safe and useful for small bowel diagnosis. This study further evaluates the utility and safety of the NaviAid™ AB in pediatric patients with suspicion of small bowel disease.

**Methods:** This prospective, open, single-center study includes patients between the ages 8-18 with known or suspected IBD. Patients underwent enteroscopy utilizing the NaviAid™ AB device from the antegrade approach, retrograde approach, or both. The balloon catheter is inserted through the instrument channel of a standard endoscope and advanced ahead of the endoscope. The balloon is then inflated to an anchoring pressure and a repetitive push-pull technique is used to easily advance the endoscope deep into the small bowel. Procedural times, depth of insertion, ease of use, findings, and adverse events were recorded.

**Figure 1: The NaviAid™ AB Device**

**Results:** Nine patients (mean age 15; range 9-17 years; 66.7% male) referred for 14 enteroscopy procedures were prospectively enrolled, utilizing the NaviAid™ AB device. Indications included known IBD, anemia, weight loss, abdominal pain, perianal disease, rectal bleeding, or diarrhea. The average depth of insertion was 86.8 cm (range 70-110 cm) from the pylorus in the antegrade approach and 62.8 cm (range 45-80 cm) from the ileocecal valve in the retrograde approach. The average advancement time utilizing the balloon catheter was 7.33 minutes for all cases. Advancement was completed when no longer deemed clinically necessary. In 100% of patients with UC, the NaviAid™ AB confirmed diagnosis and verified normal small intestine. Furthermore, the NaviAid™ AB provided the extension of disease in 100% of patients with known or suspected Crohn's disease. There were no procedural adverse events reported.
Conclusion: The NaviAid™ AB device is safe and effective in pediatric patients utilizing a conventional endoscope. The through-the-scope catheter allows deep, accurate, and easy advancement into the small bowel in shorter time compared to other procedures and may prevent the need for additional endoscopic procedures in the future.
Diagnostic approach to paediatric IBD - results from clinical practice survey

Jiri Bronsky¹, Lissy De Ridder², Frank Ruemmele³, Anne Griffiths⁴, Stephan Buderus⁵, Almuthe Christine Hauer⁶

¹Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic
²Erasmus MC-Sophia Children's Hospital, Department of Pediatric Gastroenterology, Rotterdam, Netherlands
³Hôpital Necker Enfants Malades, Department of Pediatric Gastroenterology, Université Paris Descartes, Sorbonne Paris Cité, Aphp, Paris, France
⁴The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
⁵St.-Marien-Hospital, Department of Paediatrics, Bonn, Germany
⁶Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria

Objectives and study: Despite existence of international guidelines for diagnosis and management of inflammatory bowel diseases (IBD) in children, there might be local differences in diagnostic approach even between IBD-referral centres, mainly due to availability of laboratory and imaging methods and varying expertise and local practice. The objective of this project is to study the existence of local differences by evaluating results from a survey concerning diagnostic approach in paediatric IBD.

Methods: Between 09/2016 and 12/2016, a survey on Clinical practice in paediatric IBD was performed using Surveymonkey web-based tool among members of Porto IBD working group and IBD interest group of ESPGHAN, PIBD-NET, Canadian IBD network (CIDsCANN) and Society for paediatric gastroenterology of german-speaking countries.

Results: Responses from 70 paediatric IBD centres (7 from Canada, 1 from USA and rest from Europe and Israel) were collected on 17 questions concerning diagnostic approach (focused on initial diagnosis, use of endoscopy, imaging and laboratory methods, cancer surveillance). Fifty-two percent of paediatric IBD centres report that their adult IBD colleagues see patients under the age of 18 years (usually since 16yoa). In 59% of centres, there is an IBD-dedicated histopathologist and in 66% an IBD-dedicated radiologist available. Ninety-two percent of centres report to fulfil revised Porto criteria in majority of patients. In 40% of centres, ASCA/ANCA antibodies are routinely measured in vast majority of patients at the time of diagnosis. MR enterography (MRe) is the preferred method of small-bowel (SB) imaging (91%) with 77% of centres using an IBD-specific MRe protocol. In 60% of centres a SB ultrasound is also performed in vast majority of patients at the time of diagnosis. Control endoscopy after induction therapy is routinely performed only in 8% (in CD) and 7% (in UC) of centres, however, when major change of treatment is considered, it is done in 88% (CD) and 86% (UC) of centres, respectively. Yearly cancer-surveillance endoscopies are performed since diagnosis in PSC-UC only in 12% of centres and in UC patients after 8-10 years of disease duration in 62% of centres. In 52% of centres it is done in cooperation with adult GIs.

Conclusion: Revised Porto criteria are fulfilled in majority of paediatric patients at the time of diagnosis. Small bowel is preferably examined by MR enterography. Control endoscopy is performed when major change of treatment is considered, but not routinely for evaluation of effectiveness of the induction therapy. Only minority of centres perform cancer-surveillance in PSC-IBD since diagnosis. Limitations of the survey are that potentially desirable answers might be given instead of true daily practice, and also a potential bias when most motivated and thorough people might have answered.
Assessment of the Ulcerative Colitis Endoscopic Index of Severity (UCEIS) using central video review of colonoscopies in paediatric patients with ulcerative colitis: data from the Canadian Children IBD Network.

Nicholas Carman¹, Hien Huynh², Catharine Walsh³, Amanda Ricciuto¹, Marialena Mouzaki³, Eileen Crowley¹, Peter Church¹, Thomas Walters³

¹The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
²The University of Alberta, Ped Gi Nutrition, Edmonton, Canada
³Hospital for Sick Children, Department of Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: The Ulcerative Colitis Endoscopic Index of Severity (UCEIS) is a validated endoscopic tool which measures the worst disease activity in the rectosigmoid. This is potentially problematic as paediatric disease is often pancolonic and inflammation can be patchy, especially during active treatment. To date, there are no data evaluating the UCEIS in paediatrics. Using colonoscopy videos performed in patients from the Canadian Children IBD Network, we explored the reliability of the UCEIS when applied to colonic segments proximal to the recto-sigmoid.

Methods: Video recordings of colonoscopies obtained from paediatric patients with UC undergoing endoscopic assessment at Network sites were utilised for the analysis. 4 IBD experts reviewed each video blinded to clinical information. For each anatomical colonic segment data encompassing the 3 elements of the UCEIS (bleeding, ulceration, vascular pattern) were recorded. Total UCEIS scores were calculated for each segment. In addition, the most distal segment with the highest score was identified (UCEIS-max). A global assessment of endoscopic lesion severity for the entire colon (GELS) was also recorded using a visual analogue scale. Inter-rater reliability (IRR) was measured using Intraclass correlation coefficients (ICCs). Correlation between scoring tools was measured using Spearman’s test of correlation (r).

Results: There was a broad range of endoscopic severity (median UCEIS 6 (Range 3 – 8). The IRR for each aspect of the UCEIS are displayed in Table 1. The tool performed well throughout the colon, with ‘bleeding’ being the variable demonstrating the most disagreement. When comparing standard UCEIS and UCEIS-max, in 33% of patients the maximally affected segment was proximal to the rectosigmoid. In 10% of these subjects the difference in UCEIS score was greater than 1 point. (p <0.001). Correlation with GELS was better for UCEIS-max (r = 0.79, p <0.001), than for standard UCEIS (r = 0.68, p <0.001).
**Table:** Inter-rater reliability for UCEIS variables across anatomical segments.

<table>
<thead>
<tr>
<th>UCEIS Location</th>
<th>Total</th>
<th>Vascular Pattern</th>
<th>Bleeding</th>
<th>Erosions/Ulcers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Standard – Rectosigmoid</td>
<td>0.87 (0.74 – 0.95)</td>
<td>0.80 (0.60 – 0.91)</td>
<td>0.50 (0.11 – 0.77)</td>
<td>0.88 (0.76 – 0.95)</td>
</tr>
<tr>
<td>p = &lt;0.001</td>
<td>p = &lt;0.001</td>
<td>p = 0.01</td>
<td>p = &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Descending Colon</td>
<td>0.81 (0.73 – 0.96)</td>
<td>0.89 (0.77 – 0.95)</td>
<td>0.61 (0.25 - 0.82)</td>
<td>0.86 (0.71 – 0.94)</td>
</tr>
<tr>
<td>p = &lt;0.001</td>
<td>p = &lt;0.001</td>
<td>p = &lt;0.001</td>
<td>p = &lt;0.001</td>
<td></td>
</tr>
<tr>
<td>Transverse Colon</td>
<td>0.79 (0.60 – 0.85)</td>
<td>0.90 (0.72 – 0.98)</td>
<td>0.74 (0.26 – 0.91)</td>
<td>0.69 (0.2 – 0.77)</td>
</tr>
<tr>
<td>p = 0.02</td>
<td>p = &lt;0.001</td>
<td>p = 0.01</td>
<td>p = 0.02</td>
<td></td>
</tr>
<tr>
<td>Ascending Colon</td>
<td>0.74 (0.25 – 0.95)</td>
<td>0.85 (0.53 – 0.97)</td>
<td>0.69 (0.25 – 0.88)</td>
<td>0.77 (0.1 – 0.94)</td>
</tr>
<tr>
<td>p = 0.01</td>
<td>p = &lt;0.001</td>
<td>p = 0.01</td>
<td>P = 0.05</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** UCEIS is a valuable tool in the assessment of endoscopic disease severity in paediatric UC. UCEIS, when applied in standard fashion to the recto-sigmoid shows excellent IRR amongst IBD physicians. The tool can be applied across the colon, with only a small decrease in consistency. In this group of patients diagnosed with UC, one third of patients will have the maximally affected area proximal to the rectosigmoid, highlighting the importance of complete colonoscopy in assessing disease activity in UC.
Measurement of faecal calprotectin in paediatric patients with intestinal symptoms in primary care

Isabel Casas¹, Joana Carbonell Torremorell², Alba Cebollero Agustí³, Anna Gatell Carbó², José Antonio Serrano Marchuet², Vicente Morales Hidalgo²

¹Institut Catala DE LA Salut, Pediatric Gastroenterology, Barcelona, Spain
²Institut Catala DE LA Salut, Pediatric Primary Care, Barcelona, Spain
³Consorci del Laboratorio Intercomarcal Vilafranca del Penedès, Laboratory, Barcelona, Spain

Objectives and study: Faecal calprotectin (CF) is a widely used marker in the diagnosis and monitoring of activity in inflammatory bowel disease (IBD). However it is not specific for this disease, especially in children, where its usefulness in other gastrointestinal processes is yet to be established. Our aim was to determine CF values in paediatric intestinal pathologies in a primary care setting.

Methods: A one year prospective study was conducted on 30 children (<16 years) with intestinal symptoms in a semi-urban area of Barcelona. The following variables were reviewed: demographics, medical history and diagnostic tests (FC values and endoscopic tests). The cut-off point established for CF was <50 µg / g.

Results: The mean age was 7.1 years (4m-16 years). 70% were male. The main diagnoses were rectal bleeding (43%), abdominal pain (26.6%), constipation with hematochezia (23%) and chronic diarrhea (6%). 63.4% had a positive value of FC (mean: 205 µg / g). The highest value of CF was 859 µg / g in a 6-month-old infant with a diagnosis of cow’s milk protein intolerance. 25% had a suspicion of IBD but none was confirmed. In the cases with positive FC the final diagnoses were constipation 41% (FC: 50-266 µg / g), parasitosis 17.6% (FC 47-328 µg / g), intestinal polyp 11.7% (FC 244-246 µg / g), chronic diarrhea 10.5% (FC 251-315 µg / g). FC values were negativized in 1 and 6 months. 33% required an endoscopic evaluation.

Conclusion: We have observed that FC is a good marker of intestinal inflammation not just in paediatric IBD. In primary care the monitoring of these values and their subsequent negativization would avoid an unnecessary endoscopic evaluation.
Longitudinal and functional analysis of the faecal microbiome during treatment of paediatric inflammatory bowel disease

James Ashton\textsuperscript{1}, Catherine Colquhoun\textsuperscript{2}, David Cleary\textsuperscript{3}, Tracy Coelho\textsuperscript{1}, Rachel Haggarty\textsuperscript{4}, Akshay Batra\textsuperscript{5}, Nadeem Afzal\textsuperscript{6}, Karen Scott\textsuperscript{7}, RM Beattie\textsuperscript{1}, Sarah Ennis\textsuperscript{8}

\textsuperscript{1}Southampton Children's Hospital, Paediatric Gastroenterology, Southampton, United Kingdom
\textsuperscript{2}Rowlett Institute, Aberdeen, United Kingdom
\textsuperscript{3}University of Southampton, Faculty of Medicine and Institute of Life Sciences and Global Health Research Institute, Southampton, United Kingdom
\textsuperscript{4}Southampton University Hospital NHS Trust, Southampton, United Kingdom
\textsuperscript{5}University Hospital Southampton NHS Trust, Paediatric Gastroenterology, Southampton, United Kingdom
\textsuperscript{6}Southampton Children's Hospital, Southampton, United Kingdom
\textsuperscript{7}Aberdeen, United Kingdom
\textsuperscript{8}University of Southampton, Department of Human Genetics and Genomic Medicine, Southampton, United Kingdom

Objectives and study: The human microbiome is of considerable interest to inflammatory bowel disease (IBD) researchers with one potential mechanism for disease development being aberrant immune handling of the intestinal bacteria. This study analyses the faecal microbiome through treatment in newly diagnosed paediatric IBD patients and compares to co-habiting sibling where possible.

Methods: Patients were recruited on clinical suspicion of PIBD, prior to diagnosis. Treatment-naïve faecal samples were collected, with further samples at 2 and 6 weeks into treatment. Samples underwent 16S rRNA sequencing and short chain fatty acids (SCFAs) analysis, results were analysed using QIIME and PICRUSt.

Results: Six paediatric inflammatory bowel disease patients were recruited; 4 Crohn’s disease, 1 ulcerative colitis, 1 inflammatory bowel disease unclassified, median age 12.6 (range 10 - 15.1 years); 3 patients had an unaffected healthy sibling recruited simultaneously. Microbial diversity (observed species/Chao1/Shannon diversity) was reduced in treatment-naïve patients compared to siblings and patients in remission. Principal coordinate analysis using Bray-Curtis dissimilarity and unweighted UniFrac revealed microbial shifts in Crohn’s disease over the treatment course. In treatment-naïve IBD there was reduction in functional ability for amino acid metabolism and carbohydrate handling compared to controls (p = 0.038) and patients in remission (p = 0.027). Metabolic function returned to normal after remission was achieved. SCFA revealed consistent detection of lactate in treatment-naïve samples.

Conclusion: This study adds in-depth 16S sequencing analysis on a small longitudinal cohort to the literature and includes sibling controls and patients with UC and IBDU. It highlights the initial dysbiosis, reduced diversity, altered functional potential and subsequent shifts in bacteria from diagnosis over time to remission.
Equivalent effectiveness and short term safety of infliximab biosimilars mean savings of 1,000,000 euro lost in first year; now is the time for universal adoption

Neil Chanchlani1, Kajal Mortier2, Anne Willmott3, Astor Rodrigues4, David Wilson5, John Puntis6, John Fell7, Marcus Auth8, Sonny Cheng8, Mary-Anne Morris10, Mike Cosgrove11, Rafeeq Muhammed12, Sally Mitton13, Susan Bunn14, Mark Beattie15, Huw Jenkins16, Warren Hyer17, Michael Bisset18, Andrew Fagbemi19, Richard Russell20

1Royal Free London NHS Foundation Trust, Department of Paediatrics, London, United Kingdom
2Royal College of Physicians, Department of Clinical Standards, London, United Kingdom
3Leicester Royal Infirmary, Department of Paediatrics, Leicester, United Kingdom
4Oxford University Hospital, Department of Paediatric Gastroenterology, Oxford, United Kingdom
5University of Edinburgh, Department of Paediatric Gastroenterology, Child Life and Health, Edinburgh, United Kingdom
6Leeds General Infirmary, Department of Paediatric Gastroenterology, Leeds, United Kingdom
7Chelsea and Westminster Hospital, Department of Paediatric Gastroenterology, London, United Kingdom
8Alder Hey Children's NHS Foundation Trust, Department of Paediatric Gastroenterology, Hepatology and Nutrition (Ghn), Liverpool, United Kingdom
9Queen Mary's Hospital for Children (Epsom and St. Helier University Hospitals), Department of Paediatrics, Sutton, United Kingdom
10Jenny Lind Children's Hospital, Department of Paediatrics, Norwich, United Kingdom
11Morrison Hospital, Department of Paediatrics, Wales, United Kingdom
12Birmingham Children's Hospital, Department of Gastroenterology, Birmingham, United Kingdom
13St. George's Hospital, Department of Paediatric Gastroenterology, London, United Kingdom
14Great North Children's Hospital, Department of Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom
15University Hospital Southampton NHS Foundation Trust, Department of Paediatric Gastroenterology, Southampton, United Kingdom
16Cardiff and Vale University Health Board, Department of Paediatric Gastroenterology, Cardiff, United Kingdom
17Northwick Park and St. Mark's Hospital, Department of Paediatric Gastroenterology, London, United Kingdom
18NHS Grampian, Department of Paediatric Gastroenterology, Scotland, United Kingdom
19Royal Manchester Childrens Hospital, Department of Paediatric Gastroenterology, Manchester, United Kingdom
20Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom

Objectives and study: Infliximab biosimilar drugs have been available in the UK since February 2015. Routinely collected data from the UK IBD biologics registry is the first to include Infliximab biosimilar (IFX-B) drugs, (Inflectra™ and Remsima™), as alternatives to the originator Infliximab (IFX-O) (Remicade ®). We sought to summarise the short-term effectiveness, safety, and cost of using IFX-B compared to IFX-O in biologic naïve patients.

Methods: Prospective audit of 278 patients across 27 paediatric sites between March 2015 to February 2016; 1050 IFX-O patients have been in the audit since its inception in 2011 and were used as comparators. Pre-treatment screening was with chest radiograph, Hepatitis B/C serology, and Mantoux or Gamma interferon. Disease severity, response to treatment, and remission rate was measured by Paediatric Crohn's Disease Activity Index (PCDAI) and Physician Global Assessment. Results are presented as number (S) or median (interquartile range). Cost was determined at current market value distributed and projected estimate of savings [1,2].
Results: Between Mar 2015 to Feb 2016, 278 patients: 175 (63%), 82 (29%), and 21 (8%) were newly started on IFX-O, IFX-B, and Adalimumab respectively. Male distribution (61% in IFX-O vs 60% in IFX-B) (p>0.05), age at diagnosis (12 years), and age at biologic initiation (14 years) was similar between both IFX groups.

IFX-O was commenced in 61% (n=129) of patients with Crohn’s disease (CD), 68% (n=32) of patients with ulcerative colitis (UC), and 70% of patients with inflammatory bowel disease unclassified (IBDU). IFX-B was commenced in 30% (n=63) of CD patients, 30% (n=14) of UC patients, and 25% (n=5) of IBDU patients.

At baseline, 86% (n=150) and 79% (n=65) in the IFX-O and IFX-B groups respectively received immunosuppressants, including azathioprine, mercaptopurine, and methotrexate, and 29% (n=51) and 31% (n=25) in the IFX-O and IFX-B groups, respectively, received steroids (p>0.05 for both). Median PCDAI score was 36 (20,48) (n=42) in the IFX-O group and 28 (20,40) (n=29) in the IFX-B group.

At 3-month follow up, median PCDAI score was 5 (0,11) (n=19) and 0 (0,8) (n=15) in the IFX-O and IFX-B groups respectively. Response to treatment was 85% (n=28) and 86% (n=19) with remission rates of 68% (n=25) and 79% (n=19) in the IFX-O and IFX-B groups respectively (p>0.05). IFX-B was then compared to historical patients commencing IFX-O or Adalimumab (2011 – 2015), whose response to treatment at 3-months was 74% (n=158) (p=0.05) and remission rate was 65% (n=144) (p=0.37).

Adverse events (AE) were recorded at time of initial treatment in 3/175 patients and 0/82 patients in the IFX-O and IFX-B groups respectively. At 3 months, 4/76 and 2/39 AE were reported in the IFX-O and IFX-B groups respectively (both p>0.05). When comparing IFX-B data with IFX-O or Adalimumab (2011 – 2015), <0.05% patients reported AE on initiation (p=0.26) and <0.1% of patients reported AE on follow-up (p=0.45). With a conservative estimate €1,000,000 would have been saved with universal adoption of biosimilars in patients (IFX-O, n=175) included in this audit alone.

Conclusion: At initiation and 3-month follow-up, IFX-B are as effective as IFX-O in treating IBD in comparable paediatric populations. No increase in AE was reported. Sites should adopt biosimilars for all new starts due to the cost reduction with no difference in any other parameters.

References:

Disclosure of interest: Marcus K Auth declares that he received educational travel grants from Abbvie, MSD and Nutricia.
Richard K Russell has received consultation fees, research grants, or honorarium, from MSD, Abbott, Dr Falk, Ferring and Nestle.
David C Wilson COI = MSD - Financial support for research; Abbvie - Lecture fees; Takeda – Consultancy
Sally G Mitton has a COI with Abbvie.
DUOX2 mutations in very early-onset inflammatory bowel disease

Marianna Parlato1, Fabienne Charbit-Henrion2, Patti Hayes3, Antonio Tiberti4, Marina Alo5, Salvatore Cucchiara6, Begue Bernadette7, Marc Bras7, Aurore Pouliet8, Sabine Rakotobe9, Frank Ruemmele10, Ulla Knaus11, Nadine Cerf-Bensussan1

1Institut Imagine, Inserm Umr 1163 - Intestinal Immunity and Genius Group, Paris, France
2Imagine Institute and Hôpital Necker Enfants Malades, Inserm Umr 1163 - Intestinal Immunit and Genius Group, Paris, France
3Ucd-School of Medecine, Dublin, Ireland
4La Sapienza University of Roma, Roma, Italy
5Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Pediatrics and Genius Group, Rome, Italy
6Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
7Université Paris-Descartes-Paris Sorbonne Centre and Institut Imagine, Bioinformatic Platform, Paris, France
8Institut Imagine, Genomic Platform, Paris, France
9Institut Imagine, Inserm Umr 1163 - Intestinal Immunity, Paris, France
10Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
11UCD- School of Medecine, Immunology, Dublin, Ireland

Objectives and study: By catalyzing generation of hydrogen peroxide (H$_2$O$_2$) in enterocytes, DUOX2 participates in innate defense against intestinal microbes. One mono-allelic exonic variant of DUOX2 was recently found in 15 out of 19 Crohn Disease-affected patients in a large Ashkenazi family. Here, we report the first identification of biallelic, inherited mutations of DUOX2 as a Mendelian cause of very early onset inflammatory bowel disease (VEO-IBD).

Methods: A boy born from unrelated parents developed pancolitis with bloody diarrhea at the age of three, without extra-gastrointestinal manifestation. Histology showed dense inflammatory infiltrate, mucin depletion, architectural distortion and crypt abscesses without epitheloid granuloma. Mesalamine and systemic steroids induced symptom resolution but clinical relapse occurred at steroids withdrawal. Thiopurines allowed remission but were discontinued rapidly because of increased pancreatic enzymes. He is currently in remission under mesalamine. Targeted next-generation sequencing and whole exome sequencing (WES) were performed to identify the molecular defect. Functional validation of candidate variants required transfection of wild-type (WT) or DUOX2 mutants in H661-DUOXA2 cells. Protein expression and H$_2$O$_2$ production upon thapsigargin stimulation in transfected cells were assessed by flow cytometry. Patient’s biopsies were stained for DUOX2 expression by immunochemistry.

Results: After exclusion of a known molecular defect using targeted sequencing of 68 VEO-IBD-associated genes, WES identified compound heterozygous missense variants in DUOX2, both confirmed by Sanger sequencing. Variant 1 (p.P609S, Minor Allele Frequency: 2.7 × 10$^{-4}$) was located within the first transmembrane domain, variant 2 (p.R286H) within the peroxidase-homology domain of DUOX2. R286H was absent from both public and in-house databases. Both mutations affected evolutionarily conserved residues, with changes predicted to be damaging. Cells (from an epithelial cell line) transfected with WT ors DUOX2 mutants showed comparable amounts of proteins in cell lysates. In contrast, flow cytometry revealed reduced surface expression of P609S compared to WT DUOX2, while R286H was undetectable. In accordance, DUOX2 protein expression on patient’s biopsies was markedly decreased compared to controls. H$_2$O$_2$ generation upon thapsigargin stimulation was undetectable in transfected cells expressing R286H and significantly decreased in cells expressing P609S or coexpressing the two mutants at 1:1 ratio.

Monoallelic or biallelic DUOX2 mutations are a cause of transient or permanent congenital hypothyroidism (CH). Of note, thyroid function was normal in the affected boy, in accordance with the
highly variable penetrance of DUOX2 mutations. In contrast, the child developed severe intestinal inflammation. DUOX2 is expressed in all gut segments where it is up-regulated by microbiota and inflammation-derived signals. Very rare monoallelic mutations of DUOX2 were also reported as risk factor for VEO-IBD in two patients. Together with our data, these observations strengthen the hypothesis that, alike in CH, both mono- and biallelic DUOX2 mutations can increase susceptibility to intestinal inflammation.

**Conclusion:** Our findings expand the clinical phenotype and inheritance mechanism of DUOX2 defects, and indicate that mono- and biallelic DUOX2 mutations can be a monogenic cause of IBD.
Basal faecal calprotectin as a predictor of its decrease at week 6 of exclusive enteral nutrition in paediatric patients with newly diagnosed Crohn’s disease - prospective observational study

Ivana Copova¹, Ondrej Hradsky², Kristyna Zarubova², Lucie Gonsorcikova², Kristyna Potuznikova², Tereza Drskova², Jiri Nevoral², Jiri Bronsky²

¹University Hospital Motol, Paediatrics, Prague, Czech Republic
²University Hospital Motol, Department of Paediatrics, Prague, Czech Republic

Objectives and study: Exclusive enteral nutrition (EEN) has been shown to be as effective as corticosteroids, without their side effects, in achieving clinical remission and superior in achieving mucosal healing in paediatric patients with Crohn’s disease (CD). Data of predictors of response to treatment in early phase of EEN are scarce. Primary aim of our study was to determine whether it is possible to use the difference in value of faecal calprotectin (FC) before treatment and at week 2 of treatment with EEN to predict FC decrease between week 0 and week 6.

Methods: FC was analyzed using an enzyme-linked immunosorbent assay (ELISA) in four serial stool samples prospectively collected during EEN (at week 0, 2, 4 and 6), and six weeks after induction therapy in children with newly diagnosed CD.

Results: Forty-one paediatric patients (28 boys, 16.1 ± 2.8 y) with newly diagnosed CD participated. Median FC concentration was reduced by 259 µg/g (IQR: -1.25 – 508.2) from baseline to EEN completion. Only three children achieved FC levels <100 µg/g by the end of EEN. Difference of FC concentration before EEN and at week 2 or 4 of treatment predicted decrease of FC at week 6 of EEN (p<0.00001). The FC drop of more than 8 µg/g at week 2 had specificity 1 and sensitivity 0.63 for prediction of any decrease of FC at week 6 (AUC 0.83).

Conclusion: Early decrease of FC during induction EEN therapy predicts FC levels on EEN completion. Monitoring of disease activity based on FC concentration can be useful to predict response to treatment.
Long-term follow-up in paediatric patients with Crohn’s disease with infliximab therapy: the PIT-STOP multicenter study

Áron Cseh¹, Éva Nemes², András Tárnok³, Mártta Kovács⁴, Dániel Szűcs⁵, Nóémi Vass⁵, Márta Balogh⁶, Natalia Lasztity⁷, Katalin Eszter Müller¹, András Arato¹, Antal Dezsofi¹, Gábor Veres¹

¹Semmelweis University, First Department of Pediatrics, Budapest, Hungary
²University of Debrecen, Department of Paediatrics, Clinical Center, Debrecen, Hungary
³University of Pécs, Department of Paediatrics and Paediatric Health Center, Pécs, Hungary
⁴Petz Aladár County Hospital, Győr, Hungary
⁵University of Szeged, Department of Paediatrics and Paediatric Health Center, Szeged, Hungary
⁶Markusovszky Teaching Hospital, Szombathely, Hungary
⁷Heim Pal Children’s Hospital, Budapest, Hungary

Objectives and study: Infliximab (IFX) therapy is available in Hungary since 2007 for treatment of severe paediatric Crohn’s disease (CD). According to national regulation anti-tumour necrosis (TNF) therapy must be stopped after one-year of successful treatment. However, data from adult population has already shown that the risk of relapse is high after discontinuation.

Methods: We aimed to determine the relapse rate in paediatric patients with CD and to identify risk factors of treatment failure after one-year of IFX therapy. 99 children (53 boys) were enrolled from 7 inflammatory bowel disease (IBD) centres in Hungary, retrospectively.

Results: The median age was 13.1 (11-14.7) years (median (interquartile range)) at the time of diagnosis. Disease duration before commencing IFX was 1.7 (0.9-3.3) year. Overall restart rate was 55.4% (51 restarts, 7 allergies) with reintroduction of IFX therapy in 0.8 (0.3-1.0) year. Risk factor was the need of steroid at the time of IFX therapy initiation (OR 2.940 (1.160-7.452, p=0.023). In addition, metronidazole given at the time of diagnosis was protective factor for relapse (OR 0.289 (0.095-0.883), p=0.029).

Conclusion: More than half of the paediatric patients with CD needed to restart IFX therapy which is similar to the recommencement rate shown in adult studies. Our data is unique due to our special national stop rule-regulation. Our results indicate the importance of continuation of IFX therapy after one-year treatment in paediatric patients with severe CD.
Presence and severity of ulcerations in Crohn disease contribute to the course of maintenance therapy with infliximab in children

Maciej Dadalski\(^1\), Agnieszka Wegner\(^2\), Jaroslaw Kierkus\(^3\)

\(^1\)The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
\(^2\)Public Children's Clinical Hospital, Warszawa, Poland
\(^3\)The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: The primary and secondary loss of efficacy are major problems during anti TNF-\(\alpha\) maintenance therapy. It's documented that complete remission, concurrent immunomodulators are the predictors of prolonged remission. It is questionable if presence of colonic and ileal ulcerations can contribute the CD flare. The aim of the study was to explore the contribution of presence and severity of ulcerations to the course of maintenance therapy with infliximab in children.

Methods: This is a per protocol subanalysis of CIMIT study. 77 patients with PCDAI>30 pts and endoscopic evaluation (using Simple Endoscopic Score for Crohn's Disease (SES-CD), based on 4 endoscopic variables (ulcer size, ulcerated and affected surfaces, stenosis) in 5 ileocolonic segments (ileum, right colon, transverse colon, left colon, rectum) and the endoscopic parameters are scored from 0–3) performed before induction therapy (Week 0) and after (Week 10), who finished one year maintenance therapy with infliximab 5 mg/kg were involved to the study. Clinical (PCDAI score) remission (PCDAI<10) were assessed at Week 52. Scorings of ulcer size and ulcerated surface at Week 0 and Week 10 were used as four independent variables in analysis of discrimination between: groups with clinical remission (with or without rescue therapy \(n=57\)) vs. no remission (\(n=20\)) and groups with CD flare during maintenance therapy present (\(n=34\)) vs. absent (\(n=43\)).

Results: None of the analyzed variable had significant impact on discrimination between group with clinical remission vs. no remission — all partial Wilks' Lambda > 0.98. The optimal model of discrimination had sensitivity 0.98 and specifity 0.15.

Ulcer size scoring at Week 0 had significant impact on discrimination between group with CD flare during maintenance therapy present vs. absent — partial Wilks’ Lambda = 0.93; \(p<0.05\). The optimal model of discrimination had sensitivity 0.88 and specifity 0.41. The group with CD flare during maintenance therapy present had higher scoring vs. absent - 6;3;9 vs. 4;2;6 [median;\(q1\);\(q3\)] respectively.

Conclusion: The size of ileal and colonic ulcerations contribute to the risk of CD flare during anti TNF-\(\alpha\) maintenance therapy in children.
Comparison of health related quality of life in anemic children with inflammatory bowel disease to published general IBD cohorts and healthy controls

Istvan Danko¹, Marcy Weidkamp¹

¹University of Wisconsin, School of Medicine and Public Health, Pediatrics, Pediatric Gastroenterology, Madison, United States

Objectives and study: Anemia is common in children with inflammatory bowel disease (IBD). Adverse effects of gastrointestinal symptoms on health-related quality of life (HRQL) are well documented but little is known about the impact of anemia. Our objective was to compare HRQL in children with IBD with and without anemia to published general pediatric IBD cohorts* and normative data**.

Methods: Over a 2.5-year period ending in June of 2016 all patients between ages 0-18 years with a diagnosis of IBD treated with infliximab were offered participation. Laboratory studies, disease activity and HRQL assessments were done at enrollment in the pediatric infusion center. Anemia was defined by standard WHO criteria. Remission was defined as Pediatric Crohn’s disease (CD) or ulcerative colitis (UC) activity index ≤10, normal C-reactive protein and albumin. HRQL was assessed with PedsQL 4.0 Generic Core Scales (child-reported psychosocial, physical, total scores followed by parent-reported values; range 0-100; respective scores below 66.03, 72.98, 69.71 and 64.38, 63.28, 65.42 confer risk for poor HRQL**). Mean HRQL scores were compared with two-sample t tests and the proportion of patients with risk scores were compared with Fisher’s exact test; p<0.05 defined statistical significance.

Results: 30 patients (18 males), 27 with CD (16 males), 3 with UC (2 males) participated in the study. Mean (SD) age was 10.9 (3.1) years at diagnosis and 13.1 (3.2) years at enrollment. For the entire cohort mean (SD) Hb was 11.9 (1.6) g/dl, mean (SD) HRQL scores were 77.3 (15.4), 78.8 (16.2), 77.8 (14.2), 73.7 (16.4), 78.3 (16.7), 75.0 (15.5). Of the 12 patients with active disease (40% of total, all CD), 9 (75%) had anemia and 3 (25%) had normal Hb. Mean (SD) Hb of this group was 11.4 (1.2), mean (SD) HRQL scores were 77.8 (12.8), 75.3 (14.4), 76.9 (12.3), 71.1 (14.6), 71.8 (14.3), 71.2 (12.7). There was no statistically significant difference between HRQL scores of patients with and without anemia in this group. Of the 18 patients (60% of total, 3/3 with UC and 15/27 with CD) in remission 10 (56%) had normal Hb and 8 (44%) had anemia. Mean (SD) Hb of the respective groups was 13.3 (0.8) and 11.1 (1.8) (p=0.002). Mean (SD) HRQL scores of patients with normal Hb were 85.1 (12.4), 92.4 (8.2), 87.5 (9.5), 85.6 (7.9), 92.0 (7.0), 87.6 (5.8) compared to 71.3 (19.2, p=NS), 73.0 (19.3, p=0.01), 72.0 (17.7, p=0.02), 64.3 (17.9, p=0.003), 71.9 (19.4, p=0.008), 66.4 (18.1, p=0.002) of patients with anemia. Percentage of patients with risk scores for poor HRQL in the respective scales was 0, 10, 0, 0, 0, 0 among patients with normal Hb compared to 37.5 (p=NS), 50 (p=NS), 50 (P=0.03), 62.5 (p=0.006), 37.5 (p=NS), 62.5 (p=0.007) among those with anemia. There was no statistically significant difference between mean HRQL scores of our cohort as a whole and the general IBD sample. In contrast, our patients in remission with normal Hb had significantly higher scores in all scales, and those in remission with anemia had significantly lower parent-reported psychosocial and total scores.

Conclusion: Anemia is common among children with IBD in remission and appears to place them at significant risk for poor HRQL, thus testing and treatment of anemia should be an integral part of their care. Most children in our study with active IBD also had anemia. Our data do not allow conclusions regarding the relative contribution of anemia to impaired HRQL in these patients.

Use of infliximab levels in paediatric IBD - a single centre experience

Sarumathi Dhanapal¹, Eunice Goto², Marco Deganello², Krishna Soondrum¹, Jenny Epstein², John Fell¹

¹Chelsea and Westminster Hospital NHS Trust, Paediatric Gastroenterology, London, United Kingdom
²Chelsea and Westminster Hospital NHS Trust, London, United Kingdom

Objectives and Aims: Infliximab (IFX) has been widely used in paediatric Crohn's disease patients, mainly with luminal disease refractory to standard treatment, fistulating and for extra-intestinal manifestations. Moreover, there is growing experience with its use in refractory ulcerative colitis. There is still however, limited evidence around the use of Serum Infliximab trough level (TL) in making clinical decisions with regards to escalating of the dose or cycle regime.

Risk of antibody formation if the serum Infliximab trough level is low has been reported in a few studies. This study aims to present the relevance of IFX trough levels and its clinical relevance in reaching remission.

Methods: We conducted an observational study using case notes of all paediatric IBD patients over a 22 month period treated from January 2015 to October 2016 (n=35, 25M, 10F, CD=27, UC=8, median age = 14yrs). 5 children had fistulation disease, 2 had hemicolectomy and all continued on their immunomodulatory medication (33-AZA, MTX-2, IV Steroid-1). 6 (4UC 2CD) of the 35 patients were commenced on a higher dose induction regime (7.5mg/kg-2 and 10mg/kg-4) as salvage treatment to avoid surgery. The standard dose of 5mg/kg at 0-2-6weeks was given to the rest of the patients. 35 levels were done on 35 patients between the 3rd and 6th doses.

Biochemical disease activity was assessed by serum C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), serum albumin and activity index scoring (Paediatric Ulcerative Colitis Activity index – PUCAI and weighted Paediatric Crohn’s disease activity index - wPCDAI. Data of the CD and UC groups were analyzed separately. Our lab reference range for IFX TL is 3-8 µg/ml.

Results: Out of 35 patients, 15(61%) had IFX trough levels > 3µg/ml (22CD,3UC). All Children with high/ normal therapeutic levels with CD were in remission clinically with significant improvement showing from their biochemistry results (ESR, Albumin and CRP normalizing) and disease activity score.

10 (28%) patients had low levels had low < 3µg/ml (2UC 8CD) and continued to have mild clinical symptoms with high disease activity scores. 2 children had their dose doubled and 8 children continued the same treatment 6 weekly.

Chi-square test confirmed the statistical significance of the serum Infliximab level and the remission (p value is 0.00 for CD and 0.035 for UC)

We have noted that higher TLs were not associated with side effects.

Conclusion: Adequate Serum Infliximab trough levels at dose 3-6 are associated with clinical and biochemical remission, implies that dose tailoring will result in better outcome. The activity disease score significantly reduced on all children with good TL there by improving their quality of life. There is a need for larger studies looking at serum infliximab trough levels and its relevance in clinical practice.
Long-term outcomes after restorative proctocolectomy and ileal pouch-anal anastomosis in children compared to adults

Kay Diederen1, Saloomeh Sahami2, Merit Tabbers3, Pieter Tanis2, Marc Benninga1
Angelika Kindermann1, Matthijs Oomen4, Willem Bemelman2, Justin de Jong4

1Academic Medical Center/Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Academic Medical Center, Department of Surgery, Amsterdam, Netherlands
3Academic Medical Centre, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
4Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Surgery, Amsterdam, Netherlands

Objectives and study: Restorative proctocolectomy with ileal pouch-anal anastomosis (IPAA) is the surgical treatment of choice for therapy refractory ulcerative colitis and familial adenomatous polyposis (FAP). There are only a few studies addressing the outcome of IPAA in children compared to adults. This complicates decision making in children with therapeutic refractory UC or FAP. Therefore, we aimed to compare adverse events and pouch function between pediatric and adult patients who underwent IPAA.

Methods: In this cohort study, all consecutive children (<18 years) and adults with a diagnosis of inflammatory bowel disease or FAP that underwent IPAA were included (2000–2015). The IPAA’s were performed in a Dutch tertiary referral center by the same team of colorectal surgeons in all subjects in this time period (IPAA’s 30–35/year). Demographic and surgical characteristics, and adverse events were obtained by chart review. Pouch function was assessed by phone interview using the Pouch Function Score (PFS, scale 0–30). Differences in adverse events between pediatric and adult patients were analyzed using multivariate regression analysis, corrected for the moment of enrollment during the study period.

Results: In total, 445 patients underwent IPAA: 41 pediatric (median age 15 years) and 404 adult patients (median age 39 years). Median follow-up was 24 months (IQR 8–68). In pediatric patients, overweight, previous abdominal surgeries, open procedures (i.e. colectomy) and defunctioning ileostomy were less prevalent compared to adult patients (p<0.05). All other characteristics, including type of diagnosis and duration of follow-up, were similar (p>0.05).

The occurrence of anastomotic leakage, surgical related fistulas, chronic pouchitis and Crohn’s of the pouch (in IBD patients) was not associated with pediatric age, neither was pouch failure on the long-term (table). Pediatric age at IPAA was an independent risk factor for developing anastomotic strictures (OR: 4.2 [95%CI: 1.1 - 15.8]; p = 0.032). These strictures were successfully treated through a single dilatation in all pediatric and 73% of adult patients. Current pouch function was similar between pediatric and adult patients (median PFS 5.0 vs. 6.0, p = 0.164).
Conclusion: Long-term pouch failure rates and pouch function were similar between pediatric and adult patients. There is no need for a more cautious attitude in the application of IPAA in pediatric patients based on concerns of poor outcome on the long term.

Table 1. Adverse events: pediatric vs. adult patients

<table>
<thead>
<tr>
<th></th>
<th>Pediatric (n = 46)</th>
<th>Adult (n = 426)</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Anastomotic leakage</td>
<td>14%</td>
<td>16%</td>
<td>0.88 (0.35 – 2.22)</td>
</tr>
<tr>
<td>Pouch stricture</td>
<td>10%</td>
<td>3%</td>
<td>4.22 (1.13 – 15.77)*</td>
</tr>
<tr>
<td>Fistulas related to the pouch</td>
<td>2%</td>
<td>6%</td>
<td>0.63 (0.08 – 5.21)</td>
</tr>
<tr>
<td>Chronic pouchitis</td>
<td>5%</td>
<td>8%</td>
<td>0.58 (0.13 – 2.56)</td>
</tr>
<tr>
<td>Crohn’s of the pouch*a</td>
<td>15%</td>
<td>6%</td>
<td>3.07 (0.87 – 10.82)</td>
</tr>
<tr>
<td>Pouch failure</td>
<td>10%</td>
<td>6%</td>
<td>3.01 (0.89 – 10.14)</td>
</tr>
</tbody>
</table>

* Significantly associated with adverse outcome in multivariable regression analysis.

*a in IBD patients only (n = 339)
Antibodies to infliximab trough levels in the management of children with inflammatory bowel disease

Anna Dilillo\textsuperscript{1}, Fortunata Civitelli\textsuperscript{1}, Sara Isoldi\textsuperscript{1}, Saverio Mallardo\textsuperscript{1}, Salvatore Oliva\textsuperscript{1}, Marina Aloi\textsuperscript{1}, Paolo Rossi\textsuperscript{1}, Franca Viola\textsuperscript{1}, Salvatore Cucchiara\textsuperscript{1}

\textsuperscript{1}Sapienza University of Rome, Department of Pediatrics, Gastroenterology and Liver Unit, Rome, Italy

Objectives and study: Antibodies to infliximab (ATI) and low serum infliximab (IFX) trough levels (TL) are associated with loss of response in adult patients (pts) with inflammatory bowel diseases (IBD). We aimed to evaluate the association between ATI and IFX TL and loss of response to IFX therapy in pediatric pts with IBD.

Methods: We enrolled 13 pediatric IBD pts, 5 with Crohn's disease (CD) and 8 with ulcerative colitis (UC). They were on maintenance treatment with IFX by at least 6 months and had experienced a loss of response. Both TL and ATI determinations were performed by using ELISA method (Lisa tracker-Duo IFX, Theradiag, Marn-la-Vallè, France). According to manufacturer instructions, levels of detection were 0,1 \( \mu \)g/ml for TL and 10 ng/ml for ATI. Clinical status and CRP levels were checked after drug optimization (dose increase and/or interval shortening), after six months and after one year. Clinical response was defined as the absence of symptoms related to IBD and decreasing in PCDAI and PUCAI \( \geq 15 \) points from baseline.

Results: ATI were detected in 9 pts (69,23\%), while TL were undetectable in 4 pts (30,77\%). Presence of ATI and low TL were inversely related to clinical and biological response at 6 and 12 months (\( p=0,0001 \)). 6 pts (46,15\%) with high levels of ATI (>200 ng/ml) and low TL switched to biological therapy; 2 pts (15,38\%) with ATI levels>11 ng/ml and low TL after drug optimization, and 5 pts (38,46\%) with low TL and absence of ATI after drug optimization continued biological therapy and displayed normal CRP and clinical response at 6 and 12 months.

Conclusion: Presence of ATI and IFX trough levels monitoring are useful in managing children with IBD. Presence of ATI and persistence of low TL after drug optimization are indicative of drug failure, therefore another therapy should be used. Further prospective studies are necessary to validate TL after drug optimization and to establish ATI cut-off values.
Barriers to clinical research in children with inflammatory bowel disease: the patients’ perspective

Wael El-Matary¹, Vini Deora¹

¹University of Manitoba, Pediatrics, Winnipeg, Canada

**Objectives and study:** Recruitment for clinical research in pediatric inflammatory bowel disease (IBD) could be difficult. Patients’ willingness to participate in clinical research is affected by several factors including research-related, patient-related and disease-related factors. Understanding the nature of barriers to recruitment for clinical studies is important for better planning of future research. Data on barriers for recruiting children with IBD to clinical studies are limited. The aim of this study was to examine possible barriers to clinical research in children with IBD from patients’ perspective.

**Methods:** In a cross-sectional single centre paediatric study, children with IBD or their care givers when appropriate were surveyed via a questionnaire that addressed patients’/parents’ willingness to participate in clinical studies and factors that may influence patients’ willingness to participate. Univariate logistic regression analysis was used to examine any possible effect of factors such as disease nature, type of biological samples, and parental education on willingness to participate in clinical research.

**Results:** Out of 96 children with IBD (mean age 13.9±2.78 years, 53 (55%) boys, 49 (51%) Crohn’s disease (CD)) who were consecutively recruited in the Paediatric IBD clinic, Winnipeg Children’s Hospital, Winnipeg, Manitoba, 84 (87.5%) were “definitely or probably” willing to participate in clinical research while 12 (12.5%) were neutral or unwilling to participate (P<0.01). Factors associated with increased willingness to participate included providing research blood (OR=2.1, 95% CI 1.2-4.1, P=0.03) and urine (OR=2.04, 95% CI 1.03-4.1, P=0.04) samples but not stool samples (OR=1.3, 95% CI 0.73-2.47, P=0.3) or endoscopy (OR=1.45, 95% CI 0.83-2.56, P=0.19). Patients with CD were more willing to participate (OR=3.27, 95% CI 1.11-9.66, P=0.03). Parents’ education, family income, clinical disease activity and medications such as immunosuppressive or biological medications at the time of the survey did not have any significant effect on willingness to participate.

**Conclusion:** The majority of children with IBD are willing to participate in clinical research especially in studies that include blood and urine sample collection but not stool samples or endoscopy. Children with Crohn’s disease are more likely to participate in research studies.
Biologics utilization in children with Inflammatory bowel diseases is higher and earlier than in adults: a report from the epi-IIRN group

Mira Friedman¹, Rachel Axelrod², Joseph Rosenblum³, Nir Sigman³, Iris Goren³, Natan Lederman⁴, Nurit Cohen⁵, Eran Matz⁵, Doron Dushnitsky⁵, Nirit Borovsky⁵, Matan Gavish⁵, Gili Focht¹, Malka Avitzour¹, Iris Dotan⁶, Eric I. Benchimol⁷, Dan Turner⁸

¹Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
²The Hebrew University of Jerusalem, School of Computer Science and Engineering, Jerusalem, Israel
³Maccabi Healthcare Services, Tel Aviv, Israel
⁴Meuhedet Health Services, Tel Aviv, Israel
⁵Leumit Health Services, Tel Aviv, Israel
⁶Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Department of Gastroenterology and Liver Diseases, Tel Aviv, Israel
⁷Children's Hospital of Eastern Ontario, University of Ottawa, Cheo Inflammatory Bowel Disease Centre, Ottawa, Canada
⁸Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: The diagnosis of Inflammatory bowel diseases (IBD) during childhood is associated with a more aggressive and extensive phenotype compared with adults, necessitating early introduction of effective therapy. We aimed to study differences in biologic therapy in pediatric and adult IBD patients in the Israeli population.

Methods: IBD cases were identified within the databases of three national health maintenance organizations (HMOs), covering 48% of the Israeli population. Identification as well as differentiation into Crohn's disease (CD) or ulcerative colitis (UC) patients was performed using previously validated algorithms, with the effective date of 31.12.2015. Biologic therapy was determined by pharmacy purchases as recorded by the HMOs; expenses are covered by the national public health care system, ensuring complete unbiased records.

Results: Of 19,780 IBD patients identified, 3,445 (17%) commenced on biologics by 31.12.2015. Children (<18 years) were twice as likely to be treated with biologics (n=326/1005, 32%) vs. adults (n=3119/18,775, 16%; p<0.001). The difference was more pronounced in UC than CD (CD- 41%/25%, UC- 17%/6%, for pediatrics and adults, respectively). Amongst patients diagnosed between 2005-2015, time in months from diagnosis to initiation of biologics was shorter for children (CD- median: 43 [IQR: 16-80], UC 48 [19-85]), as compared to adults (CD- 54 [25-90], UC- 66 [37-101] ; p<0.001 for both CD and UC).

Conclusion: Biologic utilization in pediatric IBD is significantly higher and earlier than in adults. The possible explanations include a more aggressive and extensive disease, differing clinical practices and the role of biologics for the treatment of growth impairment.

This study was supported by a grant from the Leona M. and Harry B. Helmsley Charitable Trust.
A switch in the prevalence ratio of Crohn’s disease vs. ulcerative colitis in Israel between 2003-2015 - a report from the epi-IIRN group


1Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
2Ben-Gurion University of the Negev, Department of Gastroenterology and Hepatology, Faculty of Health Sciences, Be’er Sheva, Israel
3Clalit Health Services, Clalit Research Institute, Chief’s Office, Tel Aviv, Israel
4Maccabi Healthcare Services, Tel Aviv, Israel
5Meuhedet Health Services, Tel Aviv, Israel
6Leumit Health Services, Tel Aviv, Israel
7The Hebrew University of Jerusalem, School of Computer Science and Engineering, Jerusalem, Israel
8Rambam Health Care Campus, Bruce Rappaport School of Medicine, Technion Israel Institute of Technology, Department of Gastroenterology, Haifa, Israel
9Chaim Sheba Medical Center, Department of Gastroenterology, Tel Hashomer, Israel
10Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Department of Gastroenterology and Liver Diseases, Tel Aviv, Israel
11Hadassah Medical Center, The Hebrew University of Jerusalem, Idbd Center, the Institute of Gastroenterology, Jerusalem, Israel
12Rabin Medical Center, Gastroenterology Department, Petach Tikva, Israel
13Children’s Hospital of Eastern Ontario, University of Ottawa, Cheo Inflammatory Bowel Disease Centre, Ottawa, Canada
14Shaare Zedek Medical Center, Department of Pediatric Gastroenterology, Jerusalem, Israel

Objectives and study: Crohn’s disease (CD) has been considered a condition limited mostly to westernized countries, while ulcerative colitis (UC) may be more common in some developing countries. We aimed to utilize data from all four Israeli health maintenance organizations (HMOs), covering 98% of the Israeli population, to determine population-based epidemiological trends of CD and UC.

Methods: IBD patients were identified from 2003 (the first year of computerization in the HMOs) until 2015 and differentiated as CD or UC patients using algorithms validated to accurately identify cases from within the dataset (case ascertainment accuracy: 99% and 94%, respectively). Standardized prevalence per 100,000 population per year were derived from the Israeli National Insurance Institute.

Results: At the end of 2015, a total of 38,291 IBD patients were residing in Israel, corresponding to a prevalence rate of 459/100,000 (0.46%), double the prevalence rate 12 years earlier (0.23%). UC was more prevalent than CD until 2010 after which CD became more common, and this difference has increased each year (CD/UC: 2003- 6306/7665 (p<0.0001), 2010- 14628/14427 (p=0.1), 2015-20196/17810 (p<0.0001), (Figure 1)). Patients in the 25-34yrs and 35-44yrs age groups contributed most to the upsurge in CD rates, suggesting a link to environmental and economic changes in Israel during childhood years.
**Conclusion:** Israeli IBD prevalence is the third highest in the world, and has nearly doubled in the past decade. The increased preponderance of CD over UC has occurred in parallel with an increase in the economic state of Israel; this possible link requires further study.

This study was supported by a grant from the Leona M. and Harry B. Helmsley Charitable Trust.
Predictors of disease progression in Manitoban children with IBD: 30 years' experience

Wael El-Matary¹, Charles Bernstein²

¹University of Manitoba, Pediatrics, Winnipeg, Canada
²University of Manitoba, Gastroenterology, Winnipeg, Canada

Objectives and study: Improving knowledge of the natural history of inflammatory bowel disease (IBD) in children may provide a better understanding of prognostic outcomes in these children. We previously showed that 9% of Manitoban children with IBD had their diagnosis changed over a 14 year-mean duration of follow up. Moreover, delayed introduction of immunosuppression was associated with higher rates of intestinal surgery in both Crohn’s isease (CD) and ulcerative colitis (UC). The aim of the current study was to examine predictors of disease progression in a cohort of children with IBD in Manitoba, Canada over a 14-year mean duration of follow up.

Methods: The Pediatric Gastroenterology Clinic at the Children’s Hospital in Winnipeg, Manitoba, Canada has provided care for nearly all children resident in the province of Manitoba and for most of the children living in Nunavut and Northwestern Ontario since 1978. The database of this clinic from January 1978 to December 2007 was reviewed and medical charts of persons with IBD diagnosed as children were examined. Predictors of changes in disease behaviour, distribution and surgical rates were determined.

Results: During the 30-year study period, 397 children (age < 17 years), of whom 221 (56%) were boys, were diagnosed with IBD. A total of 233 (59%) had CD, 141 (35%) had UC, and 23 (6%) had unclassified IBD (IBD-U). Sixty six children with CD (mean age at diagnosis 13.1± 2.1 years, mean duration of follow up 15.8±7.1 years, 44 boys) and 55 children with UC/IBD-U (mean age at diagnosis 12.8±2.8 years, mean duration of follow up 13±4.9 years, 26 boys) had complete medical records. One third of participants had changes in disease distribution and/or disease behaviour. Predictors of changes in CD included disease duration (OR 13.49, 95% CI 11.10-15.88, P<0.001 for distribution) (OR 13.28, 95% CI 10.57-15.99, P<0.001 for disease behaviour), and family history of IBD for only behavioural changes (OR 4.76, 95% CI 1.10-20.50, P=0.03) but not for distribution changes (OR=1.9, 95% CI 0.49-7.25, P=0.35). Gender was not predictive of any changes in both CD and UC. 36 (54%) participants with CD had CD-related surgery with behavioural changes predicting the need for surgery (OR=10.45, 95% CI 3.15-34.79, P<0.001) but not distribution changes (OR=2.01, 95% CI 0.69-5.89, P=0.20). Seven (18.9%) out of 37 participants with UC had colectomy. Distribution changes did not predict need for surgery (OR=0.21, 95% CI 0.02-1.91, P=0.16). There were no identified predictors of disease progression in UC.

Conclusions: Prolonged disease duration and family history of IBD are predictive of disease progression in children with CD but not in those with UC.
Accuracy of mucosal and fecal microbiota dysbiosis as a predictor of pediatric Crohn disease in Saudi Arabia

Mohammad Elmouzan1, Kirill Korolev2, Rajita Menon2, Ahmed Sarkhy3, Yassin Hamid3, Anjum Saeed3, Mona Al Asmi3, Asaad Assiri3, Harland Winter4

1King Saud University, Pediatrics, Riyadh, Saudi Arabia
2Boston University, Boston, United States
3King Saud University, Riyadh, Saudi Arabia
4Massgeneral Hospital for Children, Boston, United States

Objectives and study: Studies have revealed differing conclusions on the accuracy of predicting inflammatory bowel disease from stool microbiota. Papa, et al reported that stool samples were predictive with an area under the receiver operating curve (AUC) of 0.83.1 By contrast, the RISK study reported by Gevers, et al found in treatment naïve children that stool microbiota were a poor predictor of Crohn disease (CD) with an AUC of 0.66.2 However, Reanalysis of the RISK cohort using log-abundances increased the mean AUC to a more meaningful clinical value of 0.72.3

Objective: To compare mucosal and fecal dysbiosis in a cohort of newly-diagnosed children with Crohn disease from the Kingdom of Saudi Arabia.

Methods: Samples of mucosal biopsies and stool from 16 children with confirmed CD along with 18 children without inflammation were prospectively enrolled. At diagnosis, CD location were L1 (4 patients) and L3 (12 patients) while CD behavior was B1 in 13 and B2 in 3 patients. A total of 78 samples (51 from CD and 24 from non-IBD controls) were obtained. DNA extraction and sequencing were performed in the USA (MRDNA laboratories, Shallowater, Texas). Microbial community structure was determined using 454 pyrosequencing of bar-coded 16S rRNA genes. Sparse logistic regression was used to predict Crohn disease status based on subject’s microbiota. The accuracy of the classifier was tested by computing the ROC curve with 5-fold stratified cross validation under 100 permutations of the training data partition.

Results: All children are Saudi nationals. The mean (range) age was 13.9 (6.7-17.8) years for CD children and 13.9 (3.25-18.6) years for controls. Gender distribution indicated that 10/16 (63%) of the CD and 12/18 (67%) of the control subjects were boys. The mean area under the ROC curve for the bacterial dysbiosis classifier was significantly higher in fecal (AUC= 0.97± 0.029) than mucosal samples (AUC= 0.83 ± 0.055) (p = 1.19 ×10^{-21}). This finding is consistent with the Papa et al study1 indicating similar microbial alteration in stool and tissue, but in contrast with the results of larger studies reporting much lower dysbiosis in stool than mucosal samples.2,3

Conclusion: In this cohort of treatment naïve children, dysbiosis in the stool at the time of initial diagnosis was an excellent predictor of CD. In addition to very high accuracy, the non-invasive nature of stool sampling indicates that fecal dysbiosis is a better screening tool for CD in children.

References:
Low predictive value of histopathological scoring system for complications development in children with Crohn's disease

Ondrej Fabian¹, Ondrej Hradsky², Kristyna Potuznikova², Alena Kalfusova¹, Lenka Krskova¹, Ludmila Hornofova¹, Josef Zamecnik¹, Jiri Bronsky²

¹Motol University Hospital, Department of Pathology and Molecular Medicine, Prague, Czech Republic
²University Hospital Motol, Paediatrics, Prague, Czech Republic

Objectives and study: In pediatric Crohn's disease (CD), the benefit of microscopy in disease activity assessment and prediction of clinical outcome is, due to the focality and transmurality of the inflammation, disputable. We investigated whether histopathological scoring system predicts complications in pediatric CD and correlates with endoscopical and clinical scores.

Methods: We performed a retrospective study on 63 patients. Endoscopy in the time of diagnosis was evaluated using the Simple Endoscopic Score (SES) and histopathology with the Global Histology Activity Score, both in its original version (GHAS) and its modification (modGHAS). Pediatric Crohn's Disease Activity Index (PCDAI) was also calculated. The patients were grouped according to the presence or absence of defined complications (intraabdominal abscess or fistula, perianal fistulating disease or stricture impenetrable for endoscope or with prestenotic dilatation) during one year of follow-up, or the necessity to initiate anti-TNF treatment for persisting or relapsing active disease in the same time period. Associations were tested with Cox regression analysis.

Results: SES was higher in patients with complications. However, in case of GHAS, modGHAS and PCDAI we did not find any significant association with complicated course of disease. SES above 16 points was revealed as an independent risk factor for complications development in PCD, in contrary to GHAS, modGHAS and PCDAI. We demonstrated only a weak correlation between GHAS, modGHAS and SES and no correlation between the histopathological scoring systems and PCDAI.

Conclusion: In conclusion, the histopathological scoring system cannot be recommended as a reliable predictor of development of complications in children with CD.
Fermentation capacity of gut microbiota in patients with inflammatory bowel disease compared to healthy controls

Mhairi McGowan¹, Margarita Kokkorou², Martina Rebull ², Yunqi Koh¹, Daniel Gaya³, Richard Hansen⁴, Richard Russell⁴, Konstantinos Gerasimidis⁵

¹University of Glasgow, Human Nutrition/School of Medicine, Glasgow, United Kingdom
²University of Glasgow, Human Nutrition, Glasgow, United Kingdom
³Department of Gastroenterology, Glasgow Royal Infirmary, Glasgow, United Kingdom
⁴Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
⁵University of Glasgow, Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, Glasgow Royal Infirmary, Glasgow, United Kingdom

Objectives and study: Gut microbiota in the colon ferment undigested dietary fibre to produce short-chain fatty acids (SCFA). SCFA have beneficial effects on colonic health. Differences in microbiota composition and metabolic activity have been described between IBD patients and healthy controls. This study explored the capacity of the gut microbiota of IBD patients to breakdown dietary fibre.

Methods: Fresh faecal samples were collected from IBD patients in clinical remission and healthy controls (HC). In vitro batch culture fermentations were carried out for 5 carbohydrate/fibres and for a mixture of these 5 fibres together (hi maize, pectin, raftilose, wheat bran, cellulose). Aliquots were taken at 0 and after 48 hours of fermentation. Faecal SCFA (butyrate, propionate and acetate) concentration (umol/g) and their proportional ratio (%) were measured with Gas Chromatography.

Results: 39 IBD participants and 19 matched HC were recruited. Following 48h batch cultures, total SCFA from hi maize and raftilose in CD patients and from hi maize in UC patients were significantly lower than in healthy controls (p=0.041, p=0.003 and p=0.003 respectively) and for other fibre substrates tested: [Propionate, umol/g, CD vs HC; wheat bran: 9.99 vs 7.77, p=0.042; raftilose: 14.4 vs 11.23, p=0.005]; [% Propionate, CD vs HC; raftilose: 9.84 vs 20.4, p=0.016]. UC patients also produced lower amounts of butyrate from mixed fibres and of acetate from hi maize fermentation compared to HC (p=0.042 and p=0.045 respectively). No significant differences were observed for acetate and butyrate concentration or the production profile (% proportional ratio) or SCFA.

Conclusion: These data suggest that the microbiota of IBD patients has a lower capacity to break down fibre, compared to healthy people. The findings of this work should be complemented with changes in microbiota composition using next generation sequencing.
Comparsion of two faecal calprotectin assays in monitoring children with inflammatory bowel disease

Monika Meglicka¹, Maria Goliszek¹, Michal Szczepanski², Maciej Dadalski³, Joanna Bierla¹, Bozena Cukrowska¹, Jaroslaw Kierkus³

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
²Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
³The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland

Objectives and study: Faecal calprotectin (FC) is a good marker in monitoring mucosal healing in adults and children with inflammatory bowel disease (IBD). Its concentrations in faeces is closely related to state of mucosa observed in endoscopy. Due to increasing need in rapid, cheap testing for FC, especially in children, new point-of-care tests (POCT) are being developed. The aim of the study was to compare rapid immunochromatographic test (POCT) with standard enzyme-linked immunooassay (ELISA).

Methods: 20 paediatric patients with IBD (Crohn's disease [CD] 10, ulcerative colitis [UC] 10) were involved in the study and had elective colonoscopy performed. Each patient had FC level measured within a week before endoscopy by two assay (ELISA and POCT). Mucosa status during endoscopy was assessed with Baron score for UC and simple endoscopic score for CD (SES-CD). Full mucosal healing was defined as Baron score or SES-CD of 0. Results of FC were correlated with each other and with endoscopic findings by Spearman's rank correlation coefficient. We have identified two subgroups: those with full mucosal healing, and patients with inflamed gut mucosa. The receiver operating characteristic curves (ROC) were used as a statistical method to establish cut-off points. The area under the curve (AUC) assesses the differentiation quality of the study groups. The Deming regression was used to determine systematic differences between two measurement methods.

Results: Although both FC methods correlated significantly with r=0,66, slope and intercept differed extensively, with up to 3-fold quantitative differences between assays (y=2,8x-432). The AUC for the ELISA and POCT was 0,89 and 0,82 respectively. The selected cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation present was 686 µg/g with sensitivity 0,75 and specificity 0,88 for ELISA and 260 µg/g with sensitivity 0,83 and specificity 0,88 for POCT. The ELISA method had stronger, clinically significant correlation with presence of inflammation then POCT with r=0,66 and r=0,55 respectively.

Conclusion: FC is a good marker of mucosal healing in monitoring of children with IBD. Both the POCT and ELISA method showed comparable clinical performance in finding inflammation lesions. However the cut of points for detection of inflammation differed extensively between methods. Further efforts are needed to standardize those two assays.
Evaluation of Candida colonization of the gastrointestinal tract in children with inflammatory bowel disease

Katarína Gombošová¹, Emeše Majorová¹, Ingrid Schusterová¹, Peter Kolarčík², Iveta Fandáková³, Stella Majlingová¹, Miroslava Petrášová¹, Blanka Tarcalová¹

¹Children’s Faculty Hospital, Department of Paediatrics and Adolescent Medicine, Košice, Slovakia
²Faculty of Medicine, P.J.Šafárik University, Department of Health Psychology, Košice, Slovakia
³Synlab Ltd., Košice, Slovakia

Objectives and study: Candida organisms commonly colonize the human gastrointestinal tract as a component of the resident microbiota. Recent studies, however, show that a high level Candida colonization is associated with several diseases of the gastrointestinal tract. The aim of our study was evaluation of the occurrence of this yeast in a biopsy specimen obtained during routinely performed colonoscopy in children with inflammatory bowel disease at time of diagnosis in comparison with a control group of children.

Methods: In cohort of 38 children with IBD 23 (60.5%) children with Crohn’s disease and 15 (39.5%) with colitis ulcerosa), (mean age=15.0, SD=3.33) and in the control group of children (mean age=11.1, SD=5.30) we performed colonoscopy at time of diagnosis. According to ECCO guidelines the endoscopy of upper part of the GI tract was performed in some children, as well. We received multiple biopsy specimens for histologic and microscopic examination as well as for cultivation. As a transport medium 10% glucose solution was used. Sabouraud agar was used for cultivation and the biopsy specimen was investigated microscopically at the same time. A prolonged cultivation was performed and the result was evaluated after 10 days. The laser spectrophotometer (Malditof, Drucker Ltd. Germany) was used for identification of toy. We tested differences in the prevalence between the IBD and the control groups using the chi² test.

Results: Because of the small numbers of the patients we did not find statistically significant differences in the prevalence of our indicators. But there were several differences close to the statistical significance threshold. The IBD patients had higher prevalence (60.5% vs. 39.5%) of the overall positivity of Candida compared to the control group (chi²=3.37, p=0.066) and a higher volume of Candida in faeces (65.5% vs. 45.7%) (chi²=2.51, p=0.113).

Conclusion: Our study showed higher prevalence of Candida albicans in cultivation of the specimen of the children with IBD compared with the control group. Another interesting finding is a higher volume of candida in stool specimens of the IBD patients. Further research should use a higher number of patients and thus increase the statistical power of the study design to confirm the presence or absence of differences in the Candida positivity between the IBD patients and the control group.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-262

Effectivity of polymeric exclusive enteral nutrition of varied composition in paediatric patients with Crohn’s disease - a single center experience

Lucie Gonsorcikova1, Kristýna Zárubová1, Ondrej Hradsky1, Kristyna Potuznikova1, Ivana Copova1, Jiri Bronsky2

1University Hospital Motol, Paediatrics, Prague, Czech Republic
2Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic

Objectives and study: Exclusive enteral nutrition (EEN) has been shown to be effective in induction of remission in pediatric Crohn’s disease (CD) patients. Published studies are focused on evaluation of single enteral formula without giving the patients the possibility to choose between different tastes and composition. The aim of our study is to evaluate the efficiency and compliance in our CD patients given the possibility to choose between various types of EEN.

Methods: We retrospectively analyzed clinical and laboratory data of the CD patients (N=56, mean age 13y, range 4-17.5y, 32 males) from our department treated with EEN during the period (2011-2015). All children were given the opportunity to choose one or combination of various enteral formulas at the time of diagnosis. Median duration of induction therapy was 6 weeks (IQR 6-7 weeks) and concomitant azathioprine was given in all the patients since diagnosis. We analyzed clinical and laboratory response and remission (according to PCDAI and CRP), compliance (need for nasogastric (NG) tube) in our patients and looked for factors associated with response and remission rates.

Results: Mean PCDAI dropped down from 21 points before therapy to 7 after therapy (p<0.0001) and mean CRP dropped from 32 to 10 mg/L (p=0.0005). Sixty % of patients achieved clinical remission defined as PCDAI < 10 and 57 % of patients achieved laboratory remission defined as CRP < 5 mg/L at the end of induction therapy. Clinical response (PCDAI < 10 or drop of PCDAI at least of 12.5 points) was achieved in 77 % of patients and laboratory response (CRP < 5 mg/L or drop of at least 20 mg/L) was achieved in 76 % of patients. Twelve % of patients required NG tube since beginning of the therapy and 9 % had to switch from p.o. treatment to NG tube during the therapy. There was no difference in remission or response rate between patients receiving nutrition perorally or via NG tube. Fifty-five percent of patients have chosen EEN of multiple tastes, 45 % have chosen monocomponent nutrition. There was no difference in remission or response between these two groups. Neither disease localization nor behaviour according to Paris classification was associated with laboratory response or remission.

Conclusion: In our group of patients, free choice of polymeric enteral formula of various tastes and compositions led to remission and response rates comparable to published data on monocomponent feeds. Using NG tube, choice of multicomponent feeds and disease phenotype was not associated with remission and response rates. The study was supported by research grants VZ FNM 64203/6001, GAUK No. 136215 and No. 246216.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-263

Predictors of poor outcome in pediatric ulcerative colitis - evaluation, initial and follow-up data from CEDATA-GPGE-Registry

Raphael Benjamin Gross1, Claudia Wendt2, Tanja Weidenhausen1, Klaus-Peter Zimmer3, Jan de Laffolie1, Yenny Kho1, CEDATA-GPGE study group1

1University Giessen, General Pediatrics and Neonatology, Giessen, Germany  
2University of Giessen, Department of General Pediatrics and Neonatology, Giessen, Germany  
3Zentrum für Kinderheilkunde und Jugendmedizin, Universitätsklinikum Gießen und Marburg, General Pediatrics and Neonatology, Gießen, Germany

Objectives and study: Predictors of poor outcome (POPO) criteria in pediatric Crohn’s disease patients received widespread attention in the discussion about alternative therapeutic strategies. We aimed to identify POPO criteria within pediatric ulcerative Colitis (UC) patients from CEDATA-GPGE. Pediatric UC-patients are more likely to get a more aggressive and extensive course of disease, which can have a distinct impact on their overall health and development. Exploratory analysis was performed to identify potentially relevant items in the initial history/exam and diagnostic workup.

Methods: All UC patients within CEDATA GPGE were included if diagnosis was made within the first 18 years of life, follow-up documentation within the first three months after the first documentation and at least 2 follow-up documentations were obtained. We defined poor outcome with the presence of at least one of the following: (1) Need of therapy with azathioprine/6MP or (2) Biologics, (3) severe growth retardation (-2.5 SDS), (4) surgery and (5) inability to reach sustained remission (>1yr). Patients with those were compared to other patients with UC considering PUCAI, family history, extraintestinal manifestation, therapy and its side effects, overall symptoms, Paris-Classification/disease extent and complications.

Results: Since 2004, 390 of CEDATA-GPGE registered 1537 patients with UC were included in this study. An α<0.05 was applied. Initial PUCAI > 60 increased risk for azathioprine therapy significantly (p=0.0214, OR 2.5562[1.08-6.72]), as well as the presence of drug side effects (p=0.0014, OR 3.4531[1.51-8.87]). A positive family history increased the risk for biologics therapy significantly (p=0.032, OR 3.3021 [0.82-11.86].

Conclusion: Addressing therapeutic stratification in pediatric IBD, real-world data gain importance in evaluating and modifying therapy strategy. However, such analysis suffer from limitations towards factors influencing therapy decision. Therefore, further prospective stratification studies are necessary.
**GASTROENTEROLOGY: Inflammatory bowel disease**

G-P-265

**Association of R202Q MEFV variant and inflammatory bowel disease**

Ersin Gumus1, Aysel Yuce1, Asuman Nur Karhan1, Hulya Demir1, Inci Nur Saltik Temizel1, Hasan Ozen1

1Faculty of Medicine, Hacettepe University, Pediatric Gastroenterology, Hepatology, and Nutrition, Ankara, Turkey

**Objectives and study:** Crohn’s disease (CD) and Familial Mediterranean Fever (FMF) are systemic inflammatory diseases with uncontrolled inflammatory response. Chronic relapsing behaviour, infiltration by neutrophils at the site of injury, and abnormal regulation of apoptosis are reported to be common clinical and biologic features in FMF and inflammatory bowel disease (IBD). MEFV gene mutations have been evaluated as a potential disease modifier or susceptibility factor for IBD. There is evidence linking R202Q variant of MEFV gene with inflammatory disorders like CD and systemic onset juvenile idiopathic arthritis in adults. The aim of this study is to present two cases of paediatric CD that carry R202Q variant of MEFV gene and responded to colchicine therapy dramatically.

**Methods:** This is a case report of an unusual association between R202Q variant of MEFV gene and paediatric CD, emphasizing successful treatment with colchicine in this setting.

**Results:** The first patient was a 13-year-old girl who presented with recurrent episodes of abdominal pain, nausea, and vomiting. Her physical examination was normal. Initial laboratory and imaging studies revealed elevated acute phase reactants and fecal calprotectin levels, and diffuse thickening of the terminal ileal wall. Genetic analysis of MEFV gene for the most frequently found mutations in Turkey was unremarkable. She had a history of an appendectomy and histopathologic evaluation of the specimen revealed granulomatous lymphadenitis. After exclusion of common causes of granulomatous inflammation, upper and lower endoscopies were performed. Polypoid lesions and ulcers at the ileocecal region were detected. Histopathology revealed severe ileitis and colitis, highly suggestive for IBD. However, patient did not respond well clinically and histologically to conventional medical management for CD. Extended genetic examination of MEFV gene then revealed homozygosity for R202Q polymorphism. Good control of the episodes was achieved by colchicine treatment. Repeated colonoscopies revealed complete recovery of ileocecal lesions with normal histopathologic findings.

The second patient was an 8-year-old boy who presented with an anal abscess. He was complaining about loss of appetite and unintentional weight loss. Immunological evaluation of the patient was not suggestive for an underlying immune deficiency. In addition to elevated acute phase reactants and fecal calprotectin levels, abdominal ultrasonography revealed diffuse thickening of the distal ileal wall. Patient underwent upper and lower gastrointestinal endoscopies to rule out IBD. Colonoscopy revealed numerous superficial ulcers in the terminal ileum indicating CD. Initial genetic analysis of MEFV gene was unremarkable. Despite the immunosuppressive treatment given with the diagnosis of CD, acute phase reactants remained elevated. After a control colonoscopy which revealed persistence of ileal ulcers, heterozygosity for R202Q polymorphism was detected on extended genetic investigation of MEFV gene. Acute phase reactants turned to normal levels and abscess was healed with colchicine treatment, indicating good control of the systemic inflammation.

**Conclusion:** MEFV gene R202Q polymorphism may be associated with CD with a good response to colchicine therapy. R202Q polymorphism should be included in routine molecular diagnosis of FMF patients and regarded in the evaluation of intractable CD presenting with symptoms consistent with FMF.
Speckle tracking stress echocardiography uncovers early myocardial dysfunction in pediatric patients with inflammatory bowel diseases

Kai Hensel¹, Francisca Abellan-Schneyder², Lucia Wilke², Andreas Jenke³, Stefan Wirth²

¹Witten/Herdecke University - Helios Medical Center, Pediatrics - Center for Clinical and Translational Research, Wuppertal, Germany
²Witten/Herdecke University, Wuppertal, Germany
³Eko, Oberhausen, Germany

Objectives and study: Inflammatory bowel disease (IBD) is an established risk factor for cardiovascular disease (CVD). In adult study populations, both Crohn’s disease (CD) and ulcerative colitis (UC) have been associated with atherosclerosis and subclinical cardiac impairment. However, whether cardiac consequences present early in the course of IBD is currently unknown. This is the first study in children utilizing speckle tracking stress echocardiography (STE) to unmask altered myocardial mechanics in pediatric CD and UC.

Methods: 50 consecutive normotensive children with IBD (18 with acute inflammation, mean age 14.6 ± 2.5 years, mean disease duration 2.6 ± 2.6 years and 32 in remission, mean age 14.3 ± 2.3 years, mean disease duration 3.0 ± 3.4 years) and 60 age- and gender-matched healthy controls were examined using conventional and STE (strain and strain rate) during bicycle ergometer stress testing.

Results: Children with IBD had significantly reduced circumferential strain rate (SR) (-1.55±0.26 s⁻¹) when compared to healthy controls (1.80±0.40 s⁻¹) both at rest (p=0.002) and during stress testing (p=0.0216). Similarly, also longitudinal strain rate (p=0.0284) and circumferential and longitudinal strain was depressed in patients with IBD both at rest and during exercise (p=0.033). Interestingly, there was no significant difference in left ventricular myocardial strain between IBD patients in acute inflammation and remission (p=0.1331).

Conclusion: Pediatric patients with IBD show evidence of subclinical myocardial impairment early in the course of both CD and UC. Longitudinal studies are needed to correlate these subtle findings with clinical outcome parameters. Patients with IBD should be regularly screened for signs of CVD.
Head-to-head comparison of fecal calprotectin and calgranulin C to screen children with chronic abdominal complaints for endoscopy

Anke Heida1, Els Van De Vijver2, Stephanie Vanbiervliet3, Anneke Muller Kobold4, International CACATU Consortium5, Patrick van Rheenen1

1University Medical Center Groningen, Pediatric Gastroenterology, Groningen, Netherlands
2Antwerp University Hospital, Paediatric Gastroenterology, Antwerp, Belgium
3Ghent University Hospital, Paediatric Gastroenterology and Hepatology, Ghent, Belgium
4University Medical Center Groningen, Department of Laboratory Medicine, Groningen, Netherlands
5University Medical Center Groningen, Paediatrics, Groningen, Netherlands

Objectives and study: It has become common practice for many paediatricians to refer a child with chronic abdominal complaints for endoscopy when fecal calprotectin is over 50 ug/g. With this strategy the diagnosis inflammatory bowel disease (IBD) is rarely missed. The downside is that a considerable number of children are wrongly subjected to endoscopy. Calgranulin C is a relatively unknown fecal marker of inflammation and is potentially more specific for IBD than calprotectin. We compared the diagnostic accuracy of calprotectin and calgranulin C to see which of the two markers best predicted IBD in a large group of children and teenagers with chronic abdominal complaints.

Methods: We performed a multicenter prospective study in 19 paediatric clinics in the Netherlands and Belgium. Eligible participants were aged between 6 and 18 years, and had never undergone endoscopy in the past. They sent their stool sample to one coordinating laboratory for immediate calprotectin measurement (ELISA, BÜHLMANN Laboratories). The residual of the stool specimen was stored at -80°C for calgranulin C measurement at a later stage (INFLAMARK ELISA, CisBio Bioassays). Patients with a high risk of IBD were selected for upper and lower endoscopy (i.e. reference test), while those with a low risk were followed for 6 months for appearance of possible additional symptoms suggestive for IBD (i.e. “delayed type” reference test). We evaluated test characteristics for predefined and ideal cut-off points. Differences in specificity were tested for significance with McNemar.

Results: A total of 354 patients sent in a stool sample. At the time of writing, we have a final diagnosis in 260 of them. Forty-eight percent underwent diagnostic endoscopy, and 52% completed a 6 months follow-up. 87 patients were diagnosed with IBD. When using predefined cut-off points (calprotectin 50 ug/g and calgranulin C 0.75 ug/g), sensitivity, specificity, positive predictive value and negative predictive value were respectively 100%, 57%, 54%, 100% for calprotectin and 84%, 96%, 91%, 92% for calgranulin C. Specificity of calgranulin C was significantly higher (P<0.001). When ideal cut-off points extracted from a ROC curve, were used (calprotectin 300 ug/g and calgranulin C 0.25 ug/g), we found sensitivity, specificity, positive predictive value and negative predictive value of respectively 96%, 92%, 86%, 98% for calprotectin and 91%, 95%, 91%, 95% for calgranulin C. The specificity between markers was not statistically different anymore (P=0.19).

Conclusion: In this interim analysis we found that the calgranulin C stool test performs better than calprotectin to predict IBD, provided the use of commonly used cut-off points. Both markers perform equally well when optimal cut-off points are used.

Disclosure of interest: This study was supported by a grant from CisBio Bioassays (producer of Inflamark®). CisBio did not have a role in the design, execution, analyses, and interpretation of the data, or in the decision to submit the results.
Vitamin B12 deficiency is common in children with ulcerative colitis as well as Crohn’s disease

Samantha Ibbs¹, Rafeeq Muhammed¹

¹Birmingham Children's Hospital, Department of Gastroenterology, Birmingham, United Kingdom

Objectives and study: Crohn’s disease is a risk factor for vitamin B12 deficiency due to frequent involvement of terminal ileum. The aim is to assess the prevalence of vitamin B12 deficiency in children with Crohn's disease (CD) and Ulcerative Colitis (UC).

Methods: We performed a single-centre service evaluation of 157 patients with CD and compared them with 88 patients with UC. In patients with CD, ileal inflammation on endoscopy and MRE were recorded.

Results: Prevalence of B12 deficiency in patients with CD was 31% compared with 32% in ulcerative colitis. 6/55 (11%) patients with CD had vitamin B12 deficiency at the time of diagnosis or within 3 months of diagnosis. 20/66 (30%) had low vitamin B12 levels at 1 year of follow up. Ileal inflammation seen in endoscopy or MRI was a risk factor in the development of B12 deficiency.

5/27 (19%) patients with UC had low vitamin B12 levels at the time of diagnosis or within 3 months of diagnosis. 28/88 (32%) had low vitamin B12. 8/38 (21%) had low vitamin B12 level at 1 year of follow up.

Conclusion: Vitamin B12 deficiency is common not only in patients with Crohn's disease but also in children with ulcerative colitis. Further studies are needed to look for the reasons behind vitamin B12 deficiency in children with ulcerative colitis.
**GASTROENTEROLOGY: Inflammatory bowel disease**

G-P-269

**Functional bowel symptoms in children with quiescent IBD: role of low-grade inflammation**

Sara Isoldi¹, Saverio Mallardo¹, Salvatore Oliva¹, Franca Viola¹, Anna Dilillo¹, Marina Aloï, Giulia Biscione¹, Alessandra Lacopo², Paolo Rossi¹, Salvatore Cucchiara¹

¹Sapienza University of Rome, Italy, Pediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
²Sapienza University of Rome, Italy, Pediatrics and Childhood Neuropsichiatry, Rome, Italy

**Objectives and study:** IBS-like symptoms are common in IBD patients (pts) in apparent remission, but their real significance is still unclear. We aimed at evaluating: 1) prevalence of IBS symptoms in pediatric pts with quiescent Crohn's disease (CD) and ulcerative colitis (UC); 2) quality of life (QOL) and anxiety levels in IBD pts with and without IBS symptoms; 3) correlation between the presence and severity of IBS symptoms and extent of IBD; 4) correlation between the presence and the severity of IBS symptoms and occult inflammation assessed by fecal calprotectin (FC) levels.

**Methods:** From January 2014 to May 2016, children with quiescent CD and UC admitted to our Unit were consecutive enrolled. Remission was defined as: macroscopic normal mucosa on upper and lower GI endoscopy, including terminal ileoscopy; CRP <6 mg/L; ESR <20 mm/h; white cell count <11x10⁹/L; platelets <450x10¹²/L; no use of corticosteroids over the last 12 months; PCDAI/PUCAI <10. All CD pts underwent abdominal and pelvic MRI: those having features of active disease were excluded. IBS symptoms were defined according to ROME III criteria for IBS. Symptoms severity and QOL were evaluated using Functional Bowel Disorder Severity Index (FBDSI), Pediatric quality of life inventory (PedsQL) and the State trait Anxiety inventory for children (STAIC). Stool samples were collected from all pts for FC assay. To provide FC reference ranges for controls and IBS subjects, two further groups matched on age and sex were included.

**Results:** A total of 190 children were enrolled: 58 CD pts, 36 UC pts, 56 IBS pts and 40 healthy controls. No significant differences were found between groups for age and gender. IBS symptoms were present in 26 CD pts (44.8%), and 18 UC pts (50%), but their presence and severity did not correlate with the duration nor with the extent of IBD. PedsQL scores were lower and STAIC scores higher in IBD pts with IBS symptoms. FC levels were significantly higher in CD pts with IBS symptoms (287±23.3 mg/kg) compared to those without (58.23±15.1 mg/kg) (p=0.001). Similarly, higher levels of FC were found in UC pts with IBS symptoms (302±28.5 mg/kg) (p=0.001) compared to those without (45±18.5 mg/kg). However, symptoms severity did not strictly correlate with FC levels. IBD pts with IBS symptoms showed grater FC levels than healthy controls and IBS subjects (59±27 mg/kg and 38±24 mg/kg) (p<0.001). Besides, there was no significant difference in FC levels between asymptomatic IBD patients, healthy controls and IBS.

**Conclusion:** IBS symptoms are not uncommonly reported among pediatric pts with IBD with documented full remission, and seem to be independent from duration and extent of disease. Our data suggest that a persisting low-grade inflammation may be the underlying mechanism of IBS symptoms in apparently quiescent IBD.
Wireless capsule endoscopy complements magnetic resonance enterography and endoscopy in the evaluation of suspected small bowel Crohn’s disease in pediatric patients

David Prichard1, Zachary Hamilton2, Tom Savage3, Matthew Smyth2, Carlie Penner2, Alam Lakhani2, Matthew Carroll4, Ahmed Sarkhy5, Daniel Lemberg6, Rob Enns2, Robert Prosser8, Douglas Jamieson9, Kevan Jacobson10

1St Paul’s Hospital, Gastroenterology, Vancouver, Canada
2British Columbia Children’s Hospital and University of British Columbia, Pediatric Gastroenterology, Vancouver, Canada
3Royal Hospital for Children, Radiology, Glasgow, United Kingdom
4University of Alberta, Pediatric Gastroenterology, Edmonton, Canada
5King Saud University, Riyadh, Saudi Arabia
6Sydney Children’s Hospital and University of New South Wales, Gastroenterology, Sydney, Australia
7St Paul’s Hospital and University of British Columbia, Gastroenterology, Vancouver, Canada
8University of British Colombia, Vancouver, Canada
9British Columbia Children’s Hospital and University of British Columbia, Radiology, Vancouver, Canada
10Bc Children’s Hospital, Pediatric Gastroenterology, Vancouver, Canada

Objectives and study: Limited data exists regarding the relative ability of wireless capsule endoscopy (WCE) and magnetic resonance enterography (MRE) to identify mucosal inflammation in the small bowel (SB) of children with suspected Crohn’s Disease (CD). This study compares the ability of these modalities to identify SB inflammation in this cohort. In the terminal ileum (TI), these modalities are compared to the reference standard ileo-colonoscopy.

Methods: Participants were prospectively recruited between 09/2010 and 12/2014. Inclusion criteria: children age 10-17 years requiring ileo-colonoscopy for evaluation of suspected CD. Exclusion criteria: ulcerative or infectious colitis, contraindications to MRE (including metal foreign body, severe renal insufficiency, contrast allergy or claustrophobia) or suspected high grade SB stricture. Subsequent to endoscopy, participants underwent MRE and WCE. Inflammation identified during ileocolonoscopy and WCE was scored using the Simple Endoscopic Score – Crohn’s Disease (SES-CD) and the Lewis score respectively. Scores ≥1 and ≥135 respectively were considered active disease. For MRE, active inflammation in three defined SB segments (jejunum, proximal and distal ileum) was determined by the presence or absence of the following 5 variables: bowel wall thickening, bowel wall enhancement, fibro-fatty proliferation, hyperaemia/vascular engorgement and proximal dilation. Each finding was given a score of 1 and a score of ≥2 in any segment was considered active disease. Comparative analyses were performed using Cohen’s kappa coefficient (κ), Spearman rank correlation (ρ) and bootstrap resampling techniques.

Results: Of 35 recruited patients 23 completed the study protocol. Failure to complete the protocol was because of failure to swallow the capsule (n=7), failure to intubate the TI (n=3) or incomplete capsule studies (n=2). WCE and MRE were equally sensitive in identifying SB inflammation (17/23 [74%] vs. 15/23 [65%], P=NS). However, WCE detected more extensive SB disease relative to MRE with active disease throughout the SB in 13 [57%] vs. 1 [4%] patients. Within the TI, WCE identified numerically more patients with active mucosal inflammation than MRE or endoscopy (15 [65%] vs. 12 [52%] vs. 11 [48%] respectively, Figure). Bootstrapping methodology demonstrated that WCE is at least as sensitive as MRE or ileo-colonoscopy (both P=0.05) in identifying TI inflammation. The presence of ulcers on WCE correlated with bowel wall thickening and bowel wall enhancement on MRE (both κ=0.64, P=0.002) but not with fibro-fatty proliferation, hyperaemia/vascular engorgement and proximal dilation.
**Table:**

Terminal ileal inflammation as identified by ileo-colonoscopy, magnetic resonance enterography (MRE) and wireless capsule endoscopy (WCE) in 23 pediatric patients with suspected Crohn’s disease.

<table>
<thead>
<tr>
<th>No WCE Activity</th>
<th>Yes WCE Activity</th>
<th>No MRE Activity</th>
<th>Yes MRE Activity</th>
<th>Endoscopic Activity</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(7)</td>
<td>(1)</td>
<td>(4)</td>
<td>(1)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(8)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** WCE is as sensitive as MRE or endoscopy for identifying active SB mucosal inflammation. However, the distribution of SB CD is more extensive when evaluated by WCE than by MRE. In the absence of concern regarding stricturing or extra-luminal disease WCE can be considered for the evaluation of suspected SB CD.
Inflammatory bowel disease in children and adolescents with type 1 diabetes: analysis from the DPV database

Hildegard Jasser-Nitsche¹, Susanne Bechtold-Dalla Pozza², Elisabeth Binder³, Bettina Heidtmann⁴, Young Hee Lee-Barkey⁵, Klemens Raile⁶, Reinhard Holl⁷

¹Medical University of Graz, Graz, Austria
²Dr. von Haunersche Kinderklinik, Munich, Germany
³Univ.Klinik für Kinder- und Jugendheilkunde, Innsbruck, Austria
⁴Kkh Wilhelmstift, Hamburg, Germany
⁵Hdz Nrw, Bad Oeynhausen, Germany
⁶Klinik für Pädiatrische M.S. Diabetes, Endokrinologie, Stoffwechsel und Gastroenterologie, Berlin, Germany
⁷Institute for Epidemiology and Zibmt, Ulm, Germany

Objectives and study: While there is a clear correlation between type 1 diabetes (T1D) and certain autoimmune diseases such as celiac disease and thyroiditis, data on associations between T1D and inflammatory bowel disease (IBD) are lacking. Therefore, we investigated associations and clinical characteristics of T1D and inflammatory bowel disease (IBD). Are there any differences regarding metabolic control in patients suffering from both diseases?

Methods: Data of 65,147 patients with T1D below the age of 18 years (mean age 14 ± 3.86 years, mean diabetes duration 5.41 ± 4.2 years) of 379 centers in Germany and Austria participating in the DPV initiative (Prospective Diabetes Follow-up) were analyzed. We used multiple regression models to analyze differences in metabolic control, acute complications, insulin dose and steroid intake in patients with T1D and IBD compared to those with T1D only.

Results: In our cohort of 65,147 pediatric patients with T1D, 63 were diagnosed with IBD. Among them, 33 children and adolescents were diagnosed with ulcerative colitis (UC), 26 with Crohn’s disease (CD) and 4 with indeterminate colitis (IC). Mean BMI-SDS in patients with T1D and IBD were lower than in those with T1D only (-0.15 ± 0.12 versus 0.27 ± 0.0, p < 0.01). Patients with T1D and IBD had a significantly higher use of steroids (0.22 ± 0.05 versus 0.01 ± 0.0, p < 0.01) and significantly higher rates of severe hypoglycemia (0.33 ± 0.07 versus 0.16 ± 0.0, p < 0.01). No differences were found in HbA1c levels and insulin dose, neither differences in rates of ketoacidosis.

Conclusion: Although there were no differences in HbA1c levels, the higher frequency of severe hypoglycaemia indicates that a stable metabolic control seems to be more difficult to achieve in patients suffering from both diseases.
Maintenance treatment for ulcerative colitis in Turkey: a single center experience

Funda Ozgenc1, Miray Karakoyun2, Cigdem Omur Ecevit3, Hamiyet Hekimci Ozdemir4, Ezgi Kiran Tasci5, Gulin Erdemir2

1Ege University, Pediatric Gastroenterology, Hepatology and Nutrition, Izmir, Turkey
2Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, Izmir, Turkey
3Behçet Uz Children Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Izmir, Turkey
4Ege University Medicine School, Department of Pediatric Hematology, Izmir, Turkey
5Ege University Medicine School, Pediatric Gastroenterology, Hepatology and Nutrition, Izmir, Turkey

Objectives and study: Thiopurines is a widely used mode of treatment for inflammatory bowel diseases, but there is a limited data. Our aim was to determine outcome following thiopurine use in a single center of children diagnosed with ulcerative colitis (UC).

Methods: Forty eight UC patients who diagnosed at Ege University between 2005 and 2016 and received azathiopurine (AZA) were included in the study. Data was collected retrospectively. The diagnosis of UC was based on the conventional clinical, radiological, histological and endoscopic assessment. All UC patients in this intercept were analyzed to determine patient characteristics, characteristics of thiopurine use, effectiveness and toxicity at 4, 6 weeks and by 3 months intervals after the remission were established. Determination of remission, relapse and steroid refractoriness/dependency was guided according to ECCO consensus.

Results: Azathiopurine was started at median 1 months (0-12 months) and it was started thereafter for maintenance (n=43). Response to remission induction was obtained in 40 (93.7%) patients. The median duration of the AZA was 24 months (5-63). In 34 (85%) of the 40 children it was well tolerated until the last visit. During the follow up adverse effects occurred on total six patients. These are leucopenia, neutropenia, vomiting, diarrhea and skin rush.
Table: Baseline patient characteristics (n=48)

<p>| | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (male/female)</td>
<td>15/33</td>
</tr>
<tr>
<td>Mean age (years)</td>
<td>12.4 (+_3.5)</td>
</tr>
<tr>
<td>IBD in family (n, %)</td>
<td>5 (10.4)</td>
</tr>
<tr>
<td>Symptom (n, %)</td>
<td></td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>4 (8.33)</td>
</tr>
<tr>
<td>Diare</td>
<td>4 (8.33)</td>
</tr>
<tr>
<td>Bloody Defecation</td>
<td>23 (47.9)</td>
</tr>
<tr>
<td>All</td>
<td>11 (22.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (12.5)</td>
</tr>
<tr>
<td>Location (n, %)</td>
<td></td>
</tr>
<tr>
<td>Left colon</td>
<td>5 (10.4)</td>
</tr>
<tr>
<td>Pancolitis</td>
<td>35 (72.9)</td>
</tr>
<tr>
<td>Unknown</td>
<td>6 (12.5)</td>
</tr>
<tr>
<td>Term ileum</td>
<td>2 (4.1)</td>
</tr>
<tr>
<td>Remission induction treatment (n, %)</td>
<td></td>
</tr>
<tr>
<td>Systemic steroid+5-ASA</td>
<td>36 (75)</td>
</tr>
<tr>
<td>5-ASA</td>
<td>2 (4.2)</td>
</tr>
<tr>
<td>Systemic steroid</td>
<td>10 (20.8)</td>
</tr>
<tr>
<td>Response to induction treatment (n %)</td>
<td></td>
</tr>
<tr>
<td>Full Response</td>
<td>33 (68.8)</td>
</tr>
<tr>
<td>Partial Response</td>
<td>7 (14.6)</td>
</tr>
<tr>
<td>No Response</td>
<td>8 (16.6)</td>
</tr>
</tbody>
</table>

Conclusion: Thiopurine is useful for maintaining remission and promoting mucosal healing in UC patients. The identification of UC patients in whom clinical remission can be maintained with thiopurine and occurred adverse effects are highly important for long-term follow-up.
Primary immunodeficiencies presenting as very early onset inflammatory bowel disease - the experience of Children's Memorial Health Institute in Warsaw

Maja Klaudel-Dreszler¹, Daniel Kotlarz², Michal Szczepanski¹, Patryk Lipiński³, Aleksandra Marach³, Piotr Socha³

¹Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
²Dr von Hauner Children’s Hospital, Ludwig Maximilian University, Department of Paediatrics, Munich, Germany
³Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland

Objectives and study: Diagnostic and therapeutic management of children with very early onset inflammatory bowel disease (VEO-IBD) remains a challenge as some patients are afflicted with monogenic defects causing primary immunodeficiency (PID). Chronic diarrhea, bloody stools, failure to thrive are common for both classic IBD and PID. The aim of the study was to identify the features suggesting PID in patients with VEO-IBD.

Methods: A retrospective analysis of medical records of 22 children suspected of VEO-IBD was performed. We present 11 girls and 11 boys, aged 1-50 months (median 14 mo) at onset of symptoms. The follow-up period lasted from 6 months-10 years. We analysed clinical symptoms, spectrum of infections, immunologic and haematologic aberrations, endoscopic and histologic findings, implemented treatment.

Results: Due to the suspected PID, molecular diagnostics was performed in 14 patients; WES in 12. The diagnosis of monogenic disease has been established in 6 children: IL10R deficiency, chronic granulomatous disease (CGD), combined immunodeficiency (CID) due to LRBA mutation, Wiskott-Aldrich syndrome (WAS), familial Mediterranean fever (FMF), tricho-hepato-enteric syndrome. All patients presented with chronic diarrhea, abdominal pain and growth failure, 15 had bloody stools, 2 with PID had perianal disease, 4 (2 with PID) developed mouth ulcers, 5 atopic dermatitis, 2 (1 with CID) pyoderma gangrenosum, the girl with IL10R deficiency had persistent folliculitis; 3 (2 with PID) developed splenomegaly. Children with PID developed recurrent and/or severe infections: 4 had sepsis, 5 pneumonia; a boy with CGD had recurrent thrush. Immunological diagnostics revealed absent activity of NADPH-oxidase in a boy with CGD and hypogammaglobulinaemia in 2 girls, one with CID. The girl with IL10R deficiency had normal results of basic immunologic tests. Anaemia was present in 50% of children, thrombocytosis in 36%, leukocytosis in 22%, lymphopenia in 27%; interestingly the boy with WAS had normal platelets. The girl with CID developed chronic autoimmune thrombocytopenia and anaemia. Endoscopic and histologic examination revealed gastritis and/or bulbitis in 68% patients, colitis in 72% with the most severe inflammation in sigmoid and/or rectum. Children with PID did not present with any patognomonic changes except for perianal fistulas and abscesses. The treatment included steroids in 72% of patients, azathioprine in 50%, total or partial parenteral nutrition in 36%, biologics in 27%, 13% required surgery and 3 patients (with CID, CGD, IL10R deficiency) underwent HSCT. One child suspected of a new type of PID died from sepsis.

Conclusion:

1. The coincidence of VEO-IBD and perianal disease, severe or opportunistic infections, skin changes, splenomegaly or autoimmune cytopaenia are highly suggestive of PID.

2. Some children with VEO-IBD caused by PID do not develop abnormalities in basic immunologic tests and can be diagnosed only by molecular methods.
Hepcidin in newly diagnosed inflammatory bowel disease in children

Eva Karaskova

1University Hospital Olomouc, Department of Pediatrics, Olomouc, Czech Republic

Objectives and study: Hepcidin is a central regulatory molecule of systemic iron homeostasis. Its production is also influenced by systemic inflammation. Aims of this study were to compare hepcidin levels in newly diagnosed pediatric patients with Crohn’s disease (CD) and ulcerative colitis (UC) and to find out the association between hepcidin, laboratory and clinical parameters of inflammatory bowel disease (IBD) activity.

Methods: Seventy-six pediatric patients with IBD (53 children with CD and 23 with UC) newly diagnosed in a period from January 2012 till September 2016 were enrolled to this comparative cross-sectional study. We analyzed levels of serum hepcidin, C-reactive protein, iron, ferritin, soluble transferrin receptors, blood count and fecal calprotectin in all subjects. Serum hepcidin levels were measured by reverse-phase liquid chromatography. Pediatric Crohn’s Disease Activity Index (PCDAI) was evaluated in children with CD and Pediatric Ulcerative Colitis Activity Index (PUCAI) was used for evaluation of UC disease activity.

Results: Subjects with CD had significantly higher serum hepcidin levels compared to subjects with UC (22.6 (8.5-65.0) ng/ml versus 6.5 (2.4-25.8) ng/ml, p<0.05). Hepcidin was independently associated with ferritin in all IBD patients (p<0.05). Moreover, there was a significant positive association between hepcidin and platelets number (p<0.05) in children with CD and a negative association between hepcidin and fecal calprotectin (p<0.05) in those with UC.

Conclusion: Different hepcidin levels in newly diagnosed pediatric IBD patients confirm a different contribution of iron deficiency and/or systemic inflammation to anemia and may help with making decision of anti-anemic treatment.
Pediatric inflammatory bowel disease according to Paris classification in Daegu-Kyungpook province in Korea

Jungeun Kim, Sukjin Hong, Kwang Hae Choi, Hyo-Jeong Jang, Seung Man Cho, Juyoung Kim, Byung-Ho CHOE

1Kyungpook National University School of Medicine, Pediatrics, Daegu, Korea, Rep. of South
2Catholic University of Daegu, Pediatrics, Daegu, Korea, Rep. of South
3Yeungnam University College of Medicine, Pediatrics, Daegu, Korea, Rep. of South
4Keimyung University School of Medicine, Pediatrics, Daegu, Korea, Rep. of South
5Dongguk University School of Medicine, Pediatrics, Gyeongju, Korea, Rep. of South
6Seoul National University Bundang Hospital, Pediatrics, Seongnam-Si, Korea, Rep. of South

Objectives and study: Inflammatory disease (IBD) is heterogeneous chronic disease of unknown etiology. Recently, the incidence and prevalence of pediatric IBD is rapidly increasing in Korea. Therefore, we investigated the epidemiologic and phenotypic features of pediatric IBD in Daegu-Kyungpook province in Korea.

Methods: We enrolled 122 children with pediatric IBD who initially diagnosed at the 4 University hospitals in Daegu-Kyungpook province from July 2010 to June 2016. The clinical characteristics at diagnosis were compared according to Paris classification

Results: We enrolled total 122 children, 98 children with Crohn's disease (CD) (80.3%) and 24 with Ulcerative colitis (UC) (19.7%). The average age at diagnosis was 13.6 years, 13.7 years for CD (range 1 - 18 years) and 13.0 years for UC (range 6 - 16 years). There was no significant difference between CD and UC patients in ages at diagnosis. During the study period, there has been the increasing trend in the number of newly diagnosed children as IBD. In CD, There was a significant male predominance (74 boys, 24 girls). The age distribution at diagnosis showed A1a (0~9 years) in 5 (5.1%), A1b (10~17 years) in 88(89.8%), and A2 (above 17 years) in 5 (5.1%). Most of patients were diagnosed above 10 years. The disease activity sites according to the Paris classification were L1 (distal 1/3 ileum ± limited cecal) in 10 (10.2%), L2 (colonic) in 12 (12.3%), and L3 (ileocolonic) in 76 (77.6%), L4 in 16 (16.3%), indicating ileocolonic involvement as major type. The disease behaviors according to the Paris classification were that 87 patients (88.8%) had non-stricturing/ non-penetrating lesion (B1) and 11 patients (11.2%) had stricture or penetrating lesion, including B2 (stricturing) in 7 (7.2%), B3 (penetrating) in 2(2.0%), and B2B3 (both penetrating and stricturing) in 2 (2.0%). Perianal disease was noted in 43 patients (43.9%) and weight loss in 60 (61.2%). The average score of PCDAI at diagnosis was 41.4. In UC, the male to female gender ratio was 1:1.2 (11 boys, 13 girls) without statistical significance. Most of patients with UC (22 patients, 91.7%) were diagnosed above 10 years. The disease activity sites according to the Paris classification were E1 (Proctitis) in 5 (20.8%), E2 (Left-sided) in 3 (12.5%), E3 (Extensive) in 2 (8.3%), and E4 (Pancolitis) in 14 (58.4%), indicating pancolonic involvement as major type. The average score of PUCAI at diagnosis was 41.8. The disease severity according to the Paris classification were that 17 patients (70.8%) had S0(Never severe) and 7 patients (29.2%) had S1(Ever severe).

Conclusion: This study revealed that most of patients with CD had ileal involvement, half of CD patients had weight loss and perianal disease and pancolitis occurred in two-thirds of UC cases.
Higher morbidity of monogenic inflammatory bowel disease compared to the adolescent onset in inflammatory bowel disease

Jae Sung Ko¹, Jin Soo Moon¹, Kwang Yeon Kim¹, Kyung Jae Lee¹, Ju Whi Kim¹

¹Seoul National University College of Medicine, Department of Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Very early-onset Inflammatory bowel disease (VEO-IBD) patients develop somewhat different disease phenotype compared to adolescents and adults. Aggressive clinical course and resistance to conventional treatments usually characterize VEO-IBD. Monogenic IBD is a kind of VEO-IBD with distinct clinical manifestation. We summarized clinical characteristics of our monogenic IBD patients and compared the clinical outcome to the adolescent IBD patients.

Methods: We performed a retrospective cohort study of all children < 18 years old who were diagnosed with monogenic IBD and adolescent IBD between 2005 and 2016. VEO-IBD was defined as their presentation age was below 6. We compared height below 3rd percentile, weight under 3rd percentile, presence of perianal lesion, frequency of hospitalizations, and surgical experiences among children diagnosed with IBD according to their presentation ages.

Results: A total of 16 eligible monogenic IBD were identified: chronic granulomatous disease (CGD), hyper Ig M syndrome, hypogammaglobulinemia, immunodysregulation polyendocrinopathy enteropathy X-linked syndrome (IPEX), glycogen storage disease (GSD), congenital neutropenia, IL-10 signaling defects. Proportion for height below 3rd percentile ($p<0.005$), weight under 3rd percentile ($p<0.005$), and hospitalization ($p<0.005$) were higher in monogenic IBD group than for older children. Also, the initial PCDAI ($p=0.04$) and the incidence of surgery were higher among children diagnosed with monogenic IBD ($p<0.005$). However, there was no difference in proportion for perianal lesion ($p=0.806$) between two groups.

Conclusion: Monogenic IBD is phenotypically and genetically different disease entity from older onset IBD. It has a strong association with primary immunodeficiency. These patients do not respond to conventional therapy and are associated with high morbidity. We should consider the primary immunodeficiency in patients with VEO-IBD.
The usefulness of soluble transferrin receptor (sTfR) and sTfR/log ferritin index in the
diagnosis of iron deficiency anaemia in children with inflammatory bowel disease

Paulina Krawiec¹, Agnieszka Mroczkowska-Juchkiewicz¹, Elżbieta Pac-Kożuchowska¹

¹Medical University of Lublin, Department of Paediatrics, Lublin, Poland

Objectives and study: The diagnosis of iron deficiency anaemia (IDA) in patients with inflammatory bowel disease (IBD) is a challenging issue. The majority of traditional iron metabolism parameters are not reliable in IBD since they are influenced by accompanying inflammation. Soluble transferrin receptor (sTfR) and sTfR/log ferritin (sTfR-F) index have been reported as useful tool in the diagnosis of IDA in some inflammatory diseases. However current data on the usefulness of the sTfR and sTfR-F index in the evaluation of anaemia in children with IBD are limited. Thus, we aimed to determine the diagnostic value of sTfR and sTfR-F index for detecting IDA in children with IBD.

Methods: The study group comprised 75 children with IBD, including 46 (61%) with ulcerative colitis and 29 (39%) with Crohn’s disease. All children underwent blood tests including complete blood count, C-reactive protein, erythrocyte sedimentation rate, interleukin-6, iron, ferritin, transferrin and transferrin saturation, sTfR. The sTfR-F index was calculated based on the ratio: sTfR/log₁₀ ferritin. Anaemia was defined according to WHO criteria. IDA was recognized in anaemic patients with satTRF<20% and ferritin level<30ng/ml, anaemia of chronic diseases (ACD) was stated in evidence of inflammation, satTRF<20% and ferritin >100ng/ml. Anaemia with satTRF<20% and ferritin level ranging from 30 to 100ng/ml was considered as ACD with iron deficiency (ACD+ID). The ability of diagnostic parameters to identify IDA was examined by receiver operating characteristic (ROC) analysis. The study was approved by the local bioethical committee.

Results: In the study group 38 (51%) IBD children had anaemia, including 27 (36%) with IDA, 6 (8%) with ACD+IDA and 5 (7%) with ACD. The sTfR was significantly increased in children with IDA (median:1.63µg/ml; range: 0.72-5.27µg/ml) compared to non-anaemic children (median:1.02 µg/ml; range: 0.49-1.89µg/ml) (p=0.001). There were no differences in sTfR between patients with IDA and ACD or ACD+ID. The sTfR-F index was significantly higher in IDA (median:1.76; range: 0.64-11.05) compared to patients with ACD (median:0.55; range: 0.44-0.89), ACD+ID (median: 0.68; range: 0.65-0.96) and patients without anaemia (median: 0.72; range: 0.24-2.07) (H=25.66; p<0.0001). Both sTfR or sTfR-F index were not correlated with IBD activity and inflammatory markers. The accuracy of sTfR and sTfR-F index for the diagnosis of IDA was 81% and 71% respectively. The diagnostic power for sTfR-F index was superior to sTfR in the diagnosis of IDA in IBD children (area under ROC 0.864 vs 0.768 respectively).

Conclusion: Both sTfR and sTfR-F index are efficient, independent on inflammation and IBD activity, tools for the diagnosis of IDA. The sTfR-F index has better diagnostic utility than sTfR for the recognition of IDA in children with IBD.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-278

The NOD2/CARD15 and ABCB1/MDR1 genes polymorphism in children with inflammatory bowel disease

Paulina Krawiec1, Agnieszka Mroczkowska-Juchkiewicz1, Agnieszka Pawłowska-Kamieniak1, Katarzyna Kominek1, Elżbieta Pac-Kożuchowska1

1Medical University of Lublin, Department of Paediatrics, Lublin, Poland

Objectives and study: Inflammatory bowel disease (IBD) has been associated with several mutations in NOD2/CARD15 and ABCB1/MDR1 mutations. However, the role of genetic factor in IBD has not been fully elucidated. The aim of the study was to evaluate the polymorphism profile for NOD2 and MDR1 genes in children with inflammatory bowel disease.

Methods: Genomic DNA was extracted routinely from peripheral blood. All patients were genotyped for the polymorphism R702W, G908R and P268S in the NOD2/CARD15 gene and G2677 in the ABCB1/MDR1 gene by the polymerase chain reaction – restriction fragment length polymorphism (PCR-RFLP) method. The study was approved by the local bioethical committee.

Results: The study group comprised 40 children with IBD, including 20 (50%) with ulcerative colitis and 20 (50%) with Crohn’s disease. There was male preponderance (26/40; 65%). The mean age at IBD onset was 13.8±2.8 years. The majority of children with ulcerative colitis had pancolitis (16/20; 80%) and most patients with Crohn’s disease had ileocolonic disease with upper gastrointestinal tract involvement (8/20; 40%). The most common variant of the NOD2/CARD15 mutation was P268S. The polymorphism distribution for P268S resulted as follows: 18/40 CC (45%), 15/40 CT (37.5%), 7/40 TT (17.5%). In the study group there was no homozygous mutant of G908R or R702W polymorphism. However, heterozygous mutation of R702W was detected in 6 IBD children (15%). One child was heterozygous for G908R. There were no association between NOD2/CARD15 mutations and patients gender, location and clinical severity of IBD. In the ABCB1/MDR1 gene the polymorphism distribution for G2677T was as follows: 17/40 GG (42.5%), 14/40 GT (35%) and 9/40 TT (22.5%). In our study group, only the G2677A heterozygous mutation in the ABCB1/MDR1 gene was found in 2/40 (5%) patients. No relationship was found between ABCB1/MDR1 mutations and the phenotype of IBD.

Conclusion: The most frequent gene polymorphism in our study group consist of P268S in the NOD2/CARD15 gene and G2677T in the ABCB1/MDR1 gene. Lack of association between IBD phenotype and mutations in NOD2/CARD15 or ABCB1/MDR1 suggest that genetic factor plays in interaction with other cofactors in the pathogenesis of IBD.
Nutritional status and linear growth in children with inflammatory bowel disease

Sinem Nalcaci¹, Zarife Kuloğlu², Arzu Ensari³, Aydan Kansu²

¹Ankara University School of Medicine, Pediatrics, Ankara, Turkey
²Ankara University School of Medicine, Paediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
³Ankara University School of Medicine, Pathology, Ankara, Turkey

Objectives and study: Nutritional impairment and growth retardation is a common problem in children with inflammatory bowel disease (IBD), especially in active Crohn Disease (CD). We aimed to identify the prevalence of malnutrition and growth retardation from diagnosis to maximal follow-up in children with IBD at a single tertiary center in Turkey.

Methods: Medical records of patients (<18 years) diagnosed with IBD between 2000-2015 who were followed up for at least 1 year were analyzed retrospectively both at diagnosis and maximal follow-up (T-max). Data were collected through standardized questionnaire including demographics, clinical type and characteristics, biochemical markers, medication, disease location, behavior and activity. Disease status was classified by Paris Classification. PCDAI and PUCAI scores were categorized as "inactive disease" if PCDAI or PUCAI were <10, "mild disease" if PCDAI was ≥10 and <30 or PUCAI was ≥10 and <35; "moderate–severe disease" if PCDAI was ≥30 or PUCAI was ≥35. The z score of height/age (HAZ), weight/age (WAZ) and body mass index (BMI) (BMIZ) were determined. Growth retardation was defined as HAZ less than -2 SD, undernutrition as WAZ less than -2 SD, severe malnutrition as BMIZ less than -2 SD. Acute malnutrition was accepted as weight for height less than 90%. p-value of < 0.05 was considered to be statistically significant.

Results: Forty-six patients (mean age 107.6±67.2 months, 24 male) were enrolled. Of the 46 patients, 28 (60.9%) were ulcerative colitis (UC), 15 (32.9%) were CD and 3 (6.5%) were indeterminate colitis. Mean follow-up was 44.6 ± 34.4 ay (12-150 months). At diagnosis, perianal disease, extraintestinal manifestations and antibody positivity were present in 28.3%, 26.1%, 46.8% (15/32) respectively. Disease localisation was L2 (40%), L3 (53.3%), L4a (6.7%) in CD; E1 (10.7%), E2 (25%), E3 (14.3%), E4 (50%) in UC. Disease behavior in CD was inflammatory (93.3%) and penetrating (6.6%). A total of 95.7% patients were exposed to oral ASA, 47.8% to steroid, 34.8% to nutritional therapy, 32.6% to immunmodulatory therapy, 23.9% local ASA, 6.5% biological agents and 15.2% surgery at diagnosis or during follow-up. At Tmax, 60.8% of all patients had inactive disease. During follow-up at least once relapse was observed in 26% of patients (CD:26.7%; UC:28.7% p=n.s).

HAZ at T max was significantly lower in children with steroid exposure (p=0.025) whereas WAZ and BMIZ were not affected by steroid exposure. No difference was found in anthropometric parameters in terms of gender, age, extraintestinal disease, relapse and antibody positivity. WAZ (p=0.013) and HAZ (p=0.043) at Tmax were significantly lower in patients with high CRP level at diagnosis.
**Table:** Antropometric parameters at the time of diagnosis and maximal follow-up in 46 patients

<table>
<thead>
<tr>
<th></th>
<th>At diagnosis</th>
<th>At Tmax</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCDAI*</td>
<td>42±19,2</td>
<td>10,7±12,02</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>PUCAI*</td>
<td>33,9±13,3</td>
<td>6,07±9,1</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>HAZ*</td>
<td>-0,77 ± 1,5</td>
<td>-0,45 ± 1,3</td>
<td>0,01</td>
</tr>
<tr>
<td>WAZ*</td>
<td>-1,07 ± 2,0</td>
<td>-0,32 ± 1,2</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>BMIZ*</td>
<td>-0,7 ± 1,5</td>
<td>-0,02 ± 1,05</td>
<td>0,001</td>
</tr>
<tr>
<td>Growth retardation n (%)</td>
<td>6 (13)</td>
<td>2 (4,2)</td>
<td>0,12</td>
</tr>
<tr>
<td>Undernutrition n (%)</td>
<td>8 (17,4)</td>
<td>2 (4,2)</td>
<td>0,031</td>
</tr>
<tr>
<td>Severe malnutrition n (%)</td>
<td>8 (17,4)</td>
<td>2 (4,2)</td>
<td>0,1</td>
</tr>
<tr>
<td>Acute malnutrition n (%)</td>
<td>16 (34,7)</td>
<td>6 (13)</td>
<td>0,013</td>
</tr>
</tbody>
</table>

*Mean±SD

**Conclusion:** In our study, growth retardation and malnutrition were still present at T max, however, dramatic decrease was observed within mean 44 months. Patients with high CRP levels at diagnosis or exposure to steroid therapy were found to have a higher risk for growth failure.
Inadequate vaccination uptake in children receiving anti-TNF therapy for inflammatory bowel disease

Simone Nicol¹, Sally Lawrence¹, Kevan Jacobson¹

¹Bc Children's Hospital, Gastroenterology, Vancouver, Canada

Objectives and study: A recent Canadian study reported increasing incidence rates for paediatric IBD as 9.5 per 100,000 (in 1994) to 11.4 per 100,000 (in 2005). Childhood onset IBD is characterized by extensive intestinal involvement and an aggressive disease course, with initiation of immunosuppressive therapy essential to control inflammation and ultimately ensure mucosal healing.

Vaccine preventable infections are more frequent in IBD immunosuppressed subjects and often have a more severe disease course. In this pilot study we reviewed immunization coverage in children with IBD on anti-TNF therapy.

Methods: A retrospective chart review was performed in all patients on anti-TNF therapy attending BC Children’s Hospital in August 2016 and a letter was sent to all families to obtain updated patient immunization records.

Results: 115 patients were on anti-TNF therapy in August 2016. 43.3% of patients (N=50/115) had documented evidence of vaccination status. The median age at IBD diagnosis was 10.8 years (IQR 8.0-12.8) with median age at initiation of biologic therapy of 11.6 years (IQR 10.5-14.2). 56% (N=28/50) of patients were male and 76%(N=38/50) had Crohn’s disease, 16% (N=8/50) had UC.

At the time of IBD diagnosis 18% (N=9/50) had up to date vaccinations. Post diagnosis 31.7% (N=13/41) of patients had partial catch up in vaccination. No patient received complete catch up.

At the time of anti-TNF induction 17% (N=8/47, 3 missing values for induction date) of patients had received the full complement of live vaccinations. No patients had catch up of live vaccines prior to anti-TNF induction. No live vaccines were administered post biologic induction.

Although initial preschool immunization uptake was comparable between the IBD cohort and the BC population average for most vaccines, there was a significantly lower uptake of school vaccinations in the IBD cohort.
Table: Pediatric IBD vaccine uptake according to BC routine Immunization schedule

<table>
<thead>
<tr>
<th>Age of immunization</th>
<th>Vaccine</th>
<th>% IBD vaccinated (N eligible)</th>
<th>% BC vaccinated overall (2015)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>2 months</td>
<td>Diphtheria-Tetanus-Pertussis-Hep B- Inactivated Polio-Haemophilus B</td>
<td>90 (45/50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
<td>38 (19/50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meningitis C</td>
<td>76 (38/50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 months</td>
<td>Diphtheria-Tetanus-Pertussis-Hep B- Inactivated Polio-Haemophilus B</td>
<td>90 (45/50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
<td>42 (21/50)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6 months</td>
<td>Diphtheria-Tetanus-Pertussis-Hep B- Inactivated Polio-Haemophilus B</td>
<td>90 (45/50)</td>
<td>85</td>
<td></td>
</tr>
<tr>
<td>12 months</td>
<td>Varicella</td>
<td>66 (33/50)</td>
<td>84</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Measles Mumps Rubella</td>
<td>94 (47/50)</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Meningitis C</td>
<td>42 (21/50)</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Pneumococcal</td>
<td>42 (21/50)</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>18 months</td>
<td>Diphtheria-Tetanus-Pertussis-Inactivated Polio-Heamophilus B</td>
<td>76 (38/50)</td>
<td>75-79</td>
<td></td>
</tr>
<tr>
<td>4-6 years old</td>
<td>Diphtheria-Tetanus Pertussis-Inactivated Polio</td>
<td>86 (43/50)</td>
<td>77 (34374/44641)</td>
<td>0.13</td>
</tr>
<tr>
<td>(kindergarten)</td>
<td>Measles Mumps Rubella</td>
<td>86 (43/50)</td>
<td>93 (41516/44641)</td>
<td>0.05</td>
</tr>
<tr>
<td>Age Range</td>
<td>Vaccine Type</td>
<td>Count</td>
<td>Percentage</td>
<td>Vaccine Coverage</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------------------</td>
<td>-------</td>
<td>------------</td>
<td>------------------</td>
</tr>
<tr>
<td>11-12 years old</td>
<td>Varicella</td>
<td>31</td>
<td>82</td>
<td>0.0</td>
</tr>
<tr>
<td>(Grade 6)</td>
<td></td>
<td>(12/39)</td>
<td></td>
<td>(36750/44818)</td>
</tr>
<tr>
<td></td>
<td>Hepatitis B</td>
<td>13</td>
<td>92</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5/39)</td>
<td></td>
<td>(41232/44818)</td>
</tr>
<tr>
<td></td>
<td>Human-Papilloma-Virus</td>
<td>31</td>
<td>65</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(12/39)</td>
<td></td>
<td>(29132/44818)</td>
</tr>
<tr>
<td></td>
<td>Meningitis C</td>
<td>13</td>
<td>87</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>(5/39)</td>
<td></td>
<td>(38991/44818)</td>
</tr>
<tr>
<td>14-15 years old</td>
<td>Diphtheria-Tetanus-Pertussis</td>
<td>67</td>
<td>80</td>
<td>0.0</td>
</tr>
<tr>
<td>(Grade 9)</td>
<td></td>
<td>(12/31)</td>
<td></td>
<td>(37585/46981)</td>
</tr>
</tbody>
</table>

**Conclusion:** This pilot data demonstrates inadequate documentation of vaccination status for immunocompromised IBD patients. For those with documented evidence of vaccination status the vaccine coverage in our patients on anti-TNF therapy was poor. The vaccine status tailed off significantly in the teenage years, which may be associated with chronic ill health preventing vaccine uptake.
Effect of the baseline vitamin D level on growth outcome in pediatric Crohn disease

Eun Joo Lee1, Jin Soo Moon2, Jae Sung Ko2, Hye Ran Yang3, Ju Young Chang4, Kyung Jae Lee2

1Seoul National University Hospital, Department of Pediatrics, Seoul, Korea, Rep. of South
2Seoul National University College of Medicine, Department of Pediatrics, Seoul, Korea, Rep. of South
3Seoul National University Bundang Hospital, Seoul National University College of Medicine, Pediatrics, Seongnam-Si, Gyeonggi-Do, Korea, Rep. of South
4Seoul National University Boramae Medical Center, Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Vitamin D deficiency is common in Crohn disease (CD). The aim of the study was to examine the prevalence of vitamin D deficiency and evaluate the association between vitamin D status and growth outcome in Korean pediatric CD patients.

Methods: In this retrospective study, 17 children younger than 18 years old diagnosed with CD were enrolled and their serum 25-hydroxy vitamin D was checked between 2011 and 2015. We categorized the patients into two groups, Group 1 and Group 2. Group 1 included patients with serum 25(OH)D levels below 10 ng/mL, and Group 2 was for patients with a 25(OH)D serum levels between 10 ng/mL and 30 ng/mL. The Z-scores for height (Htz), weight (Wtz), and BMI (BMlz) were measured at baseline, 6 months, and 12 months.

Results: The mean serum 25(OH)D levels of the total 65 CD patients and 17 enrolled patients were 15.64 ± 6.9 ng/mL and 13.1±5.1ng/mL , respectively. There was no correlation at the beginning of the study between vitamin D level and growth parameters (Htz, Wtz, BMlz) or other variables including laboratory data and Pediatric Crohn Disease Activity Index. The Htz, Wtz, and BMlz in Group 1 showed no significant improvement at 6 months and 12 months follow-up. In Group 2, Wtz and BMlz showed significant improvements sustained until 12 months of follow-up. Htz showed no significant improvement at 6 months but there was significant improvement at 12 months.

Conclusion: It seems that baseline vitamin D status affects growth outcome in pediatric CD.
Implementation of an international quality improvement initiative for children with inflammatory bowel disease (IBD) - A UK site perspective of ImproveCareNow (ICN)

Claire Lee, Marco Gasparetto, Mary Brennan, Anna Folan, Deborah Cunion, Megan Maidment, Franco Torrente, Robert Heuschkel, Matthias Zilbauer

1Cambridge University Hospitals, Addenbrooke's, Paediatric Gastroenterology, Hepatology and Nutrition, Cambridge, United Kingdom

Objectives and study: ICN is the largest IBD registry worldwide aiming to improve and standardise the care of children diagnosed with IBD by creating a collaborative community of patients, families and health care providers. There are currently 95 centres participating in ICN caring for over 27,000 children and young people with IBD.

All patients with a diagnosis of IBD receiving care primarily by the participating centre are eligible for enrolment in ICN, with the exception of post-colectomy UC patients. Young people who have commenced the transition process to adult care, or who are expected to transition within 3 months are excluded from participation.

The aim for this poster is to present the experiences of a UK paediatric IBD team with joining ICN, a large collaborative network based in the US, which collects data from children with IBD for quality improvement and patient centred research.

Methods: The process of establishing ICN in our centre involved; obtaining funding, securing agreements for data transfer to the US, achieving ethical approval for research, designing appropriate information for UK children and families, and organisation of the recruitment process. Electronic Health Records (EHR) in the form of EPIC had been available in our centre since 2014, facilitating data collection and transfer to the registry held in the US.

Results: At the time of approval, 218 patients were eligible for registration for ICN. To date, 102 children have been registered (46%) and 76 (75%) of these have also given informed consent for their data to contribute towards future research. ICN sites are stratified according to the time they have been participating in ICN and the percentage of patients registered (<75% or 75% and above). This allows benchmarking with sites at the appropriate time in their journey within ICN. Early analysis shows that based on our current number of registered patients (n=102), our baseline clinical remission rate is 71%. Patients with satisfactory nutritional and growth status are 77% and 94% respectively. Focusing on treatment, 100% of our cohort received TPMT monitoring prior to commencing thiopurines, and 97% are receiving the recommended dose of thiopurine according to the ICN model care guidelines.

We have begun to embed formal pre-visit planning and population management in our weekly IBD workflow, using resources from across the ICN Exchange to modify processes in line with NHS systems. Use of the Care Stratification Score (CSS) adds value to population management by systematically identifying patients at risk of relapse, thereby focusing attention on preventative strategies.

Conclusion: ICN has great potential to transform the care, and hence clinical outcomes, of children with IBD. It also provides a unique dataset to perform future research studies, ultimately improving the lives of children and young people with IBD. As the number of patients registered to ICN increases, the data generated will become more powerful. Reports generated from the ICN registry will allow us to concentrate on areas for improvement, and also focus discussions and resources on those patients who are flagged as moderate to high risk. Following the Plan Do Study Act (PDSA) Cycle, we can set goals and actions to improve patient outcome and work collaboratively with colleagues and families.
**GASTROENTEROLOGY: Inflammatory bowel disease**

**G-P-283**

**A prospective cohort of patients receiving exclusive enteral nutrition (EEN) confirms high clinical response rates after 8 weeks of treatment: initial results from the BIG study**

Michael Logan¹, Clare Clark¹, Hazel Duncan², Lisa Richmond³, Andrew Barclay³, Richard Hansen³, Diana Flynn³, Rachel Tayler³, Konstantinos Gerasimidís¹, Richard Russell³

¹University of Glasgow, Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, Glasgow Royal Infirmary, Glasgow, United Kingdom
²Royal Hospital for Children, Department of Nutrition and Dietetics, Glasgow, United Kingdom
³Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom

**Objectives and study:** **Background:** Exclusive enteral nutrition (EEN) is the first line treatment to induce remission in active luminal paediatric Crohn’s disease (CD).

**Aim:** To prospectively characterise the efficacy of EEN during and after a course of EEN.

**Methods:** Paediatric patients attending our hospital suspected of inflammatory bowel disease were recruited to our ongoing BIG (bacteria & inflammation in the gut) study between August 2014 to June 2016. Diagnosis was based on established clinical, endoscopic and histological criteria. Patients diagnosed with CD, who undertook a course of EEN, had data and biological samples taken before, during and on completion of an 8 week course of EEN. Disease activity was defined using the weighted paediatric Crohn’s disease activity index score (wPCDAI). Anthropometry and systemic inflammatory markers of disease activity including faecal calprotectin, CRP, ESR, and haemoglobin were recorded at diagnosis and at end of EEN.

**Results:** 41 patients (12 female, median age at diagnosis 12.3y (Q1- 10.0, Q3- 14.7) were identified. In 36/41 (88%) this was the first course of EEN, the remainder were undergoing a repeat course following a relapse. 34/41 (76%) presented with disease affecting both small intestine and colon (Montreal classification L3: n = 10, L3/L4: n = 18, L2/L4: n = 6). Seven children had isolated colonic disease (L2: n = 7). All participants were treated with polymeric feeds (Modulen: N = 40; Paediasure: N = 1); 31/41 (76%) had EEN orally, the remaining 10/41 (24%) required nasogastric tube. 10/41 (24%) were non-responders; 8/10 due to symptom escalation/poor response and 2/10 were unable to tolerate EEN.

At treatment initiation, median wPCDAI was 38.8 (IQR 21.9- 57.5), 40/41 had a wPCDAI >12.5; 31/41 (76%) patients had entered clinical remission at the end of EEN (wPCDAI at EEN end <12.5). Before treatment initiation median inflammatory markers ESR, CRP, serum albumin and haemoglobin levels were 21 mm/h, 6 mg/L, 35 g/dL, and 10.3 respectively, with 63% of participants having a least one abnormal result. Three of these values had significantly improved by the end of EEN (ESR to median 7 mm/h, p = 0.012; CRP to median 6 mg/L, p = 0.004; albumin to median 38 g/dL, p = 0.0001).

All participants at time of treatment initiation had a raised calprotectin with a Median concentration OF 1305 mg/kg which declined by the end of EEN to 869.5 mg/kg (p = 0.006). There was a significant difference in calprotectin in those that respond to EEN (median 485.5) versus those who did not (median 1509.5) p = 0.02. In total, five participants had a faecal calprotectin below 250 mg/kg and, of these, four (10%) had dropped to below 100 mg/kg.

**Conclusion:** 8 weeks of EEN is associated with high rates of clinical remission in 76% of patients treated as assessed by the wPCDAI. This is paralleled by significant improvement in blood parameters and calprotectin but normalisation of calprotectin only occurs in a minority. Consideration should be given to longer courses of EEN in some patients with the aim of driving calprotectin lower to see if this improves length of subsequent remission. The BIG study will now follow the clinical course of patients following EEN, specifically looking at patients who are and are not on nutritional supplements after their course of EEN whilst examining laboratory and clinical relapse and the contribution of the microbiome.
Disclosure of interest: Richard Russell has received speaker’s fees, travel support, and participated in medical board meetings with Nestle. Konstantinos Gerasimidis received speaker’s fees from Nutricia and a research grant from Nestle. Richard Hansen has received travel support from Nutricia.
Air displacement plethysmography for assessment of body composition in children with inflammatory bowel disease

Luba Marderfeld, Neta Biran, Irit Poraz, Raanan Shamir, Assa Amit

1Schneider Children’s Medical Center of Israel, Nutrition and Dietetics Department, Petach Tikva, Israel
2Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
3Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel

Objectives and study: Growth impairment is commonly seen in children diagnosed with inflammatory bowel diseases (IBD), mainly those with Crohn's disease (CD). There is general consensus in the literature that body composition, composed of fat mass and lean mass is altered in children with IBD compared with controls. Most studies used anthropometric measures and dual energy X-ray absorptiometry (DXA) for body composition assessment, while data on the usefulness of air displacement plethysmography (ADP) for assessing body composition is available for diseases such as diabetes but has not been studied in IBD. Thus, we aimed to assess body composition in children with IBD by ADP in comparison to DXA.

Methods: In a retrospective cohort study, we measured body composition in children (6-18 years) with diagnosed IBD using both ADP (Cosmed, Italy) and DXA (lunar Prodigy Primo, GE, US). The two measurements were performed no longer than 2 weeks apart. Anthropometric and clinical parameters were recorded at the time of the first measurement.

Results: Forty children, 12 with ulcerative colitis and 28 with Crohn's disease, were evaluated (median age 14.2 (IQR 11.6-15.55 years), females 14 (35%). Median duration from diagnosis was 1 year (IQR 0.25-2.4 years). BMI z-scores -0.42±1.25 correlated positively with DXA (Spearman's r =0.511, P=0.001) and ADP (Spearman's r =0.55, P<0.0001). Mean body fat (%) was estimated as 16.47±10 and 26.34±7.45 for ADP and the DXA, respectively. Median percentile of fat mass index (FMI) was 25 (IQR 6.2-50). There was a fare correlation between two measurements (Spearman's r =0.796, P<0.0001). A significant difference was demonstrated between ADP and DXA (P<0.0001).

Conclusion: ADP is a reliable method for the assessment of body composition in pediatric IBD patients. Although the two methods were highly correlated, ADP measurements yield significantly lower scores when compared to DXA. These findings are compatible with data demonstrated for other diseases.
Subcutaneous ustekinumab provided clinical and biological benefit for 9/12 refractory pediatric Crohn’s disease

Christine Martinez-Vinson¹, Charlene Goma², Marc Bellaiche¹, Jean-Pierre Hugot¹, Jerome Viala³

¹Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris, Pediatric Gastroenterology Department, Paris, France
²Hopital Robert Debré, Gastroentérologie, Paris, France
³Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris., Departments of Pediatric Digestive and Respiratory Diseases, Paris, France

Objectives and study: Ustekinumab has shown a good safety profile and efficacy to induce and maintain remission in adult patients with refractory Crohn’s Disease (CD). Data are lacking in children.

Methods: All CD patients under 18 years who received ustekinumab were included in this retrospective observational study performed in a single tertiary pediatric centre.

Results: From January 2015 to May 2016, twelve CD patients were treated with ustekinumab, all because of failure of several lines of therapies including anti-TNF antibodies. All but one patient were followed at least one year. An initial response was achieved in 9 (75%) patients, and remission in 5 (42%). At one year, the nine responders were still receiving ustekinumab with clinical benefit and without steroids need. Seven of them (58%) were on clinical remission. One patient experienced a serious adverse event and the treatment was stopped after the first injection.
Table:

**Figure 1: Flow chart**

12 patients with refractory luminal (n=11) or perineal (n=1) Crohn’s Disease received ustekinumab induction.

One patient with a serious adverse event stopped ustekinumab after the first injection.

11 patients still under ustekinumab at 3 months.

- 9 patients (75%) with clinical benefit
  - 5 under remission (42%) did not require additional treatments

- One patient under ustekinumab needed a colectomy just after the first injection of ustekinumab. Ustekinumab was continued after surgery.

- One patient required the addition of methotrexate due to a lack of response.

The treatment was discontinued at 6 months for the patient with perineal CD which was still active.

One patient responded but he had only 3 months of follow-up at the time of the study.

7/8 responders with a one year follow-up still had a clinical benefit including 7 patients in remission.

2 patients still receiving Ustekinumab at one year with clinical benefit

9 patients with clinical benefit at one year.
Conclusion: Subcutaneous ustekinumab is effective to induce and maintain remission in severe pediatric CD refractory to anti-TNF antibodies.

Key words: Pediatric, Crohn's disease, anti-TNF-α, therapeutics.
Trough levels to infliximab at week 6 are predictive of remission at week 14, in pediatric Crohn’s disease

Christine Martinez-Vinson1, Olivier Courbette2, camille aupiais3, Stephanie WIllo4, Jean-Pierre Hugot1, Jerome Viala5

1Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris, Pediatric Gastroenterology Department, Paris, France
2Hopital Robert Debré, Service des Maladies Respiratoires et Digestives de L'enfant, Paris, France
3Hopital Robert Debré, Service de Biotatistique, Paris, France
4Centre Hospitalier de Tours, Pédiatrie, Tours, France
5Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris., Departments of Pediatric Digestive and Respiratory Diseases, Paris, France

Objectives and study: Loss of response to anti-tumor necrosis factor (TNF) agents is a common clinical problem. 40% of patients lose response within 12 months of therapy initiation.

This retrospective study aimed to analyse factors associated with remission after 14 weeks of induction treatment by IFX in children with CD.

Methods: All patients aged from 2 to 18 years old with CD meeting European Crohn’s and Colitis Organisation criteria and treated for the first time by IFX between January 2002 and March 2014 at a single tertiary pediatric center were considered for inclusion in this retrospective study. The following baseline characteristics were anonymously recorded for each patient : gender, age at CD onset, age at inclusion, duration of disease, CD classification according to Paris classification, prior exposure to CD treatments, previous intestinal resections and reasons for anti-TNF initiation. At each infusion visit (week 0, 2, 6 and 14) disease activity was determined using Pediatric Crohn's disease Activity Index (PCDAI). Four blood samples were obtained for each patient (at W0, W2, W6 and W14). The following laboratory tests were recorded: ESR, CRP, hemoglobin, hematocrit, albumin, blood levels of lymphocytes, Trough levels to IFX (TRI) and antibodies to IFX (ATIs).

Results: We analyzed 107 patients with CD, with a total of 428 visits until W14. The principal reason to start infliximab was failure of immunosuppressive therapy (60%). Infliximab proved to be an effective treatment in our cohort since 75.7% (n=81) patients were responders to infliximab and 40% (n=42) were in clinical remission whereas 24.3% (n=26) were non respondents at W14. At week 14, 107 patients were divided in three groups related to the clinical activity of their disease : lack of clinical response, partial clinical response, clinical remission. It concerns respectively 26, 39 and 42 patients.

Major baseline characteristics were not associated with clinical remission : sex, age at diagnosis, disease location, time between diagnosis and induction, age at induction. Drugs associated with infliximab at W0, W2, W6 or W14, whether it was immunosuppressive agents or corticoids were not associated with remission.

Patients with low albumin levels had a worse response at induction

Activity score at induction was also statistically associated with clinical remission: each decreasing of 10 points of activity score at induction increase of 0.48 times the risk to obtain clinical remission.

Trough residual of infliximab > 8.5 µg/ml at w6 increase of 11.3 times the risk to obtain clinical remission at w14.

Lack of growth retardation at induction increased of 3.98 times the risk to obtain clinical remission at w14.

Conclusion: Infliximab measurement in combination with evaluation of clinical severity (low body weight, growth retardation, hypoalbuminemia, severe disease) appears to be a reasonable strategy for predicting both short- and long-term treatment outcomes with IFX in the initial stage of treatment.
Early detection of response to IFX is critical for the management of CD, especially in acute severe patients: it seems that the infliximab trough level at week 6 (more than 8.5) is predictive of a remission at week 14.

Second, some patients, especially patients with low body weight, growth retardation, hypoalbuminemia and severe disease may require higher doses than standard doses.
Serum IL-9 concentration in children with inflammatory bowel disease and its correlation with the activity of disease and fecal calprotectin

Krzysztof Matusiewicz, Barbara Iwanczak, Malgorzata Matusiewicz

1Medical University Wroclaw, Department and Clinic of Pediatrics and Gastroenterology, Wroclaw, Poland
2Medical University Wroclaw, Department of Biochemistry, Wroclaw, Poland

Objectives and study: The objective of our work was the assessment of the IL-9 concentration in pediatric patients with inflammatory bowel disease, its relation to the type of disease – ulcerative colitis and Crohn’s disease, to the activity of the disease and to other laboratory parameters such as CRP, EST and fecal calprotectin.

Methods: The number of 126 children aged 6 to 17 years (average 11.7 years); 69 girls and 57 boys treated in Department and Clinic of Pediatrics and Gastroenterology Clinic of Wroclaw Medical University were included in the study: 67 with Crohn’s disease and 30 with ulcerative colitis. Control group comprised 21 children treated in our clinic who were not diagnosed with IBD. Additionally a group of children with GERD was selected. In all children IL-9 was measured, activity of the disease was described using pediatric ulcerative colitis activity index (PUCAI) or pediatric Crohn’s disease activity index, respectively. CRP and fecal calprotectin were evaluated at the same time as IL-9 was measured.

Results: The highest average value of serum IL-9 concentration was observed in active UC (106.5 pg/ml) and it was statistically significantly higher than in active CD (58.3 pg/ml), UC in remission (33.7 pg/ml) and control group (3.08 pg/ml). Serum IL-9 concentration in UC in remission was not significantly higher than that in control group. Serum IL-9 concentration in active CD tended to be higher than in CD in remission and in control group but the differences were not statistically significant, the same was observed for CD in remission where serum IL-9 concentration was higher than in control but without statistical significance. Significant positive correlations of serum IL-9 concentration with activity of the disease (correlation coefficient r=0.4, p=0.031) and fecal calprotectin were observed in UC (correlation coefficient r=0.39, p=0.038). No significant correlation was observed between serum IL-9 concentration and CRP and ESR in the whole cohort and in CU group as well as in active CU subgroup. No significant correlations between serum IL-9 concentration and CRP, ESR and disease activity were observed in CD. In selected GERD patients IL-9 was mainly below detection threshold.
Table:

IL-9 concentration and significance of the differences among groups

<table>
<thead>
<tr>
<th>Group</th>
<th>N</th>
<th>IL-9 concentration [pg/ml]</th>
<th>Control</th>
<th>GERD</th>
<th>CD remission</th>
<th>CD active disease</th>
<th>UC remission</th>
<th>UC active disease</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Average±SD</td>
<td>95% CI for the mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>21</td>
<td>3.08±7.25</td>
<td>0.3-6.48</td>
<td>X</td>
<td>ns</td>
<td>ns</td>
<td>P&lt;0.5</td>
<td>ns</td>
</tr>
<tr>
<td>GERD</td>
<td>8</td>
<td>2.33±5.91</td>
<td>-2.9-7.6</td>
<td>ns</td>
<td>X</td>
<td>P&lt;0.5</td>
<td>ns</td>
<td>P&lt;0.5</td>
</tr>
<tr>
<td>CD remission</td>
<td>36</td>
<td>30.8±64.1</td>
<td>4.4-57.0</td>
<td>ns</td>
<td>ns</td>
<td>X</td>
<td>ns</td>
<td>ns</td>
</tr>
<tr>
<td>CD active disease</td>
<td>41</td>
<td>58.3±65.1</td>
<td>34.5-75</td>
<td>P&lt;0.5</td>
<td>P&lt;0.5</td>
<td>ns</td>
<td>X</td>
<td>ns</td>
</tr>
<tr>
<td>UC remission</td>
<td>15</td>
<td>33.7±53.3</td>
<td>3.1-64</td>
<td>P&lt;0.5</td>
<td>P&lt;0.5</td>
<td>ns</td>
<td>ns</td>
<td>X</td>
</tr>
<tr>
<td>UC active disease</td>
<td>15</td>
<td>106.5±86.7</td>
<td>55.8-155.2</td>
<td>P&lt;0.5</td>
<td>P&lt;0.5</td>
<td>P&lt;0.5</td>
<td>ns</td>
<td>P&lt;0.5</td>
</tr>
</tbody>
</table>

**Conclusion:** Serum concentration of IL-9 was significantly higher in patients with active UC than in control and UC and CD in remission. In patients with UC IL-9 correlated significantly with the activity of disease and fecal calprotectin.
Prevalence of autoimmune diseases in a nationwide paediatric inflammatory bowel disease cohort

Victoria Merrick¹, Paul Henderson², Hazel Drummond³, Johan van Limbergen⁴, Richard Russell⁵, Jack Satsangi³, David Wilson⁶

¹University of Edinburgh, Child Life and Health, Edinburgh, United Kingdom
²Royal Hospital for Sick Children, Paediatric Gastroenterology, Edinburgh, United Kingdom
³University of Edinburgh, Institute of Genetics and Molecular Medicine, Edinburgh, United Kingdom
⁴Iwk Health Centre/Dalhousie University, Pediatrics, Halifax, Canada
⁵Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
⁶University of Edinburgh, Department of Pediatric Gastroenterology, Child Life and Health, Edinburgh, United Kingdom

Objectives and study: Autoimmune diseases (AIDs) affect up to 10% of individuals living in Europe and are a significant cause of morbidity. High rates of immune-mediated comorbidity and familial clustering suggest that genetic predisposition underlies AID disease susceptibility, yet few clinical studies have defined the prevalence rates of co-morbid AIDs in specific paediatric populations. We aimed to document the occurrence of Juvenile Idiopathic Arthritis (JIA) and other AIDs in a Scotland-wide cohort of paediatric inflammatory bowel disease (PIBD; diagnosed <17 years of age) patients.

Methods: The Paediatric-onset IBD Cohort and Treatment Study (PICTS) is a nationwide Scottish study of incident and prevalent PIBD patients, collecting a wide range of data, including rigorous phenotyping (Paris classification) with continuous long-term follow-up. The PICTS database was interrogated to identify patients enrolled up to 31/12/12 with a diagnosis of at least one associated AID by last follow-up; case notes were then reviewed with follow-up to 30/04/15. Cases believed to be related to use of anti-TNFα treatment were excluded; atopic diseases were excluded due to their ubiquitous presence in the Scottish population.

Results: 51 of 809 patients in the PICTS cohort had one or more associated AID; an overall co-morbid AID prevalence of 6.3%. 57% (29/51) were male; 59% (30/51) had Crohn’s disease (CD), 37% (19/51) ulcerative colitis (UC), and 4% (2/51) IBD unclassified (IBDU). Median age (range) at PIBD diagnosis was 11.5 years (2.9-16.25). Autoimmune liver disease was the most frequently occurring AID in 35% (18/51); psoriasis 24% (12/51); JIA 18% (9/51); spondyloarthropathy (SPA) 12% (6/51); coeliac disease 8% (4/51); type 1 diabetes 6% (3/51); thyroid disease 4% (2/51). 3 patients (6%) had multiple co-morbid AIDs: all psoriasis and joint disease with PIBD. Primary sclerosing cholangitis (PSC) was the predominant final liver diagnosis in 83% (15/18). Onset of PIBD preceded SPA in 100% (6/6) cases in contrast to JIA preceding PIBD in 89% (8/9) cases. There was a high prevalence of extensive disease on Paris classification; 83% (25/30) CD patients had extensive disease (ileo-colonic (L3) or greater) and 47% (14/30) had pan-enteric disease (L3+L4). 43% (13/30) had aggressive disease behaviour (B2 +/- B3); 33% stricturing (B2), 10% penetrating (B3). 71% (15/21) UC/IBDU patients had pan-colonic disease (E4); 19% (4/21) had at least one severe colitis episode (S1).

Conclusion: 6.3% of PIBD patients in this large cohort study have associated AIDs and the majority of these patients have an extensive IBD phenotype. Autoimmune liver disease (predominantly PSC) is the dominant co-morbid AID, closely followed by joint disease (JIA and SPA) and psoriasis.

Disclosure of interest: Dr Merrick has received speaker’s fees from Dr Falk; Dr Henderson has received speaker’s fees from Dr Falk; Dr Russell has received speaker’s fees, travel support, and/or performed consultancy work with MSD Immunology, Nestle, AbbVie, Dr Falk, Takeda, Napp, Mead Johnson, Nutricia, and 4D Pharma; Prof Satsangi has received financial support for research from CCUK, EC-FP7, CSO, EC-H2020, MRC, WT, lecture fees/travel support from Takeda, Ferring, Falk, MSD and consulted for Takeda; Prof Wilson has received financial support for research from MSD, lecture fees from Abbvie and consulted for Takeda.
Rapid increase in pan-treatment refractory Crohn's disease after transition to adult services: a regional cohort study

Victoria Merrick¹, Paul Henderson², Pamela Rogers², Ian Arnott³, Jack Satsangi⁴, David Wilson⁵

¹University of Edinburgh, Child Life and Health, Edinburgh, United Kingdom
²Royal Hospital for Sick Children, Paediatric Gastroenterology, Edinburgh, United Kingdom
³Western General Hospital, Gastroenterology, Edinburgh, United Kingdom
⁴University of Edinburgh, Institute of Genetics and Molecular Medicine, Edinburgh, United Kingdom
⁵University of Edinburgh, Department of Pediatric Gastroenterology, Child Life and Health, Edinburgh, United Kingdom

Objectives and study: Inflammatory bowel disease (IBD) presents in childhood in up to 15% of cases. Paediatric onset IBD (PIBD) has a more extensive and dynamically changing phenotype and a faster rising incidence than adult-onset IBD. We aimed to evaluate rates of treatment refractory disease at and then following transition to adult services.

Methods: A prospective PIBD database identified a cohort of all patients discharged from our regional service since 01/01/07. A retrospective study of patients graduating from paediatric to adult IBD services through a transition process, transition event (single joint clinic) or transfer until 31/12/13 was conducted with post transfer follow-up (FU) data at a minimum of 1 year to last adult FU (LAFU). Pan-treatment exposure (PTE) was defined as exposure to all of azathioprine (AZA) or mercaptopurine (MP), methotrexate (MTX), infliximab (IFX) and adalimumab (ADA). Pan-treatment refractory (PTR) disease as those refractory (primary non-response [PNR], loss of response [LOR] or intolerance) to all of these therapies. We used the Montreal classification to describe disease location (L) and behaviour (B) phenotypes. Psychological co-morbidity was defined as a formal psychiatric diagnosis, regular psychiatry/psychology input (or intention for this if repeated family refusal), documented anxiety or depression and deliberate self-harm.

Results: 138 patients graduated to adult services, 69% (95/138) had Crohn's disease (CD); 59% (56/95) male, 76% (72/95) with extensive disease (L3 or L3+L4) and 22% (21/95) B2 or B3 disease at time of transfer. Median (IQR) age at transfer 17.8 years (17.3, 18.4) and median (IQR) disease duration at transfer 5.4 years (4.6, 7.6). Median (IQR) length of FU post-transfer was 3.3 years (2.1, 5.1). 12% (11/95) had PTE with 4% (4/95) having PTR disease by time of transfer. PTE rates increased significantly to 26% (21/82) p=0.009 at LAFU and PTR disease to 18% (15/82) p=0.003; 13 patients lost to follow-up. 90% (19/21) of those with PTE had extensive disease and 48% (10/21) had B2 or B3 disease by LAFU. 80% (12/15) patients with PTR disease required bowel resection or a defunctioning stoma by LAFU, compared with 37% (30/82) of the whole CD cohort p=0.002. 24% (5/21) of those with PTE had significant psychological co-morbidity by LAFU.

Conclusion: Our novel data show that pan-treatment exposure in paediatric-onset CD is already significant by time of transfer to adult services and continues to increase to affect 26% of this regional cohort within a relatively short period of adult follow-up. 18% of paediatric-onset CD patients have failed all medical treatments by LAFU and 71% with PTE require resectional or defunctioning surgery to manage disease.

Disclosure of interest: Victoria Merrick, has received lecture fees from Dr Falk; Paul Henderson, has received lecture fees from Dr Falk; Ian Arnott, has received lecture fees from Tilletts and Shield, travel support and advisory board for Ferrinject; Jack Satsangi, has received financial support for research from CCUK, EC-FP7, CSO, EC-H2020, MRC, WT, lecture fees/travel support from Takeda, Ferring, Falk, MSD and consulted for Takeda; David Wilson has received financial support for research from MSD, lecture fees from Abbvie and consulted for Takeda.
Do self-selected "non-transitioned" referrals from paediatric services have lower treatment requirements?

Omar Shaikh¹, Philip Harvey¹, Rafeeq Muhammed², Rachel Cooney¹

¹University Hospital Birmingham, Department of Gastroenterology, Birmingham, United Kingdom
²Birmingham Children's Hospital, Department of Gastroenterology, Birmingham, United Kingdom

Objectives and study: Best practice guidelines stipulate children with long term health problems should have their care transitioned between paediatric services and adult health services. Our paediatric IBD patients are offered an appointment in a transition clinic, however non-attendance is high. The aim of this study is to compare treatment requirement (as a surrogate marker of disease severity) and service engagement between patients choosing to attend transition clinic (transitioned) and those not (non-transitioned patients).

Methods: All known IBD referrals from Birmingham Children’s Hospital to University Hospital Birmingham aged 16-18 years from 2010-13 were collected. Baseline demographics, disease status and treatment history were collected from both adult and paediatric settings. Post referral procedures, changes in treatment and clinic attendance data were collected.

Results: 57 patients were identified of which 33 were transitioned. Data regarding treatment prior to referral to adult services and changes post-referral are presented in table 1. Data is also presented for clinic attendance and follow-up length.

Conclusion: Fifty-eight percent of IBD patients referred from paediatric services chose to attend a transition clinic. Patients attending transition clinic are a self-selecting group in our cohort, as all are offered such a clinic appointment. Following referral both groups continue to have high therapy demands. A new course of steroids, starting Anti TNF therapy or surgical procedure was considered a surrogate for increased disease activity. Our data suggests that those attending a transition clinic are not less likely to flare, compared to those who did not attend. This is in contrast to other datasets which suggest that transition reduces disease flares. An assumption that patients choosing not to attend transition clinic have milder disease and need less intensive follow-up, is not supported by our data.
Objectives and study: The IMPACT-III is a validated, disease-specific HRQOL questionnaire for patients with inflammatory bowel disease (IBD) aged 9 to 17 years. Items within IMPACT III are grouped by domains, which cover different aspects of HRQOL. It takes 10 to 15 minutes to complete and contains 35 questions encompassing six domains: IBD symptoms, systemic symptoms, emotional functioning, social functioning, body image, and treatment/intervention.

As a means of assessing the impact of disease, all children receiving infliximab in our regional tertiary unit are encouraged to complete the IMPACT III questionnaire. Each child is encouraged to complete the questionnaire unaided on at least one hospital visit for infliximab infusion yearly. Blood investigations are routinely obtained and stools are collected for faecal calprotectin at each visit.

Aim: The aim of study is to review patient reported quality of life outcome measures in children receiving infliximab for Crohn's disease.

Methods: Completed questionnaires collected over a one year period (2015-2016) were retrospectively analysed and compared with blood investigations and faecal calprotectin obtained within 2 weeks of completing the questionnaire.

Children were excluded if they had received infliximab for less than 6 months or required infusions at greater than 5mg/kg/dose or more frequently than 8 weekly.

Results: Of the 41 children receiving infliximab during the study period, 30 completed forms were returned. Of these 18 fulfilled the inclusion criteria.

4 Children were noted to have a raised ESR and faecal calprotectin levels greater than twice the upper limit of normal. All but one patient recorded the lowest score across all domains.

One patient with one of the lowest total score recorded a near normal score for body image.
**Conclusion:** IMPACT III questionnaire is simple and easy to complete. Despite repeated hospital attendances and investigations all children with minimal disease activity scored highly. IMPACT-III questionnaire is a valuable tool in monitoring clinical response and disease activity in children receiving Infliximab.
5-year follow-up of the prospective nation-wide Hungarian Pediatric IBD Registry

Katalin Muller, Group HUPIR, Gábor Veres

Objectives and study: There is no nation-wide, 5 years follow-up epidemiological study of long-term disease course of pediatric inflammatory bowel disease (IBD), especially in the era of biologicals. The Hungarian Pediatric IBD Registry (HUPIR) is a nation-wide, prospective registry since 1st of January 2007. Follow-up data of the pediatric IBD cases diagnosed in 2010.

Methods: Newly diagnosed pediatric patients with IBD (ages 0–18 years) are registered in this prospective, nation-wide registry (HUPIR), and followed-up yearly. The questionnaire at registration includes epidemiological data, disease extension, disease activity (PCDAI, PUCAI) and initial therapy. The follow-up questionnaire consists of questions about number of relapses, therapy (medication and surgery), extraintestinal manifestation, anthropometrical data. Descriptive statistical methods were applied for data analysis and Kaplan-Meier analyses for the rates of relapses, bowel resection and biological therapy during the follow-up.

Results: Between 1st January 2007 and 31st December 2014, 1168 new IBD cases were identified (729 Crohn’s disease (CD), 365 ulcerative colitis (UC) and 74 IBD unclassified). Incidence of IBD increased from 7.1/105 to 8.7/105 during 8 years. One hundred-forty-seven newly diagnosed IBD cases (Crohn disease: n=96, ulcerative colitis: n=37, IBD-U: n=14) were registered in 2010. Median age at diagnosis was 15 years in Crohn’s disease, 13 years in UC and 12 years in IBD-U. In CD 21% of cases (17/82) had L1, 17% had L2 (14/82) and 61% had L3 (50/82) localization based on Paris Classification. Nine percent of UC patients (3/35) had proctitis, 31% of children had E2 localization (11/35), 11% of UC cases presented with extended colitis (4/35) and 49% of UC patients (17/35) had pancolitis (E4). Induction therapy in CD and UC were mainly steroid (CD: 64/96, [66%], UC: 19/37, [51%]) or mesalazine (CD: 87/96 [90%], UC: 31/37, [84%]) in Hungary.

By the end of the 5 years all data were available for 62 children (38 CD, 20 UC, 4 IBD-U). The reason for loss of cases (n=81) was mainly the transition to adult gastroenterologist (70%, 56/81). Relapse was detected in 46% of CD children (48/96), and in 50% of UC cases (18/37). Six percent of UC children (2/37) and 6% of CD patients (6/97) had steroid dependency, and 2 CD children were refractory to steroid therapy. Biologicals were applied in 22% of children with CD during the 5 years (21/96). Three children with UC got biological therapy. Bowel resection was performed in 9% of CD children during the 5 years, no colectomy was performed in UC cases (0/37).

Conclusion: Follow-up of pediatric IBD cases is difficult due to transition to adult health care. The management practice was different in Hungary from the international trends in 2010, however the disease course was similar to previous results.
Genital Crohn’s disease case series - natural history

Monica Negoita¹, Ian Sugarman², John William Lambert Puntis³, Veena Zamvar⁴, Rakesh Vora¹, Sally Grange¹

¹Leeds Teaching Hospitals, Paediatric Gastroenterology, Leeds, United Kingdom
²Leeds Teaching Hospitals, Paediatric Surgery, Leeds, United Kingdom
³Leeds, United Kingdom
⁴Leeds General Infirmary, Paediatric Gastroenterology, Leeds, United Kingdom

Objectives and study: Crohn’s Disease (CD) is an inflammatory bowel disease of increasing prevalence¹ with 25-40% patients having extra-intestinal manifestations². Genital CD lesions are rare in childhood and its management is challenging³. Our study aimed to look at the natural history of Genital CD. The response to various treatments on luminal and genital CD was also noted.

Methods: We did a retrospective case note review of patients with genital CD attending our tertiary Paediatric Gastroenterology Service. We collected data on inflammatory markers, histology, radiological investigations and CD phenotype using the Paris classification.

Results: Our cohort included 5 patients over the last 15 years (3 Males, 2 Females).

Genital CD onset ranged from 18 months to 10 years 3 months. Four patients had genital involvement several months to years before the onset of gastrointestinal symptoms. Genital CD symptoms included: scrotal oedema, erythema (3/3), penile swelling (2/3) with deviation of penis (1/3) and restricted micturition (1/3) for males; labial erythema, oedema (2/2) and perineal inflammation (1/2) for females.

Luminal CD onset ranged from 6 years to 11 years 9 months. CD phenotype was: A1aL3B3pG0, A1bL2B1pG0, A1aL2B1G0, A1aL2B1G0 and A1aL2B1G1. All had associated perianal disease of various severity, with skin tags (4/5), perianal fissures (2/5) and perianal fistula and abscesses (1/5). None of our patients had fistulating genital disease, however one had fistulating disease of the sigmoid. Other extra intestinal manifestations consisted of: seronegative arthropathy (1/5), psoriasiform dermatitis (1/5), hepatic cysts (1/5), granulomatous lung disease (1/5), delayed puberty requiring hormonal supplements (1/5). Two patients developed psychological problems leading to deliberate self-harm.

Conclusion: Genital CD is a rare, extra intestinal manifestation of CD. The onset of genital symptoms is early and has a poor response to conventional CD treatment. Most of our patients had their genital CD onset months to years before gastrointestinal CD onset. No correlation was noted between flare ups of luminal CD and of genital CD. Genital CD responded mostly to Anti-TNF treatment with some
benefit from local treatment agents. Early escalation of treatment may be considered in CD patients presenting with genital symptoms.
Serum infliximab concentrations and antibodies in pediatric inflammatory bowel disease

Samuele Naviglio¹, Eva Cuzzoni², Adriana Cifù³, Doriani Lacorte⁴, Stefano Martelossi⁵, Patrizia Alvisi⁴, Diego Favretto⁵, Marianna Lucafò², Martina Pozzi Mucelli², Andrea Taddio², Gabriele Stocco⁶, Giuliana Decorti², Martina Fabris², Alessandro Ventura⁵

¹University of Trieste, PhD School in Reproductive and Developmental Sciences, Trieste, Italy
²University of Trieste, Department of Medical, Surgical and Health Sciences, Trieste, Italy
³University of Udine, Department of Medical and Biological Sciences, Udine, Italy
⁴Ospedale Maggiore, Paediatric Department, Bologna, Italy
⁵Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Paediatric Department, Trieste, Italy
⁶University of Trieste, Department of Life Sciences, Trieste, Italy
⁷University of Udine, Department of Laboratory Medicine, Udine, Italy

Objectives and study: Anti-tumor necrosis factor (TNF) agents, in particular infliximab, have become the mainstay of treatment in refractory inflammatory bowel diseases (IBD), also in pediatric patients. Furthermore, they also seem to be promising as first line treatment in early-stage IBD, yet their widespread use in all patients could not be affordable by the national health systems. However, while the mechanism of action of anti-TNF agents has been investigated, it is still not completely understood why clinical response differs among patients. There is some evidence suggesting that the loss of response in patients treated with infliximab may be in part the result of failure to achieve and maintain adequate drug levels and/or of the formation anti-infliximab antibodies (AIA). To date, data regarding therapeutic drug monitoring of infliximab in children are incomplete. The objective of this study is to evaluate the association between pharmacokinetics (i.e, concentration of infliximab and AIA) and clinical response to infliximab therapy in pediatric IBD patients.

Methods: We studied 49 pediatric (median age 14.4, interquartile range 11.6-16.2) IBD patients (CD 34) from the Pediatric units of Bologna and Trieste, treated with standard therapeutic scheme. Serum samples were collected at week 6, 14, 22 and 54 of therapy, before infusion. Infliximab and AIA were measured using commercial ELISA assays. Clinical disease activity was determined by PUCAI (UC) and PCDAI (CD) at the end of induction therapy (week 14) and after 54 weeks of therapy. Acute adverse reactions were recorded.

Results: Clinical remission, defined as a clinical score <10, was obtained by 76.3% of patients at week 14 and by 73.9% at week 54. Median trough infliximab concentration was higher in patients with inactive disease compared to patients who did not respond to treatment at week 14 (respectively 4.1 and 0.4 µg/ml, p-value = 2.0×10⁻³) and at week 54 (respectively 4.8 vs 1.4 µg/ml, p-value = 6.9×10⁻⁵). No other significant association was found between infliximab concentration and clinical efficacy. An optimal predictor of durable sustained response to infliximab was week 14 infliximab trough level ≥3.12 µg/ml (sensitivity 89%, specificity 100%). AIA concentrations were inversely correlated with infliximab trough concentration (p-value = 1.9×10⁻¹⁴) and with the occurrence of acute severe reactions requiring therapy interruption (p-value = 0.015).

Conclusion: Measurement of infliximab trough levels at the end of induction therapy (week 14) is indicative of disease activity and of durable sustained long-term response in pediatric patients with IBD. Patients with high levels of AIA present increased probability of unsuccessful infliximab therapy. More prospective studies are needed to identify the best therapy adjustment to maintain infliximab response in patients with low trough infliximab levels at the end of induction therapy or with high AIA concentration.
Potential association between congenital chloride diarrhea and inflammatory bowel disease

Lorenzo Norsa¹, Bénédicte Pigneur¹, Olivier Goulet¹, Cécile Talbotec¹, Hélène Garnier-Lengliné¹, Frank Ruemmele¹

¹Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France

Objectives and study: Congenital chloride diarrhea (CLD) is a rare autosomal recessive disease caused by the mutation in the member 3 of the solute carrier 26 (SLC26A3). The phenotypic expression is a life-long severe watery Cl⁻ rich diarrhea. At the current stage we dispose only of symptomatic treatments. Few associations with inflammatory bowel disease (IBD) has been described in the clinical experience. However, the underlying molecular mechanisms are completely unknown.

Methods: In our center, six patients were followed on a regular basis with a diagnosis of CLD. Two patients developed IBD and their clinical presentation is described herein and compared to the four patients without IBD.

Results: The first patient is a male of Malian origin who developed a Crohn-like colitis at the age of 12. After some partially successful attempts of treatment, he is now stable on adalimumab since 2012. The second is a female of consanguineous Algerian parents who developed an ulcerative rectitis at the age of 5. She is also in remission on a 5-ASA since 6 months. No significant difference were found in gestational age, birth weight, stool’s chloride concentration at diagnosis end chloride supplementation at follow-up between patients with concomitant IBD and the others.

Conclusion: 2/6 CLD patients developed IBD in our cohort. So far no clinical markers was identified to be predictive of the development of IBD in CLD patients. The role of genetical predisposition and the colonic microbiome in this association is under investigation.
Keep an eye on inflammatory bowel disease in children

Giorgio Ottaviano¹, Samuele Naviglio², Stefano Martelossi³, Chiara Luini¹, Silvia Salvatore¹

¹University of Insubria, Varese, Italy
²University of Trieste, PhD School in Reproductive and Developmental Sciences, Trieste, Italy
³Institute for Maternal and Child Health - Irccs “Burlo Garofolo”, Paediatric Department, Trieste, Italy

Objectives and study: Ocular involvement is a recognized extra-intestinal manifestation (EIM) of both Crohn Disease (CD) and Ulcerative Colitis (UC). Data on prevalence of ocular manifestations in inflammatory bowel disease (IBD-OM) are inconsistent and there is no consensus on ophthalmological management. We aimed to evaluate the prevalence of IBD-OM in children.

Methods: We performed a systematic review of IBD-OM. In November 2016 we searched PubMed and EMBASE databases using the following queries: [1] (uveitis OR one of the following: scleritis, episcleritis iritis, iridocyclitis, choroiditis, retinitis, papillitis, ocular, eye, ophthalmologic, ophthalmic, orbital, retinal, optic, dacroyoadenitis, keratopathy, corneal, conjunctivitis, blepharitis, cataract, intraocular, “visual acuity”, blindness, uveal OR lacrimal) AND (Crohn OR “ulcerative colitis” OR “inflammatory bowel disease”), [2] (“extra(-)intestinal manifestation(s)” AND (“Crohn” or “ulcerative colitis” OR “inflammatory bowel disease”). Two authors independently reviewed search results and found a consensus on the articles to be included. Age (< 18 years) and English language restrictions were applied.

Results: We identified 3 large cohort studies on EIM of IBD pediatric patients with data about OM were reported. Prevalence of uveitis/iritis was 0.7% - 1.8%, yet in all three studies it was higher in patients who also had other EIMs (2.5% - 10.9%). No other OM were considered. Four studies reported data on small cohorts of asymptomatic children who underwent ophthalmological screening. Prevalence of asymptomatic uveitis was higher than in cohort studies on EIMs (4.1%-23.1%), with increased frequency in CD patients (CD/UC:16/1), males (M/F:13/4) and teen-agers (mean age 14.4 years). Colonic involvement was present in nearly all patients but the number of cases was too low to identify a specific risk phenotype. One study showed an increased risk of cataract in patients treated with steroids. Finally we identified 23 case reports of different IBD-OM in children which included: central retinal vein/artery obstruction, orbital myositis/pseudotumor, choroidal neovascular membrane, naso-lacrimal duct obstruction, dacroyoadenitis, dry eyes syndrome, cataract, bilateral uveitis, episcleritis, keratitis, granulomatous conjunctivitis, optical neuritis, and recurrent neuroretinitis affecting. These complications rarely preceded IBD diagnosis. Scarce data on possible association between IBD-OM and other EIMs, HLA-B27 or disease localization are available.

Conclusions: Prevalence of IBD-OM may be underestimated in children because of possible asymptomatic uveitis and no routine ophthalmological examination. The scarce data in the literature do not allow a correct management and a tailored approach in these patients. New studies on larger pediatric IBD populations are needed to identify clinical phenotypes predisposing to ocular complications and to make clear recommendations on ophthalmological follow up in IBD children.
Pediatric inflammatory bowel diseases in Turkey: results of Turkish pediatric IBD Database

Funda Ozgenc1, Zarife Kuloğlu2, Nafiye Urganci3, Tulay Erkan4, Zerrin Onal5, Sinan Sari6, Turkish Pediatric IBD Study Group7

1Ege University, Pediatric Gastroenterology, Hepatology and Nutrition, Izmir, Turkey
2Ankara University School of Medicine, Paediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
3Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
4Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
5Kanuni Sultan Suleyman Training and Education Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
6Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
7Turkish Society, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey

Objectives and study: To investigate clinical, laboratory and histological characteristics of Turkish children with IBD in a large multicenter, national database.

Methods: Pediatric IBD database (turkpedibh) was constructed and 58 representative gastroenterologists from 43 centers have consented to collect and report patient data to the database. Turkpedibh included demographic features, clinical symptoms, diagnostic work-up, treatment and response; old and new IBD cases' data was entered between October 2012 and October 2016. Data was statistically analyzed by using PAWS 18.0 for windows.

Results: During the study period, 1013 cases were collected. Duplicating cases among centers and cases with insufficient data input were excluded and analyses were made in 935 cases. Seven hundred eighty cases originated from urban areas; whereas, 152 (16.3%) cases lived in rural areas. Case load of the western border of the country (n: 418, 81%) was significantly higher than the eastern border (n: 98, 19%) (p<0.01). Ulcerative colitis (UC) was identified in 556 cases (59.5%) and Chron’s disease (CD), indeterminate disease were identified in 327 (35.0%) and 52 (5.6%) cases, respectively. Local and extensive disease was observed in 163 (51.3%) and 155 (48.7%) CD patients, respectively with a median CHAI score of 37.5 (Q1:26, Q3:50). Disease extend was identified E1 in 69 (12.7%), E2 in 150 (27.5%) and E3 in 326 (59.8%) UC cases with a median PUCAI score of 50 (Q1:30, Q3:60). Main clinical and laboratory patient characteristics are shown in table1. Treatment response in a selected group of patients with standard dose corticosteroid monotherapy was evaluated in 214 CD patients (86.3%) and 366 (92.2%) UC cases (p: 0.015). Relapse rate was 25.9% (55/214) and 32.4% (117/366) in CD and UC, respectively (p:0.103). Mean relapse free survival in steroid responders was 122 months for CD and 133+ months for UC.
**Table:** Clinical and laboratory patient characteristics

<table>
<thead>
<tr>
<th></th>
<th>Colitis Ulcerative (N=556)</th>
<th>Crohn Disease (N=327)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age (years)</td>
<td>12 (Q₁:7, Q₃:14)</td>
<td>12 (Q₁:9, Q₃:14)</td>
<td>0.033</td>
</tr>
<tr>
<td>Cases presented &lt;5 years old (n, percent)</td>
<td>63 (11.3%)</td>
<td>63 (19.3%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Male sex (n, %)</td>
<td>271 (48.7%)</td>
<td>178 (55.4%)</td>
<td>0.109</td>
</tr>
<tr>
<td>Parental consanguinity (n, %)</td>
<td>84 (16.6%)</td>
<td>78 (24.8%)</td>
<td>0.004</td>
</tr>
<tr>
<td>Main presenting symptoms (n, %)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>🧠 Abdominal pain</td>
<td>405 (72.8)</td>
<td>261 (79.8)</td>
<td>0.02</td>
</tr>
<tr>
<td>🧠 Weight loss</td>
<td>217 (39)</td>
<td>176 (53.8)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>🧠 Bloody diarrhea</td>
<td>442 (79.5)</td>
<td>94 (28.7)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>🧠 Chronic diarrhea</td>
<td>230 (41.4)</td>
<td>231 (70.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Perianal disease (n, %)</td>
<td>10 (1.8)</td>
<td>50 (15.3)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median CRP (mg/dl)</td>
<td>3.22</td>
<td>7.30</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td></td>
<td>(Q₁:0.70, Q₃:12.0)</td>
<td>(Q₁:2.50, Q₃:26.0)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Pediatric IBD is predominant in western parts of Turkey in urban residence. Ulcerative colitis prevails in Turkish children and tends to be extensive disease with relevant steroid response.
A prospective 52-week mucosal Healing and deep remission assessment of small bowel and colonic Crohn's disease as detected by colon capsule endoscopy

Salvatore Oliva¹, Fortunata Civitelli¹, Marina Alo¹, Franca Viola¹, Francesca Maccioni², Paola Papoff³, Stanley Cohen⁴, Salvatore Cucchiara¹

¹Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
²Sapienza University of Rome, Radiological Sciences, Oncology, and Pathology, Rome, Italy
³Sapienza University of Rome, Picu, Department of Paediatrics, Rome, Italy
⁴Children's Center for Digestive Health Care, Atlanta, United States

Objectives and study: There are no data on long-term mucosal healing (MH) and deep remission (DR) in children with Crohn’s disease (CD). Previously, we reported prospectively assessed MH and DR rates on the entire GI tract by performing two CCE over 24 weeks in children with CD, in comparison with biomarkers, magnetic resonance enterography (MRE) and SB contrast ultrasonography (SICUS). This extension evaluates MH and DR in the same cohort of patients at 52-week follow-up. The long-term efficacy of a “treat-to-target” strategy was also evaluated at the end of the study.

Methods: Children with known CD were prospectively recruited and underwent imaging studies followed by CCE, at 0, 24 and 52 weeks. The Lewis score (LS) and Simple endoscopic score for Crohn’s disease (SES-CD) were calculated for SB and colon, respectively. C-reactive protein (CRP) and fecal calprotectin (FC) were also evaluated for their association with clinical activity, imaging and CCE findings. Clinical remission was defined as PCDAI<10. SB and colonic MH were defined as LS<135 and SES-CD ≤1, respectively; moderate-to-severe inflammation was defined as LS >790 or SES-CD >7. Biomarker remission (BR) was defined as a combination of clinical remission (PCDAI<10) and normal biomarkers. Deep remission (DR) was defined as a combination of BR and MH. Therapy was calibrated according to CCE results at baseline and week 24.

Results: Of 48 patients (pts) recruited, 46 completed the 52-week evaluation (2 developed an ileo-cecal valve stricture). At baseline, 22 were clinically active and 26 were in remission. After a “treat to target strategy”, at week 24, only 8 were in clinical activity, while 40 were in remission. CCE identified DR in 26/40 (54%) of the remission group; while in 8 with mild clinical activity (100%) showed a partial MH (according to baseline evaluation). At 52 weeks, CCE showed DR in 28 (58%); with the detection of new lesions in 4 and a complete MH in 6 (with previous partial MH at 24 weeks). MRE and SICUS had good concordance in evaluating DR (24/28, 86%), but did not identify mucosal lesions in 4 as well as mucosal improvements after therapy (p<0.05). FC and CRP were not able to accurately evaluate DR in either groups at 24 and 52 weeks (BR in 65% and 69%, respectively). The DR and MH rates increased over the time (23% to 58%) and by using CCE and a treat to target strategy.

Conclusion: This study evaluates long-term MH and DR rate in children with CD and indicates that CCE is effective for monitoring long as well as short term DR and MH of the entire GI tract and in directing therapy for pediatric patients with CD. Additional studies are needed to explore these issues further.

Disclosure of interest: Salvatore Oliva, Conflict with Medtronic
Stanley Cohen, Conflict with Medtronic
20 years single tertiary centre experience of medical and surgical management of paediatric perianal Crohn’s disease

Raj Parmar, Christos Tzivinikos, Venkatesh Krishnappa, Sarang Tamhne, Marcus Auth

1 Alder Hey Children's Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition (Ghn), Liverpool, United Kingdom
2 Alder Hey Children's NHS Foundation Trust, Department of Paediatric Gastroenterology, Hepatology and Nutrition (Ghn), Liverpool, United Kingdom

Objectives and study: Perianal Crohn disease (PCD) is defined as inflammatory changes around the anus, including tags, fissures, fistulae, abscesses or stenosis. There is no consensus of the exact classification of the fistulae nor in their medical and surgical management. In this study, we reviewed characteristics of our cohort of paediatric Crohn's perianal disease and perianal fistulising disease (CD-PAF) including their management and long term outcomes.

Methods: A retrospective study conducted in one of UK’s major tertiary paediatric gastroenterology and surgical unit. Patients were identified using medical coding and relevant information collected using hospital inpatient records, clinic letters and hospital electronic patient record database system. We collected data for period 1994 – 2010 for perianal disease and from 2010-2016 with focus on perianal fistulising disease.

Results: Study period (1994-2010): total of 59 PCD cases were identified. Out of which Male:Female ratio is 1.5:1. Age at diagnosis of PCD ranges 2 -16 years, with mean age 11 years. Most common perianal lesion was fissure (n=35), followed by abscess (n=24), fistula and skin tag (each n= 19) and anal stenosis the least with 5 cases. In terms of initial surgical procedure, most common was abscess drainage (17), followed by examination under anaesthesia (EUA) in 14 cases. Seton insertion was done in only 10 cases. We have noticed significant difference in medical management approach in pre and post diagnosis of PCD (figure 1). Use of both azathioprine and mesalazine increased by approx. 8 fold (Azathioprine 44:6 and mesalazine 41:5). Use of Infliximab nearly doubled (7:4) and steroid use increased by 4 fold (31:8). Majority of cases (45) were started on exclusive enteral nutrition at initial diagnosis of CD. Adalimumab was prescribed in only 2 cases. On long term follow up nearly half of cases i.e. 29 out of 59 cases required major bowel surgery including hemicolectomy, pan-proctocolectomy and stoma formation.

Study period (2010-2016): we have identified n=24 cases of fistulising disease. Male: female ratio is 2.4:1. Mean age at diagnosis of CD-PAF was 12.5 years. In terms of surgical procedure most common was EUA (21) followed by abscess drainage (18) and seton insertion done in 9 cases. Use of immunosuppressant (Azathioprine) doubled from n=12 to n=23 in pre-and post fistula phase. Use of biologics (Infliximab, biosimilar, adalimumab) quadrupled from 5 to 20 in pre and post fistula phase. Clinical fistula healing in half of cases was partial healing i.e. 14 followed by complete healing in 6 and no healing in 4 cases.
Conclusion: Our study shows that diagnosis of PCD and CD-PAF lead to major changes in medical approach to treatment. Our unit has started using biologics from 2007 which is demonstrated by higher prescription of anti-TNFs in second study period. Significant proportion of fistulising patient had partial or complete clinical and radiological healing. It is worth recognising that irrespective of intensive combined medical and surgical input paediatric PCD carries risk of major bowel surgery which has huge implications in terms of morbidity and increased mortality from complications. There is huge variation in medical and surgical management even inter unit variation. There is need for further registry and interventional studies of combined medical and surgical approach to guide optimum future management.
Immunization status of children and adolescents with inflammatory bowel disease or autoimmune hepatitis in Germany

Luana Cagol1, Klara Frivolt2, Andreas Krahl3, Elke Lainka4, Patrick Gerner5, Dietrich Ney6, Jan Vermehren7, Michael Radke8, Stefan Trenkel8, Sibylle Koletzko2, Carsten Posovszky1

1University Medical Center Ulm, Department of Pediatric and Adolescent Medicine, Ulm, Germany
2Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
3Children's Hospital „prinzessin Margaret“, Darmstadt, Germany
4University Hospital Essen, Clinic for Paediatrics II, Essen, Germany
5Zentrum für Kinder- und Jugendmedizin, Department of Pediatric and Adolescent Medicine, Freiburg, Germany
6Katholisches Kinderkrankenhaus Wilhelmstift, Hamburg, Germany
7University Medical Center Regensburg, Department of Pediatric and Adolescent Medicine, Regensburg, Germany
8Klinikum Westbrandenburg, Department of Pediatric and Adolescent Medicine, Potsdam, Germany

Objectives and study: Long-term immunosuppressed patients with inflammatory bowel disease (IBD) and autoimmune hepatitis (AIH) are at risk of severe infections with vaccination preventable diseases. Several recent studies demonstrated insufficient immunization coverage in children and adolescents with IBD. Therefore, we evaluated the vaccination rate of children and adolescents with IBD and AIH in Germany.

Methods: As part of the German multicentre clinical trial called „VARICED“, the immunization rate of patients with IBD and AIH below 18 years of age was assessed from the certificate of vaccination, medical history of chicken pox and by analysing varicella zoster virus (VZV) IgG and measles virus IgG antibody titres by ELISA.

Results: To date 229 patients (51% female, mean age at diagnosis 9.9 years) are registered: 137 have Crohn’s disease (CD), 53 ulcerative colitis (UC), 19 IBD-unclassified (IBD-U) and 20 AIH. The majority of the patients (n=190, 83%) are on immunosuppressive therapy (AIH 100%, CD 89%, UC 68%). A complete basic immunisation consisting of 4 doses of a hexavalent vaccine were given to 89% of the total cohort. A combined inoculation for measles, mumps, and rubella (MMR) was documented in 225 (98%) patients, 208 (92%) received two doses. However, 10% of the immunized patients did not display sufficient measles IgG antibodies irrespective of the vaccination mode. VZV vaccination was introduced in 2004 to the vaccination schedule from the German Standing Committee on Vaccination (STIKO). A good implementation with 90% was found in the birth cohorts from 2005 onwards. In children born before 2005 (n=190) only 22% received VZV vaccination catch up. VZV vaccination was documented in only 77 (34%) patients, but 17 patients (23%) did not display sufficient VZV IgG titres. Already 144 (63%) patients had a medical history of chicken pox. However, three of them did not have verifiable VZV IgG antibodies. In addition, 17 patients had neither a history of a chicken pox infection nor VZV inoculation, but 11 out of them were found to have sufficient VZV IgG titres.

Conclusion: There is a good implementation of the vaccination schedule from the German Standing Committee on Vaccination (STIKO) in the group of children and adolescents with IBD and AIH. Our data suggests a gap in VZV immunity in birth cohorts before 2005 in Germany. Moreover, neither the certificate of vaccination nor the medical history of chicken pox infection is reliable for assessing VZV immunity. Serologic investigations demonstrated that some non-immunized patients may undergo occult immunization, and immunized patients did not present sufficient VZV or measles IgG titres. Thus, we recommend VZV and measles IgG serology within the check-up in newly diagnosed patients and VZV and measles vaccination before initiating immunosuppressive therapy, if applicable.
Objectives and study: Children suspected of IBD (Inflammatory Bowel Disease) often undergo multiple diagnostic tests, including upper endoscopy and colonoscopy with biopsies, as well as MR (Magnetic Resonance) or CT (Computed Tomography) enterography. It is crucial to promptly select patients with a great risk of IBD diagnosis among children with symptoms including abdominal pain and diarrhoea before applying invasive diagnostic tools. In this study the frequency of particular symptoms in patients with IBD compared to a group of children with FGID (Functional Gastrointestinal Disorders) was analysed. Moreover, we tried to show the usefulness of basic blood tests and ultrasonography in the selection of patients with suspicion of IBD.

Methods: The retrospective study was performed on a group of 96 children with IBD and 27 subjects with FGID hospitalised between 2007 and 2015. Based on medical charts we analyzed the presence of symptoms such as abdominal pain and diarrhoea as well as basic laboratory tests: BPT (Blood Platelet Count), ESR (Erythrocyte Sedimentation Rate) and concentration values of CRP (C-reactive protein). Detailed sonographic evaluation of the small bowel wall thickness was performed with a linear high-frequency transducer (3-13 MHz. Phillips, model HD 11XE). All patients underwent colonoscopy with ileum biopsy. The diagnosis of IBD was confirmed by histopathologic examination in all cases. The FGID diagnosis was based on Rome III Diagnostic Criteria.

Results: The studied groups consisted of 66 girls (53.7%) and 57 boys (46.3%). The mean age of the patients at the time of the study was 13.0 years. Abdominal pain was more frequently observed in the group of children with FGID than in patients with IBD (92.6% vs. 77.1%, p<0.05) while diarrhoea was noted mainly in the IBD group compared to the FGID one (81.2% vs. 51.8%, p<0.05). Median levels of ESR, CRP and BPC were significantly higher in the IBD group compared to the FGID group (24.5 ± 16.7 vs. 4.33 ± 4.0; 2.9 ± 3.3 vs. 0.5 ± 0.0; 399.9 ± 92.1 vs. 253.0 ± 62.9; p<0.05). Setting the platelet count cut-off at 330x10^3 entailed specificity of 88.9% and sensitivity of 71.9%. The mean terminal ileum wall thickening was higher for Crohn’s Disease (3.5 mm ± 2.5) than for Ulcerative Colitis (2.3 ± 1.2) and FGID (1.9 ± 1.1) (p<0.05). The standard value of 3 mm induced specificity amounting to 81.5% and sensitivity of 34.4%.

Conclusion: In order to eliminate unnecessary exposure to ionizing radiation and the possible complications during endoscopy, first clinical approach in children with abdominal pain and diarrhoea should include a thorough medical history, simple laboratory tests and terminal ileum wall ultrasound.
Pulmonary necrobiotic nodules: a rare manifestation of Crohn’s disease in paediatric patients

Jesús Gónzalez1, Gemma Pujol1, Cristina Molera Busoms1, Jordi Costa2, I Masiques3, Javier Martin de Carpi4

1Hospital Sant Joan de Déu, Unit for the Comprehensive Care of Pediatric Inflammatory Bowel Disease, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
2Hospital Sant Joan de Déu, Paediatric Pneumology Department, Barcelona, Spain
3Hospital General de Granollers, Paediatric Gastroenterology Department, Granollers, Spain
4Sant Joan de Deu Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain

Objectives and study: Pulmonary manifestations of Crohn’s disease are very unfrequent in paediatric patients. The findings of pulmonary nodules suppose an important challenge in diagnosis and treatment of these patients. We present the second reported case of necrobiotic pulmonary nodules in a paediatric patient and the first one treated with anti-TNF alpha on initial diagnosis.

Case description: A 14-year-old male, with no personal history of interest, who was admitted to hospital because of diarrhea, abdominal pain, anorexia and weight loss for three months. On physical examination the patient had affected appearance, pallor, supraumbilical pain and an anal fissure. The initial blood tests showed microcytic anemia, iron deficiency, hypoalbuminemia, thrombocytosis, elevated inflammatory markers (erythrocyte sedimentation rate, C-reactive protein and Fecal Calprotectin). Esophagogastroduodenoscopy, ileocolonoscopy and MR enterography were compatible with colonic Crohn’s disease. The patient started treatment with exclusive enteral nutrition, however it was discontinued after two weeks due to persistent digestive symptoms and poor adherence to treatment. In the examination prior to initiating anti-TNF alpha therapy (Infliximab), the chest X-Ray showed bilateral nodular lung lesions of peripheral distribution and the patient began to experience high fever, dyspnea, chest pain, musculoskeletal and dermatological manifestations. PET-CT showed hypermetabolic pulmonary nodular lesions, predominantly peripheral and a single cavity lesion. Autoimmune and infectious tests and tumor markers were negative. Lung biopsy was performed and the histological results reported necrobiotic abscessed nodules in relation to extraintestinal manifestation. Anti-TNF alpha treatment was initiated at standard doses aiming for improvement of digestive, musculoskeletal and dermatological symptoms in the first 24 hours and analytical, radiological and pulmonary function findings in 4 weeks.

Conclusion: Pulmonary necrobiotic nodules represent a rare extraintestinal manifestation of Crohn’s disease in pediatric patients (only one case has been reported in the literature). Anti-TNF alpha therapy can be an effective treatment, as occurs with another extraintestinal manifestations.
Shared decision making in the choice of anti-TNF in paediatric Crohn’s disease

Gemma Pujol, Jesús Gónzalez, Johanna Martínez Osorio, Belinda García, Víctor Vila Miravet, Javier Martín de Carpi

1Hospital Sant Joan de Déu, Unit for the Comprehensive Care of Pediatric Inflammatory Bowel Disease. Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
2Sant Joan de Déu Hospital, Barcelona, Paediatric Gastroenterology, Hepatology and Nutrition Unit., Barcelona, Spain

Objectives and study: Infliximab (IFX) and Adalimumab (ADA) are the two approved anti-TNFα drugs for Paediatric Crohn’s disease (P-CD) treatment showing comparable efficacy and safety for induction and maintenance of remission. In our center, some patients and parents are invited to participate in the choice of the anti-TNF. Our aim is to analyze baseline characteristics and outcomes of this group of patients, comparing these results with those from patients who are not given this option of shared decision.

Methods: retrospective study of P-CD patients (<18 years) who initiate anti-TNFα therapy at some point of the disease evolution in a tertiary Hospital between July 2007 and December 2015. T-student test was used for quantitative variables and Chi-square for qualitative ones.

Results: Sixty-six patients were included; 56% (n=37) were given the option to choose the drug and 44% (n=29) were not. There were not statistically significant differences between sex, age and disease duration between both groups. The reasons for not offering a shared decision making were: 20 with specific clinical presentation (8 perianal disease, 6 extra-intestinal manifestations requiring the anti-TNF, 3 B2-B3 phenotype, and 3 combination of features), 3 for socio-familial reasons (3 IFX), 1 start treatment in other center (IFX) and 5 the cause was not known (4 IFX and 1 ADA). In the group that participated in the election of the treatment 89% (n=33) chose ADA versus 11% (n=4) that preferred IFX, while in the other group 72.4% (n=21) started IFX and 27.6% (n=8) initiated ADA, showing significant statistically differences (p<0.05) between both groups. Analyzing PCDAI at the start of anti-TNFα, a lower mean value (19.59) was observed in the choice versus non-choice group (33.69) (p<0.05). Regarding remission rate at 6 and 12 months after starting biologic treatment no statistically significant differences were found between those who chose (100% and 95.2%) and those who did not (84.6% and 89.5%), nor among those who chose ADA or IFX (p>0.05).

Conclusion: The choice of the anti-TNF-α drug by a selected group of patients with P-CD and their families does not influence the response to the drug and the course of the disease, being a safe practice that allows their involvement in decision making regarding treatment options. In our series, most of our patients choose ADA, probably in relation to the possibility of outpatient administration.
Risk of colectomy in patients with pediatric-onset ulcerative colitis

Firas Rinawi1, Assa Amit2, Rami Eliakim3, Yael Mozer – Glassberg1, Vered Nachmias Friedler1, Yaron Niv4, Yoram Rosenbach1, Ari Silbermintz1, Noam Zevit5, Raanan Shamir6

1Schneider Children's Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach - Tikva, Israel
2Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Hospital, Petach Tikva, Israel
3Sheba Medical Center -Tel Hashomer, Department of Gastroenterology, Tel Aviv, Israel
4Rabin Medical Center -Tel Hashomer, Department of Gastroenterology, Petach Tikva, Israel
5Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Petach-Tikva, Israel
6Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel

Objectives and study: Data describing the incidence and risk factors for colectomy in pediatric ulcerative colitis (UC) is inconsistent. Our aim was to describe the colectomy rate and to identify risk factors associated with colectomy in a large cohort of children with UC with long term follow up.

Methods: We performed a retrospective chart review of pediatric UC cases that were diagnosed at Schneider Children's Medical Center of Israel between 1981 to 2013. Potential predictors for colectomy including age at diagnosis, gender, disease extent, severity indices and different therapeutic regimens during disease course were assessed.

Results: Of 188 patients with pediatric onset UC, 34 (18%) underwent colectomy. Median follow-up was 6.9 years (range, 1-30). Kaplan – Meier survival estimates of the cumulative probability for colectomy were 4% at one year and 17% at 10 years from diagnosis. Multivariate Cox models showed that male gender (HR 4.2, P = 0.001) and severe disease at diagnosis reflected by Pediatric Ulcerative Colitis Activity Index (PUCAI) score ≥ 65 (HR 8.9, P < 0.001) were associated with increased risk for colectomy. Age, disease extent, ethnicity, family history of inflammatory bowel disease, early introduction of immunomodulators, treatment with anti-tumor necrosis factor α agent or diagnosis prior to the year 2000 did not affect the risk of colectomy.

Conclusions: Male sex and higher PUCAI score at diagnosis are independent risk factors for colectomy while anti-tumor necrosis factor α treatment and diagnosis during the "biologic era" are not associated with diminished long-term surgical risk.
Clinical and phenotypic differences in inflammatory bowel disease among Arab and Jewish children in Israel

Firas Rinawi1, Assa Amit2, Husam Basher3, Sarit Peleg4, Raanan Shamir5

1Schneider Children's Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach - Tikva, Israel
2Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Hospital, Petach Tikva, Israel
3Haemeq Medical Center, Pediatric Department A', Afula, Israel
4Emek Medical Center, Director of Paediatric Gastroenterology Unit, Afula, Israel
5Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel

Objectives and study: Data regarding disease phenotype among the Arab population in Israel or in the neighboring Arab countries is scarce. Our aim was to assess differences in patient's characteristics and disease phenotype of inflammatory bowel disease (IBD) among Arab and Jewish children living in Israel.

Methods: We performed a retrospective chart review of pediatric IBD cases, including Crohn's disease (CD) and ulcerative colitis (UC), which were diagnosed at Schneider Children's Medical Center and HaEmek Medical Center in Israel between 2000 to 2015. Demographic, clinical and phenotypic parameters were compared between Arabs, Sephardi and Ashkenazi Jews.

Results: Seventy one Arab children with IBD (39 CD and 32 UC) were compared with 145 Ashkenazi (115 CD and 30 UC) and 143 Sephardi Jewish children (96 CD and 47 UC). There were no differences in gender or age between groups. Arab CD patients had significantly higher short pediatric Crohn's disease activity index (shPCDAI) at diagnosis compared with both Sephardi and Ashkenazi Jews (45 versus 40 and 35, p=0.017). Sephardi and Ashkenazi Jewish CD patients had significantly more stenotic behavior (24% and 26% versus 5%, p=0.03) and less perianal involvement (15% and 11% versus 31%, p=0.014) compared with Arab patients. Arab children with UC had more severe disease at diagnosis compared to Sephardi and Ashkenazi Jews reflected by higher Pediatric UC Activity Index (PUCAI) (45 versus 35 ad 35 respectively, p=0.03) and more involuntary weight loss (>10% during less than 6 months) at diagnosis (33% versus 20% and 21%, p=0.001). UC disease extent did not differ between the groups. Arab patients had significantly lower proportion of ASCA positivity (in CD) and p-ANCA positivity (in UC) than both Sephardi and Ashkenazi Jewish children (23% versus 53% and 65%, p=0.002 and 35% versus 60% and 75%, p=0.002) respectively.

Conclusion: Arab and Jewish children with IBD differ in disease characteristics and severity. Whether genetic or environmental factors are the cause for these differences is yet to be determined.
Clinical significance of "low transaminase levels" in children with inflammatory bowel disease

Murat Cakir¹, Elif Sağ¹, Fatih Unal², Erhun Kasırğa³

¹Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
²Bursa, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Bursa, Turkey
³Celal Bayar University School of Medicine, Department of Paediatric Gastroenterology, Manisa, Turkey

Objectives and study: Liver involvement, ranges from transient elevated liver enzymes to end-stage liver disease that requires transplantation, is a common extra-intestinal manifestation of inflammatory bowel disease (IBD) in children. On the other hand, low transaminase levels (LTLs) (ALT and/or AST ≤5 U/L) may be seen in some patients during initial or follow-up laboratory examinations. It was shown that LTLs is associated with vitamin B6 deficiency, sarcopenia and increased risk of long term mortality in adult patients. Vitamin B6 deficiency and malnutrition are common finding in children with IBD. Therefore, we aimed to analyze the clinical importance of LTLs in children with IBD.

Methods: Medical records of 85 children (47 F, 11.9 ± 4 years) in 3 medical centers with IBD (51 UC, 32 CD and 2 IC) were reviewed. Patients with LTLs were analyzed in detail including demographic findings, clinical presentation and outcome.

Results: LTLs were found in 22 patients within 6 months after initial admission (25.8%). Demographic and clinical findings of the patients with and without LTLs are shown in Table 1. LTLs were more common in females and patients with CD and folic acid levels were low in patients with LTLs (p<0.05 for all).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>With LTLs (n=22)</th>
<th>Without LTLs (n=63)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean± SD, years</td>
<td>12.4 ± 3.1</td>
<td>11.8 ± 4.2</td>
<td>0.51</td>
</tr>
<tr>
<td>Gender, female n (%)</td>
<td>21 (95.4)</td>
<td>26 (41.2)</td>
<td>0.00001</td>
</tr>
<tr>
<td>Type of IBD, CD, n (%)</td>
<td>12 (54.5)</td>
<td>20 (31.7)</td>
<td>0.04</td>
</tr>
<tr>
<td>Underweight / Stunted, n (%)</td>
<td>6 (27.2) / 2 (9)</td>
<td>9 (14.2) / 6 (9.5)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Hemoglobin, mean± SD, g/dl</td>
<td>11.1 ± 3.4</td>
<td>11.6 ± 1.8</td>
<td>0.33</td>
</tr>
<tr>
<td>CRP, mean± SD, mg/l</td>
<td>4.1 ± 5.5</td>
<td>4.2 ± 5.2</td>
<td>0.93</td>
</tr>
<tr>
<td>ESR, mean± SD, mm/h</td>
<td>31.5 ± 21.8</td>
<td>32 ± 26.5</td>
<td>0.94</td>
</tr>
<tr>
<td>Vitamin B12, mean± SD, pg/ml</td>
<td>340.1 ± 209</td>
<td>323.9 ± 188.5</td>
<td>0.75</td>
</tr>
<tr>
<td>Folic acid, mean± SD, ng/ml</td>
<td>5.2 ± 3.3</td>
<td>8.6 ± 5.9</td>
<td>0.019</td>
</tr>
<tr>
<td>Ferritin, mean± SD, mg/l</td>
<td>48.2 ± 86.9</td>
<td>53.2 ± 90.9</td>
<td>0.83</td>
</tr>
</tbody>
</table>

Additionally; LTLs were seen in 10 patients (11.7%) during the follow-up (44.1 ± 46.7 months). Three of 10 patients underwent surgical resection during the follow-up, whereas only 1 in other patients (30% vs. 1.33%, p=0.0046, OR: 31.7).
Conclusion: This is the first study about the association of IBD with LTLs. LTLs were more common in patients with CD and associated with low folic acid levels during initial admission. Additionally, it may be a predictor of surgical resection during the follow-up.
Tacrolimus as bridging strategy to vedolizumab treatment in two pediatric patients with severe ulcerative colitis with failure of TNF-alpha antagonists

Anna Schneider¹, Daniel Ortner¹, Katharina Paulmichl², Verena Heu³, Michaela Achleitner³, Daniel Weghuber²

¹University Hospital of Salzburg, Department for Pediatric Gastroenterology, Salzburg, Austria
²Paracelsus Medical University, Department of Pediatrics, Salzburg, Austria
³University Hospital of Salzburg, Department for Pediatric Nutrition, Salzburg, Austria

Objectives and study: Vedolizumab is a humanized integrin-antagonist, which is approved in adults with moderate to severe inflammatory bowel disease (IBD). Previous studies showed that vedolizumab is superior to placebo for induction of remission and has a low side effect profile, but there is limited data in pediatric patients. Importantly, literature shows that vedolizumab takes up to 14 weeks to reach its maximum effect, suggesting that a bridging therapy might be necessary. Tacrolimus has been shown to induce remission in up to 70% of patients with severe ulcerative colitis (UC), while long-term remission can only be achieved in a minority of patients with additional risk of substantial side effects.

Case outline Patient 1: A 2002 born girl was diagnosed with UC in September 2014. Initially, corticosteroids as well as a maintenance therapy with mesalazine and azathioprine were given. Azathioprine was discontinued due to side effects and after another flare TNF-α antagonist adalimumab was started. Under this therapy the patient had five severe flares in eleven months, although dosage was extended in the end, and was therefore switched to infliximab. After a promising initial response, another severe relapse occurred. During all flares the patient required intravenous (iv.) corticosteroids, was anemic and had a dramatic worsening of her general condition and nutritional state. As two TNF-α antagonists had failed and the disease took a steroid-refractory course, it was decided to start with an off-label therapy with vedolizumab in a weight adjusted dosage (6 mg/kg at week 0, 2, 6 and 8 weekly thereafter). Given the severity of the disease, tacrolimus was used as bridging strategy (initially through levels of 10-15 ng/ml tapered down to 3-5 ng/ml after 3 months).

Case outline patient 2: A 2004 born boy was diagnosed with UC in December 2015 and was initially treated with corticosteroids, mesalazine and azathioprine. Later mesalazine was added. Due to a relapse, therapy was then switched to infliximab. After 3 infusions no response was detectable and iv. corticosteroids had to be given. As no remission could be induced by this regimen the decision was made to start vedolizumab with tacrolimus as a bridging therapy under the same conditions and dosages as in patient 1.

Methods: Case report study with two patients.

Results: In patient 1 partial clinical remission was achieved after 4 weeks of combined treatment with tacrolimus and vedolizumab and steroid-free remission was reached after 12 weeks. It is now planned to end tacrolimus treatment while expecting vedolizumab to exert its full effects.

Patient 2 reached steroid-free remission already two weeks after induction and remained stable until now. In the meantime it was possible to reduce and finally end tacrolimus.
Table:

<table>
<thead>
<tr>
<th>Vedolizumab and Tacrolimus</th>
<th>PUCAI Patient 1</th>
<th>PUCAI Patient 2</th>
<th>CRP Patient 1 (mg/dl)</th>
<th>CRP Patient 2 (mg/dl)</th>
<th>f Calpr. Patient 1 (ug/g stool)</th>
<th>f Calpr. Patient 2 (ug/g stool)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>75</td>
<td>60</td>
<td>5.8</td>
<td>1.3</td>
<td>5910</td>
<td>1630</td>
</tr>
<tr>
<td>Week 2</td>
<td>60</td>
<td>10</td>
<td>3.9</td>
<td>0.2</td>
<td>na</td>
<td>37</td>
</tr>
<tr>
<td>Week 6</td>
<td>40</td>
<td>10</td>
<td>7.5</td>
<td>0.1</td>
<td>597</td>
<td>na</td>
</tr>
<tr>
<td>Week 14</td>
<td>10</td>
<td>10</td>
<td>1.0</td>
<td>0.1</td>
<td>na</td>
<td>9.0</td>
</tr>
</tbody>
</table>

PUCAI… pediatric ulcerative colitis activity index  
CRP…. C - reactive protein  
f Calpr. … Fecal calprotectin

**Conclusion:** Whether or not vedolizumab will show to be effective in maintaining remission remains to be seen in our patients. However, tacrolimus could be considered as a bridging strategy when initiating vedolizumab in severe cases of pediatric patients with UC.

**Disclosure of interest:** Daniel Weghuber, Conflict with: Takeda Pharmaceutical
Short and long-term surgical outcomes and pouch function following proctocolectomy and pouch formation in paediatric UC: a multicentre-retrospective cohort study from the Porto IBD working group of ESPGHAN

Objectives and study: We aimed to evaluate contemporary surgical complications rate and pouch function following proctocolectomy and ileal pouch anal anastomosis (IPAA) in children with ulcerative colitis (UC)/inflammatory bowel disease unclassified (IBDU) undergoing the procedure before 18 years of age. Outcomes related to pouchitis are reported separately.

Methods: This was a multicentre longitudinal retrospective study involving 17 paediatric IBD centres from the Porto group of ESPGHAN. An electronic REDcap system was used to collate explicit baseline characteristics, clinical, management and surgical data, including short and long term outcomes.

Results: A total of 129 children after IPAA were included (50% male; 93% UC and 7% IBDU). Mean age at diagnosis was 10.5±4.2 years and median disease duration to colectomy was 17 months (IQR 8-36 months). Median post-operative follow-up was 40 months (IQR 26-72 months). Nineteen patients (15%) underwent proctocolectomy before age 10. A two-staged procedure was performed in 76 patients (59%), 3-stage in 45 (35%) and one-stage in 8 (6%). 48 patients (38%) underwent a laparoscopic (lap) assisted colectomy. Median number of bowel movements (BM)/24 hours one year after surgery was 5 (IQR 4-6; range 2-12). 42 patients (40%) had nocturnal BM one year post surgery even when pouchitis-free, of whom 48% had up to 1 nocturnal BM and 52% had greater than 1. One month and one year post-IPAA, 31 (28%) and 31 (28%) children used anti-diarrheal medication, respectively. Physician global assessment (PGA) of overall pouch performance was rated good or excellent in 71 (66%) patients at 1 month, 79 (71%) at 1 year post-IPAA, and 86 patients (74%) at last follow-up. Neither number of BM nor PGA were associated with surgical technique (lap/open) or with age <10 at colectomy.
Within 1 month after colectomy, 41 patients (34%) had surgical complications. The most common complications were small bowel obstruction in 14 (12%) and wound infection in 9 patients (7%). Within 1 month of pouch formation 33 patients (30%) had surgical complications. There was no association between surgical complications and surgical technique (lap/open). Patients with colectomy before age 10 had significantly more surgical complications at 1 year post IPAA. Pouch related outcomes included pouch stricture in 14 (11%) patients, pouch fistula in 12 (9%), prolapse in 3 (2.3%), pelvic floor in one (0.8%) and anal sphincter dysfunction in 1 (0.8%).

Conclusion: Surgical complications occurred in many children undergoing IPAA for UC/IBDU. Age younger than 10 years at proctocolectomy was associated with higher long term surgical complications but comparable pouch function. Pouch function was rated excellent or good in the majority of patients at last follow-up (74%).
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-309

Incidence and geographic differences of inflammatory bowel disease in children (<19 years) in the Pilsen Region - prospective study

Jan Schwarz¹, Dominika Cvalinová¹, Josef Sýkora¹

¹Charles University, Faculty of Medicine in Pilsen, Faculty Hospital, Department OD Paediatric, Pilsen, Czech Republic

Objectives and study: The objective of this study was to assess the incidence of inflammatory bowel disease (IBD) in the Pilsen Region (PR) in children up to 19 years and estimate, whether there are any geographic or demographic differences in the incidence.

Methods: The data of newly diagnosed IBD patients <19 years of age were prospectively collected from 1st January 2000 to 31st December 2015 in computerized clinical database. We included only patients who meet the diagnostic criteria for IBD and came from PR. The population based catchment was determined from census data. We calculated the incidence by relating the number of new diagnosed cases to the size of the paediatric population-at-risk during each calendar year. After completing the analysis, we compared the incidence in different districts of the region for the whole period of 15 years.

Results: A total of 170 new IBD cases [105 Crohn's disease (CD), 48 ulcerative colitis (UC) and 10 IBD- U unclassified (IBDU)] were identified. The median age at IBD diagnosis was 14.2 years; 59.4% male. A male preponderance in IBD (p=0.026) as well as CD (p=0.016) was observed. The average incidence of IBD per 100000 person-years was 10.0, (6.2 for CD, 2.8 for UC, and 1.0 IBD-U) for children < 19 years. Between 2000-2015, the incidence increased for IBD patients (p=0.01) and CD in particular (p=0.001), while the incidence for UC (p=0.09) and IBDU (p=0.339) remained unchanged. Children from sparsely and densely populated area were not equally affected. A higher incidence was demonstrated for children living in more urban areas (5 to 10000 inhabitants; p<0.01).

Table: The demographic characteristic of newly diagnosed paediatrics patients (<19 years) in Pilsen Region (2000-2015).

<table>
<thead>
<tr>
<th></th>
<th>CD</th>
<th>UC</th>
<th>IBDU</th>
<th>IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>total patients</td>
<td>105</td>
<td>48</td>
<td>17</td>
<td>170</td>
</tr>
<tr>
<td>male</td>
<td>68</td>
<td>24</td>
<td>9</td>
<td>101</td>
</tr>
<tr>
<td>female</td>
<td>37</td>
<td>24</td>
<td>8</td>
<td>69</td>
</tr>
<tr>
<td>median, y (range)</td>
<td>14.1 (1.4-18.1)</td>
<td>14.6 (2.7-18.3)</td>
<td>14.1 (2.5-17.7)</td>
<td>14.2 (1.4-18.3)</td>
</tr>
<tr>
<td>average incidence</td>
<td>6.2</td>
<td>2.8</td>
<td>1.0</td>
<td>10.0</td>
</tr>
</tbody>
</table>

Conclusion: The pediatric-onset IBD has risen considerably, especially for CD in this population. Geographical differences and the modulating effect of urbanization suggest possible environmental effects on the pathogenesis of IBD.
Paediatric IBD patients do not meet the daily recommendations of vitamin D and calcium intake: survey based analysis in a tertiary centre

Rita Shergill-Bonner, Nikki Acton, Sara Sider, Sibongile Chadokufa, Bonita Huggett, Neil Shah, Mila Baycheva, Alexisandra Zambrano Perez, Fevronia Kiparissi

Great Ormond Street Hospital for Children Foundation Trust, Dept of Gastroenterology, London, United Kingdom

Objectives and study: Achieving optimal levels of vitamin D (VitD) and calcium (Ca) is essential for developing children, especially in patients with inflammatory bowel disease (IBD). VitD and Ca play a major role in bone health and recently VitD has shown to potentiate the effect of anti-inflammatory treatments. However, achieving a sufficient oral intake is difficult in this group taking into account young age, modern eating habits and the nature of IBD itself. The purpose of this study was to evaluate if children with IBD seen in our centre achieve optimal Vit D and Ca intake according to recommendations made by the British Scientific Advisory Committee on Nutrition and the UK Department of Health, Dietary Reference Values.

Methods: A prospective dietetic survey was conducted among sequential IBD children seen in clinics over a 12 month period. Ca and VitD intakes were assessed through a 24-hour recall of dietary intake and food frequency questionnaire. Children who had been placed on restricted diets for allergic disease were excluded as well as children under 4 years. Included patients were classified according to age into 2 groups: 4-10 and 11-18 years. Sources of VitD were divided into dairy, oily fish, fortified cereals and egg. Analysis was performed using absolute values, percentages and means in Microsoft Excel.

Results: Survey was conducted in 151 patients; this represents 68.3% of all IBD patients under follow-up. 94 patients were included for analysis and 57 were excluded. 43/94 (45.7%) were females. Overall, only 26.6% and 21.3% of the surveyed population achieved the current recommended intake for Ca and VitD respectively. In the younger group, only 7/31 (22.6%) met the current VitD recommendations, the same figure repeats with regards Ca intake. In the older group, only 13/63 (20.6%) and 18/63 (28.6%) met the Ca and VitD recommendations respectively. In both groups dairy was the main source of vitamin D (61.3% young ones and 58.7% older ones). Less than 1/3 of the patients have an optimal intake of oily fish (intake 19% for children and 30% for adolescents).

Conclusion: 73.4% (age 4-10yrs) and 78.7% (age 11-18yrs) of the population surveyed did not achieved the current recommended intake amounts for Ca and VitD respectively. Paediatric IBD patients living in the UK do not meet the minimum requirements of VitD and Ca intake and therefore are at risk of having poor bone health, calcium homeostasis imbalance and VitD deficiency. In the great majority, Ca and VitD sources come from diary whereas the contribution of oily fish and egg as a VitD source is minimal. We recommend that paediatric IBD patients receive frequent counselling on healthy eating habits and proactive intake monitoring. Routine VitD supplementation recommended by local authorities must be followed as there is an insufficient VitD taken orally among these populations.
A team approach for exclusive enteral nutrition in Crohn’s disease results in high adherence and remission rate

Anna Andersson¹, Lotta Söderberg¹, Maria van der Pals¹

¹Skåne University Hospital, Department of Pediatrics, Malmö, Sweden

Objectives and study: Exclusive enteral nutrition (EEN) is known to be a safe and effective treatment for induction of remission in paediatric Crohn’s Disease (CD). However, the diet is challenging for the patient and adherence is often low as a result. The purpose of this study was to assess the adherence to EEN in the setting of a team based approach aimed to support the patient through the duration of the EEN-treatment. In brief, a two-member team consisting of a paediatric nurse and dietician followed the patients at an outpatient clinic with weekly visits and phone consultations as needed. The duration of EEN was eight weeks, plus 2-4 days of step up and step down. Encouragement, coaching and motivation to continue the treatment were mediated by the team.

Methods: All newly diagnosed CD patients from October 2015 through October 2016 were included in this study. Data was retrospectively collected from the patients’ electronic medical records. Age, gender, type of nutrition, Paediatric Crohn’s Disease Activity Index (PCDAI score), fecal calprotectin and adherence to the treatment were evaluated.

Results: In total, 17 patients with a mean age of 14.9 years (10-17 years) were diagnosed with CD. Seven (41 %) of those were girls and 10 (59 %) were boys, p=NS. Thirteen (76 %) patients were prescribed EEN at the discretion of the attending paediatrician. Of those, 11 (65%) completed the treatment and 2 changed therapies due to a more serious disease course. No patients were non-adherent to EEN. Mean PCDAI score decreased from 40 (27.5-65) to 21 (15-27.5), with a mean decrease of 17, p=0.0001. Mean fecal calprotectin decreased from 520 mg/kg (72-1204 mg/kg) to 280 mg/kg (<25-985 mg/kg), p=0.01.

Conclusions: Adherence to EEN-treatment can be effectively achieved by a multidisciplinary team approach. As expected exclusive enteral nutrition also appears to induce remission in paediatric Crohn’s Disease.
Peripheral regulatory T cells in pediatric inflammatory bowel disease: a major impairment in ulcerative colitis

Caterina Strisciuglio¹, Alessandra Vitale¹, Marianna Santopaoło², Elena Scarpato³, Erasmo Miele³, Annamaria Staiano¹, Riccardo Troncone⁴, Carmen Gianfrani⁵, Giuseppe Matarese⁶

¹Second University of Naples, Department of Woman, Child and General and Specialistic Surgery, Naples, Italy
²University Federico II, Department of Molecular Medicine and Biotechnology Science, Naples, Italy
³Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy
⁴University Federico II, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Naples, Italy
⁵Institute of Protein Biochemistry (Ibp), Cnr and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Naples, Italy
⁶Universita DI Napoli Federico II, Department of Molecular Medicine and Biotechnology Science, Napoli, Italy

**Objectives and study:** In inflammatory bowel disease (IBD), the inflammation is initiated by a dysfunctioning interplay between the intestinal microbiota and the innate mucosal immune system, resulting in excessive activation of adaptive immunity. The regulatory T cells (Tregs) play a critical role in maintaining immune homeostasis and limiting autoimmune responses by modulating the function of both the innate and adaptive immune cells. CD4+ T cells that express Foxp3 and Tr1 cells comprise the major regulatory populations in the intestine. In this study, we aimed to characterize these two type of Tregs in IBD paediatric patients at diagnosis.

**Methods:** The Tregs were analysed from peripheral blood mononuclear cells (PBMCs) in 17 children with Crohn’s disease (CD), 19 with ulcerative colitis (UC), and 14 non-IBD controls (HC) children. We have identified Tregs using two different mix of monoclonal antibodies; mix 1 (CD4/CD25/FOXP3/CD62L/PD1/CTLA4/CCR7/ki67) for Foxp3+, and mix 2 (CD45/CD4/CD25/CD49b/LAG3/Beta7 Integrina/ki67) for Tr1. The frequency and phenotype of these populations were analyzed by flow cytometry (BD FACS CANTO II).

**Results:** We observed a significantly increase of Tr1 cells, identified as CD4+LAG3+CD49b+ cells in IBD compared to HC children (p= 0.04 for CD and p= 0.002 for UC). In addition, we found a higher frequency of CD4+CD25+ cells in UC patients compared to HC (p=0.02); however the expression of Foxp3+ in the CD4+CD25+ gated cells was higher in both CD and HC when compared to UC, p=0.04 and p=0.02 respectively. Furthermore, the CD4+Foxp3+ in HC showed an increased expression of CD62L+ compared to both CD (p=0.01) and UC (p=0.004), the same result was found for CTLA4 expression, but it reached statistically significance only when compared to UC (p=0.01). We also observed a higher frequency of CCR7+ cells, in the gate of CD4+Foxp3+, in CD (p=0.007) and HC (p=0.003) compared to UC.

**Conclusion:** We characterize for the first time the expression of Tr1 cells in paediatric IBD and we find that they are increased at the diagnosis probably for a compensative mechanism. Differently, the frequency of Foxp3+ is reduced in UC patients but not in CD, however the expression of the adhesion and activation markers, such as CD62L and CTLA4, is impaired in both forms of IBD compared to HC, whereas CCR7 expression is reduced only in UC. Our results suggest that in paediatric IBD Treg are altered in functionality and not in the frequency, with a major impairment of Foxp3+ Treg in UC compared to CD.
Evaluation of Free Vitamin D levels in IBD paediatric patients: the role of inflammation

Caterina Strisciuglio¹, Sabrina Cenni², Francesca Paola Giugliano², Erasmo Miele³, Grazia Cirillo¹, Massimo Martellì⁵, Alessandra Vitale¹, Carlo Tolone¹, Annamaria Staiano², Emanuele Miraglia Del Giudice¹, Laura Perrone¹

¹Second University of Naples, Department of Woman, Child and General and Specialistic Surgery, Naples, Italy
²Federico II University, Department of Translational Medical Science, Section of Paediatrics, Naples, Italy

Objectives and study: An association between total 25-hydroxyvitamin-D (T-25OH-D) deficiency and Inflammatory Bowel Diseases (IBD) has already been described. However, existing studies do not consider the effect of inflammation on vitamin D metabolism, and the free 25-hydroxyvitamin-D (F-25OH-D) and the Vitamin-D-Binding Protein (VDBP) are usually not evaluated. The aim of our study was to investigate the levels of T-25OH-D, F-25OH-D and VDBP in a cohort of IBD paediatric patients and to correlate these values with the disease activity and the main inflammation markers.

Methods: Between January 2015 and May 2016 we enrolled all consecutive children with a new diagnosis of IBD (group A), a group of IBD patients at follow-up in clinical remission (group B) and a group of age- and sex- matched healthy controls (group C). In each subject T-25OH-D, F-25OH-D and VDBP levels were measured with an enzyme-linked immunosorbent assay (ELISA). Comparison between groups were made using the non-parametric Mann-Whitney test. For each IBD patient, the activity scores of disease and the inflammation markers C-reactive protein (CRP) and fecal calprotectin (FC) were measured and correlated to T-25OH-D and F-25OH-D levels by a linear regression test. CRP was also measured in the control group and it was related to VDBP by a linear regression test for all the groups.

Results: Sixty-four consecutive children were enrolled (group=n): group A=37, group B=27 and group C=18. Levels of T-25OH-D were higher in group A than in group B (19.9±1.7 ng/ml vs 14.2±1.3 ng/ml; p=0.01) but were lower in both groups A and B when compared to group C (19.9±1.7 ng/ml vs 28.2±2.8 ng/ml; p=0.008 and 14.2±1.3 ng/ml vs 28.2±2.8 ng/ml; p<0.001, respectively). The values of F-25OH-D were higher in group A compared to both group B (5.3±0.3 pg/ml vs 3.6±0.3 pg/ml; p=0.001) and C (5.3±0.3 pg/ml vs 3.2±0.3 pg/ml; p=0.001). Finally, levels of VDBP were lower in both groups A and B when compared to group C (196.1±3.3 ng/ml vs 286.9±22.1 ng/ml; p<0.001 and 170.6±2.9 ng/ml vs 286.9±22.1 ng/ml; p<0.001, respectively). A significant direct correlation was found between F-25OH-D and activity index of disease (r²:0.18; p<0.001). A direct correlation, not reaching statistical significance, was also found between F-25OH-D and both CRP and FC. Moreover, between all IBD patients and controls we found an indirect correlation between VDBP and CRP, not reaching statistical significance.

Conclusion: IBD children, both at diagnosis and at follow up, have lower levels of T-25OH-D compared to healthy controls. However due to the lower level of VDBP, F-25OH-D is not different between IBD patients in follow up and controls, and it is even higher in IBD patients at the diagnosis. Inflammation inversely correlates to VDBP and is associated with higher levels of F-25OH-D levels, which is the more meaningful marker of vitamin D function. Therefore IBD patients, despite their deficiency in T-25OH-D, have normal or even higher levels of F-25OH-D.
The prevalence of MEFV gene variants in cases of inflammatory bowel disease and its effect on clinical and laboratory values

Gokhan Tumgor¹, Mehmet Agin¹, Atil Bisgin², Mustafa Yilmaz³

¹Cukurova University Medical Faculty, Dept. of Pediatric Gastroenterology, Hepatology and Nutrition, Adana, Turkey
²Cukurova University Medical Faculty, Medical Genetics, Adana, Turkey
³Cukurova University Medical Faculty, Pediatric Allergy and Immunology, Adana, Turkey

Objectives and study: Inflammatory bowel disease (IBD) is characterized by irregular mucosal immune response of the GIS, although the pathogenesis is as yet unclear. Familial Mediterranean Fever (FMF) is a genetic disease characterized by recurring febrile episodes and inflammation of the serous membranes. The purpose of this study was to investigate the effect on IBD of the MEFV gene variants seen in FMF.

Methods: 46 patients aged 0-18 under monitoring with a diagnosis of IBD by the Çukurova University Faculty of Medicine Pediatric Gastroenterology Department between January 2012 and January 2016 were included in the study. Variants of the 12 MEFV gene, the most commonly seen in Turkey, were investigated in all patients using genetic methods. The allele and genotype levels of the variants determined were compared between the patient groups using appropriate genetic statistical techniques. Cases were evaluated in terms of clinic and demographic characteristics and laboratory values.

Results: The prevalences of MEFV mutations in all cases of IBD were 15% R314R (HT), 14% D102D (HT) and 12% G138G (HT). Analysis of allele and genotype levels revealed higher C allele of the D102D T>C variant, G allele of the G138G A>G variant, A allele of the A165A C>A variant and A allele of the R202Q G>A variant in patients with UC, but that the wild type of the R202Q G>A variant was common in cases of CD. In addition, the D102D T>C / R314R C>T haplotype was significantly more prevalent in the UC group. AAA was determined in six cases of FMF. UC was present in two of these and CD in four. When laboratory values of cases diagnosed with IBD+FMF were compared with those of cases diagnosed with IBD alone, sedimentation, CRP and IgG values were statistically significantly higher in the IBD+FMF group (p<0.05).

Conclusion: The prevalence of MEFV gene variants in cases of UC was higher than that in the normal population, suggesting that risk groups with a disposition to UC need to be identified with an expansion of haplotyping studies and need to be given genetic counseling. If acute phase markers are high in cases diagnosed with IBD of FMF despite treatment, care should be taken over the possibility of the two conditions being comorbid.
Evaluation of carotid intima-media thickness and aortic stiffness in patients with inflammatory bowel disease

Nafiye Urganci¹, Tugce Kurtaraner², Taliha Oner³, Merve Usta¹

¹Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
²Sisli Etfal Training and Research Hospital, Department of Pediatrics, Istanbul, Turkey
³Siyami Ersek E&R Hospital Istanbul, Child Cardiology, Istanbul, Turkey

Objectives and study: Due to the limited data on the relationship between childhood onset inflammatory bowel disease (IBD) and atherosclerosis, the comparison of carotid intima-media thickness (CIMT) and aortic stiffness parameters of early atherosclerotic markers with healthy controls in children with IBD diagnosed cases is aimed.

Methods: A total of 84 cases including 42 healthy controls and 42 children with IBD who were examined between 2002-2015 in Pediatric Gastroenterology outpatient clinic and had no risk factors for atherosclerosis, were enrolled in our study. Biochemical studies of the cases were done. Aortic stiffness, aortic strain and aortic distensibility parameters were measured from aortic diameter by transthoracic echocardiography. Common carotid artery intima-media thickness was assessed by B-mode ultrasound.

Results: Carotid intima-media thicknesses were 0.42±0.07 mm in IBD cases and 0.40±0.06 mm in control group and the difference between two groups was not statistically significant. Aortic stiffness of the aortic elasticity parameters calculated by echocardiography was significantly higher in patients with IBD, while aortic strain and distensibility were significantly lower. In cases with IBD, there was a significant correlation between CIMT and age.

Conclusion: The impairment of the aortic elasticity parameters in IBD cases may be indicative of early atherosclerosis. We can explain the fact that we do not find any difference in CIMT values between two groups, the age of our cases is young and the follow up period is short. On the contrary, we find increase in aortic stiffness, decrease in aortic distensibility and strain values so we think that these parameters may be indicative of early atherosclerosis in young children and more number of cases may be a guide.
Choice of exclusive enteral nutrition (EEN) induction therapy is associated with increased small bowel imaging and detection of ileal disease extension in pediatric Crohn’s disease

Jessica Connors¹, Sana Basseri¹, Gamal Mahdi¹, Angela Noble¹, Mohsin Rashid¹, Anthony Otley¹, Johan van Limbergen¹

¹Iwk Health Centre / Dalhousie University, Pediatrics, Halifax, Canada

Objectives and study: Paediatric Crohn’s disease (CD) is characterized by extensive involvement at diagnosis and further disease extension occurs in up to 20% of patients. EEN is recommended as first-line induction therapy although corticosteroids (CS) are still used commonly. It is unknown whether choice of induction therapy alters disease extension. Our aim was to compare disease extension in an observational cohort of paediatric CD patients initially managed with either EEN or CS.

Methods: Disease location (according to the Paris classification) was assessed from diagnosis up to 10 years follow-up in 131 pediatric CD patients (diagnosed between 2001 to 2013 at a pediatric tertiary care institution). All patients had upper and lower endoscopy at diagnosis. L4a and/or L4b involvement was grouped as L4. Macroscopic involvement defined by the presence of endoscopic mucosal ulceration and/or radiological findings were confirmed by histology, if available.

Results: Of 131 patients reviewed, 91 (35 CS and 56 EEN) had at least 4 years follow-up and were included. L1, L2, and L3 phenotypes (+/- L4) at diagnosis was comparable between groups, however there was a trend towards greater L1 (21 vs 9%, p=0.14) and less L2 disease (16 vs 31%, p=0.19) in the EEN-group compared with the CS-group. At diagnosis, 32% of patients had maximum disease extension (L3+L4). Of the remaining 62 patients eligible to exhibit extension, 10 did and all were initially treated with EEN. Extension to the ileum (L2→L3) was more common (8/10) than extension to the colon (L1→L3, 1/10) or upper gut (L4, 1/10), p=0.007. Immunomodulators (IMM) were used less within the first year in the EEN group compared with the CS group: 8weeks-21/56 (37%) vs 20/35 (57%), p=0.02; 6months-56 vs 82%, p=0.004; 1year-62 vs 86%, p=0.02. By 6 months, 4/10 children who extended their disease location were on IMM and 5/10 at 1 year. By 2 years, 89% of EEN and 91% of CS group had been on IMM (p=0.74). There was a trend towards less anti-TNF use at 2 years in the EEN group (23%) compared with CS (40%), p=0.09. There was disparity in the choice of follow-up imaging investigations between CS and EEN-treated patients. EEN patients had an increased frequency of WBC-labelled scans (32% vs 14%, p=0.06). Small bowel follow-through and/or MREnterography were performed in 10/35 (29%) of CS- versus 36/56 (64%) of EEN-treated patients (p=0.0009). Proportions of patients who underwent follow-up upper endoscopy were comparable between groups (p=0.32), whereas lower endoscopies were performed in 42% of CS versus 21% of EEN-treated patients (p=0.05).

Conclusion: Choice of EEN as induction therapy is associated with significantly increased use of imaging of the small intestine and detection of ileal disease extension. Further prospective studies are needed to assess disease progression in CS- versus EEN-treated patients.
Impact of exclusive enteral nutrition primary treatment on body mass composition in newly-onset paediatric Crohn's disease

Agata Wasilewska¹, Anna Stochel-Gaudyn¹, Katarzyna Ponanta-Gawron², Dorota Drożdż¹, Małgorzata Sładek¹

¹University Children’s Hospital, Jagiellonian University Medical College, Department of Paediatrics, Gastroenterology and Nutrition, Krakow, Poland
²Jagiellonian University Medical College, Department of Paediatrics, Gastroenterology and Nutrition, Krakow, Poland

Objectives and study: Crohn’s disease (CD) is characterized by imbalance between innate and adaptive immunologic response and proinflammatory cytokines dominance, causing chronic inflammation. In children that inflammatory condition is associated with weight loss (up to 85% cases) and altered body composition (fat free mass deficiencies – 94%), which is present even in children with proper body mass index (BMI). The electrical bioimpedance is an effective method to assess body mass compartments (FM – fat mass/FFM- fat free mass) and phasal angle (PA) - regarded as a marker of nutrition. The Exclusive Enteral Nutrition (EEN) induces remission in up to 85% of children with mild to moderate newly diagnosed CD, but its favorable effects on body mass composition (BMC) is present even with the absence of mucosal healing.

The aim of the study was to assess BMC alterations in children with newly diagnosed CD and to evaluate the influence of EEN on gaining steroid-free remission (with negative inflammatory markers – C reactive protein (CRP) and calprotectin) and to define EEN impact on BMC.

Methods: 45 children (aged 7-17) with newly diagnosed mild or moderate Crohn’s disease (Paediatric Crohn’s Disease Activity Index - PCDAI <40 points), with disease location: L1, L2, L3 and disease phenotype: B1 according to the Paris classification, qualified to EEN induction remission treatment, were enrolled in to the study. 23 children without any gastroenterological disorders, served as controls. FM, FFM and PA were measured by electrical bioimpedance analysis, laboratory tests were performed twice in studied group (before and after 6 weeks period of EEN) and once in controls.

Results: 36 children (80%) gained remission after 6-weeks of EEN (PCDAI<10), 24 children (53%) reached normal CRP – level and 9 (20%) reached remission with normal CRP - level and calprotectin. On diagnosis 28 (65%) children had proper body weight, 16 (35%) were underweight (BMI< 5 centile). Lower FFM and PA, in accordance to general population, were observed in 40 (88%) and 28 (62%) children also in patients with proper BMI (5-84 centile) – 85% and 60,7% respectively. Decreased FM was present in 25 (55%). In comparison to the control group deficits of FFM and FM were observed in 75% and 35% respectively. In children who gained remission after completion EEN, increase in FFM occurred more often (73% vs 60%) and was higher (8 vs 6,5%). BMI was positively correlated to FM, but did not correspond to FFM (p<0,01). PA – measured before and after gaining remission – positively correlated to BMI and negatively to PCDAI (p <0,01).

Conclusion: EEN is an effective therapy for induction remission in paediatric CD and has positive influence on body mass composition, even in patients who did not gain remission. BMI is not sufficient enough to be the only tool in assessing the alterations in body composition. PA and FFM changes may be used to monitor response to EEN treatment in children.
Study on association of human leukocyte antigen-I polymorphisms with pediatric inflammatory bowel diseases

Haijiao Xia1, Ying Huang1

1Children's Hospital of Fudan University, Shanghai, China

Objectives and study: The purpose of this research is to study human leukocyte antigen-I (HLA-I) gene polymorphisms and analyze the association between HLA-I predisposing genes and clinical characteristics of pediatric inflammatory bowel disease with Han nationality.

Methods: Forty-five cases of pediatric inflammatory bowel disease with Han nationality were investigated for HLA-I alleles by PCR-SSO. Controls include 283 healthy Han Chinese people, their HLA-I alleles were based on NCBI MHC database. The two groups’ allele frequencies were compared using the Chi-squared test or Fisher’s exact test, when appropriate. Association between HLA-I predisposing genes and disease were analyzed by calculating the odds ratio(OR)and 95% confidence interval (95%CI).

Results: 1. The correlation between HLA-I gene polymorphisms and inflammatory bowel disease:

Frequencies of HLA-A*02:01, A*30:01, A*68:01, HLA-B*13:02, B*15:11, B*39:01, B*40:06 and HLA-C*06:02 in inflammatory bowel disease patients were 24.44%, 11.11%, 4.44%, 11.11%, 8.89%, 6.67%, 11.11%, 15.56%, respectively, which were significantly higher than those(9.89%, 3.18%, 0.00%, 3.53%, 0.35%, 0.35%, 2.47%, 5.30%)in controls, and the ORs(95% CI)were 2.946(1.345-6.453), 3.806(1.214-11.928), 3.291(1.261-8.590), respectively, the P-value were 0.005, 0.030, 0.018, 0.040, 0.001, 0.015, 0.020, respectively. Frequency of HLA-A*02:03 in inflammatory bowel disease patients was lower than the control group (6.67% vs 19.79%), and the OR was 0.290, 95%CI:0.087-0.968, the P-value was 0.033. There was statistically significant difference in allele frequencies between the two groups.

2. The association between HLA-I predisposing genes and clinical characteristics of inflammatory bowel disease:

There was no significant difference between HLA-I predisposing genes and patients’ age and gender (P>0.05). Compared to controls, the frequency of HLA-B*40:06 increased significantly in colonic Crohn’s disease patients (33.3% vs 2.5%, OR=19.714, 95%CI:3.082-126.102, P=0.012), and the frequencies of HLA-A*30:01, HLA-B*15:11, HLA-C*06:02 increased significantly in Crohn’s disease patients with upper gastrointestinal disease (25.0% vs 3.2%, OR=10.148, 95%CI:1.794-57.390, P=0.032; 25.0% vs 0.4%, OR=94.000, 95%CI:7.466-1183.567, P=0.002; 37.5% vs 5.3%, OR=10.720, 95 %CI: 2.338-49.156, P=0.009, respectively). The difference of allele frequencies between the two groups was statistically significant.

Conclusion: HLA-A*02:01, A*30:01, A*68:01, HLA-B*13:02, B*15:11, B*39:01, B*40:06 and HLA-C*06:02 may be the predisposing genes in pediatric patients with inflammatory bowel disease with Chinese Han nationality, and HLA-A*02:03 may be a protective factor for inflammatory bowel disease. Among them, HLA-A*30:01, HLA-B*15:11, B*40:06 and HLA-C*06:02 are associated with the extent of Crohn’s disease.
Inflammatory bowel disease in children is a challenging diagnosis when overlaps with coeliac disease

Alexandra Zambrano Perez1, Rita Shergill-Bonner1, Fevronia Kiparissi1, Nikki Acton1, Neil Shah1, Keith Lindley1

1Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom

Objectives and study: Inflammatory bowel disease (IBD) and coeliac disease (CD) are conditions associated with chronic inflammation of the gastrointestinal tract. Underlying aetiology includes genetic susceptibility, abnormal immune response and various environmental factors not fully understood to date. Both entities can overlap in paediatric patients although this is uncommon and difficult to confirm. We present our experience with patients who developed both conditions during early years of life.

Methods: We retrospectively reviewed all IBD patients seen in our centre who also had a diagnosis of coeliac disease over a 10-year period. Data were collected from electronic notes and laboratory registries. Demographics, consultations, laboratory and endoscopic findings were extracted to a STATA database. Descriptive analysis was performed using absolute value, percentage and mean functions through STATA software version 14.

Results: Only 8/578 patients were found to have both diagnosis, this accounts for 1.4% of all paediatric IBD patients seen in our centre (mean 57 new patients per year, past 10 years). 5 of them were female, 1 male had Down syndrome, and 1 patient had incomplete records. Mean age of diagnosis was 7.1 and 8.9 years for CD and IBD respectively. In terms of the IBD subtype, 4 patients suffered of Crohn's disease, 3 of ulcerative colitis and 1 of IBD unclassified. 3 patients were diagnosed with both entities within 3 months, other 4 had a previous history of CD and developed IBD years later (mean in years 3.0), despite having a well-controlled disease. Positive anti-transglutaminase (TTG) serology was found in 4/7 patients. Endoscopic findings were difficult to interpret, complementary specific biopsy immunostaining, small bowel imaging (MRI, CT) and video capsule endoscopy were required in order to support both diagnoses. Endoscopic assessment when there was a previous diagnosis of CD obeyed to persistent gastrointestinal symptoms despite normal TTG values, these 4 known CD patients had significant IBD features including granulomata and cryptitis in small bowel (3/4) and pancolitis (1/4).

Conclusion: Inflammatory bowel disease can overlap with coeliac disease in paediatric IBD patients although this association is rare. IBD can follow the appearance of CD years later despite TTG normalization and can also present at the same time of CD. Proving the coexistence of IBD and CD in children is a challenge, and requires of a multidisciplinary team involving expert histopathologists, gastroenterologists, dietitians and clinical laboratory scientists. IBD must be considered in CD patients with new onset of gastrointestinal symptoms or in CD patients whose gastrointestinal symptoms do not seem to respond to a gluten-free diet.
Vitamin D levels in paediatric IBD patients living in England

Alexsandra Zambrano Perez, Rita Shergill-Bonner, Fevronia Kiparissi, Nikki Acton, Sara Sider, Sibongile Chadokufa, Bonita Huggett, Kosmas Kailidis

1Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom

Objectives and study: Children living in England are prone to develop low Vitamin D (VitD) levels due to a limited sun exposure and often a limited oral intake. These factors are greatly exacerbated in children suffering of inflammatory bowel disease (IBD) as the disease usually relates to malabsorption, lack of appetite, food refusal, indoor resting and little sun exposure as a skin cancer precaution when using immunosuppressors. Vitamin D level monitoring has become a standard of quality in IBD care over the past years as there is good evidence that low vitamin D levels are detrimental in children for their bone health and possible for the disease itself. Our aim was to assess guidelines compliance for yearly VitD monitoring and determinate the frequency of VitD deficiency and insufficiency among our patients.

Methods: We retrospectively reviewed all VitD levels performed locally and from district hospitals for IBD patients diagnosed over the past 5 years. Data were collected from electronic notes and laboratory registries. VitD insufficiency was defined when levels were 25-75nmol/L and deficiency when <25nmol/L. We compared the proportion of patients who were yearly assessed, patients with normal and insufficient levels, and IBD subtype (Crohn's disease (CD), ulcerative colitis (UC) and IBD unclassified (IBDU)). Demographics, laboratory findings, and treatment were extracted to a STATA database. Descriptive analysis was performed using absolute value, percentage and mean functions. Results: 51% (n=96) of patients under follow-up had VitD determination at least once over the past 3 years. When grouped by year, 21 patients had vitamin levels in 2014, 43 in 2015 and 66 in 2016. This represents a 3 fold increase within an average IBD population of 188 patients. 15.6 % (15/96) were VitD deficient (6 CD, 5 IBDU, 4 UC) at least in one determination, 60.4% (58/96) were VitD insufficient (26 IBDU, 24 CD, 8 UC) at least in one determination over the past 3 years. All patients who were VitD deficient had normal levels after 2-3 months of VitD treatment. Not all the patients were advised to continue on prophylactic vitamin D after recovering from low levels. 56% of patients with levels greater than 100 nmol/L were on prophylactic supplementation (400-800IU).

Conclusion: A considerable improvement in the standard of care has been achieved by increasing the yearly rates of VitD determination among our patients. VitD deficiency and insufficiency were common among IBD patients as described in other geographic regions. VitD monitoring enable us to identify patients at risk of abnormal bone health and to promptly commence vitamin D supplementation when low levels are found.
Endoscopic relapse-rate in Crohn’s disease patients treated postoperatively by anti-TNF for residual disease

Kristýna Zárubová¹, Ondrej Hradsky¹, Ivana Copova¹, Richard Škába², Blanka Rousková², Lucie Poš², Jiří Bronsky³

¹University Hospital Motol, Paediatrics, Prague, Czech Republic
²University Hospital Motol, Paediatric Surgery, Prague, Czech Republic
³Second Faculty of Medicine, Charles University and University Hospital Motol, Paediatrics, Prague, Czech Republic

Objectives and study: Anti-tumour necrosis factor alpha (anti-TNF) is one of the most important modalities in the treatment of Crohn’s disease (CD) in children. There is lack of evidence in prevention disease recurrence in children after ICR treated by anti-TNF and no prospective endoscopic study in these patients. In this study we observed endoscopic recurrence rate in patients treated for residual disease by anti-TNF (adalimumab (ADA) or infliximab (IFX)) after ileocaecal resection (ICR). All patients were treated with anti-TNF also before surgery.

Methods: We collected prospective (endoscopic, laboratory, PCDAI) and retrospective (disease phenotype and behaviour at the time of diagnosis, indication for surgery) data from paediatric patients with CD, who underwent ICR between April 2011 and October 2015. These children had residual disease (perianal, colonic or upper GI tract involvement) and were treated both pre- and postoperatively with ADA (n=5) or IFX (n=9). We performed endoscopy after ICR (median time to first endoscopy was 6 months (1.5 – 27) and evaluated disease recurrence defined as more than 5 aphtous lesions in neoterminal ileum, diffuse aphtous ileitis or diffuse inflammation with large ulcers, nodules or narrowing. We also repeated endoscopies to maximum follow-up of 60 months. All patients had at least one endoscopy, mean was 2 endoscopies per patient (min. 1, max. 4).

Results: From 59 patients who underwent ICR, fourteen (mean age 14.8 years, (range 9.6 – 17.3), 57 % males) fulfilled inclusion criteria to this study. Four patients (28.5 %) had disease recurrence at the time of first postoperative endoscopy and they needed escalation of therapy (shorter interval, higher dose) or change to other therapeutic modalities. From the relapse group, 2 patients were treated with ADA and 2 with IFX. Three patients had disease recurrence on first endoscopy after 6 months, one patient after 19 months.

Conclusion: Approximately one third of patients treated by anti-TNF for residual disease after ICR has recurrence at the time of first postoperative endoscopy (median 6 months) and need escalation or change of the therapy.

Supported by research grants VZ FNM 00064203/6001 a GA UK No. 136215
Antibiotic resistance to Helicobacter pylori in paediatric patients in North Israel

Sarit Peleg¹, Yoram Keness², Philippe Trougouboff³, Rasha Khalilie⁴

¹Emek Medical Center, Director of Paediatric Gastroenterology Unit, Afula, Israel
²Director of Clinical Microbiology Laboratory, Emek Medical Center, Afula, Israel
³Head of Hematopathology Unit, Tissue Diagnosis and Cancer Research Institute, Emek Medical Center, Afula, Israel
⁴Paediatric Department B, Paediatric Gastroenterology Unit, Emek Medical Center, Afula, Israel

Background: First line eradication therapy for Helicobacter Pylori (HP) infection usually consists of Proton Pump Inhibitor, Amoxicillin plus one of two Antibiotics: Clarithromycin or Metronidazole. Reduced therapeutic efficacy is explained by low compliance or antibiotic resistance. Antibiotic susceptibility testing for clarithromycin is recommended before initial clarithromycin based triple therapy in areas with a known high resistance rate (>20%). In European countries, the reported prevalence of Clarithromycin resistance in children ranges from 12% to 20%, and 13% in the United States. In Israel, 25% for naïve patients, while 42% for those previously treated for HP. Primary Metronidazole resistance ranges from 15% to 43% in European children and 25% in the United States. In Israel, 19% for naïve patients, while 52% for those previously treated for HP.

Objectives: To investigate the rate of HP resistant strains to antibiotic treatment in paediatric population in Emek Medical Center.

Methods: Study group included 100 patients aged 1-18 years. Tests for HP that were performed included rapid urease test, biopsy and culture. Antibiotic susceptibility to Amoxicillin, Clarithromycin, Metronidazole, Tetracycline, and Levofloxacin was determined by E-test.

Results: 41% of the children were infected with HP, 37 Jews (90.2%) and 4 Arabs (9.7%). Mean age was 11.3±4.1 years. The prevalence rate of resistance to Clarithromycin was 15.1% and to Metronidazole 12.1%, which is lower than previous studies from Europe, United States and Israel with the same age population. No resistance was found to Amoxicillin, Tetracycline or Levofloxacin.

Conclusion: HP resistance to Clarithromycin and Metronidazole is lower in our study with respect to data obtained from Europe, USA and other studies from Israel, perhaps due to lower use of these antibiotics in our area. In our area, Metronidazole and Clarithromycin can be considered as part of the first line treatment for children infected with HP.
Helicobacter pylori infection and eradication rate with standard triple therapy in children with coeliac disease

Nevzat Aykut Bayrak, Burcu Volkan, Esra Polat, Günsel Kutluk

1Diyarbakir Children's Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
2Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
3Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: In recent decades, the incidence of celiac disease (CD) has increased independent of the improvements in new screening methods. In contrast to CD, incidence of Helicobacter pylori (Hp) infection has been decreasing even in developing countries. According to the hygiene hypothesis, decreased exposure to bacteria may trigger autoimmunity. There is a few number of studies arguing the inverse relationship between CD and Hp infection, and data regarding children are even scarce. The aim of this study was to evaluate the association between Hp and CD in children as well as any difference in Hp eradication rates.

Methods: Children who underwent endoscopy between July 2015 and September 2016 in three pediatric gastroenterology centers were included in the study. The presence of Hp infection was confirmed by both histopathology and the rapid urease test. All Hp infected patients received lansoprazole for a month and amoxicillin plus clarithromycin for 14 days. Eradication was assessed by Hp stool antigen after 8-12 weeks. Patients with the history of previous Hp eradication, antibiotic therapy or acid suppressive drug use in last 4 weeks and chronic renal, cardiac or neurologic disease were excluded. The ones who had the diagnosis of CD were compared with the children who underwent endoscopy in the same period and had another diagnosis.

Results: Of 1086 endoscopies performed in the study period, 942 cases were eligible for the study. A total of 332 CD patients (mean age: 8.8±4.2 years, 48.1% girls) and 610 controls (mean age: 9.5±4.8 years, 56.6% girls) were included into the study. Hp infection rate was significantly lower in CD group (31.1% vs 66.4%, χ²=52.2, OR: 2.65 95% CI: 1.84-3.21, p<0.01). There was no correlation between the severity of Hp infection and modified Marsh scores in CD patients (r²= -0.196, p>0.05). Hp eradication rate was indifferent between groups (67.5% vs 61.8%, p>0.05).

Conclusion: In this cohort where Hp infection is common even in childhood population, the frequency of Hp infection was significantly lower in CD children. Hp eradication rate with standard triple therapy was higher among CD cases compared to the controls but without statistical significance. Hp infection might have a protective role in the development of CD.
Decreasing frequency of Helicobacter pylori infection in a cohort of 1893 children from the region of Silesia, Poland

Agata Chobot1, Jolanta Porębska1, Agnieszka Krzywicka1, Alicja Żabka1, Katarzyna Bąk-Drabik2, Wojciech Pieniążek1, Andrzej Dubik1, Jarosław Kwiecień2

1Clinical Hospital No1, Zabrze, Poland
2School of Medicine With the Division of Dentistry in Zabrze, Medical University of Silesia, Department of Pediatrics, Katowice, Poland

Objectives and study: Past data suggest presence of Helicobacter pylori (Hp) infection in approximately 15-30% of children in Poland. A decrease has been described in analyzes carried out in Western and Eastern Europe. This study aimed to estimate the prevalence of Hp infection in the region of Upper Silesia, Poland.

Methods: During 5 years (Sept 2009-Sept 2014) we studied 1892 children (1027 (54.3%) females, 865 (45.7%) males) aged 3-18 years from the region of Upper Silesia, Poland. These were children qualified for participation in the „Good diagnosis-Treatment-Life” program (financed by the European Economic Area Financial Mechanism, PL 0361) that is run by the Clinical Hospital No1 in Zabrze, Poland. For all participants a questionnaire regarding nutritional status (weight and height) and presence of symptoms possibly related to Hp infection was obtained. Hp status was investigated using the 13C-labelled urea breath test (UBT) (IRIS, Wagner GmbH).

Results: 211 (11.2%) children - 107 female and 104 male - had a positive and 1681 (88.8%) a negative UBT result. Mean age of Hp positive individuals was lower than in Hp negative children (respectively 9.8 and 10.3 years), but did not reach statistical significance (p=0.094). Slightly lower mean body weight Z-score (-0.42 vs -0.24 SDS, p=0.025) as well as mean height (-0.48 vs -0.23 SDS, p=0.014)was found in Hp positive children than in those with negative results. Frequency of abdominal pain, nausea, halitosis and poor appetite was similar in Hp positive and negative children (78.7% vs 77.3%; 19.9% vs 18.8%, 66.8% vs 67.1% and 54% vs 50.6% respectively, for all p=ns).

Conclusion: In the region of Upper Silesia, Poland Hp infection seems to affect approximately every tenth child, which is less than reports in the past. Presence of Hp infection in children seems to be associated with slightly lower weight and height, but does not appear to be associated with more frequent presence of symptoms such as abdominal pain, nausea, halitosis or poor appetite.
Comparison of clinical outcomes and FOXP3, IL-17A responses in Helicobacter pylori infection in children versus adults

Eda Yörgüç1, Hacer Fulya Gulerman1, Burcu Güven1, İsmail Hakkı Kalkan2, Mahi Balci3, Mustafa Çağlar Yörgüç4

1Kirikkale University Faculty of Medicine, Pediatric Gastroenterology, Kirikkale, Turkey
2Kirikkale University Faculty of Medicine, Gastroenterology, Kirikkale, Turkey
3Kirikkale University Faculty of Medicine, Pathology, Kirikkale, Turkey
4Kirikkale State Hospital, Pediatrics, Kirikkale, Turkey

Objectives and study: Helicobacter Pylori (H. Pylori) plays a significant role in development of both chronic active gastritis and peptic ulcer in children and it is substantially acquired in childhood period. Confronted by that microorganism in childhood period increases risk of the development of serious diseases in adult such as atrophic gastritis, gastric adenocarcinoma and mucosa-associated lymphoid tissue lymphoma (MALT). Immune response of H. Pylori that is defined as carcinogen bacteria in children should be well established. Effects of T helper 17 (Th17) and regulatory T cell (Treg) groups on various diseases have investigated in recent years. There are few studies in literature based on the relationship between this subject and H. Pylori.

Methods: 40 pediatric and 40 adult cases were taken into the investigation designed as a case-control study. Revised Sydney System evaluation and number of FOXP3, IL-17A cells which are the markers of Treg and Th17 were evaluated in gastric tissue in the study. Also, every case is evaluated with clinical follow-up questionnaires. Data were analyzed with SPSS (IBM Corporation, Armonk, NY, US) statistical software package version 22.0.

Results: Clinical symptoms and findings of both groups were similar. Mean FOXP3 value of children were significantly higher, mean IL-17A values of children were lower than adults in cases with H. Pylori (+) (p <0.001). IL-17A and FOXP3 values were significantly higher in H. Pylori (+) children and adults, compared to H. Pylori (-) cases (p <0.001). Statistically significant moderate negative correlation is seen between bacterial density and IL-17A; statistically significant strong positive correlation is observed between FOXP3 and bacterial density in H. Pylori (+) pediatric cases.

Table: Comparison of IL-17A and FOXP3 in H. pylori (+) children and adults

<table>
<thead>
<tr>
<th>GROUP</th>
<th>Children Mean ±SD</th>
<th>Adults Mean ±SD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>IL-17A</td>
<td>104.11±21.86</td>
<td>173.51±11.94</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>FOXP3</td>
<td>89.62±23.60</td>
<td>58.58±7.52</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Children Th17 / Treg balance, we see that proper registration of Tregs, which is a factor that increases the susceptibility to persistent infections. Development of a vaccine or more effective therapy in children would be a great improvement in this field.
GASTROENTEROLOGY: Peptic disease and helicobacter pylori

G-P-329

Could 13C urea breath test be a diagnostic test for Helicobacter pylori infection in children

Burcu Güven 1, Hacer Fulya Gulerman 1, Birgül Kaçmaž 2, Eda Yörgüç 1

1Kirikkale University Faculty of Medicine, Pediatric Gastroenterology, Kirikkale, Turkey
2Kirikkale University Faculty of Medicine, Microbiology and Clinical Infection Department, Kirikkale, Turkey

Objectives and study: Helicobacter pylori (H. pylori) is common cause of dyspepsia besides peptic ulcer, gastric cancer and MALT lymphoma. Although severe diseases are seen in adults, the infection is usually acquired during childhood. Because of that, it is more important to diagnose H. pylori infection in children correctly. Not only the easier and applicable test, but also as far as noninvasive test should be chosen. In our study, we aimed to identify the sensitivity and specificity of 13C urea breath test (UBT) for diagnosis of H. pylori infection.

Methods: Urea breath test was applied to 200 children with epigastric pain and/or nausea which last for more than a month, aged 4-18 years. Esophagogastroduodenoscopy (EGD) was performed and tissue samples were taken from antrum. Gastric mucosa samples were graded using Sydney Scoring System. UBT results were compared with histopathology. This was designed as a cross-sectional, case-control study. Data were analyzed with SPSS (IBM Corporation, Armonk, NY, US) statistical software package version 22.0.

Results: Overall 193 children were included in study population. Seven cases were excluded. The mean age of study population was 13.50±2.98 years. 71 (36.8 %) patients had positive and 122 (63.2%) had negative UBT results. Upper gastrointestinal endoscopy was performed to 60 of 71 patients with positive UBT and 30 of 122 patients with negative UBT. The sensitivity and specificity of UBT were 85.1% (CI 95% 75.3-92.9) and 100% (CI 95% 83.2-100) respectively. Positive and negative predictive values were 100% (CI 95% 94-100) and 66.7% (CI 95% 47.2-82.7) respectively. There was a positive correlation between the level of DOB values and the density of Helicobacter pylori (p<0.01) and inflammatory activity (p<0.01).

Table: The relationship between UBT results and density of Helicobacter pylori

<table>
<thead>
<tr>
<th>Density of Helicobacter pylori</th>
<th>Grade 0</th>
<th>Grade 1</th>
<th>Grade 2</th>
<th>Grade 3</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>UBT (+)</td>
<td>0</td>
<td>7</td>
<td>21</td>
<td>32</td>
<td>60</td>
</tr>
<tr>
<td>UBT (-)</td>
<td>21</td>
<td>3</td>
<td>4</td>
<td>2</td>
<td>30</td>
</tr>
<tr>
<td>Total</td>
<td>21</td>
<td>10</td>
<td>25</td>
<td>34</td>
<td>90</td>
</tr>
</tbody>
</table>

Conclusion: Dyspepsia is a common symptom and most of the patients have functional dyspepsia instead of other H. pylori related diseases. We should distinguish that is functional or organic disease. In addition to detailed history and physical examination, we need a noninvasive diagnostic test initially. UBT can be a safe, cost effective diagnostic test for this propose.
Helicobacter pylori antibiotic sensitivity patterns and risk factors for antibiotic resistance in a multi-ethnic South East Asian cohort

James Huang¹, Si Ying Sheryl Lim², Seng Hock Quak³

¹Khoo Teck Puat- National University Children's Medical Institute, National University Health System, Singapore, Singapore
²Yong Loo Lin School of Medicine, National University of Singapore, Singapore, Singapore
³National University Health System, Paediatrics, Singapore, Singapore

Objectives and study: The clinical characteristics and antibiotic sensitivity patterns of Helicobacter pylori (H.pylori) infection in children may vary according to geographical regions, and there is a lack of paediatric data from South-East Asia. We aim to analyse antibiotic resistance profiles, risk factors for resistant strains, and the impact on eradication outcomes in a multi-ethnic paediatric cohort with positive H. pylori cultures diagnosed at National University Hospital, Singapore.

Methods: We identified 32 positive H. pylori cultures from gastric antral biopsies taken between 2008-2016. Clinical, endoscopy, prescription and urea breath test records were retrospectively analysed. Antibiotic sensitivity was tested based on the disc diffusion method - an inoculum of 0.2ml H. pylori suspension was spread on a chocolate blood agar plate, followed by drying and antibiotic discs were placed on the surfaces of dried agar plates at the following dosages: amoxicillin (10µg), ciprofloxacin (5µg), clarithromycin (15µg), metronidazole(50µg), tetracycline (10µg). Resistance was defined based on the diameter of inhibitory zones: amoxicillin(18mm), ciprofloxacin(30mm), clarithromycin(30mm), metronidazole(28mm), tetracycline(4mm). All statistical analyses was performed by STATA/SE 13.1, with linear regression for continuous variables and logistic regression for categorical variables.

Results: The mean age was 13.8 (6.0-17.0) years with an approximately equal gender distribution (male : 56.9%). Duodenal erosions/ulcers were more prevalent (28.1%) than gastric ulcers (9.4%). Resistance rates of the H pylori isolates were: clarithromycin (21.9%), metronidazole (21.9%) and ciprofloxacin (9.4%). All isolates were sensitive to amoxicillin and tetracycline although a younger age (p=0.009) and a prior history of failed eradication (p=0.043) had a significant association with a reduced inhibitory zone diameter for amoxicillin, while this was not observed with tetracycline. On a univariate regression analysis, significant factors increasing antibiotic resistance in general, were a younger age (p=0.015), immigrant status [non-native Singaporean](p<0.001) and longer duration of symptoms at presentation (p=0.018). In the multivariate model, only immigrant status (p<0.001) and duration of symptoms (p=0.006) remained strongly significant. Mono-resistance occurred in 15.6% (5/32); dual resistance occurred in 12.5% (4/32), of which all were resistant to clarithromycin/metronidazole; triple resistance was rare at 3.1% (1/32) to clarithromycin/metronidazole/ciprofloxacin.

Successful primary eradication is significantly dependent on clarithromycin sensitivity (p=0.005); treatment failure occurred in 24.0% of patients, of which all had received amoxicillin/clarithromycin. All cases subsequently achieved successful eradication with bismuth-based quadruple therapy regimes.

Conclusion: We report equally high resistance rates to both clarithromycin and metronidazole, and clarithromycin resistance was the single most important cause for primary eradication failure. Certain factors such as immigrant status, prolonged duration of symptoms and a young age at infection may predict antibiotic resistant strains, and alternatives to clarithromycin-based regimes should be sought as first-line therapy.
Treatment of Helicobacter pylori in children: a single centre experience

An-Sofie Lemmens¹, Koen Huysentruyt¹, Bruno Hauser¹, Annieta Goossens², Denis Pierard³, Toni Lahoutte², Yvan Vandenplas⁴

¹Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
²Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Brussels, Belgium
³Uz Brussel, Labo Microbiologie, Brussels, Belgium
⁴Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives and study: New ESPGHAN guidelines for the management of Helicobacter pylori (HP) in children were recently published. In a preliminary presentation of these guidelines at the previous ESPGHAN annual meeting a longer duration and higher dosage of antibiotic therapy was proposed to obtain a better eradication rate. This study aimed to 1) investigate local success rates of HP eradication and 2) local HP resistance rates to standard antibiotics.

Methods: A retrospective chart review (2010-2016) was performed of children that underwent a ¹³C-urea breath test (UBT) in case of suspicion of a HP infection. A true positive UBT (cut-off at ≥3 δ‰) was defined as a confirmed presence of HP on anatomic pathology and/or a positive culture. Resistance to antibiotics were determined through minimum inhibitory concentration (MIC) values, using the Eucast clinical breakpoints. Statistical analysis were done using SPSS, proportions between groups were compared using a χ² or Fisher Exact test, difference in continuous variables were determined using the Mann Whitney U test. A significance level of 0.05 was used for all tests.

Results: We assessed the files of 353 children undergoing a UBT, of which 81 (22.9%) were positive. In 63 (77.8%) patients a confirmatory gastroscopy was performed, 7 patients (11.1%) had a false positive UBT (values ranging from 3.1 to 63.2 δ‰). Overall, the median (Q1; Q3) age and weight (z score) were 8.3 (5.7; 11.6) years and 0.34 (-0.7; 1.1) respectively; 40 (49.4%) of the population was female. A post-treatment UBT to confirm eradication of treatment was performed after 70/104 (67.3%) treatment courses. Forty-two children received 1 treatment course, 18 children two courses, 4 received three and one four eradication courses. A confirmed eradication was achieved for 73.3% of the children treated for the first time and 88.9% treated for the second time. The most frequently used treatment strategies were amoxicillin-clarithromycin-PPI (ACP) (85.5%) and amoxicillin-metronidazole-PPI (AMP) (10.4%), duration varied between 7 and 10 days. ACP treatment was used significantly more in a first eradication attempt than in a second or more attempt (p<0.001), whilst the proportion of children treated with AMP was significantly higher (p<0.001) when it was second (or more) eradication course. Overall HP resistance rates for clarithromycin and metronidazole were 15.0% and 11.9% respectively. We did not find an association between treatment success and sex, resistance to clarithromycin (p=1.00), resistance to metronidazole (p=1.00), family history of HP infection (p=0.657), prior episodes of HP-infection (p=0.432), age (p=0.878) or duration of antibiotic therapy (0.225).

Conclusion: HP eradication was successfully for three quarter of the children treated for the first time and 90% of those treated for the second time. We could not identify any factors associated with treatment success, probably due to small sample size. Local antibiotic resistance rates are comparable with those reported in literature.
Clinical study of tailored therapy in Helicobacter pylori infection treatment in pediatrics

Dongdan Li¹, Xiwei Xu²

¹Beijing Children’s Hospital of Capital Medical University, Beijing, China
²Beijing Children’s Hospital, Capital Medical University, Gastroenterology, Beijing, China

Objectives and study: To discuss the efficacy of tailored therapy based on H. pylori invitro culture, drug sensitivity and cytochrome P450 genetic polymorphisms (CYP2C19), to explore the cause of eradication failure in pediatrics and improve the eradication rate of Helicobacter pylori.

Methods: A total number of 128 pediatric patients at Beijing Children’s Hospital with Helicobacter pylori infection of upper gastrointestinal tract, confirmed by 13C-urea breath test and gastroscope, were all failed on standard triple therapy. Gastric mucosal biopsy samples were used to collect H. pylori strains, and examine drug sensitivity and cytochrome P450 genetic polymorphisms. Two antibiotic medications were selected according to drug sensitivity and PPI was taken based on cytochrome P450 genetic polymorphisms. Patients with Clarithromycin sensitive choose amoxicillin and clarithromycin, patients with clarithromycin resistance choose amoxicillin and Tinidazole. Patients with rapid extensive metabolizer choose rabeprazole, patients with poor metabolizer and intermediate metabolizer choose omeprazole. The course of treatment was ten days. 13C-urea breath test was performed again 4 weeks after the therapy to assess eradication status.

Results: The study of 128 cases of patients, with 45 famelas and 71 males. Clinical manifestations include: abdominal pain (97 cases), vomiting (23 cases), anorexia (23 cases), abdominal distension (19 cases), belching (19 cases), acid reflux (18 cases), nausea (6 cases). H. pylori antibiotic resistance rate: Amoxicillin (0.8%), Clarithromycin (86.7%), Levofloxacin (60.9%), Metronidazole (40.6%), Acheomycin Neotetrine (0.8%). Cytochrome P450 genetic polymorphisms: Rapid extensive metabolizer (46.1%), Poor metabolizer (5.5%), Intermediate metabolizer (48.4%). A total of 128 cases include 79 successful and 49 failed cases, eradication rate was 61.7%. Adverse drug reactions accounted for 2.3%.

Conclusion: Tailored therapy based on H. pylori culture, drug sensitivity and cytochrome P450 genetic polymorphisms has certain significance to improve the H. pylori eradication rate and choke H. pylori resistance rise.
**Clinical characteristics of Helicobacter pylori - negative, non-steroidal anti-inflammatory drug - negative duodenal ulcer disease in children: a single university hospital experience**

Manabu Tagawa¹, Hiroki Wada², Takuro Sato³, Ryo Sumazaki⁴

¹University of Tsukuba, Department of Child Health, Faculty of Medicine, Ibaraki, Japan
²Kensei General Hospital, Department of Pediatrics, Ibaraki, Japan
³Ibaraki Children's Hospital, Department of Pediatrics, Ibaraki, Japan
⁴University of Tsukuba, Department of Child Health, Faculty of Medicine, Ibaraki, Japan

**Objectives and study:** There have been some studies that report an increased rate of *H. pylori*-negative, non-steroidal anti-inflammatory drug (NSAID)-negative duodenal ulcer disease in adults and children. The prevalence and clinical characteristics of these ulcer diseases in children differ among countries, especially between Europe and Asia. We therefore investigated clinical characteristics and outcomes of *H. pylori*-negative, NSAID-negative duodenal ulcer disease in our pediatric patients who underwent upper endoscopic procedures.

**Methods:** We retrospectively collected data from paediatric patients (age 18 or younger) who underwent upper gastrointestinal endoscopic examinations between April 2011 and March 2016. The resulting demographic, clinical, endoscopic, and laboratory data were reviewed. The diagnosis of *H. pylori* infection was based on endoscopic findings, histological results, rapid urease test, urea breath test, stool antigen test and serum antibody test. NSAID users were defined by medical history of taking NSAID from patient and their parents.

**Results:** Out of the 285 endoscopic procedures in 148 children, a total of 7 (4.7%) children had duodenal ulcers, mucosal erosion or scars. Among 7 patients, *H. pylori* infection was only detected in one adolescent with a duodenal ulcer. There were no NSAID users. The clinical characteristics of 6 patients with *H. pylori*-negative, NSAID-negative duodenal ulcer disease were as follows: mean age 10.3 years (range 1 year to 15 years), 4 male (one with trisomy 21, one with agenesis of the corpus callosum) and 2 female. Clinical symptoms included abdominal pain, hematemesis, melena and shock. One male patient had a duodenal perforation and was treated conservatively without complication. Among five patients with haemorrhagic duodenal ulcer disease, one needed surgery because of difficulty in endoscopic hemostasis. Three patients had recurrent disease and one underwent angiographic intervention to obtain hemostasis. Three patients underwent a long period of medication because of recurrence. As a late complication, one had duodenal stenosis and needed surgery. Serum gastrin level in 6 patients was within normal range.

**Conclusion:** *H. pylori*-negative, NSAID-negative duodenal ulcer diseases are uncommon, but life-threatening when resulting in gastrointestinal bleeding. Some patients require urgent treatment with surgery or endoscopic hemostasis. Since there is a high risk of recurrence, some patients might also require long-term medication. This case therefore calls for studies with large numbers of patients to examine the intricacies of this specific type of duodenal disease.
Helicobacter pylori infection in children: how to overcome antimicrobial resistance?

Marco Manfredi¹, Silvia Iuliano¹, Federica Gaiani², Pierpacifico Gismondi¹, Carmen Madia¹, Giuseppina De Caro¹, Gian Luigi de' Angelis²

¹Pediatric Clinic, University Hospital of Parma, Parma, Italy
²Unit of Gastroenterology and Digestive Endoscopy, University Hospital of Parma, Parma, Italy

Objectives and study: Helicobacter pylori (Hp) infection can cause several gastrointestinal diseases over the years, if not eradicated. The best therapeutic approach in terms of efficacy and safety has not yet been identified.

Treatment failure is often due to antibiotic resistances, both in adults and children. A different combination of the available antibiotics may improve the eradication rate. As the availability of antibiotics in children is limited, we wanted to test the efficacy of sequential therapy (esomeprazole (Eso) 0.8-1.3mg/kg/die + Amoxicillin (AMO) 50-60mg/kg/die b.i.d. for the first 5 days followed by Eso 0.8-1.3mg/kg/die + Clarithromycin (CLA) 15-20mg/kg/die and Tinidazole (TIN) 20-30mg/kg/die b.i.d. for the next 5 days) regardless the culture development, to verify if this regimen could overcome antibiotic resistances.

Methods: Children with Hp infection, admitted to the Department of Paediatric Gastroenterology of Parma between July 2013 and July 2015 were recruited. The confirmation of Hp infection was made using at least two tests among detection of faecal antigen, rapid urease test, urea breath test, histological detection and culture on biopsies. All the patients underwent esophagogastroduodenoscopy (EGDS) with biopsies, histological examination and microbiological culture. Data about demographics, country of origin, symptoms, EGDS findings and antimicrobial susceptibility towards AMO, metronidazole (MET), and CLA were collected. All patients received sequential therapy.

Results: Fifty-three children were enrolled, mean age 9.48 years. Thirty-two patients came from Italy (60.4%), 6 from Northern-Africa (11.3%), 9 from Eastern-Europe (17%), 4 from Southern-Sahara (7.5%) and 2 from Asia (3.8%). Fourteen patients were asymptomatic, while the other cases presented with abdominal pain (47.1%), pyrosis (7.6%), vomit (5.7%) or a combination (13.2%). Endoscopy showed a nodular gastric mucosa in 77.4% of cases, while all patients had a chronic non-atrophic gastritis at histology. The culture developed in 86.8% of cases. Out of these, 20 patients (43.5%), resulted susceptible towards all the tested antibiotics, 14 showed an isolate resistance to MET (30.4%) and 12 to CLA (26.1%). One child had a combined resistance towards both MET and CLA. By using sequential therapy, we obtained an overall eradication rate of 88.7%. Among the 20 patients who resulted susceptible to all antibiotics, an eradication rate of 95% was obtained. The infection was eradicated in 92.8% of patients with MET resistance, in 75% of those with CLA resistance, including the child with combined resistance, and in 85.7% of patients in which the antimicrobial susceptibility testing did not develop.
### Table:

<table>
<thead>
<tr>
<th>Antibiotic resistance (n°tot) (%)</th>
<th>Italian (n° eradicated/ n° tot) (%)</th>
<th>Immigrant (n° eradicated/ n° tot) (%)</th>
<th>Eradication rate, n° (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CLA-R (12) (26.1%)</td>
<td>8/9 (88.9%)</td>
<td>N-A 1/1 (100%)</td>
<td>9 (75%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E-E 0/2 (0%)</td>
<td></td>
</tr>
<tr>
<td>MET-R (14) (30.4%)</td>
<td>8/8 (100%)</td>
<td>N-A 1/2 (50%)</td>
<td>13 (92.8%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E-E 1/1 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asia 1/1 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>S-S 2/2 (100%)</td>
<td></td>
</tr>
<tr>
<td>Full-susceptible (20) (43.5%)</td>
<td>12/12 (100%)</td>
<td>N-A 2/2 (100%)</td>
<td>19 (95%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E-E 3/4 (75%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Asia 1/1 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>S-S 1/1 (100%)</td>
<td></td>
</tr>
<tr>
<td>Culture failed (7) (13.2%)</td>
<td>2/3 (66.7%)</td>
<td>N-A 1/1 (100%)</td>
<td>6 (85.7%)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>E-E 2/2 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>S-S 1/1 (100%)</td>
<td></td>
</tr>
<tr>
<td>Total (53) (100%)</td>
<td>30/32 (93.8%)</td>
<td>17/21 (80.9%)</td>
<td>47 (88.7%)</td>
</tr>
</tbody>
</table>

**Conclusion:** Considering the limited availability of antibiotics in paediatrics, sequential regimen could be a valid option for the eradication of *Hp* infection as first-line therapy, at least in Italy.
Usefulness of ultrasonography in the early diagnosis of peptic ulcer disease in children

Yeoun Joo Lee, Sang Wook Mun, Eun Ha Hwang, Peter Chun, Jae Hong Park

1Pusan National University School of Medicine, Pediatrics, Yangsan, Korea, Rep. of South

Objectives and study: To assess the clinical usefulness of transabdominal ultrasonography (TUS) for detection of gastroduodenal peptic ulcer disease (PUD).

Methods: Twenty-four patients who were admitted Pusan National University Children's Hospital due to acute abdomen or gastrointestinal bleeding and were diagnosed with PUD by endoscopy and underwent TUS were included. Clinical data were collected retrospectively by reviewing medical records of patients between Jul 2010 and Jul 2015. TUS was performed with an 8-15 MHz linear scanner. When the thickness the gastric wall on sonography exceeded 1 cm or when part of the wall appeared significantly thicker than the adjacent, and when the thickness of the duodenal wall exceeded 0.5 cm, the patient was suspected as having gastric ulcer (GU) or duodenal ulcer (DU), respectively. Comparison for sensitivity of TUS in diagnosing PUD according to body weight was done using logistic regression test. \( P \)-values less than 0.05 were considered statistically significant.

Results: A total 24 patients (19 male, 5 female) were included. The mean age of the patients was 10.6±4.5 (range: 3.0-17.9) years. Chief complaints were abdominal pain (66.7%), gastrointestinal bleeding (20.9%) and vomiting (12.5%). Duration between symptom presentation and diagnosis was 7.0±7.7 days. Sensitivity of TUS in diagnosing PUD was 66.7% in GU and 38.9% in DU. The mean age and body weight of 11 patients suspected with PUD on TUS (4 GU, 6 DU, 1 combined) were 8.9±4.7 years and 28.3±15.5 kg. The mean age and body weight of 13 patients who were not diagnosed on TUS (2 GU, 9 DU, 2 combined) were 12.1±4.1 years and 46.4±14.4 kg. Sensitivity of TUS in diagnosing PUD according to body weight of patient was 88.9% in patient under 30 kg and 20.0% over 30 kg \( P=0.007 \). There were no statistical differences between sensitivity of TUS in diagnosing PUD and age, and localization of lesion.

Conclusion: The ultrasound investigation of the stomach and duodenum is a highly efficient method for the detection of PUD in children, especially in those who have lower body weight. Ultrasonography can be used in the preliminary diagnostic work-up prior to further invasive tests.
Helicobacter pylori antibiotic resistance in Armenian children: preliminary data

Tatevik Shahinyan\(^1\), Gayane Amaryan\(^2\), Christian Braegger\(^3\)

\(^1\)Arabkir Medical Centre, Institute of Child and Adolescent Health, Gastroenterology and Hepatology Service, Yerevan, Armenia
\(^2\)“Arabkir” Medical Centre-Institute of Child and Adolescent Health, Gastroenterology and Hepatology Service, National Pediatric Familial Mediterranean Fever Centre, Yerevan State Medical University, Pediatrics, Yerevan, Armenia
\(^3\)Children’s Research Centre, University Children’s Hospital, Division of Gastroenterology and Nutrition, Zurich, Switzerland

**Objectives:** The prevalence of Helicobacter pylori (Hp) is highly variable in relation to geography, ethnicity, age and socioeconomic factors, reaching 70% in developing countries [1]. High incidence of Hp in children appears to be a contributing factor to high incidence of gastric cancer in adult population in several areas [2]. Successful eradication is an important factor in prevention of Hp complications. A leading factor limiting treatment effectiveness is antibiotic resistance. Surveillance of antibiotic resistance rate in different geographic areas is recommended [3]. Aim of the present prospective clinical study is to determine antibiotic resistance of Hp in hospitalized Armenian children with gastroduodenal (GD) disease.

**Methods:** 45 symptomatic children with suspected GD disease were selected from April to December 2016 (23 boys and 22 girls, aged 2.5 - 18y). Hp associated gastritis, duodenitis or peptic ulcer disease (PUD) were diagnosed according to clinical, laboratory, endoscopic and histological criteria. Patients were enrolled according to clinical criteria (chronic dyspeptic symptoms - nausea, vomiting, regurgitation, early satiety; recurrent epigastric pain). Exclusion criteria were antibiotics <1 month and PPI <2 weeks prior to referral; decompensated cardio-respiratory disorders; coagulopathy; and pharmacotherapy for epilepsy, asthma, and familial Mediterranean fever. Biopsies were taken from antral part of the stomach (1 for histology and rapid urease test; 1 for culture), duodenal bulb, and distal oesophagus. Biopsies for culture were transferred to the lab in special transport media (Portagerm) within 15 minutes and drawn to Columbia agar with 5% sheep blood and selective Hp media. Histological examination was done according to the updated Sydney criteria. Specimens were stained by Giemsa for detection of Hp.

**Results:** Hp associated disease was diagnosed in 37 out of 45 patients (34 gastritis and duodenitis, 3 PUD). Eight from 45 children (17.8%) were excluded from the study due to both histology and culture negative results for Hp. Cultures were positive for Hp in 14 of 37 patients (37.8%). Determination of antibiotic susceptibility was possible in 12 strains. All but 2 were resistant to metronidazole (83.3%), 4 were resistant to clarithromycin (33.3%), 3 were resistant to both metronidazole and clarithromycin). A high rate of doxycycline resistance was found (66.6%). All strains were susceptible to amoxicillin and levofloxacin, 6 strains were tested and found susceptible to nifurantel.

**Conclusion:** Preliminary data indicate a high resistance rate to metronidazole (83.3%) and clarithromycin (33%) in Armenian children with Hp associated GD disease. Surprisingly more than half of all specimens were resistant to doxycycline despite of limited use of this antibiotic in pediatric practice. High susceptibility to nifurantel might be useful for further development of specific eradication schemes for Armenia.

The prevalence on Helicobacter pylory in children with syndrome od dyspepsia in Trans-Baical territory

Vladimir Shcherbak¹

¹Chita State Medical Academy, Pediatric Department of Postgraduing Training, Chita, Russian Federation

Objectives and study: Helicobacter pylori, according to The Kyoto consensus (2015) is one of the major pathogens that cause functional dyspepsia. In Russia, there are only a few data on the prevalence of Helicobacter pylori in children. Objective: To study the prevalence of Helicobacter pylori infection in children with the syndrome of dyspepsia in the Trans-Baikal Territory.

Methods: The study involved 550 patients with functional dyspepsia aged 8-15 years. With abdominal pain syndrome was 423 children with post-prandial dyspepsia - 127. Helicobacter pylori Ig M was examined by ELISA in the serum. For the ELISA we used the following equipment: shaker-thermostat Elmi ST-3 (Latvia), automatic washer Atlantis 4 (UK), Immunoassay Analyzer Awareness Technology (USA). Voluntary informed consent was taken in all patients.

Results: Antibodies to Helicobacter pylori were found in 313 (57%) patients. Titer 1:10 was in 13 (2.4%), 1:20 in 62 (11.4%), 1:40 in 115 (20.9%), 1:60 122 (22.3%) patients. Prevalence of Helicobacter pylori infection in children with the syndrome of dyspepsia in the Trans-Baikal region was not significantly different from other regions of Russia. According to the 7 statement of the Kyoto consensus (2015) Helicobacter pylori may be a cause of dyspepsia symptoms in patients. According to the 8 statement of the Consensus Helicobacter pylori-associated dyspepsia should be considered as a special form of the disease.

Conclusion: Thus, the prevalence of Helicobacter pylori infection in children with the syndrome of dyspepsia in the Trans-Baikal Territory is 57%.
**Helicobacter Pylori eradication in children**

Nadia Siala¹, Mohamed Charfi², Zied Khlayfia², Ines Kasraoui², Ilhem Fetni², Haifa Ouerda², Sonia Halioui², Ahmed Maherzi²

¹Hôpital Mongi Slim, Service de Pédiatrie, and Genius Group, La Marsa, Tunisia
²Mongi Slim Hospital, Sidi Daoud, La Marsa, Tunisia

**Objectives and study:** To compare the eradication rate of helicobacter pylori (Hp) between 2 therapeutic protocols in children.

**Methods:** Prospective study from April 2016 to November 2016 in a pediatric department in Mongi Slim Hospital (Tunis-Tunisia). We included all children with chronic Hp gastritis. Children were randomly treated with one of the two following protocols: Protocol A (Amoxicillin+Clarithromycin+Metronidazole+PPI during 10 days) and Protocol B (Amoxicillin+Clarithromycin+PPI during 5 days then Amoxicillin+Metronidazole+PPI during 5 days). The eradication control was practiced at least after 2 months by Breath Test (BT) or endoscopy.

**Results:** 52 children were enrolled. The sex-ratio was 1.2. The median age was 8.7 years (13months to 15years).

Abdominal pain was the most frequent reason of consultation (N=36), vomiting (N=10), anorexia (N=6).

The median duration of the symptoms was 12months (15 days – 72 months). The upper endoscopy was done in all cases and showed: erythematous antral gastritis (N=18), nodular antral gastritis (N=29) and normal mucosa (N=5). Histopathologic examination showed chronic Hp gastritis in all cases. Hp activity was intense (N=5), moderate (N=30), low (N=17).

28 received protocol A and 24 received protocol B. Clinical improvement was noted after an average delay of 5.3 days (2-15). The control of eradication was done by BT (N=23) and upper endoscopy (N=29). The BT was negative in 20 cases and the biopsy was negative in 20 cases.

The eradication rate in patients treated with protocol A was 71% and in patients treated with protocol B was 91%.

**Conclusion:** Protocol B seems to be more efficient for Hp eradication. Multicenter studies with largest number of children are necessary to evaluate treatment efficiency.
**GASTROENTEROLOGY: Peptic disease and helicobacter pylori**

**G-P-339**

**Chronic Helicobacter pylori infection in adolescents with Functional Gastrointestinal Disorders (FGIDS) defined by questionnaire on pediatric gastrointestinal symptoms Rome III version (QPGS-RIII): study in region with high infection prevalence (Central Siberia)**

Sergey Tereshchenko¹, Elena Anisimova², Nina Gorbacheva³

¹Scientific Research Institute of Medical Problems of the North, Department of Child's Physical Health, Krasnoyarsk, Russian Federation
²Krasnoyarsk State Medical University, Krasnoyarsk, Russian Federation

**Objectives and study:** Many worldwide studies have shown no relation between recurrent abdominal pain (RAP) and chronic Helicobacter pylori (Hp) infection in children and adolescents; however, there are some limitations for final conclusion. First, most studies did not make any separation for definitive FGDIS subtypes and even for upper and low RAP patterns; second, data regarding this relation are mostly available for regions with low Hp prevalence; third, the age should be taken into consideration as the important factor. We aimed to investigate the relation between FGIDS and Hp presence in Siberian adolescent (region with high Hp prevalence).

**Methods:** 246 adolescents with RAP complaints aged 11-17, referred to a pediatric gastroenterology center (Krasnoyarsk, Siberia, Russia), were screened by QPGS-RIII and tested to Hp positivity (Hp antigen ELISA monoclonal test in stool, Immundiagnostik, Germany). No tested adolescent had erosions or ulcer according to upper endoscopy. The rates of FGIDs in accordance to QPGS-RIII scoring instructions were as follows: functional dyspepsia (FD) – 17, irritable bowel syndrome (IBS) – 61, abdominal migraine (AM) – 14, functional abdominal pain (FAP) – 19, functional abdominal pain syndrome (FAPS) – 14. Two-sided Fisher’s exact test with Yates’ correction was used.

**Results:** Significant positive association was detected between FD group and Hp presence and negative for IBS adolescents (Table 1).

**Table:** Hp positivity percentages in adolescents with different FGIDS

<table>
<thead>
<tr>
<th>Helicobacter pylori status</th>
<th>No FGIDs</th>
<th>FD</th>
<th>IBS</th>
<th>AM</th>
<th>FAP</th>
<th>FAPS</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive Hp stool test</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>52.9 %</td>
<td>76.5 %</td>
<td>37.7 %</td>
<td>42.9 %</td>
<td>57.9 %</td>
<td>50.0 %</td>
<td>0.067</td>
</tr>
<tr>
<td>(64/121)</td>
<td>(13/17)</td>
<td>(23/61)</td>
<td>(6/14)</td>
<td>(11/19)</td>
<td>(7/14)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** We suppose that RAP diagnostics in adolescents with upper abdomen pain pattern with high frequency (several times a week or every day) should include Hp testing in region with high infection prevalence, although, eradication usefulness in this subgroup of patients requires further investigation. Low Hp prevalence in adolescents with IBS may be resulted by higher socioeconomic status, antibiotics overuse or even some protective role of Hp chronic infection in this patients group.

The reported study was funded by Russian Foundation for Basic Research, Government of Krasnoyarsk Territory, Krasnoyarsk Region Science and Technology Support Fund to the research project № 16-44-240668.
Infectious markers and autoantibodies against microsomes gastric parietal cells in chronic gastritis in children

Galina Volynets¹, Anatoly Khavkin¹

¹Pirogov Russian National Research Medical University (Rnrmu), Gastroenterology, Moscow, Russian Federation

Objectives and study: Determine the frequency of occurrence of markers most widespread of infections at a chronic gastritis (CG) in children.

Methods: The study included 145 children (mean age 10.1±0.3 years) with upper digestive tract diseases (UDT); continuous study without preliminary qualification selection. Among them allocated a group of 128 patients with endoscopically and morphologically diagnosed with chronic gastritis. In biopsies of the mucosa gastric by the PCR method was carried out DNA determination H. pylori and identification of specific DNA herpesviruses (Epstein-Barr virus - EBV, cytomegalovirus - CMV, herpes simplex virus type 1 and 2 - HSV1-2, herpes virus human type 6 - HHV6). The method of indirect immunofluorescence on a fluorescent microscope "LUMAM-P1" using the antibody conjugate to human IgG with flyuorestseinizotiosionat were determined autoantibodies against microsomes gastric parietal cells (APCG).

Results: H.pylori in children with disorders UDT detected in 65 patients (45%), EBV-specific DNA in the gastric mucosa - in 44 patients (30%), CMV - have 4 (2.8%) children, HSV1-2 - have 2 patients (1%). APCG in children with disorders UDT were detected in the 58 cases out of 145 (40%), and the 128 cases of CG (45%). If there are in gastric mucosa a EBV DNA APCG are defined in 40 of 44 cases (90.9%).

Conclusion: Autoimmune gastritis, which are markers of autoantibodies against gastric parietal cells microsomes, diagnosed in children with UDT pathology in 40% of cases, and at a chronic gastritis - a 45% of cases. Among the most widespread in the population infections markers in gastric mucosal H.pylori are determined DNA and EBV. The presence of APCG and, consequently, autoimmune gastritis, EBV is associated with DNA a gastric mucosal.
Clinical profile and factors associated with non-alcoholic fatty liver disease (NAFLD) among overweight and obese children: a prospective study

Sarabeth De Castro¹, Maria Estela Nolasco¹, Randy Urtula¹, Adrienne Michelle Lu¹

¹Philippine Children's Medical Center, Section of Pediatric Gastroenterology, Hepatology and Nutrition, Quezon City, Philippines

Objectives and study: In the past decades, the prevalence of childhood overweight and obesity had increased worldwide. Childhood obesity has been associated with a wide range of serious health complications and increased risk of premature adult illnesses. Non-alcoholic Fatty Liver Disease (NAFLD) was of concern because of limited data among children. The study aims to determine the prevalence and demographic/clinical factors associated with Non-alcoholic Fatty Liver Disease (NAFLD) among overweight and obese children.

Methods: The study was a cross sectional study among overweight and obese participants aged 2-18 years old. Study period was from October 2015 to June 2016. A total of 96 subjects were included. Frequencies and percentages of clinical characteristics were determined. Chi-square and linear regression analysis for different factors were performed.

Results: A total of 96 subjects were included in the study with four drop-outs as they opted to withdraw consent and refuse to proceed. Among the 92 subjects, 26 (28%) were overweight while 66 (72%) were obese. The M:F ratio was 1.8:1 and majority belonged to 6-10 years old (44%). As to socioeconomic class, majority (59%) were from the low income group. The overall prevalence of NAFLD among overweight and obese subjects was 29.3%. None of the clinical factors (age, gender, socioeconomic status, BMI, waist circumference, actual caloric intake and dietary fat consumption) were significantly associated with NAFLD. Analysis of biochemical factors revealed that alanine aminotransferase, aspartate aminotransferase, serum triglycerides and total cholesterol were found to be associated with NAFLD.

Conclusion: The growing epidemic of obesity further increases the risk of developing NAFLD. There was a high prevalence of NAFLD among overweight and obese children. Screening among the pediatric population may aid in early identification and prevent its progression. With analysis of different factors, ALT, AST, serum triglycerides and total cholesterol were independently related with NAFLD. Among which, AST was the primary predictor while total cholesterol was the least predictor identified.
Biliatresone, a toxin model of biliary atresia in animals, causes reversible damage to extrahepatic bile ducts, and its toxicity is related to Rhou and Sox17

Orith Waisbourd-Zinman¹, Sophia Fried², Alyssa Kriegermeier³, Pierre-Marie Lavrut⁴, Pierre Russo³, Raanan Shamir⁵, Rebecca Wells⁶

¹Schneider Children's Medical Center of Israel, Gastroenterology, Nutrition and Liver Diseases, Petach Tiqva, Israel
²Schneider Children's Medical Center of Israel, Petach Tiqva, Israel
³Children's Hospital of Philadelphia, Philadelphia, United States
⁴University of Pennsylvania, Philadelphia, United States
⁵Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
⁶University of Pennsylvania School of Medicine, Philadelphia, United States

Objectives and study: Biliary atresia (BA) is a fibrotic disease of unknown etiology affecting the extrahepatic bile ducts (EHBDs) of newborns. The isoflavonoid biliatresone, which causes rapid decreases in glutathione (GSH), leads to a BA-like disease in newborn livestock and larval zebrafish as well as to EHBD obstruction in neonatal mouse EHBD explants. As biliatresone represents a new model of BA, our goal was to understand the nature of toxin-associated injury, the potential recovery and the molecular mechanisms involving injury in the EHBD.

Methods: Cholangiocyte organoids with open lumens were generated by growth in 3D culture. EHBD were isolated from neonatal BALB/c mice (days 0-3), cultured in a high oxygenation incubator (95% O₂), treated with biliatresone and allowed to recover for varying lengths of time. We investigated molecular pathways by real time PCR and by silencing and overexpressing proteins. Target proteins were assessed in human livers by comparing immunostaining of human biliary atresia and normal liver tissues.

Results: Biliatresone treatment for 24h caused loss of lumens in >50% of organoids at a molar concentration of 6.1μM. In neonatal EHBD explant cultures, biliatresone associated ductal damage was observed after 4h, along with lumen obstruction and increased subepithelial staining for α-smooth muscle actin (α-SMA) and collagen observed after 24h treatment. Explants treated for up to 24h recovered lumen integrity after 24h of washout, with a partial decrease in α-SMA staining. The molecular pathway of the toxin was related to the WNT signaling pathway. Biliatresone caused an increase in Rhou and a concomitant decrease in Sox17. Both overexpression of Rhou and silencing of Sox17 resulted in lumen obstruction of cholangiocyte organoids in 3D culture. Staining human biliary atresia livers demonstrated increased Rhou staining of intrahepatic cholangiocytes at the time of BA diagnosis compared to non-BA liver biopsies.

Conclusion: Biliatresone has direct toxic effects on cholangiocyte organoids and neonatal bile duct explants. The neonatal EHBD has significant capacity for repair, although there is likely a point of irreversibility. The molecular pathway of biliatresone toxicity includes decreases in Sox17 and increases in Rhou. In vivo, this is a potential cause of lumen obstruction and may be an important part of the pathophysiology of BA.
A comparison of primary sclerosing cholangitis with and without associated inflammatory bowel disease: data from the pediatric PSC consortium


1Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
2The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada
3State University of New York Buffalo, Buffalo, United States Minor Outlying Islands
4Prince Salman North West Armed Forces Hospital, Tabuk, Saudi Arabia
5University of California San Francisco, San Francisco, United States Minor Outlying Islands
6The Dana-Dwek Children's Hospital, Tel Aviv, Israel
7Alder Hey Children's NHS Foundation Trust, Department of Paediatric Gastroenterology, Hepatology and Nutrition (Ghn), Liverpool, United Kingdom
8Mayo Clinic, Rochester, United States Minor Outlying Islands
9Our Lady's Children's Hospital, Crumlin, Dublin, Ireland
10University of Rochester Medical Center, Rochester, United States Minor Outlying Islands
11University of Colorado School of Medicine, Aurora, United States Minor Outlying Islands
12University of Utah, Salt Lake City, United States Minor Outlying Islands
13Children's Hospital Research Institute of Manitoba, DIV Gi, Winnipeg, Canada
14Mayo Clinic, Rochester, United States
15Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
16CHU Lille, Reference Center for Congenital and Malformative Esophageal Disease (Cracmo), Division of Gastroenterology, Hepatology and Nutrition, Lille, France
17Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
18Emory University School of Medicine, Atlanta, United States Minor Outlying Islands
19University Children's Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia
20Seoul Asan Medical Center, Seoul, Korea, Rep. of South
21Helsinki University, Department of Pediatric Gastroenterology, Helsinki, Finland
22Royal Manchester Children's Hospital, Department of Paediatric Gastroenterology, Manchester, United Kingdom
23Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
24University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
25Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
26Columbia University College of Physicians and Surgeons, New York, United States Minor Outlying Islands
27Texas Children's Hospital, Houston, United States Minor Outlying Islands
28Children's National Medical Center, Washington, United States Minor Outlying Islands
29University College Dublin, Dublin, Ireland
30Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece
31Memorial University, St-John's, Canada
Objectives and study: Primary sclerosing cholangitis (PSC) frequently co-exists with inflammatory bowel disease (IBD). Data comparing IBD-associated PSC and isolated PSC in children are sparse. We aimed to evaluate disease characteristics and long-term outcomes of PSC in children with and without IBD in a large, multicenter pediatric cohort.

Methods: We examined data from the Pediatric PSC Consortium, a collaboration of 36 centers. We performed a survival analysis from time of PSC diagnosis to any of: 1) a portal hypertensive complication (ascites, encephalopathy or esophageal varices), 2) a dominant biliary stricture requiring stent, dilation or drainage, 3) liver transplantation, 4) cholangiocarcinoma and/or 5) liver-related death. Multivariate Cox regression was used to examine the association between IBD and the risk of progression to adverse liver outcomes, adjusting for age, gender, a small or large duct phenotype, overlap with autoimmune hepatitis (AIH), ursodiol use, as well as baseline MELD score and AST to Platelet Ratio Index (APRI).

Results: 571/751 PSC patients (76%) had concomitant IBD (83% ulcerative colitis (UC), 17% Crohn disease (CD)). PSC without IBD was characterized by more females, a greater proportion of AIH overlap (51 vs. 28%), and a higher baseline MELD (4 vs. 0), APRI (1.57 vs. 0.68), and ALT (286 vs. 176), all p<0.001. Small vs. large duct involvement and GGT were similar in both groups. The probability of portal hypertensive and biliary complications within 5 years of diagnosis in the PSC vs. PSC-IBD groups was 31 vs. 21%, and 24 vs. 12%, respectively (p<0.01), despite a 5% prevalence in both groups at baseline. Event-free survival at 5 years was worse in PSC vs. PSC-IBD (58% vs 73%, p<0.001). In univariate analysis, concomitant IBD, a small duct phenotype and a lower baseline MELD score were independently-associated with a higher probability of event-free survival. In multivariate analysis, only MELD score was associated with outcomes (HR 1.09 [95% CI 1.05-1.13]). Event-free survival did not differ between UC and CD phenotypes.

Table: Univariate and Multivariate Analyses Examining Event-Free Survival in Pediatric PSC

<table>
<thead>
<tr>
<th></th>
<th>Univariate HR (95% CI)</th>
<th>p</th>
<th>Multivariate HR (95% CI)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory bowel disease</td>
<td>0.66 (0.49-0.88)</td>
<td>0.006</td>
<td>0.88 (0.56-1.37)</td>
<td>0.577</td>
</tr>
<tr>
<td>Large duct disease</td>
<td>1.4 (1.01-1.92)</td>
<td>0.042</td>
<td>1.40 (0.87-2.24)</td>
<td>0.167</td>
</tr>
<tr>
<td>PSC+AIH overlap</td>
<td>0.99 (0.75-1.32)</td>
<td>0.990</td>
<td>1.01 (0.68-1.49)</td>
<td>0.971</td>
</tr>
<tr>
<td>Male gender</td>
<td>0.88 (0.67-1.14)</td>
<td>0.342</td>
<td>1.02 (0.69-1.49)</td>
<td>0.937</td>
</tr>
<tr>
<td>Ursodiol therapy</td>
<td>0.99 (0.68-1.44)</td>
<td>0.94</td>
<td>0.81 (0.5-1.32)</td>
<td>0.403</td>
</tr>
<tr>
<td>Age at diagnosis of PSC</td>
<td>1.00 (0.97-1.03)</td>
<td>0.868</td>
<td>0.97 (0.93-1.02)</td>
<td>0.239</td>
</tr>
<tr>
<td>APRI</td>
<td>1.02 (0.99-1.05)</td>
<td>0.280</td>
<td>0.99 (0.95-1.02)</td>
<td>0.472</td>
</tr>
<tr>
<td>MELD</td>
<td>1.07 (1.05-1.10)</td>
<td>&lt;0.0001</td>
<td>1.09 (1.05-1.13)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>
Conclusion: PSC-IBD patients experienced fewer adverse liver outcomes during follow-up compared to patients with no IBD. The presence of concomitant IBD or a small duct PSC phenotype appeared to be protective in univariate analysis. However, this association was lost when controlling for baseline disease severity in a multivariate analysis. PSC-IBD patients had lower MELD scores and surrogate markers of fibrosis at baseline. It is unclear if this difference in baseline disease characteristics reflects a lead-time bias (due to routine liver enzyme monitoring in IBD patients and earlier diagnosis of PSC), or rather an intrinsically more aggressive cholangiopathy in patients without IBD. Further analysis of IBD activity and colectomy rates in this cohort is underway.
Cirrhotic cardiomyopathy pre- and post liver transplantation: incidence and clinical impact in a single centre analysis

Norman Junge 1, Claudia Junge 2, Julian Schröder 1, Eva-Doreen Pfister 1, Ulrich Baumann 3

1 Hannover Medical School, Paediatric Gastroenterology and Hepatology, Hannover, Germany
2 Hannover Medical School, Paediatric Cardiology and Intensive Care Medicine, Hannover, Germany
3 Medizinische Hochschule Hannover, Paediatric Gastroenterology and Hepatology, Hannover, Germany

Objectives and study: Cirrhotic cardiomyopathy (CCM) is defined by a combination of distinct cardiac changes associated with hepatic cirrhosis: diastolic dysfunction, systolic dysfunction and QT interval prolongation. In adults CCM has been found to have a significant incidence and some studies show impact on outcome pre- and post- paediatric liver transplantation (pLT). In children, data is scarce. Our aim was to evaluate incidence of CCM in our single centre pLT-cohort before and one year after pLT, to correlate these findings to histological stage of liver fibrosis and to evaluate clinical impact of these changes on patient outcome.

Methods: We evaluated liver fibrosis histological at the time of LT (in explanted liver) and echocardiography findings (end-diastolic left ventricular diameter [LVIDd], end-diastolic left ventricular posterior wall thickness [LVPWTd], left ventricular mass index 2 [LVMI]) pre pLT and one year after pLT (6.8 months prior and 14.6 months after LT) in 282 children consecutively transplanted from 2002-2013 at our centre. Signs of CCM were compared by z-Score 1,3 analysis with healthy children and patients with advanced fibrosis (ISHAK Fibrosis Score 4-6) were compared to patients with less advanced liver fibrosis (ISHAK Fibrosis Score 0-3). Clinical impact of CCM was tested by correlation of CCM to one year survival after pLT and to duration of hospital/ intensive care unit (ICU) stay. Statistical analysis was performed with SPSS and Fisher Test, Wilcoxon and one-way Anova.

Results: 198 patients (4.3 years average age (0.2-18); females n=97) fulfilled inclusion criteria (no primary heart disease, no metabolic liver disease with associated heart disease no primary portal thrombosis). 169 patients had advanced fibrosis (85.4%), 29 were found to have minor fibrosis (ISHAK 1-3) (14.6%). Z-Scores of LVIDd (0.98±1.15 vs. -0.1±1.37; P<0.001), LVM (-0.42±0.11 vs. -1.55±0.29; P<0.001) and the LVMI (124.2±69.7 vs. 76.6±39.1; P=0.001) were significantly higher in patients with advanced fibrosis and pathological LVIDd z-Scores (>2SDS) were significantly more frequent in this group (2.62% (32/169) vs. 2.19% (1/29); P=0.03). All changes disappeared after pLT with significant decrease of LVIDd z-Score and LVMI in patients with advanced fibrosis after pLT (LVIDd 0.99 vs. 0.08; P<0.001, LVMI 121.42 vs 66.52). Cardiac findings however, did not affect the one year survival after pLT but were associated with a significantly longer stay in an intensive care unit.

Conclusion: CCM in pLT candidates is not uncommon but clinical impact remains unclear and should be evaluated in prospective studies.

References:
2. (Devereux-Formula): LV-Masse=0,8(1,04(LVEDD+IVSd+LVPWd)3-LVEDD3))+0,6 (g)
Objectives and study: Giant cell hepatitis with Coombs-positive haemolytic anaemia (GCHCHA) is a rare and severe form of immune-mediated hepatitis in infancy, characterized by giant cell transformation on liver biopsy and autoimmune haemolysis. Modalities in treatment remain controversial. We aimed at describing features and outcomes of a European multicentre patient cohort.

Methods: We analysed retrospectively all cases of GCHCHA diagnosed or consulted upon by other centres at King's College Hospital, London (UK) and Hospital Papa Giovanni XXIII, Bergamo (Italy) between 1990 and 2012. Clearance of jaundice, resolution of coagulopathy and stable reduction of transaminase levels defined response to treatment (complete response [CR]: transaminase levels ≤ 2-fold ULN; partial response [PR]: if > 2-fold ULN).

Results: Twenty-one patients (F:M 13:8), median age 7 months (range, 2-19) at diagnosis, were followed for a median time of 38 months. Haemolytic anaemia was the initial presenting symptom before diagnosis of liver disease in 4. Jaundice, hepatomegaly and pallor were observed in 76%, 71%, 66% at diagnosis, respectively; 5 had INR > 2. Five had positive autoantibodies (SMA in 5, associated with ANA and AMA in 1) and 3 had an associated autoimmune disease (coeliac disease in 2 and bullous pemphigoid in 1). Seven patients (33%) died after a median of 17 months; liver transplant and haematopoietic stem cell transplantation (HSCT) were performed as rescue in one patient each, both of whom died. Fourteen patients (66%) are alive, 11 have normal transaminase levels, and 4 are off-therapy. Outcome did not correlate with age, transaminase, bilirubin and haemoglobin levels at onset, or with time of treatment initiation. First-line treatment consisted of prednisone and azathioprine (AZA) in all patients at a median time of 2 weeks from presentation. Second-line treatments comprised mycophenolate mofetil (MMF), cyclosporine A, immunoglobulins, rituximab (RIT), alemtuzumab (ALE). Among 3 children with initial CR to steroids + AZA, one died after 3.5 months for a relapse despite rescue therapy with MMF and ALE. Of 10 children with PR, 5 had an early relapse during steroid tapering and died after 1-18 months despite treatment escalation; one is alive after rescue with ALE; 4 relapsed 0.5-3 months after steroid withdrawal, but responded to RIT and are alive. Eight children did not respond to steroid + AZA; 7 of them were rapidly rescued with RIT
(6) and ALE (1) and survived, while one died after a non-ablative HSCT. Overall, RIT rescue therapy was attempted in 13, leading to CR in 10, PR in 2 and no response in 1.

**Conclusion:** GCHCHA is a severe immunologic disorder generally responding to steroid treatment. Patients at risk of relapse and death must be identified promptly, on the basis of rapid worsening of liver function during steroid tapering. Rituximab is an effective rescue treatment when used early in patients with refractory disease.
Early development of nonalcoholic fatty liver disease in genetically predisposed children with overweight and obesity does not coincide with metabolic derangements.

Kylie Karnebeek1, Jogchum Plat2, Anita Vreugdenhil1

1Centre for Overweight Adolescent and Children’s Healthcare (Coach), Maastricht University Medical Centre, Department of Paediatrics, Maastricht, Netherlands
2Maastricht University, Department of Human Biology, School of Nutrition and Translational Research in Metabolism (Nutrim), Maastricht, Netherlands

Objectives and study: Non-alcoholic fatty liver disease (NAFLD) is now one of the most common chronic liver diseases in children and a health threat particularly in children with overweight and obesity. Single nucleotide polymorphisms in genes encoding PNPLA3 (rs738409) and TM6SF2 (rs58542926) contribute significantly to the development of NAFLD. It is however unknown whether liver pathology and disturbances in metabolism and cardiovascular risk coincide in carriers and non-carriers of these risk alleles. Therefore, we assessed metabolic derangements, genetic predisposition for NAFLD and liver transaminase levels in children with overweight and obesity.

Methods: One hundred and seventy-four children (49% boys) from the Centre for Overweight Adolescent and Children’s Healthcare (COACH) at the Maastricht University Medical Centre were genotyped for PNPLA3 I148M and TM6SF2 E167K. Anthropometric, metabolic, cardiovascular and liver-related parameters were determined.

Results: Anthropometric parameters did not differ significantly between carriers and non-carriers of the risk alleles. ALT and AST were significantly higher in carriers of the PNPLA3 G minor ‘risk’ allele (ALT; CC 21.00 (17.00;28.00); CG 26.50 (18.00;34.50); GG 29.00 (23.00;51.00)(p=0.004) and AST; CC 24.00 (19.00;30.00); CG 27.50 (21.00;40.00); GG 30.00 (26.00;36.00)(p=0.004)) as compared to the major allele. The odds ratio for having ALT levels above the normal range increased for every PNPLA3 G allele, with an OR of 2.51 (1.22;5.18; p=0.013) for PNPLA3 CG genotype and 5.54 (1.53;20.02; p=0.009) for the GG genotype, compared to CC genotype. Interestingly, carriers of the PNPLA3 risk allele did not show a deteriorated metabolic profile as compared to non-carriers. The TM6SF2 T allele carriers also showed a tendency towards increased ALT and AST, but a significantly healthier metabolic profile, i.e. lower serum total cholesterol (p=0.024), LDL cholesterol (p=0.015) and triglyceride concentrations (p=0.003) compared to the major allele. Carrying the TM6SF2 T allele in addition to the PNPLA3 ‘risk’ allele, did not significantly increase the odds ratios for increased ALT concentrations.

Conclusion: Children with overweight and obesity carrying risk alleles in PNPLA3 have significantly higher liver transaminase levels then non-carriers. The early development of nonalcoholic fatty liver disease in genetically predisposed children with overweight and obesity does not coincide with metabolic derangement. This suggests that hepatic aberrations and metabolic disturbances apparently develop as independent entities in this specific population. Furthermore, these children with a high liver health risk may not be identified by focussing on metabolic and cardiovascular parameters in conventional risk assessments.
Alpha-1 Antitrypsin as an anti-inflammatory therapy to improve the efficacy of hepatocyte transplantation

Charlotte Lee¹, Anil Dhawan², Ragai Mitry¹, Simon Walker¹, Valeria Iansante¹, Raquel Fernandez Dacosta¹, Celine Filippi¹, Sharon Lehec¹, Anil Chandrashekran¹, Terry Strom³, Maria Koulmanda³, Emer Fitzpatrick⁴

¹Institute of Liver Studies, King's College London, London, United Kingdom
²King's College Hospital, Paediatric Liver, GI and Nutrition Centre, London, United Kingdom
³Beth Israel Deaconess Medical Center, Cambridge, United States
⁴Paediatric Liver, GI and Nutrition Centre, King's College Hospital, London, United Kingdom

Objectives and study: Hepatocyte transplantation is a promising alternative to liver transplantation for liver-based metabolic disease, though long-term benefits have not yet been demonstrated. This is partly due to the rapid clearance of hepatocytes by the innate immune response. We investigated the use of alpha-1 anti-trypsin (AAT) as an immunomodulatory agent to improve engraftment thus establishing a critical mass for long-term efficacy. AAT is a serine protease widely used as an intravenous infusion in patients with alpha-1 anti-trypsin deficiency but also in islet transplantation and autoimmune conditions in clinical trials.

Methods: Effects on Human Hepatocytes (HH) treated in vitro with 1-4mg/ml AAT for 20 min were determined by MTT, albumin and urea assays. AAT was added to a Chandler loop of ABO-matched human blood containing HH (incubated at 37°C, rotated at 24rpm to mimic portal vein blood flow) and compared to a loop containing HH alone. Platelet consumption and coagulation were measured up to 1 hour. Plasma was analysed for cytokine expression (Randox Array). Hepatocytes were isolated from Sprague Dawley rats. Littermates underwent tail vein injection of AAT (120mg/kg) or saline (control) prior to the intrasplenic transplantation of 2x10⁷ CM-DIL labelled hepatocytes. At 48hr and 1 week post-transplant, liver was collected for immunohistochemical analysis and RNA extracted for cytokine PCR array (Qiagen).

Results: AAT did not affect HH viability, urea or albumin production (N=6, P>0.05). Loops containing AAT and HH showed significantly higher platelet counts than HH alone (156 v 62 x10⁹ cell/L)(N=6 P<0.001), and no thrombus formation. The addition of AAT inhibited the increased expression of pro-inflammatory cytokines IL-1β(1.7 v 3.9ng/ml), IL-6(0.4 v 1.1ng/ml) and IFN-γ(0.4 v 1.3ng/ml)(N=5, P<0.05). Loops containing AAT and HH showed higher concentrations of anti-inflammatory IL-1RA compared to non-treated loops (913 v 719ng/ml)(N=5, P<0.05). At 48 hours and 1 week, AAT treated rats had a significantly higher engraftment of CM-DIL labelled hepatocytes in cryosections of the liver (48h:7.1%±1 v 3.6%±0.5, 1 week:14.1%±1.4 v 5.4%±0.8). 13 and 11 genes were downregulated and 3 and 8 genes upregulated in AAT-treated rats at 48 hr and 1 week respectively using RT-PCR array as compared to control-treated animals.

Conclusion: Intravenous infusion of AAT at the time of hepatocyte transplantation may provide local inhibition of coagulation, improve cell engraftment and has the potential to significantly improve the clinical outcome of the technique by increasing the critical cell mass.
Common variant p.D19H of the hepatobiliary sterol transporter ABCG5/8 affects cholesterol homeostasis in children with gallstones

Marcin Krawczyk1, Olga Niewiadomska2, Irena Jankowska2, Krzysztof Jankowski3, Zbigniew Kulaga4, Jolanta Gozdowska5, Dariusz Lebenstejn6, Sabina Wiecek7, Dieter Lutjohann8, Frank Lammert9, Piotr Socha10

1Universitätsklinikum Saarland, Klinik für Innere Medizin II, Homburg, Germany
2The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutrition Disorders and Pediatrics, Warsaw, Poland
3Dept. Internal Medicine and Cardiology, Medical University of Warsaw, Poland, Warszawa, Poland
4The Children's Memorial Health Institute, Public Health, Warsaw, Poland
5Medical University of Warsaw, Departament Transplantation Medicine and Nephrology, Warsaw, Poland
6Medical University of Białystok, Departament of Pediatrics, Gastroenterology and Allergology, Białystok, Poland
7Medical University of Silesia, Department of Paediatrics, Katowice, Poland
8University of Bonn, Institute of Clinical Chemistry and Clinical Pharmacology, Bonn, Germany
9Saarland University Medical Center, Saarland University, Department of Medicine II, Homburg, Germany
10Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Introduction: Lately we demonstrated that presence of the p.D19H variant in the hepatobiliary cholesterol transporter ABCG5/8 increases the risk of developing gallstones in children (Krawczyk/Socha, ESPGHAN 2016). In humans cholesterol derives from de novo synthesis or intestinal absorption. Serum levels of cholesterol precursors and plant sterols represent valid surrogate markers for cholesterol biosynthesis and intestinal absorption, respectively. The comparison of serum surrogate markers informs about the sources of cholesterol and its transport in a given individual. The aim of the current study was to assess the effects of the p.D19H polymorphism on cholesterol homeostasis in children with gallstones.

Materials and methods: In total, we measured serum concentrations of cholesterol precursors and plant sterols using gas chromatography / mass spectrometry (GC/MS) in 52 children with gallstone disease recruited in the Children’s Memorial Health Institute, Warsaw. Gallstone disease was confirmed by either abdominal sonography in patients with gallbladders in situ, or by the history of cholecystectomy. Fasting serum specimens for sterol measurements, each containing butylated hydroxytoluene, were collected at the time of the clinical evaluation and stored at -70°C. The ABCG5/8 p.D19H variant was genotyped using TaqMan assays.

Results: Among recruited children 15 carried at least one copy of the proliithogenic ABCG5/8 [p.19GG] allele and 37 carried the common ABCG5/8 [p.19GG] genotype. Patients carrying the proliithogenic allele had significantly lower concentrations of the natural phytosterol sitosterol (P=0.045) and decreased serum phytostanols, i.e. campestanol (P=0.028) and sitostanol (0.029). In line with these results, the ABCG5/8 p.D19H variant was associated with decreased ratios of phytosterols to cholesterol precursors (sitosterol:desmosterol, P=0.008; campesterol:desmosterol, P=0.013).

Conclusion: The ABCG5/8 proliithogenic variant p.D19H is associated with increased output of cholesterol in the setting of relatively low intestinal cholesterol absorption in children. This trait is present already at young age and might substantially contribute to the increased gallstone risk among carriers of the ABCG5/8 p.D19H risk allele.
Prevalence, clinical spectrum and outcome of pediatric drug induced liver injury

Aditi Kumar, Sanjeev Kumar Verma, Vikrant Sood, Rajeev Khanna, Nikhil Mehra, Dinesh Rawat, Seema Alam

1Institute of Liver and Biliary Sciences, Pediatric Hepatology, New Delhi, India
2King George Medical University, Pediatrics, Lucknow, Up, India
3Pediatric Hepatology, New Delhi, India
4Institute of Liver and Biliary Sciences, Pediatric Hepatology, Delhi, India

Objectives and study: Drug-induced liver injury (DILI) presents with a broad spectrum of clinical, biochemical and histologic abnormalities. Limited available literature in pediatric population regarding its overall spectrum makes it a diagnostic challenge. This study was thus planned to study the prevalence, clinical spectrum and the outcome of DILI in children.

Methods: A retrospective review of 36 children and adolescents under 18 years of age, diagnosed as DILI as per departmental protocol was done. Details regarding symptomatology, clinical presentation, Roussel Uclaf Causality Assessment Method (RUCAM) scale, drugs implicated, biochemical abnormalities (also for classification based on R value into hepatocellular, cholestatic, or mixed patterns) and outcome were noted.

Results: DILI constituted 3.7 % (36 out of 972 children) of children with liver disease. Clinical presentation was as acute liver failure, acute hepatitis, acute on chronic liver failure and chronic liver disease in 16 (45%), 12 (33.3%), 5 (13.7%) and 3 (8%) cases respectively. Cases were divided into the hepatocellular (50%), cholestatic (27.8%), and mixed pattern (8 cases, 22.2%) based on R value. Percentage distribution of RUCAM categories was as follows: highly possible (16.7%), possible (47.2%) and probable (36.1%). Complementary and alternative medicines (CAM) and antitubercular (ATT) drugs accounted for 39% and 33% cases of DILI respectively. Of the 35 cases followed up over a median duration of 9 months (2 to 19 months), 4 (11%) patients died, five (14%) patients either progressed to or persisted as chronic DILI. Presence of ascites (Odd’s ratio/OR 49.5, 95% Confidence Interval/CI 4.8 to 505.9, p value 0.001) and high serum total IgG levels (mean difference 8.68, 95% CI 4.71-12.65, p-value 0.004) were significantly associated with unfavourable outcome (death or chronicity).

Conclusion: Pediatric DILI is still an under reported entity with significant morbidity. More than three-fourths DILI in this cohort is accounted for by CAM and ATT group of drugs. Role of RUCAM in pediatric DILI still needs further scrutiny. Presence of ascites and high IgG are poor prognostic marker for DILI, which needs confirmation by larger prospective studies.
Cryopreservation of hepatocyte microbeads for clinical transplantation

Nataruks Chaijitraruch¹, Anil Dhawan², Robin Hughes³, Celine Filippi³, Sharon Lehec³, Ragai Mitry³

¹King Chulalongkorn Memorial Hospital, Chulalongkorn University, Paediatrics, Bangkok, Thailand
²King's College Hospital, Paediatric Liver, GI and Nutrition Centre, London, United Kingdom
³Institute of Liver Studies, King's College London, London, United Kingdom

Objectives and study: Intraperitoneal transplantation of hepatocyte microbeads is an attractive option for the management of acute liver failure. Encapsulation of hepatocytes in alginate microbeads supports their function and prevents immune attack of the cells. Establishment of banked cryopreserved hepatocytes microbeads is important for emergency use. The aim of this study was to develop an optimised protocol for cryopreservation of hepatocyte microbeads for clinical transplantation using modified freezing solutions.

Methods: Four freezing solutions with potential for clinical application were investigated. They consisted of a) University of Wisconsin (UW) contained 10% dimethyl sulfoxide (DMSO) and 5% (300mM) glucose, b) Histidine-tryptophan-ketoglutarate (HTK) contained 10% DMSO and 5% glucose, c) CryoStor CS10 and, d) Bambanker. All freezing solutions were evaluated on non-encapsulated human and rat hepatocytes. The best two freezing solutions that resulted in high cell viability and function after thawing were then selected for study of hepatocytes microbeads cryopreservation. Then, cytoprotective agents: a pan-caspase inhibitor (benzyloxycarbonyl-Val-Ala-DL-Asp-fluoromethylketone; ZVAD), an antioxidant (desferoxamine; DFO), and buffering and mechanical protection (human serum albumin; HSA) were examined in order to improve the microbeads cryopreservation protocol.

Results: Human and rat hepatocytes cryopreserved with UW/DMSO/glucose and CryoStor CS10 showed better post thawing cell viability, attachment and hepatocyte-functions than with HTK/DMSO/glucose, and Bambanker. The two freezing solutions which gave better results were studied with human and rat hepatocytes microbeads (HMBs and RMBs). Similar effects on cryopreserved microbeads morphology (external and ultrastructural), viability and hepatocyte-functions post thawing were observed over 7 days in culture. UW/DMSO/glucose, as a basal freezing medium, was used to investigate the additional effects of cytoprotectants. ZVAD (60µM) had beneficial effect on cell viability, greater than with DFO (1mM), HSA (2%) and basal freezing medium alone. Improvements in the ultrastructure of encapsulated hepatocytes, and a lower degree of cell apoptosis were observed with all three cytoprotectants. ZVAD trending to provide the greatest effect. Cytochrome P450 activity was significantly higher in the three cytoprotectants groups than with fresh microbeads.

Conclusion: Developing an optimised cryopreservation protocol by adding cytoprotectant such as ZVAD could improve the outcome of cryopreserved hepatocyte microbeads for future clinical use.
**HEPATOLOGY: Basic Science**

H-O-012

**Tunnelling nanotube-based mitochondria transfer from MSCs to human hepatocytes: a potential rescue mechanism for hepatocytes with impaired mitochondria?**

Raquel Fernandez Dacosta¹, Anil Dhawan², Charlotte Lee¹, Valeria Iansante¹, Ragai Mitry¹, Sharon Lehec¹, Emer Fitzpatrick³, Simon Walker¹, Celine Filippi¹

¹Institute of Liver Studies, King's College London, London, United Kingdom
²King's College Hospital, Paediatric Liver, Gi and Nutrition Centre, London, United Kingdom
³Paediatric Liver, Gi and Nutrition Centre, King's College Hospital, London, United Kingdom

**Objectives and study:** Hepatocyte transplantation is a promising alternative to whole liver transplantation for children with either acute liver failure or liver-based metabolic diseases. However sustaining the function of cryopreserved hepatocytes isolated from marginal grafts remains a challenge. Mesenchymal stromal cells (MSCs) enhance hepatocyte viability and metabolism, through mechanisms not yet fully understood. We hypothesized that MSCs rescue hepatocyte function via the transfer of mitochondria through tunneling nanotubes (TNT). Therefore, the aims of this study were to (i) assess if a TNT-based transfer of mitochondria occurs between MSCs and hepatocytes; (ii) to study TNT composition and formation inhibition, and (iii) to determine if TNT inhibition stops mitochondria transfer and affects MSCs trophic effects on hepatocytes.

**Methods:** Mitochondrial transfer from MSCs to hepatocytes was followed over 24h of co-culture using FACS as well as live- and fixed-cell microscopy, after staining of MSCs mitochondria with MitoTracker Red. TNT presence in the co-cultures was studied by fluorescent microscopy. Characterization of TNT was performed by immunofluorescence to detect actin and tubulin expression. TNT-disruption was tested by dosing actin polymerization inhibitors: Latrunculin A (LatA) and Cytochalasin D (CytD). MTT and Annexin V/PI assays were used to assess LatA/CytD cytotoxicity. Mitochondrial transfer after TNT inhibition was quantified by FACS.

**Results:** Hepatocytes containing MSCs mitochondria were detected as early as 2h after co-culture onset, using live microscopy (n=3) and confirmed by FACS (n=3), with statistical significance at 4 and 6h of co-culture (21±6 and 27.6±10%, p<0.05 vs monocultures). TNT containing red-labelled MSCs mitochondria were observed between co-cultured MSCs and hepatocytes. Actin was identified as the main TNT structural component. 0.5µM LatA achieved TNT inhibition without cytotoxic effect on the cells, leading to a decrease in the number of hepatocytes with MSCs mitochondria.

**Conclusion:** Our preliminary studies show that MSCs do transfer mitochondria to primary hepatocytes through actin-based TNT, which might be the responsible mechanism for the beneficial effects of MSCs on hepatocyte function. This data is helpful to further advance our knowledge in transplanting MSCs, either alone or together with hepatocytes, for the treatment of paediatric liver disease.
SCYL1 deficiency, a disorder of intracellular trafficking: a new cause of infantile cholestasis with a variable neurological phenotype

Dominic Lenz¹, Patricia McClean², Penelope Bonnen³, Christian Thiel¹, Beate Straub⁴, Inga Harting⁵, Urania Kotzaeridou¹, Emma Blakely⁶, Robert Taylor⁶, Thomas Meitinger⁷, Stefan Kölker⁸, Holger Prokisch⁹, Georg Friedrich Hoffmann¹⁰, Tobias Haack¹¹, Christian Stauffner¹

¹University Hospital Heidelberg, Department of General Pediatrics, Heidelberg, Germany
²Leeds Teaching Hospitals NHS Trust, Department of Paediatric Hepatology, Leeds, United Kingdom
³Baylor College of Medicine, Department of Molecular and Human Genetics, Texas, United States
⁴University Mainz, Institute of Pathology, Mainz, Germany
⁵University Hospital Heidelberg, Department of Neuroradiology, Heidelberg, Germany
⁶Institute of Neuroscience, Newcastle University, Welcome Trust Centre for Mitochondrial Research, Newcastle, United Kingdom
⁷Technische Universität München, Institute of Human Genetics, Munich, Germany
⁸Zentrum für Kinder- und Jugendmedizin, Universitätsklinikum Heidelberg, Department of General Pediatrics, Heidelberg, Germany
⁹Helmholtz Zentrum München, Neuherberg, Germany
¹⁰Universitätsklinikum Heidelberg, Department of General Paediatrics, Heidelberg, Germany
¹¹University of Tübingen, Institute of Medical Genetics and Applied Genomics, Tübingen, Germany

Objectives and study: Inborn errors of intracellular trafficking are an emerging group of diseases associated with infantile hepatopathy, such as NBAS deficiency which we recently described as a relatively frequent cause of recurrent acute liver failure with onset in infancy. Mutations in SCYL1 were currently identified as the molecular cause of “Spinocerebellar ataxia, autosomal recessive 21”, a syndromal disorder characterized by peripheral neuropathy, cerebellar atrophy, ataxia and recurrent episodes of liver failure in three individuals from two families. SCYL1 is involved in retrograde transport scaffolding for key components of coat protein complex I (COPI) coats and regulating Golgi morphology. So far, very little is known regarding the hepatic phenotype of this new disease and the pathomechanism of liver damage has not been targeted.

Methods: Patients with biallelic SCYL1 mutations were identified within a whole exome sequencing study of individuals with infantile cholestasis or liver failure of unknown aetiology. Deep clinical phenotyping was performed, including a detailed workup of laboratory and metabolic analyses focusing on the hepatic phenotype. Liver biopsies were studied by immunohistochemistry and transmission electron microscopy (TEM). Functional studies on patients’ fibroblasts including SCYL1 western blot, glycosylation studies and analyses of endoplasmic reticulum stress were performed.

Results: Four patients from three families with biallelic mutations in SCYL1 were identified: two individuals from one family homozygous for a missense mutation and the others each homozygous for nonsense mutations in SCYL1. All mutations are novel and pathogenicity of the missense mutation was proven by absent protein levels of SCYL1 in patients’ fibroblasts. The main clinical phenotype was recurrent cholestatic liver dysfunction with onset within the first 2 years of life, whereas the neurological phenotype was mild, variable and with a later onset. Liver crises were all triggered by minor febrile infections, were less frequent with age and did not always lead to full blown liver failure. Liver dysfunction was transient, but liver fibrosis developed; one patient underwent liver transplantation. TEM demonstrates disorganized Golgi morphology in hepatocytes. In one patient, pronounced glycosylation abnormalities were observed during liver crisis but not during symptom-free interval suggesting deregulated Golgi function.

Conclusion: Biallelic mutations in SCYL1 are a new cause of infantile cholestasis or liver failure with recurrent episodes triggered by infections. A neurological phenotype is possible, but has a later onset and may be mild with secondary microcephaly as the only abnormality in infancy. Our results emphasize that pathophysiology of SCYL1 deficiency is linked with impaired Golgi homeostasis. Recurrent cholestatic liver dysfunction triggered by febrile infections, with or without neurological symptoms, should prompt genetic analysis of SCYL1.
Stereotactic radiofrequency ablation (SRFA) - a new option for treating liver lesions not eligible for surgical therapy in pediatric patients

Hetzer Benjamin¹, Thomas Müller¹, Georg-Friedrich Vogel¹, Daniela Karall³, Gabriele Kropshofer³, Reto Bale⁴

¹Medical University of Innsbruck, Paediatrics I, Innsbruck, Austria
²Tirol Klinken, Paediatrics I, Innsbruck, Austria
³Interventionelle Onkologie - Mikroinvasive Therapie an der Abteilung für Radiologie, Department of Radiology, Innsbruck, Austria

Objectives and study: Liver tumors in childhood are rare, but may be associated with a range of therapeutic and surgical problems. Surgical resection or liver transplantation are the primary treatment options for malignant tumors. To date, only little has been reported about the application of SRFA in paediatric liver patients. We describe successful stereotactic radiofrequency ablation (SRFA) of focal hepatic lesions including adenoma, hepatocellular carcinoma, hepatoblastoma, myofibroblastic tumor and hepatic cysts associated with alveolar eccessoccosis in six paediatric patients aged between five months and 17 years.

Methods: SRFA is a known interventional treatment of liver malignancies in adult patients not eligible for surgical therapy. This method is a potentially local curative ablation method which is based on the application of high-frequency alternating current between probes in tissue and skin electrodes, causing targeted heat of more than 60 °C. Thereby controlled tumor destruction without open resection is possible. Stereotaxy enables a high precision of electrode placement, which is mandatory to assure patient safety and technical success and to avoid major complications. In addition, the stereotactic multielectrode/electrode position approach allows for generating overlapping ablations for successful treatment of even large tumors.

To this day, the youngest patient to whom SRFA was successfully applied for removal liver lesions in our centre, is a five-month-old girl diagnosed with Beckwith- Wiedemann syndrome. As bridging therapy before transplantation SRFA was used in a seven-month-old girl with hepatocellular carcinoma and another nine years old girl with hepatoblastoma. In a 17-year-old girl with an inflammatory myofibroblastic tumor (ALK-1- positive) and two liver lesions SRFA was successfully applied.

Not only in oncology patients SRFA was used. Also in a 16-year-old patient with liver adenomas caused by the metabolic disease tyrosinemia type I (TYR I) with α-fetoprotein (AFP) elevation as well as in a 16-year-old girl with echinococcus multilocularis lesions SRFA was executed.

Results: SRFA application was applied successfully to all six patients. In all patients follow up imaging by ultrasound and MRI showed stable conditions of the necrotic ablation areas with no new lesions. The condition of the two patients with HCC and hepatoblastoma was stable before transplantation. The patient diagnosed with Beckwith- Wiedemann syndrome has yet not shown yet any new lesions for more than 4 years after treatment. In the TYR I patient, elevated AFP values promptly returned to normal and she was discharged in good clinical condition just one day after intervention. One patient developed pleural effusion one day after SRFA requiring pleural drainage for few days. Large scars were avoided and there was a reduced tissue damage compared to conventional liver surgery.

Conclusion: SRFA technique may be a promising and safe alternative to surgical resection of focal liver lesions in paediatric patients.

Disclosure of interest: Reto Bale, is a co-inventor of the Atlas aiming device and a co-shareholder in its financial returns. The other authors declare that they have no conflict of interest.
Farnesoid X receptor agonist GW4064 protect against short bowel syndrome-associated liver disease via attenuating bile acid dysmetabolism

Yi Cao¹, Wei Cai²

¹Shanghai Jiao Tong University, Department of Pediatric Gastroenterology and Nutrition, Xin Hua Hospital, School of Medicine, Shanghai, China
²Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Pediatric Surgery, Shanghai, China

Objectives and study: The mortality associated with liver disease was observed in patients with short bowel syndrome (SBS). Bile acid (BA) dysmetabolism may be one of the putative mechanisms, and farnesoid X receptor (FXR) is the key regulator of BA synthesis. Therefore, we explored the effect of FXR agonist GW4064 on SBS-associated liver disease (SBS-ALD).

Methods: Sprague dawley (SD) rats were randomized into three groups, including: sham, SBS model, and GW4064 treatment. Both of the SBS model and GW4064 treatment groups were underwent 80% small bowel resection (SBR), while the sham group was experienced sham operation. Rats from treatment group were further subjected to GW4064 (30mg/kg) intraperitoneal injection every other day. After two weeks, Liver histology and serum transaminases were examined. Metabolomic studies detailed the alterations in BA composition of hepatic tissues, stool and serum. Gene expression of hepatic FXR target genes was assessed. Serum concentration of FGF15 was determined.

Results: Liver histology in SBS model group performed inflammatory cells infiltration, hepatocyte ballooning and microvesicular steatosis. Compared to those in the sham group, serum transaminases such as alanine aminotransferase (ALT) (28.30±1.47 vs. 21.78±1.74, P=0.004) and aspartate aminotransferase (AST) (29.21±3.15 vs. 9.20±1.90, P=0.000) were increased, γ-glutamyltransferase (GGT) (6.67±1.00 vs. 4.49±1.34, P=0.244) was on the rise and serum total bile acids (TBA) (36.38±2.66 vs. 68.66±6.46, P=0.002) was reduced. BA composition of hepatic tissues reflected a larger proportion of primary and secondary unconjugated BAs, and those of stool and serum showed secondary unconjugated BAs ratio increased. Hepatic regulation of BA synthesis was characterised by a blunted hepatic FXR activation response, and serum FGF15 (51.10±12.38 vs. 195.62±33.52, P=0.000) level was declined. Gene expression of the key enzymes such as cholesterol 7α-hydroxylase (CYP7A1) (1.51±0.79 vs. 0.94±0.20, P=0.367), sterol 12a-hydroxylase (CYP8B1) (0.25±0.04 vs. 0.15±0.02, P=0.027) and sterol 27 hydroxylase (CYP27A1) (1.20±0.19 vs. 0.77±0.07, P=0.021) in the BA synthesis was activated.

Compared with SBS model group, both of the liver histology and serum transaminase activity (ALT: 19.48±1.18 vs. 28.30±1.47, P=0.000; AST: 14.27±1.78 vs. 29.21±3.15, P=0.000; GGT: 5.24±1.57 vs. 6.67±1.00, P=0.441) were improved in the treatment group, which demonstrated the attenuation of SBS-ALD. Serum TBA (65.87±9.23 vs. 36.38±2.66, P=0.003) was rebound. BA compositions of hepatic tissue, stool and serum were recovered and closer to those of sham group. Expression levels of hepatic FXR target genes were activated and serum FGF15 level (105.73±17.60 vs. 51.10±12.38, P=0.114) was rebound. Consistent with it, expression levels of CYP7A1 (0.20±0.12 vs. 1.51±0.79, P=0.048), CYP8B1 (0.20±0.12 vs. 0.25±0.04, P=0.009) and CYP27A1 (0.55±0.04 vs. 1.20±0.19, P=0.001) were statistically down-regulated.

Conclusion: We propose a pathological scenario in which a large loss of bile acid following SBR results in BA dysmetabolism in the liver and consequent hepatic damage. GW4064 activated FXR target genes to suppress BA synthesis key enzymes, and then restored hepatic BA composition to
improve liver injury. These findings provide an insight into the clinical treatment of liver disease in patients with SBS.
Transjugular Intrahepatic Portosystemic Shunt (TIPS): a valuable treatment option for the management of portal hypertension in children. A single centre experience

Angelo Di Giorgio¹, Roberto Agazzi², Mara Colusso³, Maurizio Cheli⁴, Michele Colledan⁵, Lorenzo D’Antiga⁶

¹Paediatric Liver, GI and Transplantation, Asst Papa Giovanni XXIII, Bergamo, Italy
²Radiology, Asst Papa Giovanni XXIII, Bergamo, Italy
³Papa Giovanni XXIII Hospital, Paediatric Surgery, Bergamo, Italy
⁴Paediatric Surgery, Asst Papa Giovanni XXIII, Bergamo, Italy
⁵General Surgery and Transplantation, Asst Papa Giovanni XXIII, Bergamo, Italy
⁶Papa Giovanni XXII Hospital, Paediatric Hepatology-Gastroenterology and Transplantation Unit, Bergamo, Italy

Objectives and study: In adults, TIPS insertion is a common procedure for treating severe portal hypertension (PH). In the paediatric population the use of TIPS is limited because this radiological procedure is considered technically challenging and also associated with high risk of hepatic encephalopathy and shunt dysfunction. In this study, we aimed to review and update our results on TIPS placement in children, to assess its feasibility and efficacy to treat severe complications of PH.

Methods: We retrospectively reviewed the patients who underwent TIPS at our centre in the last 10 years. Indications included the complications of PH unresponsive to medical and endoscopic treatment in absence of end-stage liver disease. We included patients with cirrhotic and non-cirrhotic PH and those who developed PH after liver transplantation (LT). An covered stent was placed following the measurement of portosystemic pressure gradient (PPG). During the follow up serum ammonia and doppler ultrasonography were performed 3 monthly.

Results: 24 patients were selected, one was excluded due to low portosystemic gradient. TIPS procedure was performed in 23 patients (M/F = 10/13; median age 10.2 years [range 2.2-17.4], median weight 30.0 Kg [11.5-96.0]) with portal vein thrombosis (n 5, of whom 1 transplanted), Budd-Chiari syndrome (n 3), cystic fibrosis (CF, n 3), congenital hepatic fibrosis (n 2), intestinal failure associated liver disease (n 2), biliary atresia (n 2, 1 transplanted), sclerosing cholangitis (n 1), non syndromic bile duct paucity (n 1, transplanted), Alagille syndrome (n 1, transplanted), hepatoportal sclerosis (n 1), intrahepatic cholestasis (n 1), veno-occlusive disease (n 1, transplanted). Indications for TIPS included persistent ascites in 7 patients and recurrent gastrointestinal bleeding in 16. TIPS was successfully placed in 22/23 (96%) patients. The median PPG before and after TIPS was 18 (12-35) and 8 mmHg (3-12) respectively (p<0.01). Complications of PH resolved completely in 18/22 (82%), partially in 3 (14%), persisted in 1 (4%). Median serum ammonia before and after TIPS was 41 (20-96) and 74 mol/L (41-100) respectively (p<0.01); no patients developed overt encephalopathy. Five patients (23%) developed shunt dysfunction requiring a revision. Median follow up was of 1.6 years (0.2-5.7). At last follow up all patients had a patent TIPS, 9 (41%) required LT after a median time from TIPS of 0.8 years (range 0.1-4.9), 12 still have a patent shunt and 1 (with CF) died from respiratory tract infection.

Conclusion: TIPS insertion is technically feasible in children with both native liver and split liver graft. TIPS is effective in normalising PPG and control the severe complications of PH both in children with non-cirrhotic PH, as a permanent porto-systemic shunt, and in those with cirrhotic PH, as a bridge to LT. A slight increase in serum ammonia is common after TIPS insertion, but does not cause over encephalopathy. A regular radiological survey and, if required, a shunt revision may maintain a patent shunt in the long-term.
Post liver transplant class II donor specific HLA antibodies of the DQ subtype with MFI>5000 are predictive of allograft dysfunction

Sharat Varma1, Jérome Ambroise2, Mina Komuta3, Dominique Latinne4, Raymond Reding4, Francoise Smets4, Xavier Stephenne5, Isabelle Scheers6, Etienne Sokal6

1Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium
2Université Catholique de Louvain, Center for Applied Molecular Technologies, Bruxelles, Belgium
3Clinique Universitaire St Luc, Pathology, Brussels, Belgium
4Cliniques Universitaires Saint-Luc, Brussels, Belgium
5Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
6Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Background and aims: Liver allograft fibrosis is often seen on protocol liver biopsies and class II donor specific HLA antibodies have been implicated. Evidence lacks to determine appropriate MFI cut off values or on relative importance of subtypes.

Patients and methods: Cross-sectional study including stable LT recipient children having undergone protocol biopsy between 2012-2015. Biopsies were assessed for fibrosis and inflammation. HLA antibody detection using Luminex platform was done, pre-LT and simultaneous to protocol biopsy. Data evaluation and statistics: Impact of HLA antibodies and other variables was analyzed using cumulative logistic regression. Then Polyserial correlation coefficients were computed for MFI of antibody subclasses and histological characteristics and Receiver Operating Characteristic curves used to determine MFI threshold.

Results: 102 children were included, allograft fibrosis and portal fibrosis correlated to presence of post-LT class II DSA (OR=6.13, p=0.01 and OR=5.18, p=0.02 respectively). Allograft inflammation significantly correlated to presence of post-LT class II DSA in the portal area (OR=8.02, p<0.01). Higher polyserial correlation coefficients with portal inflammation and fibrosis were found for DQ (PCC=0.77 and 0.50) than for DP or DR antibody subclasses. The DQ subclass enabled to discriminate between low and high inflammation and fibrosis (AUC=0.83, p=0.02 and AUC=0.74, p=0.10). A cut-off of 5000 MFI enabled a sensitivity (83.3 % for inflammation and 75.0 % for fibrosis) and specificity (71.4 % for inflammation and 57.1 % for fibrosis).

Conclusion: Among the post-LT class II DSA, DQ subclass with MFI >5000 is associated with allograft inflammation and fibrosis in the portal area.
Genetic profiling of children with cholestatic liver disease: experience of a large pediatric liver transplant centre

Mohamed Shagrani1, Dieter Clemens Broering2, Jessica Burkholder2, Mohamed Abouelhoda3, Nada Altassan4, Fowzan Alkuraya5

1King Faisal Specialist Hospital & Research Center/Alfaisal University, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia
2King Faisal Specialist Hospital and Research Centre, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia
3King Faisal Specialist Hospital and Research Center, Riyadh, Saudi Arabia
4King Faisal Specialist Hospital & Research Center, Department of Genetics, Riyadh, Saudi Arabia
5King Faisal Specialist Hospital & Research Center /Alfaisal University, Department of Genetics, Riyadh, Saudi Arabia

Objectives and study: Advanced cholestatic liver disease is a leading referral to pediatric liver transplant centers. In our country (S.A.) genetic familial and metabolic liver diseases are the leading indication for liver transplantation which is not the case in any other population as biliary atresia is the leading cause anywhere else. This is reflecting the urgency for the need of our own gene panel for diagnosis and prevention specially with our current high volume pediatric liver transplantation service where in the year of 2016 we performed 55 Pediatric liver transplantation in one centre.

Methods: Recent advances in the molecular classification of this group of disorders promise a highly personalized management although the genetic heterogeneity also poses a diagnostic challenge. Using a next-generation sequencing-based multi-gene panel for the first time, we performed retrospective analysis of 98 pediatric patients who presented with advanced cholestatic liver disease. Either post or pre pediatric liver transplantation.

Results: A likely causal mutation was identified in the majority (66%) which higher than any published data so far We did manage to reverse diagnosis in 50 % of cases present as primary diagnosis as Wilson disease to be MDR 3 disease (PFIC3) Progressive familial intrahepatic cholestasis which will change the whole management, we diagnose 7 children with TJP2(Tight junction protein 2) rarely been reported to cause cholestatic liver disease and we showed that it has clear oligogenic presentation. In our cohort it showed that PFIC3 and PFIC2 are more prevalence than PFIC1. In addition to refining the clinical diagnosis, the panel results provided molecular explanation for a number of important clinical observations including risk of recurrence post-transplantation, which highlights the promise of applying our assay prospectively to personalize the management of these patients.

Conclusion: In summary, we describe the successful use of a next generation sequencing-based multi-gene panel to molecularly characterize a large cohort of pediatric patients with advanced cholestatic liver disease.

Our results highlight the important contribution of genetic causes in this cohort and the promise of this approach when applied prospectively to personalize the diagnosis and management of these patients. We are totally believe that this new genetic panel in KFSHRC will change the future of pediatric liver diseases in all aspects and will open a new era of translation and personalized medicine research.
Epidemiology of hepatitis C infection in children and young people in the UK

Line Modin1, Afam Arshad2, Bryony Wilkes3, William Irving4, Jennifer Benselin3, Carla Lloyd5, Deirdre Kelly6

1Hospital Lillebaelt, Department of Paediatrics, Kolding, Denmark
2The Homestead, Stoke-on-Trent, United Kingdom
3Hcv Research UK, Nottingham, United Kingdom
4University Hospital, Microbiology, Nottingham, United Kingdom
5Birmingham Children's Hospital, Liver Unit, Birmingham, United Kingdom
6The Liver Unit, Hepatology, Birmingham, United Kingdom

Objectives and study: To describe the mode of infection, genotype, and long-term liver damage of chronic hepatitis C (CHC) in a cohort with childhood acquired hepatitis C virus infection (HCV) in the UK.

Methods: Retrospective review of patients with acquired HCV infection in childhood. Data for patients with an estimated age at first HCV infection between 0-18 years were requested from a national clinical database (HCV Research UK) covering 43 adult and 7 paediatric centres. Data on demographics, virology and clinical details collected between July 2012 and October 2016.

Results: Overall 1085 patients, 72% males, were included. Data expressed as median (range) age of infection in years. The most prevalent mode of infection was recorded as intravenous drug abuse: 570 (16 (10-17)). Blood products: 252 (11 (0-17)). Perinatal exposure: 123 (0 (0-1)). Other risk factors: 140 (15 (0-18)). The genotype (G) was recorded in 951 G1: 536 (56%), G2: 51 (5%), G3: 336 (35%), G4: 27 (3%), and G5: 1 (0.1%).

Liver disease according to risk group is in Table. Cirrhosis was found in 338 (31%); hepatocellular carcinoma (HCC) in 55 (5%); and liver transplantation (LTx) in 48 (4%). The time between first infection and development of cirrhosis was identical in all risk groups (median 33 years, range 1-50) (p=0.76). Patients with perinatal exposure (10/123) developed cirrhosis at an earlier age (median 36 years, range 17-53) compared to the intravenous drug abuse group (median 48.5 years, range 33-68), blood recipient group (median 45.5 years, range 23-61), and other risk factor group (median 51.5 years, range 12-65), (p<0.001). The number of patients with cirrhosis was significantly less in the perinatal risk group (8.1%, 10/123) compared to the intravenous drug abuse group, blood transfusion risk group and mixed risk group (36.0%, 205/570; 32.1%, 81/252; 30.0%, 42/140) (p<0.001) but the majority of patients with perinatal exposure are less than 33yrs (106/123, 86%) at time of data analysis, whereas (10/17, 59%) above the age of 33yrs have developed cirrhosis, suggesting that this group may be at particular risk.
Table:

<table>
<thead>
<tr>
<th>Liver disease</th>
<th>Intravenous drug abuse (n= 570)</th>
<th>Receipt of blood products (n= 252)</th>
<th>Perinatal exposure (n= 123)</th>
<th>Other$^1$ (n= 140)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cirrhosis, n (%)</td>
<td>205 (44)</td>
<td>81 (32)</td>
<td>10 (8)</td>
<td>42 (30)</td>
</tr>
<tr>
<td>Age at cirrhosis, yrs, median (range)$^2$</td>
<td>48.5 (33-68)</td>
<td>45.5 (23-61)</td>
<td>36 (17-53)</td>
<td>51.5 (12-65)</td>
</tr>
<tr>
<td>Years from first infection to cirrhosis, yrs, median (range)$^2$</td>
<td>33 (17-51)</td>
<td>32 (12-48)</td>
<td>36 (17-53)</td>
<td>36 (1-50)</td>
</tr>
<tr>
<td>HCC, n (%)</td>
<td>38 (7)</td>
<td>11 (4)</td>
<td>0</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Age at time of HCC, yrs, median (range)$^3$</td>
<td>55 (47-68)</td>
<td>53 (37-63)</td>
<td>-</td>
<td>53 (48-54)</td>
</tr>
<tr>
<td>Years from first infection to HCC, yrs, median (range)$^3$</td>
<td>39 (30-51)</td>
<td>39 (23-53)</td>
<td>-</td>
<td>37 (31-39)</td>
</tr>
<tr>
<td>LTx, n (%)</td>
<td>28 (5)</td>
<td>13 (5)</td>
<td>1 (1)</td>
<td>6 (4)</td>
</tr>
<tr>
<td>Age at time of LTx, yrs, median (range)$^4$</td>
<td>50 (36-66)</td>
<td>46 (27-63)</td>
<td>-</td>
<td>53 (44-54)</td>
</tr>
<tr>
<td>Years from first infection LTx, yrs, median (range)$^4$</td>
<td>33 (20-50)</td>
<td>37 (16-49)</td>
<td>-</td>
<td>36 (28-39)</td>
</tr>
</tbody>
</table>

HCC: Hepatocellular carcinoma, HCV: Hepatitis C virus, LTx: liver transplantation.
$^1$Born abroad, tattoos, surgery, dental, unknown. $^2$Missing data from 50 patients with cirrhosis.
$^3$Missing data from 7 patients with HCC. $^4$Missing data from 5 LTx patients.

**Conclusion:** The main route of HCV infection in young people (<18yrs) in the UK is intravenous drug abuse with serious long-term liver disease developing in 31%. Detection of HCV should be aimed at relevant risk groups and anti-viral therapy should be made available in childhood to prevent long-term liver disease and spread of HCV.
Predicting HCC development in children with PFIC2

Sharat Varma1, Raphael Fredrick2, Anne Spraul3, Charlotte Mussini3, Xavier Stephenne4, Emmanuel Jacquemin4, Etienne Sokal5, Emmanuel Gonzales3

1Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium
2Université Catholique de Louvain, Brussels, Belgium
3Bicêtre Hôpital, Paris-Sud University, Ap-Hp, Paris, France
4Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
5Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Background and aims: Progressive familial intrahepatic cholestasis type 2 (PFIC2) is an autosomal recessive disorder with defective bile salt export pump (BSEP) which results in cholestatic liver disease and in 15% hepatocellular carcinoma (HCC). As intra-hepatocytic bile accumulation is considered to be the driver of oncogenesis in PFIC2, we hypothesized that risk of HCC would correlate to functional capability of BSEP.

Methods: From two participating centers, sixty-two children with PFIC2 were identified, of which seven who developed HCC were included. Clinical, genetic, histological information was collected and 3D homology modelling was done to determine the severity of structural alterations in BSEP. Functional ability of the BSEP was assessed by the clinical response to medical therapy and severity of structural change in the BSEP as assessed by 3D homology modelling.

Results: PFIC2 was diagnosed at a mean of 3.7 months (1-10 months) and HCC was discovered 52 months later (11-150 months). At diagnosis BSEP was absent in 85% (6 of 7) while one had canalicular localization. The diagnostic features of HCC were elevated AFP in 71% (5 of 7) and ultrasound characteristics in 85% (6 of 7). Functional ability of BSEP was retained in 28% (2 of 7). These both demonstrated clinical response to medical therapy and had mild structural alteration of BSEP on 3D modelling.

Conclusion: There is high incidence of HCC in PFIC2, and can occur in presence of normal AFP. The functional capability of BSEP can be predicted by structural modelling and does not correlate to risk of oncogenesis.
Hyperparathyroidism prior to liver transplantation is associated with early ACR in children

Elisa Anghileri¹, Vladimir Cousin², Carla Colombo³, Laetitia Marie Petit⁴, Valérie McLin¹

¹University Hospitals Geneva, Pediatrics, Geneva, Switzerland
²Geneva University Hospital, Pediatrics, Geneva, Switzerland
³Cystic Fibrosis Center, Milano, Italy, Milan, Italy
⁴Hopitaux Universitaires de Geneve, Pediatrice, Geneva, Switzerland

Introduction: In adults, the number of episodes of acute cellular rejection (ACR) has been shown to compromise long-term liver allograft survival. It is commonly accepted that children may be more prone to ACR than adults, and allograft longevity in pediatric recipients is of the utmost importance. Factors predisposing to ACR are not understood. Recently, the immunomodulatory properties of vitamin D have been increasingly recognized. Given that children typically undergo liver transplant (LT) for cholestatic conditions which are characterized by fat-soluble vitamin deficiencies, we asked whether perturbations in pre-LT vitamin D metabolism may predispose to ACR in a representative cohort of pediatric LT recipients.

Methods: We conducted a retrospective, single center study of children who underwent liver transplantation between 2005 and 2013. Serum 25 (OH) vitamin D levels and other factors related to vitamin D metabolism were collected from pre-LT records, while immune complications such as ACR, autoimmune hepatitis, CMV and EBV infections were collected from post-LT clinical charts during 2 years of follow up.

Results: Fifty-three patients were included in this study. No significant correlations were identified between serum 25 (OH) D levels, ACR and other post LT immune complications (p> 0.05). However, the development of ACR was associated with pre-LT hyperparathyroidism (p = 0.008) and with the absence of a pre-LT nutritional support (p = 0.048).

Conclusion: This study suggests that pre-LT hyperparathyroidism may be associated with ACR. This surprising finding is compatible with long-standing abnormalities in vitamin D metabolism prior to transplant, as hyperparathyroidism is slower to correct than serum vitamin D levels. In other words, in spite of normalized or near-normal serum vitamin D levels which can correct quickly through nutritional supplementation, long-standing abnormalities in vitamin D metabolism pre-LT, the hallmark of which is hyperparathyroidism, may pre-dispose to ACR, thereby possibly impacting long-term graft survival, although this needs further validation.
Transient elastography measurements of spleen stiffness as a predictor of clinically significant varices in children with portal hypertension

Harry Sutton¹, Emer Fitzpatrick², Mark Davenport¹, Anil Dhawan¹, Tassos Grammatikopoulos³

¹King’s College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom
²Paediatric Liver, GI and Nutrition Centre, King’s College Hospital, London, United Kingdom
³King’s College Hospital, Institute of Liver Studies, London, United Kingdom

Objectives and study: Assess the feasibility and prognostic value of spleen stiffness measurements (SSM) by transient elastography (TE; Fibroscan) in the prediction of clinically significant varices (CSV+ve) in children, defined as oesophageal grade ≥II or gastric grade 2 with red spots.

Methods: A total of 204 children (110M) underwent single TE measurement between September 2015- May 2016. Children with hypersplenism, defined as splenomegaly and platelet count <150x10⁹/L, or GI bleeding underwent oesophagoduodenoscopy (OGD), within 6 months from elastography study. Clinical and laboratory data were collected and validated variceal prediction scores were calculated at time of TE.

Results: 189 children (103M) had chronic liver disease (CLD), 15 (7M) portal vein thrombosis (PVT). OGD was performed in 68 children due to evidence of hypersplenism. CSV+ve were identified in 37 children including 8 who had emergency OGD due to acute GI bleeding. In all patients median age, platelet count, haemoglobin, INR, albumin, bilirubin, alanine aminotransferase, spleen size z-score, Clinical Prediction Rule (CPR), King’s Variceal Prediction Score (KVaPS) and SSM were 7 years (range, 2 mo-19yr), 198x10⁹/L (25-619), 125.5g/L (52-165), 1.1 (0.8-2.7), 43g/L (23-55), 10µmol/L (1-246), 43.5IU/L (7-444), 2.89 (-2.4-16.6), 126.8 (69.8-289.1), 97.3 (14.7-134.9) and 16.5kPa (1.6-75), respectively. In CLD patients median liver stiffness measurements (LSM) and KVaPS were 8.6kPa (range, 2.4-75) and 99.1 (14.7-134.9). In all children there was significant difference in CSV+ve and CSV-ve groups in SSM (52.5kPa vs. 16.5kPa, p=0.001) and CPR (104.1 vs. 136.6, p<0.001). SSM, CPR, KVaPS and LSM were compared in the assessment of CSV+ve in patient’s groups (Table). The optimal cut-off for SSM (23.7kPa), CPR (115) and KVaPS (76) had PPV and NPV of 59% and 96%, 39% and 95%, and 44% and 87%, respectively. Children with GI bleeding had median SSM, CPR and KVaPS of 27.8kPa (range, 16.4-75.0), 102.5 (69.8-111.7) and 70.1 (36.6-90.8), respectively.

Table:

<table>
<thead>
<tr>
<th></th>
<th>All patients</th>
<th>CLD</th>
<th>PVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>SSM AUROC</td>
<td>0.92</td>
<td>0.90</td>
<td>1.00</td>
</tr>
<tr>
<td>SSM sensitivity/specificity</td>
<td>89%/81%</td>
<td>87%/81%</td>
<td>100%/100%</td>
</tr>
<tr>
<td>CPR AUROC</td>
<td>0.83</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>CPR sensitivity/specificity</td>
<td>83%/77%</td>
<td>83%/77%</td>
<td></td>
</tr>
<tr>
<td>CPR specificity</td>
<td>77%</td>
<td>77%</td>
<td></td>
</tr>
<tr>
<td>KVaPS AUROC</td>
<td>0.87</td>
<td></td>
<td></td>
</tr>
<tr>
<td>KVaPS sensitivity/ specificity</td>
<td>78%/80%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSM AUROC</td>
<td>0.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LSM sensitivity/ specificity</td>
<td>82%/78%</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Vol. 64, Supplement 1, April 2017
Conclusion: In children with portal hypertension SSM was the greatest predictor of CSV+ve as well as in the individual CLD and PVT subgroups. SSM can be used as a non-invasive screening tool for children with hypersplenism to stratify the risk of having CSV+ve.
Ductular reaction is associated with concurrent fibrosis on protocol biopsy from liver transplant recipient children

Sharat Varma¹, Mina Komuta², Jérome Ambroise³, Caroline Bouzin⁴, Etienne Sokal⁵

¹Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium
²Clinique Universitaire St Luc, Pathology, Brussels, Belgium
³Université Catholique de Louvain, Center for Applied Molecular Technologies, Bruxelles, Belgium
⁴University Catholique de Lovain, Brussels, Belgium
⁵Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Objectives and study: Ductular reaction (DR) is identified by using CK7 staining and represents a ductular phenotype, possibly arising from proliferation of cholangiocytes and progenitor cells. DR has been linked to hepatic fibrosis progression in HCV and hemochromatosis. It is frequently seen on protocol biopsies (PB) post-liver transplant (LT) and given its origin it’s unclear if its linked to fibrogenesis or hepatocyte regeneration after an insult. This was analyzed in the current study using paired PB’s to test if CK7 quantification on the baseline PB could predict the course of fibrogenesis in the follow up PB.

Methods: Children who underwent LT from 2012 to 2014 and had ≥2 PB at an interval of 1-2 years between each other were included. The first PB was labeled as “baseline biopsy” and the successive biopsy as “follow-up biopsy.” The change of fibrosis severity between the “baseline” and “follow-up” biopsy was termed as “prospective change in fibrosis.” Each biopsy was evaluated for inflammation and fibrosis using the Metavir and LAFSc system. The baseline biopsy was stained with CK7 and digitally evaluated to obtain “CK7 – positive area percentage” i.e. CK7-stained area expressed as percentage of the total biopsy area. The association between CK7-positive area percentage on baseline biopsy and “prospective change in fibrosis” scores, ductular reaction, lobular inflammation, and portal tract inflammation was assessed using ordinal logistic regression models.

Results: Our study included 64 pared PB from 32 children. The baseline PB stained for CK7, were taken at a mean of 2.89 years post-LT. The time interval between the two paired PB’s was 1.41 years. CK7-positive area percentage was significantly associated with baseline fibrosis, extent of ductular reaction (p=.006) and portal tract inflammation (p=.01). There was a no significant association between the CK7-positive area percentage of the baseline biopsy and the “prospective change in fibrosis” as assessed by the Metavir score (p=.36) or cumulative LAFSc (p=.25) or with recipient or donor age, donor type, HLA antibodies, or recipient or donor gender.

Conclusion: Ductular reaction, CK7 expression is significantly associated with extent of portal tract inflammation and concurrent severity of fibrosis but does not predict the future course of fibrogenesis.
The impact of IBD on the course and progression of PSC

Mohana Sathiaseelan¹, Rishi Bolia¹, Winita Hardikar¹, Jeremy Rajanayagam¹

¹Royal Children’s Hospital, Gastroenterology, Hepatology and Clinical Nutrition, Parkville, Australia

Objectives and study: The association between Primary Sclerosing Cholangitis (PSC) and Inflammatory Bowel Disease (IBD) is well established. The impact of IBD on the course and progression of PSC however, remains unclear. Our aim was to evaluate the prevalence of IBD in patients diagnosed with PSC and determine its relationship to clinical significant hepatobiliary endpoints.

Methods: Retrospective analysis of children aged ≤ 18 years diagnosed with PSC with or without IBD in accordance to standard definitions between 1998 and 2016. Patients were followed from tertiary paediatric care through transition until last follow-up within an adult liver service. Outcomes of interest included: (1) abnormal LFT’s at last follow up (2) biliary complications (i.e., admissions for cholangitis and/or dominant strictures requiring intervention) (3) clinically significant portal hypertension (4) need for liver transplantation (5) post-transplantation disease recurrence (6) cholangiocarcinoma and (7) survival.

Results: 51 children (28 female) were diagnosed with PSC at a median age of 11.3 years and followed over a median duration of 54 months (IQR 32-88). At last review, IBD was present in 37 (73%) patients, of which 23 had their diagnosis confirmed prior to or near the time of presentation with PSC. 31 had Ulcerative Colitis, 3 Crohn’s Disease and 3 IBD-Unspecified, with the predominant disease phenotype for all groups being pancolitis (92%). A comparison of outcomes for children with PSC with or without IBD is shown in Table 1. There were no hepatobiliary malignancies or deaths in our cohort. At the time of last follow up, 27/37 (73%) patients with IBD were in clinical remission. A sub-analysis of patients in IBD remission versus those with active disease showed patients in remission have a significantly lower likelihood of having deranged LFT’s at last follow up (30% vs 70%, p= 0.03). No other endpoints were significant.

Table: Comparison of outcomes in children diagnosed with PSC with and without IBD

<table>
<thead>
<tr>
<th></th>
<th>PSC</th>
<th>No IBD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abn LFT’s at last follow-up</td>
<td>n=37</td>
<td>n=14</td>
</tr>
<tr>
<td>Biliary complications</td>
<td>6 (16%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Clinically sig. portal hypertension</td>
<td>10 (27%)</td>
<td>4 (29%)</td>
</tr>
<tr>
<td>Liver transplantation</td>
<td>7 (19%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>Post-transplant disease recurrence</td>
<td>4 (11%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

Conclusion: Better IBD management may lead to improved liver function in children with PSC. Large cohort longitudinal studies are required to assess if IBD disease control alters the progression of liver disease.
Graft fibrosis and long-term outcome after paediatric liver transplantation

Steffen Hartleif, Jeremy Rajanayagam, Vladimir Cousin, Dominique Debray, Jake Demetris, Helen Evans, Björn Fischler, Emmanuel Gonzales, Annette S. Gouw, Wolfram Haller, James Hodson, Stefan G. Hubscher, Florence Lacaille, Silvia Malenicka, George V. Mazariogos, Valérie McLin, James E. Squires, Ekkehard Sturm, Henkjan Verkade, Deirdre Kelly

1Childrens Hospital University of Tuebingen, Paediatric Gastroenterology and Hepatology, Tuebingen, Germany
2Birmingham Children’s Hospital, The Liver Unit, Birmingham, United Kingdom
3Geneva University Hospital, Pediatrics, Geneva, Switzerland
4Hôpital Bicêtre, Paris, France
5University of Pittsburgh Medical Centre, Pittsburgh, United States
6Starship Child Health, Department of Paediatric Gastroenterology, Auckland, New Zealand
7Dept. of Pediatrics, Karolinska University Hospital, Clintec, Stockholm, Sweden
8University Medical Center Groningen, Groningen, Netherlands
9Birmingham Children’s Hospital, Department of Paediatric Gastroenterology, Birmingham, United Kingdom
10Queen Elizabeth Hospital, Birmingham, United Kingdom
11Necker-Enfants Malades Hospital, Gastroenterology, Hepatology and Nutrition, Paris, France
12Astrid Lindgren Children’s Hospital, Karolinska University Hospital Huddinge, Paediatric Gastroenterology, Hepatology and Nutrition, Stockholm, Sweden
13Children’s Hospital of Pittsburgh, Pittsburgh, United States
14University Hospitals Geneva, Pediatrics, Geneva, Switzerland
15Dept of Paediatrics, University of Groningen, University Medical Center Groningen, Paediatrics, Groningen, Netherlands
16The Liver Unit, Hepatology, Birmingham, United Kingdom

Objectives and study: The histological prevalence of allograft fibrosis in asymptomatic paediatric liver transplant (LT) recipients is well documented. But, the impact of fibrosis on long-term outcome remains unclear. In this retrospective study, we aim to determine risk factors and to analyse clinical outcomes for children with liver allograft fibrosis in 10-year protocol biopsies.

Methods: We reviewed clinical data and long-term outcomes of 289 asymptomatic (ALT<50 IU/L) children who underwent 10-year (+/- 2 years) protocol biopsies in 8 international liver transplant centres. Histological findings were correlated with clinical endpoints including re-transplantation and survival. The median follow-up was 17 years (8 - 24 years) after LT.

Results: In the 10-year biopsies, normal or near normal histology was reported in 68 (24%); periportal or central fibrosis without bridging in 135 (47%); 59 (20%) had bridging fibrosis and 27 (9%) had cirrhosis. Significant predictors of graft fibrosis vs. no fibrosis included recipients negative for CMV at time of transplant (OR 1.87; p=0.044)); prior episodes of biopsy-proven rejection (OR 1.84; p=0.038)); and maintenance immunosuppression including steroids at 10 years (OR 1.92; p=0.019)). There was a trend towards an association with positive serum autoantibodies, although this did not reach statistical significance (p=0.057). Fibrosis was not found to be significantly associated with transplant related factors such as, cold ischemia time (p=0.112), age at transplantation (p=0.898), or type of graft (p=0.873), and laboratory parameters such as elevated IgG (p=0.240) at 10 years post LT.

In a subgroup of n=115 patients, 5-year protocol biopsies were available and reviewed. Analysis of serial biopsies revealed that fibrosis was progressive at least one stage in 46% of patients. In 38% of patients, there was no change in fibrosis stage while 16% showed improvement by one or more stages. In a multivariate regression model, the presence of positive auto-antibodies at 10 years post-transplant (n=70) was associated with progression of fibrosis (OR 6.29; p=0.005)).

A Kaplan-Meier analysis for patient and allograft survival did not demonstrate reduced allograft survival in patients with periportal/central fibrosis and bridging fibrosis in comparison to patients
without fibrosis at 10-year biopsy. However, patients with cirrhosis at 10 years had a significantly (p=0.028) higher risk of death (2 out of 27 patients) or re-transplantation (3 out of 27 patients) by the end of the second decade after LT.

**Conclusion:** 76% of patients transplanted in childhood developed fibrosis in protocol liver biopsies 10 years post transplant, which is potentially progressive in most cases. While many patients with fibrosis are stable, severe fibrosis or cirrhosis on 10-year protocol biopsy may lead to graft loss or mortality by the end of second decade post paediatric LT.
HEPATOLOGY: General Hepatology

H-O-026

Altered systemic bile acid homeostasis contributes to liver disease in pediatric patients with intestinal failure

Yongtao Xiao¹, Wei Cai¹

¹Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Department of Pediatric Surgery, Shanghai, China

Objectives and study: Intestinal failure (IF)-associated liver disease (IFALD), as a major complication, contributes to significant morbidity in pediatric IF patients. However, the pathogenesis of IFALD is still uncertain. We here investigate the roles of bile acid (BA) dysmetabolism in the unclear pathogenesis of IFALD.

Methods: Serum levels of FGF19, IL-6 and, TNF-α were measured in pediatric IF patients and matched healthy controls using ELISA assay. Liver injury and fibrosis were determined by histology, TUNEL analysis and Masson’s trichrome stain. Ultraperformance liquid chromatography-tandem mass spectrometry (UPLC-MS) was used to measure the bile acid (BA) composition in serum and liver.

Results: It found that the histological evidence of pediatric IF patients exhibited liver injury, which was characterized by liver bile duct proliferation, inflammatory infiltration, hepatocyte apoptosis and different stages of fibrosis. The BA compositions were altered in serum and liver of pediatric IF patients, as reflected by a primary BA dominant composition. In IF patients, the serum FGF19 levels decreased significantly, and were conversely correlated with ileal inflammation grades (r =-0.50, p < 0.05). In ileum, the inflammation grades were inversely associated with farnesoid X receptor (FXR) expression (r =-0.55, p < 0.05). In liver, the expression of induction of the rate-limiting enzyme in bile salt synthesis, cytochrome P450 7a1 (CYP7A1) increased evidently.

Conclusion: In conclusion, ileum inflammation decreases FXR expression corresponding to reduce serum FGF19 concentration, along with increased hepatic bile acid synthesis, leading to liver damages in IF patients.
Table: Liver biochemistry, serum lipids, glucose and inflammatory cytokines in the patients

<table>
<thead>
<tr>
<th>Variable</th>
<th>Control</th>
<th>Patients</th>
<th>p value</th>
<th>Correlation with FGF19</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=21</td>
<td>n=23</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Liver enzymes</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma alkaline phosphatase, ALP(U/L)</td>
<td>51.76±69.24</td>
<td>90.34±66.99</td>
<td>0.08</td>
<td>-0.34</td>
</tr>
<tr>
<td>Plasma alanine aminotransferase, ALT(U/L)</td>
<td>23.23±16.01</td>
<td>55.77±19.91</td>
<td>&lt;0.01</td>
<td>-0.19</td>
</tr>
<tr>
<td>Plasma aspartate aminotransferase, AST(U/L)</td>
<td>36.35±16.66</td>
<td>61.67±27.51</td>
<td>&lt;0.01</td>
<td>-0.3</td>
</tr>
<tr>
<td><strong>Markers of cholestasis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Plasma total bilirubin(µmol/L)</td>
<td>5.33±2.55</td>
<td>6.24±1.35</td>
<td>0.15</td>
<td>-0.15</td>
</tr>
<tr>
<td>Plasma conjugated bilirubin(µmol/L)</td>
<td>3.16±1.43</td>
<td>3.19±2.26</td>
<td>0.97</td>
<td>-0.07</td>
</tr>
<tr>
<td><strong>Serum lipids</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum HDL cholesterol (mmol/L)</td>
<td>0.76±0.26</td>
<td>0.63±0.19</td>
<td>0.09</td>
<td>0.07</td>
</tr>
<tr>
<td>Serum LDL cholesterol (mmol/L)</td>
<td>1.50±0.56</td>
<td>1.83±0.45</td>
<td>0.04</td>
<td>0.02</td>
</tr>
<tr>
<td>Serum total cholesterol, TC (mmol/L)</td>
<td>2.00±0.47</td>
<td>2.4±0.61</td>
<td>0.02</td>
<td>-0.16</td>
</tr>
<tr>
<td>Serum triglycerides, TG (mmol/L)</td>
<td>0.79±0.31</td>
<td>1.13±0.60</td>
<td>0.03</td>
<td>0.08</td>
</tr>
<tr>
<td>Plasma glucose (mmol/L)</td>
<td>3.80±1.16</td>
<td>3.21±0.88</td>
<td>0.21</td>
<td>0.18</td>
</tr>
<tr>
<td><strong>Markers of inflammation</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Serum IL-6(pg/mL)</td>
<td>13.28±21.78</td>
<td>50.63±45.99</td>
<td>&lt;0.01</td>
<td>-0.32</td>
</tr>
<tr>
<td>Serum TNF-α(pg/mL)</td>
<td>0.41±0.2</td>
<td>0.89±0.43</td>
<td>&lt;0.01</td>
<td>-0.33</td>
</tr>
</tbody>
</table>
Extra-hepatic involvement in paediatric autoimmune liver disease

Giulia Paolella¹, Marcello Farallo¹, Irene Degrassi¹, Federica Nuti¹, Gabriella Nebbia¹

¹Fondazione Irccs Ca' Granda Ospedale Maggiore Policlinico, Service of Pediatric Hepatology and Nutrition, Milan, Italy

Objectives and study: Autoimmune liver disease (AILD) is a chronic and progressive inflammatory liver disease that evolves spontaneously to cirrhosis and liver failure. AILD comprises autoimmune hepatitis (AIH), and autoimmune sclerosing cholangitis/overlap syndrome (ASC), the latter associated with signs of cholangiopathy. AIH is classified in two subgroups, according to the presence of different autoantibodies: AIH type 1 (ANA/ASMA positivity) and AIH type 2 (LKM1/LC1 positivity). AILD is often associated with extra-hepatic diseases (EDs) which can precede or follow liver involvement. In this study we aimed to assess the EDs frequency in our AILD paediatric series.

Methods: A retrospective evaluation of 38 AIH children and 9 ASC children (23 males and 24 females; age range at diagnosis of AILD: 3 years and 2 months-16 years and 10 months, median age: 9 years and 6 months) referred to our Paediatric Liver Centre. Thirty-six children were referred primarily to our centre for a suspicion of liver disease, the remaining eleven patients were initially followed for EDs by other centres and only subsequently they showed liver disease. Patients were screened for celiac disease, ulcerative colitis, autoimmune thyroiditis, autoimmune skin disease (e.g. scleroderma, psoriasis), rheumatoid arthritis, diabetes, lupus, etc.

Results: Mean duration of follow-up was 9 years and 3 months. As a total, 21 out of 47 patients (44.7%) showed EDs: 9 ulcerative colitis (42.8%), 5 autoimmune thyroid diseases, 4 celiac disease (19%), 3 autoimmune skin disease (14.3%), 3 rheumatoid arthritis (14.3%), 2 lupus erythematosus (9.5%), 1 autoimmune thrombocytopenia (4.8%) and 1 type-1 diabetes (4.8%). Furthermore 6/21 patients (28.6%) had more than one EDs. In 8 out 9 (88,9%) children with ulcerative colitis, ASC was present.

Conclusion: Several studies have reported the association between AILD and EDs, whereas there are only few paediatric cohorts studies. Our study showed a high prevalence of EDs in AILD children. This very high percentage could be related to the frequent referral to our centre by other highly specialized pediatric services. Our data suggest the importance to look for EDs in AILD patients, conversely AILD has to be excluded in EDs children with abnormal liver function tests.
Next generation sequencing: identifying atypical Alagille syndrome and NOTCH2 variants

Luis Alvarez, Loreto Hierro, Sixto García-Miñaur, Luiz Stark Aroeira, Pilar Martínez, Sara Andueza, Carmen Camarena, Angela De la Vega, Carmen Díaz, Paloma Jara

1“la Paz” University Hospital, Health Research Institute-Idipaz, Madrid, Spain
2“la Paz” University Hospital, Paediatric Liver Service, Madrid, Spain
3“la Paz” University Hospital, Institute of Medical & Molecular Genetics –ingemm, Madrid, Spain

Objectives and study: Alagille syndrome is caused by mutations in JAG1 (chromosome 20p12.2) or NOTCH2 (chromosome 1p12-p11). Distribution is reported to be 98% JAG1 and 2% NOTCH2. Molecular testing in liver diseases has recently evolved to next generation sequencing (NGS) using customized liver genes panel, which allows exploring JAG1 and NOTCH2 in a wider clinical spectrum. We aimed at reviewing the results of molecular analysis of JAG1 and NOTCH2 performed in children with liver disease at Hospital La Paz-Madrid.

Methods: Procedures resulting in the genetic diagnosis of Alagille Syndrome were reviewed. NGS (liver panel) became available in 2016. The capture technology is SECAP EZ (Roche, Nimblegen) in a MiSeq platform (Illumina) and was applied to identify mutations in children with features of Alagille syndrome (ALGS), either new cases or showing normal JAG1 in previous era of JAG1 sequencing and MLPA. NGS was also applied to study liver disease of unknown origin.

Results:
1) Sanger sequencing identified 64 children with JAG1 mutation (62 one mutation, 2 mutations in two siblings). MLPA found a large deletion in JAG1 in 2 cases.

2) NOTCH2 sequencing (performed by Dr N. Spinner) identified 1 case. His apparently unaffected mother carried the same mutation (included in: Kamath BM et al. J Med Genet 2012)

3) NGS:
3.a) 5 cases of JAG1 mutation were identified: 1 classical ALGS in whom previous JAG1 Sanger sequencing was normal, 1 new case of classical ALGS, 2 siblings suspected of high-GGT familial disease who displayed isolated liver disease (but evolved to kidney failure a decade after liver transplantation), and 1 child treated elsewhere with partial biliary diversion who resembled PFIC (ABCB11 and ATP8B1 sequencing had ruled out PFIC 2 and PFIC1).

3.b) 5 cases of NOTCH2 mutation were found. Four cases had undergone JAG1 Sanger sequencing (normal) and 3 ABCB4 sequencing (normal). One was a classical ALGS (deafness, facies, kidney, liver and cardiac disease), 1 had presumed ALGS (liver disease, facies, cardiac murmur, embriotoxon), 2 children displayed a high-GGT chronic liver disease but no other features of the syndrome (one of them additionally displayed 2 mutations in FOXA2, transcriptional activators for liver-specific genes), and 1 suffered familial cirrhosis (no features of ALGS) and underwent NGS study with a suspicion of MDR3 defect (1 mutation in ABCB4 was found additionally).

4) Familial studies.
Out of total 77 cases, hereditary disease was clinically observed in 12 (15.5%). JAG1 Sanger sequencing was performed in parents (57 individuals) of 33 cases (2 were twins) of sporadic ALGS: 1
father and 6 mothers with JAG1 or NOTCH2 mutation were identified. Thus 8 of 33 (24%) sporadic children were hereditary and 76% “de-novo”.

5) Clinical evolution

Today, 33 (43%) children are alive with own liver, 4 (5%) died with complications of liver or cardiac disease, and 39 (50%) underwent liver transplantation (1 multivisceral for jejunal atresia). Four (5%) underwent kidney transplantation.

Conclusion: Combination of JAG1 study upon clinical suspicion plus NGS with or without suspicion of Alagille syndrome, led to a series of 77 patients. Of them 69 (89.6%) displayed JAG1 mutation, 2 (2.5%) JAG1 deletion, and 6 (7.8%) NOTCH2 mutation. Alagille syndrome was not clinically presumed in 6 (7.8%): 4% of JAG1 and 50% of NOTCH2. Sporadic cases resulted most frequently as consequence of “de-novo” mutation (76%).
Impact of IL28B gene polymorphism on virological response to pegylated interferon/Ribavirin therapy in Egyptian children with HCV genotype-4 chronic hepatitis

Ahmed Megahed1, Ahmed Abdalla1, Khaled Zalata2, Abeer Fathy1, Tarik Barakat1, Mona Abd El-Latief1, Shreen El-Zainy1, Suzy Abd El-Mabood3

1Mansoura University Children’s Hospital, Mansoura University, Pediatrics; Gastroenterology, Hepatology and Nutrition, Mansoura, Egypt
2Mansoura University, Pathology, Mansoura, Egypt
3Mansoura University Children’s Hospital, Mansoura University, Pediatrics, Mansoura, Egypt

Objectives and study: IL28B polymorphism reflection upon response to interferon based HCV therapy has been reported in many adult studies; for children only few reports are available. In the current work we evaluated the reflection of IL28B polymorphism on treatment response to pegylated interferon alpha plus ribavirin therapy in children with chronic genotype -4 HCV infection.

Methods: The study included 55 naive children with chronic HCV genotype -4 hepatitis; 33 male and 22 females with age ranged from 4 to 17 years (mean 11.20 ± 3.64). Liver biopsy; basal HCV RNA viral load; liver function tests; in addition IL28B polymorphism at position – 3176 C/T (rs 12979860) were performed for all patients. HCV PCR was performed at 12; 24; 48 completed weeks of pegylated interferon alpha/ ribavirin therapy, and 24 weeks after as indicator for sustained virological response (SVR).

Results: Out of the studied 55 children, 37 (67.3%) had basal mild viremia, and 18 (32.7%) were of moderate viremia. Fifty one out of the 55 children were F0/F1; only two children had advanced fibrosis (F3/F4). Sustained virological response (SVR) was achieved in 26 (47.3%) children. Basal HCV RNA was significantly lower among children with SVR; 21 (80.2%) of responders were of mild viremia versus 16 (55.2%) of non-responders (P = 0.04). Regarding IL28B polymorphism, CC; CT and TT genotypes were reported in 19; 23 and 13 children respectively. Among responders CC; CT and TT genotypes were reported in 14 (53.8%); 6 (23.1%) and 6 (23.1%) children respectively. While in non-responders CC; CT and TT genotypes were reported in 14 (53.8%); 6 (23.1%) and 6 (23.1%) children respectively. While in non-responders CC; CT and TT genotypes were reported in 5 (17.3%); 17 (58.6%) and 7 (24.1%) children respectively, (P= 0.009). Age, gender, fibrosis stage and necroinflammation were of no significant differences among responders and non-responders.

Conclusion: Treatment response to Pegylated IFN/Ribavirin therapy in children with HCV genotype -4 is significantly correlated with basal HCV RNA viremia as well IL28B polymorphism. Testing for IL28B polymorphism may be considered as a prerequisite to pegylated interferon/ribavirin therapy in children with HCV genotype-4.
There is no role of routine monitoring of thiopurine metabolites in children with autoimmune hepatitis

Rishi Bolia¹, Jeremy Rajanayagam¹, Winita Hardikar¹

¹Royal Children's Hospital, Gastroenterology, Hepatology and Clinical Nutrition, Parkville, Australia

Objectives and study: Azathioprine therapy is the mainstay in the maintenance of remission in children with autoimmune hepatitis (AIH). The ability to measure thiopurine metabolites has allowed for optimization of azathioprine dose in inflammatory bowel disease, but its role has not been defined and validated for AIH. We aimed to study the role of the measurement of thiopurine metabolites in children with AIH.

Methods: Retrospective chart review (year 2001 onwards) of children (< 19 years) with AIH, who have been on treatment with azathioprine for a period of at least 6 months. Baseline characteristics, clinical course and outcome, TPMT genotyping, thiopurine metabolites and their corresponding liver function tests were recorded. Children were stratified according to the therapeutic response to determine the relationship of thiopurine metabolites to outcome. Patients with a AIH / PSC overlap, on concomitant immunosuppressive agents [apart from low dose (< 5 mg./day) prednisolone] or an intercurrent illness that could have contributed to deranged liver function tests (LFT’s) were excluded while analysing the correlation between thiopurine metabolites and LFT’s. Standard definitions were used for defining treatment response and disease flare.

Results: The records of 56 children [23 boys, age 11 (0.7 – 18 years) at diagnosis] with a total median follow – up duration of 50 (8-182) months were reviewed. Forty – five had Type I AIH, while 6 and 5 had Type II and seronegative AIH respectively. An AIH/PSC overlap was seen in 18(32.1%) patients. All patients received prednisolone and azathioprine as a part of their initial treatment regimen. Azathioprine was started at a dose of 0.7 – 1 mg/kg and was then titrated and increased to a maximum dose of 1.7 – 2.5 mg/ kg.

TPMT genotype testing was done in 45 patients .45/50 (90%) of the patients were homozygous normal (extensive metabolisers) while 5 were heterozygous (intermediate metabolisers). Azathioprine toxicity was seen in 4 patients (Nausea- 2, pancreatitis – 1, Bone marrow suppression – 1). After exclusions, a total of 106 values of thiopurines metabolites were available. 56 were performed at the time of remission and 50 were performed when remission was not maintained. There was no difference in 6-Thioguanine (6-TG) levels when children in remission were compared to those who were not in remission [274 (100 – 1030) vs. 257.5 (24 – 538), p = 0.56]. No correlation was observed between 6 TG levels and the ALT levels (r = -.08, p = 0.42). A correlation was seen between 6- Methyl Mercaptopurine (6–MMP) levels and ALT levels (r = 0.23, p = 0.01).

Four patients who had an incomplete response were found to have a shifted metabolism (preferential generation of 6 MMP). All were started on allopurinol and went into biochemical remission. Inappropriately low thiopurines metabolites ( all < 100) helped in identifying 5 patients who were not compliant to the drug. Ensuring compliance helped in regaining response.

Conclusion: There is no role of routine monitoring of thiopurines metabolites to guide azathioprine dosing in children with AIH. Judicious measurement in patients with non – response, incomplete response or a flare helps in identifying children with a shifted metabolism or those who are non – compliant to therapy.
Early screening for inflammatory bowel disease in children with autoimmune liver disease

Dhamyanthi Thangarajah¹, Elena Cernat¹, Shola Doherty¹, Babu Vadmalayan¹, Nedim Hadzic¹, Marianne Samyn²

¹King's College Hospital, Paediatric Liver, Gi and Nutrition Centre, London, United Kingdom
²King's College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom

Objectives and study: Autoimmune liver disease (AILD), in particular autoimmune sclerosing cholangitis (ASC) is associated with inflammatory bowel disease (IBD). Faecal calprotectin (FC), screens for bowel inflammation without the need for invasive endoscopic evaluation. The aim of this study was to review the investigations and outcomes of IBD and AILD in children with a primary diagnosis of AILD and to identify possible risk factors for development of IBD in children with AILD.

Methods: Children with AILD were identified from electronic case notes between 2007 and 2010, they were diagnosed and treated as per centre protocol. Those with IBD prior to AILD were excluded. Diagnostic endoscopy for IBD was performed, based on GI symptoms and/or elevated FC (>60U/g). Data were documented at time of liver diagnosis; endoscopy and last liver follow up. Patients were classified as AILD-IBD or AILD. Statistical analysis was carried out using Social Sciences (SPSS) version 23.

Results: 37(12 male) children, diagnosed with AILD (ASC 11), 23 underwent diagnostic endoscopy after a median time from diagnosis of 27.6 [20.1 to 53.9] weeks. 20/23 reported GI symptoms and FC was elevated in 13/18. 13/23 had a diagnosis of IBD (AILD-IBD group) (UC (n=12), IBD-U (n=1)), 11 had pancolitis and 2 left sided disease. Endoscopy was normal in 10/23 (AILD group). No difference in gender or diagnosis of ASC between the 2 groups. At presentation of AILD, the AILD-IBD group were significantly leaner in terms of weight and BMI, had lower haemoglobin, with a trend for younger age at presentation (table). GI symptoms and FC >60 U/g were significantly more prevalent in the AILD-IBD group. At endoscopy, 22 were on treatment for AILD with prednisolone and 13 with an additional agent (azathioprine or mycophenolate mofetil). Biochemical remission for AILD was achieved in 45% at endoscopy and in 74% at last liver follow up (median 4.1 [3.5 to 5.0] years) with no difference for both groups. All patients are alive however in the AILD-IBD group 1 underwent an isolated liver transplantation and 1 required a subtotal colectomy. One girl underwent LT combined with subtotal colectomy after decompensation of her liver disease.
### Table:

<table>
<thead>
<tr>
<th></th>
<th>AILD-IBD</th>
<th>AILD</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (male)</td>
<td>13 (5)</td>
<td>10 (3)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>12.5 [10.3 to 14.6]</td>
<td>14.4 [12.0 to 15.5]</td>
</tr>
<tr>
<td>ASC (n)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>48.8 [38.8 to 55.9]</td>
<td>61.5 [52.9 to 75.4]*</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.7 [152.3 to 168.0]</td>
<td>164 [154.4 to 168.9]</td>
</tr>
<tr>
<td>BMI</td>
<td>19.2 [18.1 to 20.2]</td>
<td>22.5 [19.5 to 27.2]*</td>
</tr>
<tr>
<td>Haemoglobin (g/l)</td>
<td>113.0 [90.5 to 122.0]</td>
<td>127.5 [118.5 to 146.5]*</td>
</tr>
<tr>
<td>AST (IU/l)</td>
<td>235.0 [113.5 to 470.5]</td>
<td>461.0 [241.0 to 1039.0]</td>
</tr>
<tr>
<td>IgG (g/l)</td>
<td>25.2 [16.2 to 37.8]</td>
<td>25.1 [19.2 to 30.1]</td>
</tr>
<tr>
<td>Faecal calprotectin (U/g)</td>
<td>298.5 [114.5 to 439.8]</td>
<td>42.5 [34.6 to 66.3]*</td>
</tr>
<tr>
<td>GI Symptoms (n)</td>
<td>12</td>
<td>8</td>
</tr>
<tr>
<td>Faecal calprotectin &gt;60 U/g</td>
<td>11/12</td>
<td>2/6</td>
</tr>
</tbody>
</table>

**Conclusion:** 35% of children presenting with AILD were subsequently diagnosed with IBD. Possible risk factors for development of IBD in AILD are low haemoglobin, being leaner and younger at diagnosis. An elevated FC and the presence of GI symptoms are useful to assess the need for diagnostic endoscopy when considering diagnosis of IBD in the context of AILD. As concurrent immunosuppression, may mask mild symptoms and signs of IBD a lower threshold for endoscopy should be considered in these patients.
Transaldolase deficiency in 12 patients: phenotype, outcome and perspectives of treatment

François-Xavier Mauvais, Coraline Grisel, Anais Brassier, Jean-baptiste Arnoux, Chris Ottolenghi, Pascale de Lonlay, Florence Lacaille

1 Necker-Enfants Malades, Metabolic Diseases, Paris, France
2 Necker-Enfants Malades, Biochemistry, Paris, France
3 Necker-Enfants Malades, Gastroenterology-Hepatology-Nutrition, Paris, France

Objectives and study: Transaldolase (TALDO) deficiency is an inherited disorder of the pentose phosphate pathway, resulting in a multi-visceral perinatal disease. In neonates, the typical features are hepatosplenomegaly, jaundice, cutis laxa, telangiectasia, hypertrichosis, abnormal external genitalia, and a normal neurological examination. Thrombocytopenia, anemia and liver failure are also frequent. In the literature, both the nature and severity of presentations are highly heterogeneous, from a rapid death from organ failure or a progressive disease that will eventually result in cirrhosis or kidney failure. However, the treatments according to clinical features are still mainly elusive. We aimed to precise the clinical and biological phenotype of TALDO deficiency and to identify decision-making criteria that would improve the management of patients.

Methods: This retrospective study included 12 children, after exclusion of the data of a prematurely terminated pregnancy. We compared the characteristics of our patients to the 27 children reported in the literature. We also divided our cohort into two groups, and compared their characteristics according to the outcome..

Results: Seven boys and 5 girls from 6 families, 5 consanguinous, were followed from 1994 to 2016. The main clinical features were similar to the published cases, except a higher frequency of consanguinity and dysmorphism, and a lower frequency of thrombocytopenia in our cohort: 11/12 vs 12/27, p=0.01, 12/12 vs 12/27, p<0.001 and 6/12 vs 25/27, p=0.01, respectively. Two groups were defined depending on outcome, dead (group A, n=6) or alive (group B, n=6) at last follow-up. While dysmorphism was present at birth in all the children, the frequency of severe liver failure and renal abnormalities was higher in group A: 6/6 vs 2/6 p=0.05 and 4/6 vs 1/6, p=0.08, respectively. All patients in group A died before the age of 9 months from liver failure (n=3) or following liver transplantation (n=1), malnutrition (n=1), and multi-organ failure and infection (n=1). At last follow up, children in group B had a normal development but progressive organ damages, including cirrhosis, (n=3) and renal abnormalities (n=2).

Conclusion: Our results suggest the presence of two presentations and outcomes of TALDO deficiency: a severe and rapidly fatal neonatal disease that might benefit from early liver transplantation; and a slowly progressive neonatal form with favorable long-term outcome for which close attention should be paid to prevent and treat organ damage, including with liver or kidney transplantation as needed.
Role of PNPLA3 polymorphism in Wilson's disease: what role in metabolic syndrome and neurologic phenotype?

Giusy Ranucci1, Maria Teresa Petti1, Massimo Giovanni Zuin2, Rosa Zampino3, Margherita Matarazzo4, Emanuele Miraglia Del Giudice5, Raffaele Iorio1

1University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
2Università DI Milano, Milano, Italy
3University of Naples Federico II, Department of Medical, Surgical, Neurological, Metabolic and Geriatric Sciences, Naples, Italy
4University of Naples Federico II, Department of Translational Medical Sciences, Section of Internal Medicine, Naples, Italy
5Second University of Naples, Department of Woman, Child and General and Specialist Surgery, Naples, Italy

Objectives and study: The earliest characteristic alterations of the liver pathology in Wilson disease (WD) include steatosis, which is sometimes indistinguishable from non-alcoholic fatty liver disease (NAFLD). A genetic polymorphism in rs738409, in the patatin-like phospholipase domain (PNPLA3), seems to have a role in NAFLD and a recent paper also supports its influence in steatosis in WD patients. This study evaluated the role of PNPLA3 variant in a large cohort of WD patients as potential modifiers of metabolic syndrome and neurologic phenotype.

Methods: We enrolled 76 patients (47 males) with a median age of 15 years (1-58), followed at the Pediatric Hepatology Unit of University "Federico II" of Naples and at the Liver Unit of San Paolo Hospital of Milan. In the subgroup analysis to analyze correlation between polymorphism and response to treatment, it was considered as non-responder patients with persistent abnormal ALT and urine copper excretion despite treatment, excluding patients not-adherent to treatment.

Results: Median BMI of our WD population was 20.6 kg/m2, and only two patients were obese. Fifty patients (65%) showed dyslipidemia. Steatosis at ultrasound was present in 73 patients (96%). In particular, severe steatosis was described in eleven patients (14%), only two patients were under 18 years. In 31 patients there was a moderate steatosis (47%). The genotype frequencies for PNPLA 3 p148M were distributed as follows: 51% CC, 37 CG, 12% GG. Patients with GG phenotype showed higher ALT levels than CC (p:0.035). Contingency analysis showed higher prevalence of severe steatosis in GG group (89%, p<00.1). GG polymorphism seemed to correlate with an earlier onset (p: 0.021), while grade of steatosis did not correlate with age at onset (p>0.05). Neurologic phenotype at onset distribution was so distributed: CC 20%; CG 16%; GG 33%. GG polymorphism seems to correlate with response to treatment (p:0.019) and in particular in CC group 100% patients were responder, while 26% of CG and 45% %of GG were non responder.

Conclusion: Our study shows that PNPLA3 polymorphism might modulate liver injury in WD patients. In particular, it seems to correlate with metabolic syndrome parameters, especially with steatosis, so that GG variant was responsible of a severe phenotype and a worse response to treatment.
Objectives and study: Lysosomal acid lipase deficiency (LAL-D) is a progressive multisystem disease that is an underappreciated cause of cirrhosis, severe dyslipidemia, and early-onset atherosclerosis. In the phase 3 ARISE trial (NCT01757184) the primary endpoint of ALT normalization and multiple secondary efficacy endpoints were met after 20 weeks of exposure to sebelipase alfa (SA) in adults and children with LAL-D. This study aimed to examine the biochemistry outcomes in ARISE following long-term treatment with SA.

Methods: Affected patients (N=66; median age 13 y, range 4–58 y) were randomized to placebo (PBO) or SA at 1 mg/kg every other week for 20 weeks; following which 65 patients entered an ongoing, open-label extension phase in which they all received SA. Reported here are efficacy data at 76 weeks of SA exposure for all patients.

Results: Safety results from the open-label period involve patients with between 86 and 152 weeks of SA exposure (Week 22 to Jan 26, 2016). After 76 weeks of SA exposure, 52% of patients (32/61) achieved ALT normalization and 65% (37/57) achieved AST normalization; 87% reached ALT ≤1.5 x ULN and 95% reached AST ≤1.5 x ULN. The PBO group that crossed over to SA during the open-label period exhibited marked and sustained improvements in ALT and AST, which mirrored that seen in the SA group during the double-blind phase. Further, those in the SA group who continued receiving SA in the open-label period had sustained the improvements achieved in the 20 week double-blind period. Mean baseline values for LDL-C (199.2 mg/dL), non-HDL-C (230.0 mg/dL), and triglycerides (153.9 mg/dL) decreased by −28%, −27%, and −17%, respectively, after 76 weeks of SA exposure; mean HDL-C (baseline 32.5 mg/dL) increased by 23%. Most AEs in the open-label period were mild to moderate in severity. The most commonly experienced AEs were headache, nasopharyngitis, cough, and pyrexia. Four patients had serious AEs (one was treatment-related, an infusion-associated reaction). Twelve patients (19%) experienced infusion-associated reactions, which were mild or moderate in severity in all but one subject. There were no discontinuations due to an AE. Six (9%) of the 66 patients had at least one positive anti-drug antibody (ADA) sample; of these, two developed neutralizing antibodies. The safety profile for ADA-positive patients was consistent with that of the overall study population. SA was well tolerated; the long-term safety profile was similar to the profile seen during the double-blind portion.

Conclusion: Long-term treatment with SA produced early and rapid improvements in markers of liver injury and lipid abnormalities which were sustained.

Disclosure of interest: This study was sponsored by Alexion Pharmaceuticals, Inc. K.N. Furuya and B.K. Burton are investigators in the ARISE study. B.K. Burton has received funding for the conduct of clinical studies from Alexion Pharmaceuticals, Inc., BioMarin, Shire, Genzyme, and Ultragenyx; funding for independent research and/or education from BioMarin and Shire; and consulting fees and honoraria from BioMarin, Shire, Alexion, Genzyme, and Regenxbio. S. Marulkar, M. Friedman, and R. Tripuraneni are employees of Alexion Pharmaceuticals, Inc., and may own stock/stock options in the company.
Molecular characterization of novel variants for improved diagnosis in children having Wilson disease

Friedrich Bernick¹, Magdalena Naorniakowska², Sarah Guttmann¹, Sara Reinartz Groba¹, Andree Zibert¹, Hartmut Schmidt³

¹Clinic for Transplantation Medicine, University Clinic Muenster, Muenster, Germany
²Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
³Universitätsklinikum Münster, Münster, Germany

Objectives and study: Wilson disease (WD) is a rare autosomal recessive disorder of copper accumulation, especially in the liver and brain. Lifelong treatment involves mostly copper chelating compounds. If untreated, WD leads to death. WD patients may present liver disease in childhood or teenage years, while those with neurological or psychiatric symptoms are usually diagnosed in their twenties. Diagnosis is however difficult to perform, due to a high phenotypic variability and different onset of the disease. A distinctive criterion for WD diagnosis is a mutation in the copper transporter gene ATP7B. More than 600 disease-causing mutations of ATP7B are currently described. Novel variants with an unknown disease-causing phenotype can hamper establishment of diagnosis. There is a high clinical demand to classify novel ATP7B variants for rapid diagnosis and to start effective therapy in childhood.

Methods: Children were admitted to our hospital and diagnosed according to an established WD scoring system. DNA derived from peripheral blood was analyzed using ABI BigDye terminator reagents. Stable cell lines were generated by retroviral vectors expressing the variants in a human hepatoma ATP7B knockout cell line (PLoS ONE, 9: e98809, 2014). Functional characterization was achieved by determination of the copper transport using MTT assay and by determination of intracellular copper using atomic absorption spectrometry (AAS). Protein stability was assessed at different temperatures using Western blot analysis. Intracellular trafficking was determined by confocal fluorescence microscopy.

Results: The two children were borderline positive for WD with a score of 4 and 3, respectively (cut off score ≥ 4). Two novel variants of ATP7B, p.L168P and p.S1423N, were detected in one child, while p.L168P was associated as a compound heterozygote with the most frequent disease-causing mutation p.H1069Q in the other child. Using viability assays of stable cell lines, variants p.L168P and p.S1423N were demonstrated to have significant functional activity. However, activity of the variants was reduced as compared to wild type ATP7B. A comparison of p.L168P and p.S1423N expressing cells with p.H1069Q revealed a higher activity of the novel variants suggesting that both amino acid changes result in a relative mild phenotype. Intracellular copper determination as well as assessments of protein stability further corroborated the functional phenotype of the two variants.

Conclusion: Our functional analysis of novel ATP7B variants in children having presumably WD may represent a valuable methodology that adds to the established scoring system for diagnosis. To our knowledge this is the first report of a functional characterization of novel ATP7B variants in children for early start and improvement of therapy.
Transgene expression of interleukin-37 in IL-10ko mice inhibits colon carcinogenesis and colitis-associated liver disease

Steffeni Mountford¹, Andrea Ringleb¹, Rahel Schwaiger¹, Mayr Doris², Charles Dinarello³, Philip Bufler¹

¹Dr. von Hauner Children’s Hospital Ludwig-Maximilians-University Munich, Pediatric Gastroenterology and Hepatology, Munich, Germany
²Institute of Pathology, Ludwig-Maximilians-University Munich, Germany
³University of Colorado, Department of Medicine, Infectious Diseases, Aurora, United States

Objectives and study: Inflammatory bowel disease is associated with an increased risk of developing colon cancer. Interleukin (IL-) 37 is a fundamental inhibitor of innate immunity by reducing systemic and local inflammation. IL-37 exhibits intra- and extracellular functionality and we recently identified the IL-37 receptor composed of IL-18 receptor 1 and single Ig IL-1R-related molecule (SIGIRR). IL-37 protein is expressed in healthy and diseased human bowel and liver tissue and shows a similar expression pattern as IL-18. In the present study, we tested whether transgene IL-37 expression protects against colon inflammation and carcinogenesis as well as liver disease secondary to chronic colitis in IL-10ko mice.

Methods: IL-37tg mice (C57Bl6) were crossbred with IL-10ko (C57Bl6) mice. Homozygous IL-10ko/IL-37tg mice were selected by genotyping. At 6 weeks of age mild colitis was induced by 2% dextran sulphate sodium (DSS) in drinking water for 5 days (IL-10ko n=10, IL-10ko/IL-37tg n=5). Subsequently, cyclooxygenase 2 inhibitor celecoxib (500 µg/mouse) was applied by gastric gavage on day 7, 10 and 13 to trigger colon carcinogenesis as described (Glauben et al. Gut 2008). Mice were sacrificed on day 171. Endpoints were clinical parameters, cytokine response in LPS-stimulated whole blood and explanted colon cultures as well qPCR analysis of livers. Cytokine measurements were performed by Elisa (IL-6) and Bioplex assay (IL-1β, IL-10, IL-17, IFNγ, TNFα). Colon inflammation, number of adenoma/carcinoma and colitis-associated liver inflammation were analyzed by histology.

Results: During the DSS-induction phase IL-10ko and IL-10ko/IL-37tg mice had a similar weight loss due to mild acute colitis. From day 115 there was a significantly improved weight gain in IL-10ko/IL-37tg mice. Colon length was similar in both groups. Whole blood assays showed similar basal cytokine levels. However, after LPS response, IL-10ko/IL-37tg compared to IL-10ko mice released less IL-6 (p=0.03), IL-1β (p=0.03), IFNγ (p<0.0001), TNFα (p<0.003), but more IL-10 (p<0.0001) in supernatants of ex vivo stimulated whole blood. Ex vivo colon cultures showed a trend towards lower levels of pro-inflammatory cytokine production in IL-10ko/IL-37tg mice. Hemoglobin levels were higher in IL-10ko/IL-37tg mice (p=0.013). 6/10 IL-10ko mice developed colon adenoma (1) and carcinoma (6). Only one adenoma but no carcinoma was detected in the colon of IL-10ko/IL-37tg mice. Colitis-induced liver inflammation and profibrotic cytokines as measured by qPCR were markedly less in IL-10ko/IL-37tg mice.

Conclusion: In conclusion, IL-37 transgene expression protects IL-10ko mice from colon carcinogenesis and liver inflammation secondary to chronic colitis. It remains unclear whether IL-37 has direct tumor suppressing and antifibrotic properties.
Morphofunctional changes of gallbladder and biochemical parameters of lipid metabolism in children with liver steatosis

Svetlana Babiy¹, Natalya Zavgorodnya², Irina Konenko³

¹Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine*, Laboratory of Biochemistry, Dnipropetrovsk, Ukraine
²Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine*, Pediatric Gastroenterology Department, Dnipro, Ukraine
³Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine*, Department of Minilinvasive Endoscopic Interventions and Instrumental Diagnostics, Dnipropetrovsk, Ukraine

Objectives and study: To investigate peculiarities of structural and functional disorders of gallbladder among children with non-alcoholic fatty liver disease. The study was conducted in 51 children in the age of 10–17 years. Patients were divided into four groups: the 1st - consisted of 11 children - with biliary normokinesia without steatosis; the 2nd – 20 children with biliary hypokinesia without steatosis; 3rd – 11 children with biliary normokinesia and steatosis, and the 4th – 9 children with biliary hypokinesia and steatosis. All patients had given their agreement to participation in the study.

Methods: Anthropometric parameters were measured: height, weight, abdominal circumference, body mass index (BMI). Functional state of gallbladder was investigated with the help of ultrasound (SH-2000 HONDA ELECTRONICS) in real time scale, on an empty stomach and after breakfast. Diagnosis of liver steatosis was realized by measurement of the controlled attenuation parameter (CAP) with «FibroScan® 502Touch» F60156 (Echosens, France). Such biochemical parameters as total cholesterol (CHL), triacylglicerols (TG), levels of high density lipoprotein-cholesterol (HDL), low density lipoprotein-cholesterol (LDL) and very low density lipoprotein-cholesterol (VLDL) were defined, atherogenic coefficient (AC) was calculated according to Friedewald formula.

Data of American National Cholesterol Education Program and The National Health and Nutrition Examination Survey (USA) were used as lipid metabolism reference criteria in children. The normal CHL levels for 1 – 19-year-old children are 2,96–4,4 mmol/l, TG - 0,40–0,9 mmol/l, HDL - 0,99–1,59 mmol/l, LDL - 1,63–2,59 mmol/l and VLDL - 0,22–0,40 mmol/l. Data from all groups were compared using the Student unpaired t-test by SPSS 9.0 for Windows.

Results: Present study shows overweight (in 15% of patients), obesity (in 85% of patients), increasing of gallbladder volume on 30 – 50% (p<0,05), density of gallbladder wall on 12–16 % (p<0,05) and its echogenicity on 24 % (p<0,05) in children with steatosis versus group without steatosis and normokinesia of gallbladder. Positive correlation between wall thickness and steatosis has been established.

Hypercholesterinemia was observed in every group, its frequency was 50% higher among patients with gallbladder hypokinesia: 60% - in 1st group and 29% - in 4th, respectively. Thus, hypertriacylglycerolemia prevalenced among patients with steatosis. The mild atherogenic dyslipidemia was found in the 3rd group. There were TG level increasing in 1,4 times (p < 0,05) and VLDL – in 1,5 times (p < 0,05), in comparison with 1st group. Dyslipidemia in patients from 4th group was combined with decreased PL level in blood serum in 1,5 times (p < 0,05), HDL – in 1,5 times (p < 0,05) and CH/PL ratio increasing in 3,6 times (p < 0,05) compared with 1st group.

Conclusion: Our data demonstrate that hepatic steatosis formation is associated with gallbladder volume elevation, gallbladder wall thickness and echogenicity increasing, gallbladder motility impairment probably due to fat accumulation and cholesterol/phospholipids relation disruption. Decreased gallbladder contractility lead to dislipidemia, such as hypercholesterinemia development whereas steatosis is associated with hypertriacylglycerolemia. We recommend an obligatory functional gallbladder state correction in children with fatty liver.
Clinical variants of galactosatmia type 1

Tatyana Bushueva¹, Tatiana Borovik¹, Vera Skvortsova¹, Galina Yatsik², Elena Roslavtseva¹, Ekaterina Zakharova³, Alexander Pushkov⁴, Natalia Zhurkova⁴

¹Scientific Centre of Children’s Health, Healthy and Sick Child Nutrition Department, Moscow, Russian Federation
²Scientific Center for Children’s Health, Department of Rehabilitation for Young Children With Consequences of Perinatal Pathology, Moscow, Russian Federation
³Medical Genetics Research Center, Laboratory of Hereditary Metabolic Diseases, Moscow, Russian Federation
⁴Scientific Center for Children’s Health, Laboratory of Molecular Genetics and Cell Biology, Moscow, Russian Federation

Objectives and study. Clinical forms of galactosaemia type I depend on activity of the enzyme galactose-1-phosphate uridyltransferase (GALT). The aim of the study was to compare some indicators of liver function, type of mutation, as well as the effectiveness of diet therapy in patients with severe and milder course of galactosaemia.

Methods: Blood levels of total galactose (TG), total bilirubin (TB), alanine aminotransferase (ALT), aspartate aminotransferase (AST), GALT activity and genotype in 67 full-term infants with galactosaemia type I. 2 groups of infants: group 1 with severe (n= 39), group 2 with milder course of the disease (n=28) were compared. TG and GALT activity were determined in dry blood spots by fluorometric method. Serum levels of TB, ALT, AST were estimated by automatic biochemical analyzer before and with a diet therapy. The most frequent mutations in the GALT gene were identified by molecular-genetic methods.

Results: Severe clinical symptoms (hepatomegaly, splenomegaly, vomiting) were observed in 100% of infants in group 1: jaundice in 28 (72%), hemorrhages in 9 (23%), anaemia in 8(21%), congenital cataract in 6(15%). In group 2 68% of infants had hepatomegaly, 11% had splenomegaly, 21% had vomiting. Blood levels of TG were 68.7±14.5 mg/dl in group 1 and 15.7±2.54 mg/dl in group 2 (p=0.000). In group 1 the most frequent mutations were: homozygous for the mutation 188R (62%), and K285N (10%), heterozygous Q188R/N314D (10%), Q188R/S135L (18%). In group 1 92% of newborns had GALT activity less than 10%, and in 8% infants it was 10% to 25%. In group 2 the most frequent mutations were heterozygous Q188R/N314D (68%), K285N/N314D (25%), and homozygous N314D/N314D (7%). GALT activity was more than 25% in 64% infants, and 10-25% in 36%.

The hepatic indices were significantly higher in group 1: TB 163 ± 126 mmol / l and 25.8 ± 2.5 mmol / l (p=0.000); ALT 182 ± 35.5 U/L и 40.1 ± 19.2 U/L (p=0.002), AST - 191.3 ± 35.9 U/L and 105±14 U/L (p=0.034) respectively.

Soy-based infant formulas were used in 19 (28%), hydrolyzed protein lactose free formulas in 21 (32%), lactose free milk formula in 27(40%) of infants.

After one months on the lactose free diet the blood level of TG had decreased to 2.4 ± 0.51 mg/dl in group 1 (p = 0.000) and to 2.3 ± 0.37 mg/dl in group 2 (p = 0.000). The levels of TB and transaminases matched the reference values and had no differences between groups.

Conclusion: The severity of symptoms depends on the degree of GALT enzyme reduction and therefore, the higher levels of total galactose, more pronounced in Q188R homozygotes. Use of lactose-free formulas based on soy isolate, hydrolyzate or milk protein had the same efficacy.
Liver copper concentration in differential diagnosis between presymptomatic Wilson disease and primary sclerosing cholangitis

Maciej Dadalski¹, Magdalena Naorniakowska¹, Piotr Socha¹

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland

Objectives and study: Liver copper concentration is regarded to be a sensitive and specific diagnostic test in Wilson disease (WD). Concentrations above 250µg/g dry weight have high Positive Predictive Value in adults, whereas concentrations below 50µg/g practically exclude diagnosis of WD. Previous studies have suggested that the majority of patients with the primary sclerosing cholangitis (PSC), had increased hepatic copper. There is no data concerning liver copper in children with WD in comparison with PSC.

Methods: 74 patients with WD diagnosed according to Ferenci score were the study group. 15 patients with PSC or overlap syndrome (autoimmune hepatitis/PSC) were the control group. They all have liver biopsy performed with liver copper measurement. Sensitivity and specificity were assessed for cutoff value of 250µg/g and discriminant ability and optimal cutoff point were established with ROC curve analysis.

Results: Liver copper concentrations were 882; 626; 1124 [median, Q1, Q3] µg/g and 54,5; 31,6; 117 µg/g in study and control group respectively. For cutoff point of 250µg/g, the sensitivity was 0.96 (0.89; 0.99 [95% CI]) - 3 out of 74 patients had liver copper under 250µg/g; and the specificity was 0.88 (0.63; 0.98) – 2 out of 15 patients had liver copper over 250µg/g. Area under ROC curve was 0.985. The optimal cutoff point for our groups was 304µg/g with sensitivity 0.96 (0.89; 0.99) and specificity 0.93 (0.68; 0.998).

Conclusion: Liver copper concentration has high discriminant ability in differential diagnosis between presymptomatic WD and PSC, however optimal cutoff point (304 µg/g) should be slightly higher.
Cerebrotendinous Xanthomatosis presenting as neonatal cholestasis: early treatment with chenodeoxycholic acid can prevent neurological damage

Irene Degrassi, Giuseppe Giordano, Chiara Amoruso, Marcello Farallo, Giulia Paolella, Federica Nuti, Gabriella Nebbia

Fondazione Ircss Ca' Granda Ospedale Maggiore Policlinico, Service of Pediatric Hepatology and Nutrition, Milan, Italy
Institute of Pediatric Research, University of Padova, Mass Spectrometry and Metabolomic Laboratory, Women's and Children's Health Department, Padova, Italy

Objectives and study: Cerebrotendinous xanthomatosis (CTX) is an autosomal recessive inborn error of primary biliary acids synthesis. The deficiency of Sterol 27-hydroxylase, due to a mutation of the CYP27A1 gene, is responsible of accumulation of cholestanol and toxic precursors. Only a few cases have been described as neonatal cholestasis at the onset, which generally regresses, while neurological involvement is ongoing. Few pediatric cases have been reported: neonatal cholestasis, steathorrhoea and diarrhoea have been described. Most cases present in the second or third decades of life with juvenile cataract, tendon xanthomas and a progressive neurologic disorder in adulthood. Chenodeoxycholic acid (CDCA) is the only effective therapy reducing formation of cholestanol and bile alcohols through a negative-feedback mechanism and preventing their accumulation in different organs. The aim of this study is to describe the case of a female child presenting as neonatal cholestasis at two months of life.

Methods: Diagnosis of CTX was made by Liquid-chromatography-mass-spectrometry on the basis of the presence of cholestanepentols glucuronide in the urine. The diagnosis was confirmed by dosage performed by mass-spectrometry of cholestanol in serum and genetic analysis of the CYP27A1 gene. Therapy with CDCA was started with a dosage of 15 mg/kg/die. In the following 10 years liver function tests, plasma cholestanol and urinary cholestanepentols were serially controlled. Neurological impairment was assessed with electroencephalography, electroneurography, brain magnetic resonance and neurocognitive tests.

Results: A female infant of 74 days of age presented hepatosplenomegaly, normocholic stools, a moderate increase of aminotransferases and severe conjugated hyperbilirubinemia, with gamma-GT within normal values. We excluded most frequent aetiologies of neonatal cholestasis: extrahepatic biliary tract obstructions, infectious agents, alpha1-antitrypsin deficiency and most frequent other metabolic diseases. Abdominal ultrasonography revealed only slightly brilliant liver. Liver biopsy showed giant cell hepatitis with intracellular and intracanalicular cholestasis, inflammatory changes and focal hepatocellular necrosis. Urinary biliary acids were performed revealing a profile compatible with a diagnosis of CTX. Plasma cholestanol dosage was 3.140 µg/dl (n.v. 470 µg/dl). Molecular genetic analysis revealed a homozygosis for a deletion of 1.9 kb with loss of exon 7,8,9 in the CYP27A gene. Cholestasis spontaneously regressed at the age of 6 months; nevertheless therapy with CDCA was started at the age of 8 moths, without side effects. In the following 10 years the therapy was monitored by keeping serum cholestanol and urinary cholestanepentols within normal limits. During the follow up the child showed normal physical and mental development, with normal electroencephalography, electroneurography, brain magnetic resonance and neurocognitive tests. Liver function tests and ophthalmological findings were normal as well.

Conclusion: In front of a case of neonatal cholestasis after having excluded the most frequent etiologies, we recommend to focus on inborn errors of metabolism of biliary acids. Early diagnosis of CTX is crucial, considering that CDCA is an efficient therapy in this condition and can prevent accumulation of cholestanol in tissues with consequent neurologic impairment.
HEPATOLOGY: General Hepatology

H-eP-007

Change in liver fibrosis in children and adults with lysosomal acid lipase deficiency after 52 Weeks of sebelipase alfa (ARISE trial)

Zachary Goodman¹, Barbara Burton², Lakshmi Alaparthi¹, Fanny Monge¹, Mark Friedman³

¹Inova Fairfax Hospital, Falls Church, United States
²Northwestern University, Feinberg School of Medicine, Chicago, United States
³Alexion Pharmaceuticals, Inc., New Haven, United States

Objectives and study: Lysosomal Acid Lipase Deficiency (LAL-D) is a rare genetic, progressive disease that frequently leads to fibrosis, cirrhosis, and ultimately liver failure. In an animal model of LAL-D, sebelipase alfa (SA) improved liver pathology with resolution of hepatomegaly, liver fibrosis and restoration of normal architecture. In the phase 3 ARISE trial (NCT01757184), the primary endpoint of alanine aminotransferase (ALT) normalization and several secondary endpoints were met with SA treatment at 20 weeks (wks) in children and adults with LAL-D. This study evaluated the effect of treatment with SA on liver fibrosis stage in LAL-D patients (pts).

Methods: 66 pts enrolled in the ARISE trial were randomized to placebo (PBO; N=30) or SA (N=36) at 1 mg/kg every other wk for 20 wks, after which 65 pts rolled over to open-label treatment with SA. Liver biopsy was performed at baseline, Wk 20 and/or Wk 52. Reported here are the liver fibrosis changes through Wk 52 using the Ishak staging system (0-6).

Results: 20 pts (age 5-59 yrs) had paired liver biopsies taken at baseline and Wk 52: 8 of whom had cirrhosis (stage 5 or 6) at baseline. 12 pts received SA for 52 wks, and 8 received SA for 30 wks (Wk 22 to 52). 10 of the 20 pts also had biopsy after 20 wks of SA exposure. Change in fibrosis stage from baseline to Wk 52 is shown in the table. Of the 8 pts who had a 1 Ishak stage reduction in fibrosis, 5 had cirrhosis at baseline. Of the 6 pts who had a 2 stage reduction, 1 had cirrhosis at baseline. 5 of the 6 had stage 3 at baseline and experienced a mean percentage change at 52 wks of -60.5% in ALT, -40.3% in LDL-C and -31.6% in liver fat content (via MRI). During 52 wks of the study, 62 pts had ≥1 adverse event (AE); most of which were unrelated. 10 pts had infusion associated reactions (IARs). 5 pts had Serious Adverse Events (AEs); 1 was considered related to treatment (an IAR). SA was stopped and the pt was reintroduced to SA following a brief desensitization protocol and remains on study drug. No pt discontinued the study due to an AE.

Table:

<table>
<thead>
<tr>
<th>Wks of SA exposure</th>
<th>N</th>
<th>≥2-stage Reduction</th>
<th>1-stage Reduction</th>
<th>No change</th>
<th>Increase</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20</td>
<td>10*</td>
<td>0</td>
<td>2</td>
<td>5</td>
<td>3</td>
</tr>
<tr>
<td>30</td>
<td>8</td>
<td>0</td>
<td>4</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>52</td>
<td>12</td>
<td>6</td>
<td></td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

*N limited to pt population that also consented to Wk 52 biopsy

Conclusion: Of the 12 pts treated with SA for 52 wks, 8 had reduction in fibrosis stage, 3 had no change and one had an increase. Longer duration of treatment tended to show greater reductions in fibrosis. These reductions were accompanied by reductions in liver fat, ALT, and LDL-C and support the value of early and long term SA treatment in LAL-D.

Disclosure of interest: This study was sponsored by Alexion Pharmaceuticals, Inc. Zachary Goodman has received research support from Gilead Sciences, Galectin Therapeutics, Intercept, Alexion Pharmaceuticals, Inc., Conatus, Cempra, Nitto Denko, Tobira, and Exalenz. Barbara Burton has received funding for the conduct of clinical studies from Alexion Pharmaceuticals, Inc., BioMarin, Shire, Genzyme, and Ultragenyx; funding for independent research and/or education from BioMarin and Shire; and consulting fees and honoraria from BioMarin, Shire, Alexion Pharmaceuticals, Inc., Genzyme, and Regenxbio. Lakshmi Alaparthi and Fanny Monge have nothing to disclose. Mark Friedman is an employee of Alexion Pharmaceuticals, Inc. and may own stock/stock options in that company.
Liver steatosis, as measured by ultrasonographic hepatorenal index, does not coincide with an abnormal cardiometabolic risk profile in children with overweight and obesity

Kylie Karnebeek¹, Simon Robben², Jogchum Plat³, Anita Vreugdenhil¹

¹Centre for Overweight Adolescent and Children’s Healthcare (Coach), Maastricht University Medical Centre, Department of Paediatrics, Maastricht, Netherlands
²Maastricht University Medical Centre, Department of Radiology, Maastricht, Netherlands
³Maastricht University, Department of Human Biology, School of Nutrition and Translational Research in Metabolism (Nutrim), Maastricht, Netherlands

Objectives and study: Non-alcoholic fatty liver disease (NAFLD) is prevalent in children with overweight and obesity. The ultrasonographic hepatorenal index (HRI) is a non-invasive, reproducible and highly sensitive measurement to quantitatively assess hepatic steatosis. Although NAFLD is generally assumed to be the hepatic manifestation of the metabolic syndrome, it is unknown whether an increased HRI is associated with a deteriorated (cardio)metabolic risk profile in children. Therefore, we here studied the association between the HRI with anthropometric, metabolic and cardiovascular risk parameters in children with overweight and obesity.

Methods: Liver ultrasonography was performed in 117 children (44% male) with overweight (n=29), obesity (n=48) and morbid obesity (n=40) from the Centre of Overweight Adolescent and Children’s Healthcare (COACH) at the Maastricht University Medical Centre (Maastricht UMC+). The HRI was calculated as the ratio between ultrasonographic hepatic and renal brightness. Anthropometric, metabolic, cardiovascular and liver-related parameters were determined.

Results: The ultrasonographic hepatorenal index is associated with higher alanine transaminase (ALT) levels (R=0.257, p=0.007) and inversely associated with age (R= - 0.295, p=0.002) and systolic blood pressure z-score (R= - 0.232, p=0.017), but not with other anthropometric or cardiometabolic risk parameters. ALT levels were associated with BMI z-score (R=0.423, p<0.001), waist circumference z-score (R=0.474, p<0.001) and waist-to-hip ratio z-score (R=0.463, p<0.001), but not with cardiometabolic risk parameters. In children with the highest hepatorenal indices, i.e. the upper tertile, the HRI is associated with ALT levels (R=0.446, p=0.009) and gamma-glutamyl transferase (GGT) levels (R=0.346, p=0.049), but not with anthropometric and cardiometabolic parameters.

Conclusion: A higher ultrasonographic hepatorenal index reflecting increased accumulation of fat in the liver is not associated with a deteriorated cardiometabolic risk profile in children with overweight, obesity and morbid obesity. Additionally, ALT levels are not associated with a deteriorated cardiometabolic profile. This suggests that in obese children NAFLD exists independent from deviating cardiometabolic risk markers. Besides implications for mechanistic understanding of NAFLD development, these findings have clinical relevance since recognizing children at risk for NAFLD apparently demands other parameters then anthropometric and cardiometabolic risk markers.
Cholestasis - a very rare manifestation of Gaucher disease type 2

Aco Kostovski¹, Nikolina Zdraveska²

¹University Children's Hospital, Pediatric Gastroenterohepatology, Skopje, Macedonia
²University Children's Hospital, Skopje, Macedonia

Objectives and study: Gaucher disease (GD) type 2 is a rare lysosomal storage disorder with usual onset between 3 and 6 months of age leading to progressive neurodegeneration and death within the first 2 years of life. Very rare Gaucher disease can occur in neonates. The early course of neonatal onset type 2 GD variants is not well known. Neonatal cholestasis is an extremely rare presentation of Gaucher disease type 2 in infants and reports in literature are scarce.

Methods: Case study of a 3-day old newborn with Gaucher disease type 2 will be presented. Review of the literature and analysis of previously described cases of early onset Gaucher disease with neonatal cholestasis and hepatosplenomegaly will be provided.

Results: The newborn was admitted because of cholestasis associated with severe thrombocytopenia and hepatosplenomegaly since birth. It was third child in the family; the older sibling died at age of 9 months with suspected, but not confirmed Gaucher disease. Consanguinity was not reported. Laboratory analysis showed thrombocytopenia (20 x10⁹/l), elevated conjugated bilirubin (183 µmol/l) and serum transaminases (AST-749 U/l, ALT-331 U/l). All investigations for structural, viral and metabolic causes of cholestatic jaundice were negative. Bone marrow aspirate did not reveal any engorged cells. The diagnosis was made with enzymatic and molecular studies. Sequence analysis of GBA gene revealed two homozygous mutations p.[H294Q];[D448H]. The clinical course was marked by progression of hepatosplenomegaly, severe cholestasis, portal hypertension and ascites, followed by neurological deterioration (hypertonus, feeding difficulties). The patient died at age of 2.5 months because of liver failure. Only symptomatic treatment was provided. We identified three previous case reports in the literature of early onset Gaucher disease with neonatal cholestasis, hepatosplenomegaly and subsequent development of neurological signs.

Conclusion: Although extremely rare neonatal cholestasis can be the first sign of Gaucher disease making the diagnosis very difficult because the focus is on more prevalent neonatal illnesses. Gaucher disease should be considered in the diagnostic approach of infants with cholestatic jaundice even if, initially the bone marrow aspirate do not reveal typical cells.
**Objectives and study:** Congenital portosystemic shunts are rare vascular malformation that can lead to pulmonary hypertension, encephalopathy & liver tumors. They were classified as type I (end-to-side portocaval fistula with no visible portal flow in the liver) & type II (side-to-side portocaval fistula) shunts. Type I shunts are often referred to as congenital absence of the portal vein (CAPV), and are still considered an indication for liver transplantation, whereas surgical or percutaneous closure is usually feasible for type II shunts. Here, through a case report and a review of all published patients, we show that what is initially diagnosed as CAPV may conceal a hypoplasic portal vein that can successfully be closed by surgical ligation.

**Methods:** A 2-year-old girl was referred for liver transplantation in the context of recent diagnosis of CAPV. She was asymptomatic and showed a hypertrophic left liver lobe, without any complication. Her blood tests were normal excepted for moderately elevated serum ammonia levels. MRI confirmed the diagnosis of a type Ib portosystemic shunt (with superior mesenteric and splenic veins joining to form a short portal trunk ending into the inferior vena cava). Percutaneous venogram confirmed the absence of the portal vein. Nevertheless, a second direct catheterization of the shunt with temporary shunt occlusion allowed us to visualize an hypoplasic portal vein arising from the posterior face of the shunt. Pressure was measured at 12 mmHg in standard conditions and 36 mmHg upon temporary occlusion. We decided for a two-step occlusion. A partial banding was carried out without significant complication (normal liver tests, minimal transient ascites). The shunt was permeable, with a measurable portal flow, at follow-up Doppler ultrasound. Two months later, moderate elevation of liver enzymes (3xULN) and mild ascites were detected, but resolved spontaneously within a few weeks. The shunt was not detected anymore, and the Doppler study showed a normal portal flow. A percutaneous venogram confirmed the total closure of the shunt and the permeability of the portal vein. The child is asymptomatic at 6-month follow-up.

**Results:** 202 cases of extrahepatic shunts were reported since 1979, of which 134 were described as “CAPV”. 38 patients (19%) had percutaneous or surgical shunt closure (12 & 26, respectively), whereas 25 patients (12.4%) received a liver transplantation. Among all transplanted patients, only 4% had a preoperative percutaneous venogram with temporary shunt occlusion.

**Conclusion:** Overall, the case reported here exemplifies what emerges from published literature: a precise evaluation of the shunt with percutaneous venogram and temporary occlusion is warranted in all patients with suspected CAPV. It allows detecting otherwise invisible hypoplasic portal veins that allow tore establish a physiological hepatic circulation and avoid liver transplantation.
Health related quality of life in children and adolescents with autoimmune hepatitis

Engy Mogahed¹, Mona El-Raziky², Mariam El-Moslemany³, Eman Taher⁴

¹Kasr Alainy School of Medicine, Pediatrics, Cairo, Egypt
²Kasr Alainy School of Medicine, Cairo University-Pediatric Liver Unit, Cairo, Egypt
³Ministry of Health Hospital, Cairo, Egypt
⁴Kasr Alainy School of Medicine, Cairo, Egypt

**Objectives and study:** Autoimmune hepatitis (AIH) is a chronic inflammatory disease that can be associated with significant morbidity and shortened survival compared to the general population. The aim of our study was to assess health related quality of life (HRQOL) among paediatric patients with AIH and compare them to healthy controls.

**Methods:** This was a case control study conducted on 30 AIH patients and 30 age and sex matched normal healthy controls. HRQOL was assessed by using World Health Organization Quality Of Life BREF questionnaire (WHOQOL-BREF) for cases and controls and with chronic liver disease questionnaire (CLDQ) for cases.

**Results:** The mean ±SD age of the patients was 13.62 ± 3.06 years. Children with AIH showed significant lower HRQOL scores compared to normal controls as regards physical, psychological and environmental domains of WHOQOL ($p < 0.001$). There was a negative correlation between frequency of complications of therapy and WHOQOL physical domain ($r = -0.501$, $P=0.005$). As regards CLDQ we found a moderate reduction in QOL among AIH patients. Female sex was a significant negative predictor for activity and worry domains of CLDQ. Age was a significant negative predictor for emotional domain as older children were associated with lower emotional domain scores ($P=0.039$).

**Conclusion:** Paediatric patients with AIH have significantly lower HRQOL compared to healthy individuals with special concerns related to female sex, patients with older age and patients with lower social level. Physical functioning is compromised with prolonged steroid therapy.
HEPATOLOGY: General Hepatology

H-eP-012

Tight-junction protein-2 (TJP2) defect: increasing the clinical spectrum

Luis Alvarez1, Gema Muñoz Bartolo2, Luiz Stark Areira3, Pilar Martínez3, Sara Andueza1, Loreto Hierro2, Esteban Frauca2, Dolores Lledín2, Carmen Díaz2, Paloma Jara2

1“La Paz” University Hospital, Health Research Institute-Idipaz, Madrid, Spain  
2“La Paz” University Hospital, Paediatric Liver Service, Madrid, Spain  
3“la Paz” University Hospital, Institute of Medical & Molecular Genetics –ingemm, Madrid, Spain

Objectives and study: Mutations in the tight junction protein 2 gene (TJP2) (chromosome 9q12) were recently described as a cause of progressive familial intrahepatic cholestasis (PIFC) (Sambrotta M. Nat Genet 2014). Descriptions are scarce to date. Our aim was to describe the characteristics of 3 new patients with TJP2 defect.

Methods: Cases of unexplained liver disease with PFIC phenotype underwent further studies once BSEP, FIC1, and bile acid synthesis defects were ruled out. In 2 patients, a first study of TJP2 immuno-histochemistry showed absence of canalicular and ductal staining. Next generation sequencing (NGS) was then performed using customized liver genes panel, as well as in others within a project of research in a series of children with unknown liver diseases. The capture technology is SECAP EZ (Roche, Nimblegen) in a MiSeq platform (Illumina). We describe the genetic and clinical characteristics of 3 cases of TJP2 homozygous mutation.

Results: The clinical data of 3 patients with TJP2 (NM_001170630) defect were:

1) Case 1 ( exon 6: c. 1000C>T  (p.R334X)). Born to consanguineous parents of Lebanese origin, presented with neonatal cholestasis and giant-cell transformation in liver biopsy. Biochemical profile was AST 331 IU/L, ALT 186 IU/L, Total Bilirubin (TB) 7 mg/dL, Direct Bilirubin (DB) 3.6 mg/dL, GGT 91 U/L. Jaundice maintained, mild pruritus started at 9 months of life. Progression to ascites and liver insufficiency occurred at 11 month. Severe hypoglycemia led to multiple studies including brain MRI with normal findings. Living donor liver transplantation (LT) was performed when she was 13 months old. Explant showed cirrhosis, cholestasis, and a 3-mm nodule with high-grade dysplasia. She had no complications after LT (follow-up 1 year)

2) Case 2 (exon 5: c. 892G>T (p.E298X)). Born to consanguineous Moroccan parents, she presented with neonatal cholestasis, first data were TB 17 mg/dL, AST 396 IU/L, ALT 186 IU/L, GGT 91 U/L. Pruritus started at 8th month. Cholestasis and growth failure led to LT (split liver) at 22 months of age. Explant showed bridging fibrosis and cholestasis. Follow up lasting 7 years after LT showed normal graft function, she initiated absence seizures with normal motor and psychic development. Brain MRI identified cerebellum dysgenesia.

3) Case 3 (exon 20: c.2986delC  (p.S966AfsX8)). Born to Spanish consanguineous parents, she had hip dysplasia and clef palate. Cholestasis and pruritus were detected at age 1 year; TB 8 mg/dL, DB 7 mg/dL, AST 60 IU/L, ALT 31 IU/L, GGT 28 IU/L. Liver biopsy at 2 years showed mild portal fibrosis. She displayed a mild liver disease in the follow-up; TB decreased (to <4mg/dL) since 5th year. She has an extended follow up (32 years) with mild pruritus, and no liver failure. However liver appears nodular in MRI (multiple nodules, maximum size 1.5 cm) with normal alpha-fetoprotein levels.

Conclusion: Three patients with TJP2 defect were identified and had various severity of liver disease. One case is alive with own liver at 32 years old. Associated anomalies (cerebellum, palate, hip) were observed in 2 cases.
**HEPATOLOGY: General Hepatology**

H-eP-013

**Serum alanine aminotransferase levels in children: what is normal?**

Natasha Ng¹, Suzanne Davison¹

¹Paediatric Liver Unit, Leeds General Infirmary, Leeds, United Kingdom

**Objectives and study:** Serum alanine aminotransferase (ALT) is widely recognised for its role in detecting liver disease and injury. Despite routine use in clinical practice, normal reference ranges are difficult to establish and are likely to be both age and gender specific. Elevation of ALT above the adult reference range (female < 19IU/l male < 30IU/l) has been proposed as threshold for decision making in management of chronic hepatitis B (HBV) in both adults and children. However, current paediatric reference ranges suggest that ALT up to 60IU/l may be normal. In contrast, need for treatment of chronic hepatitis C (HCV) infection is not determined by ALT elevation. After successful eradication of HCV RNA and in the absence of co-morbidity, ALT would be expected to be normal. Monitoring ALT before and after therapy could help determine whether pre-treatment values within the laboratory reference range are truly normal, or whether a significant decrease after HCV clearance suggests that a lower range is the true normal. **AIM:** To determine ALT values in children before and after HCV eradication to determine whether current paediatric ALT reference range or the adult reference range, which is significantly lower, is more appropriate as a guide of liver inflammation.

**Methods:** A retrospective study of consecutive children treated for chronic HCV infection at a single centre. Response to treatment was determined by HCV RNA level and ALT values before and at end of treatment were ascertained. ALT values were defined as either (i) “abnormal” if above the laboratory reference range, (ii) “laboratory normal” if within the laboratory reference range but above adult reference range or (iii) “adult normal” if within adult reference range.

**Results:** Of 53 children who received treatment for HCV infection, 10 were excluded because of co-morbidity (4) or lack of treatment response (6). Forty-three children were therefore studied: 23F:20M, median age at starting treatment was 8y2m (4y5m -15y11m). Before treatment median ALT was 42 IU/l (11-140), and was “abnormal” in 16 (37%), (median 1.8 x ULN, range 1.3-2.9), “laboratory normal” in 21 (49%) and “adult normal” in 6 (14%). At the end of treatment, ALT had improved in all children, and was “abnormal” in none, “laboratory normal” in 14 (33%) and “adult normal” in 29 (67%). Of 21 with “laboratory normal” values pre-treatment, ALT decreased to “adult normal” values at end of treatment in 15 (71%). In the remaining 6, all female, ALT fell from median pre-treatment level of 40 IU/l (21-45) to median end of treatment ALT of 19.5 IU/l (19-24).

**Conclusion:** This study revealed that ALT levels improved in children following eradication of HCV. The decrease in ALT, even in those who had “laboratory normal” ALT before treatment, suggests that the upper limit of normal in paediatric reference ranges may be too high. These findings may have significant implications on the management of children with chronic liver disease in which ALT values are used to determine the need for treatment (such as HBV infection) or to evaluate treatment response (such as autoimmune hepatitis).
Cyclosporin A induces remission in steroid resistant AIH and AIH/PSC overlap syndrome.

Marcin Osiecki¹, Malgorzata Wozniak¹, Maciej Dadalski¹, Marek Woynarowski¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland

Objectives and study: Autoimmune hepatitis (AIH) is a progressive inflammatory liver disease of unknown origin. Up to 49% of AIH cases may be concurrent with primary sclerosing cholangitis (PSC). Response to initial treatment is achieved in 90% AIH patients. In cases refractory to steroids, cyclosporin A (CsA) is introduced to induce remission. Our aim was to assess its efficacy in such an indication.

Methods: It is a retrospective, single center study. We describe a clinical characteristic of 33 children (18F, 15M), mean age 14 years, mean disease duration 37 months who underwent CSA treatment in the course of AIH and AIH/PSC in years 2005-2015. The primary endpoint was biochemical and histological remission/response at month 24 and the secondary one - liver transplantation rate. The clinical outcomes were related to biochemical, histological and demographic data at the beginning of CsA therapy.

Results: Biochemical and histological remission was achieved at month 24 in 11 out of 33 cases (33%). Liver transplantation has to be performed in 6 out of 33 (18%) cases. Statistical analysis showed that remission group had significantly higher number of platelets than group with no remission at the beginning of the CsA therapy: 215;103;343 vs. 91;65;186 [median;q1;q3] respectively.

Conclusion: CsA leads to remission in up to one third of AIH, AIH/PSC cases refractory to steroid therapy. Liver transplantation rate in this group is 18%. Patients with symptoms of hypersplenism have worse prognosis of CsA therapy.
Metabolically healthy obese children and adolescents are at risk of liver steatosis and subclinical atherosclerosis

Lucia Pacifico¹, Francesco Massimo Perla¹, Enea Bonci¹, Gian Marco Andreoli¹, Ala Hamdan¹, Ester De Luca¹, Claudio Chiesa²

¹Sapienza University of Rome, Rome, Italy
²National Research Council, Rome, Italy

Objectives and study: Childhood obesity is associated with metabolic complications such as insulin resistance, hypertension, dyslipidemia and inflammation, which may eventually lead to the development of cardiovascular disease (CVD) and type 2 diabetes. Nonetheless, some obese children do not show any of these cardiometabolic disturbances, and they are called metabolically healthy obese (MHO). It has been suggested that 30% of obese adult patients are metabolically healthy, and that this group have similar insulin sensitivity to lean individuals, lower visceral and liver fat and lower intima media thickness of the carotid artery (cIMT) compared with metabolically unhealthy obese (MUO) patients. Some studies have also shown that CVD risk in MHO subjects is similar to normal-weight metabolically healthy individuals. To date, studies on the MHO phenotype in pediatric population are very limited. The aims of the present study were to 1) determine the prevalence of MHO phenotype in a large cohort of obese children and adolescents; and 2) compare anthropometric and cardiometabolic features with MUO children and adolescents.

Methods: This cross-sectional study included 552 overweight/obese adolescents [mean age, 10.5 (SD, 2.9) years] who were classified as MHO (no cardiometabolic risk factors) or MUO (≥ 1 cardiometabolic risk factors), on the basis of age- and gender-specific cut-off points for fasting glucose, triglycerides, total cholesterol, high-density lipoprotein cholesterol (HDL), low-density lipoprotein cholesterol, non-HDL cholesterol, homeostasis model assessment of insulin resistance (HOMA-IR), and systolic and diastolic blood pressure. All study subjects had abdominal ultrasound examination for assessment of liver steatosis. Carotid artery ultrasound for evaluation of cIMT was performed in a subset of study population (n= 246).

Results: Among the study children and adolescents, 31.7% (175 of 552) had MHO phenotype, and they were more likely to be younger and in earlier stages of pubertal development compared to the MUO group. Compared with MUO phenotype, youth classified as MHO also displayed a lower body mass index-standard deviation score (BMI-SDS) and waist circumference, lower blood pressure, and lower serum lipids, aminotransferases, HOMA-IR levels, and high-sensitivity C-reactive protein (HSCRP) concentrations as well as decreased cIMT values. Liver steatosis was diagnosed in 258 of 552 (46.7%) subjects, of whom 61 belonged to the MHO group (34.8%, 61 of 175 MHO). When we compared MHO subjects with and without liver steatosis, we found that those with liver involvement were older, and had higher WC, while no differences were found with respect to BMI-SDS, serum lipids, HOMA-IR, and HSCRP levels. cIMT values were significantly high in MHO youths with liver steatosis. Multiple logistic regression analysis revealed that the risk factor for increased cIMT in MHO subjects was fatty liver [odds ratio, 4.27 (confidence interval, 1.16-15.7); P< 0.05] after adjustment for clinical variables.

Conclusion: In a large cohort of strictly defined metabolically healthy obese children and adolescents we found that 35% of them had liver steatosis, which might explain the increased cIMT in the MHO phenotype. The presence of fatty liver should be assessed to determine whether youths are actually in a metabolically benign state for the prevention of CVD.
The impact of nonalcoholic fatty liver disease and patatin-like phospholipase 3 rs738409 gene polymorphism on renal function in overweight/obese children

Lucia Pacifico1, Enea Bonci1, Alessia Di Costanzo1, Laura D'Erasmo1, Ester De Luca1, Marcello Arca1, Claudio Chiesa2

1Sapienza University of Rome, Rome, Italy
2National Research Council, Rome, Italy

Objectives and study: Paralleling the worldwide epidemic of obesity, nonalcoholic fatty liver disease (NAFLD) has become the most common cause of chronic liver disease in both adults and children. It is now clear that NAFLD is not only a risk factor for liver failure and liver carcinoma, but also it is associated with a spectrum of extrahepatic diseases traditionally linked to metabolic syndrome such as type 2 diabetes, and cardiovascular disease. Also, emerging evidence suggests that NAFLD is associated with an increased risk of chronic kidney disease, defined by a decline in the glomerular filtration rate (GFR) and/or microalbuminuria and/or overt proteinuria. Genome-wide association studies have identified rs738409 C>G, which encodes the I148M variant in the patatin-like phospholipase domain-containing 3 protein (PNPLA3) as a strong determinant of NAFLD. Presently, there are very few data regarding the influence of PNPLA3 rs738409 polymorphism on renal function in subjects with NAFLD. Thus, in this study we sought to assess whether PNPLA3 rs738409 gene polymorphism influences renal function in overweight/obese Caucasian children and adolescents with and without NAFLD.

Methods: We studied 226 overweight/obese children, 94 with NAFLD [hepatic fat fraction (HFF) ≥ 5% on magnetic resonance imaging] and 132 without NAFLD. A decline in kidney function was defined as eGFR <90 mL/min/1.73m² and/or microalbuminuria (24-h urinary albumin excretion ≥ 30 and ≤ 300 mg).

Results: A greater prevalence of eGFR <90 mL/min/1.73m² was observed in patients with NAFLD compared to those without liver involvement (22.3% vs 4.3%; P < 0.0001). The proportion of children with abnormal albuminuria was also higher in the NAFLD group compared to those without NAFLD, although it did not reach statistical significance (10.3% vs 3.3%; P = 0.07). The frequencies of PNPLA3 C/G and G/G genotypes were significantly higher in the NAFLD patients than in the non-NAFLD subjects (69.1% vs 36.7%; P < 0.0001). The genotype distribution in both groups was in Hardy-Weinberg equilibrium (P > 0.05). We found that in the NAFLD group the presence of rs738409 G allele was significantly associated with lower body mass index-standard deviation score, higher aminotransferase concentrations, higher HFF, and a lower mean eGFR. Moreover, among the NAFLD patients, the prevalence of reduced eGFR (i.e. eGFR < 90 mL/min/1.73m²) was significantly more common among carriers of PNPLA3 C/G and G/G genotypes [18 (27.7%)] than in those with PNPLA3 C/C genotype [2 (6.9%); P < 0.05]. In children without liver involvement, no significant association was found between the presence of rs738409 G allele and eGFR.

Conclusion: Obese children with NAFLD, particularly those with the PNPLA3 G allele, have a moderate decline in renal function. A determination of this polymorphism may help to identify youth at high risk for renal disease at an early pre-clinical level. Nonetheless, future multicentre studies involving a larger population of overweight/obese youths may help to better understand the role of PNPLA3 in renal disease.
Two dimensional shear wave elastography in children: linear versus convex probe

Corina Pienar, Puiu-Iulian Velea, Diana Gherhardt, Tudor-Voicu Moga, Alina Popescu, Ioana Ciucă, Ioan Sporea

1“Victor Babes” University of Medicine and Pharmacy, Pediatrics, Timisoara, Romania
2“Victor Babes” University of Medicine and Pharmacy, Gastroenterology, Timisoara, Romania

Objectives and study: To compare the measurements acquired with the linear and convex probe and to assess the intra-observer reproducibility of a two dimensional shear wave elastography (2D-SWE GE) technique.

Methods: We conducted a prospective study that included 70 children (age range: 3-17 years, 37.1 % girls, mean body mass index 24.73±7.2 kg/m2). Our study population consisted of obese children (n=35) and a control group: normal weight children without liver disease (n=35). Liver stiffness measurements were performed using 2D-SWE.GE (Logiq E9, GE Healthcare, Chalfont St Giles- UK). For each child one examiner performed 10 liver stiffness measurements with both a linear and a convex probe. To assess the intra-observer reproducibility, we calculated, for each probe, the medians for the first five and the last five measurements, respectively. We then calculated the interclass correlation coefficients (ICCs) for the two medians.

Results: Overall, we found significantly higher measurement values for the linear probe: 7.8±5.1 kPa vs 4.1±0.9 kPa, p= 0.001. The measurements were also higher for the linear probe, both in obese and controls: 9.9±6.1 kPa vs 4.2±0.8 kPa, p= 0.01 and 6.5±4 kPa vs 3.9±1 kPa, p= 0.235. As for the intraobserver reproducibility, we found no differences between the two sets of measurements for both the linear (8.2±5.8 kPa vs 8.1±5.6 kPa, p= 0.25) and the convex probe (4.2±0.9 kPa vs 4.3±0.9 kPa, p= 0.33). The agreement between measurements was excellent for both probes: ICC= 0.956 (95% CI: 0.922-0.975) and ICC= 0.927 (95% CI: 0.883-0.955).

Conclusion: Measurements acquired with the linear and convex probe are not superimposable. 2D-SWE GE is a reproducible method for liver stiffness measurements in children.
**HEPATOLOGY: General Hepatology**

H-eP-018

**Alpha-1 antitrypsin deficiency rare allelic variants Plowell and Mheerlen causing early onset transient liver disease**

Marco Poeta\(^1\), Claudia Mandato\(^2\), Lucia Nazzaro\(^3\), Valeria Marchetti\(^1\), Andrea Catzola\(^1\), Anna Giulia Elena De Anseris\(^3\), Ilaria Ferrarotti\(^4\), Paolo Siani\(^2\), Pietro Vajro\(^1\)

\(^1\)Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi, Italy  
\(^2\)Aorn Santobono-Pausilipon, Pediatrics, Naples, Italy  
\(^3\)Aou San Giovanni DI Dio e Ruggi D'aragona, Pediatrics, Salerno, Italy  
\(^4\)Irccs Fondazione Ospedale San Matteo, Pavia, Italy

**Objectives and study:** Alpha1Antitripsin deficiency (A1ATD) (OMIM#613490) due to heterozigous Pi\(^*\)MZ or Pi\(^*\)MS common variants is occasionally associated with transient liver disease in the first months of life. Data concerning possible hepatic involvement in the presence of heterozygosity for “rare” alleles are infrequently reported. Here we describe three cases of male infants from Campania region (Italy) with transient cholestasis and elevated aminotransferases who were affected by heterozygous A1ATD: two had rare variants (Plowell and Mheerlen) and one a common variant (MS).

**Methods:** A1ATD was investigated by nephelometry, isoelectric focusing (IEF) phenotype analysis, SERPINA1 gene sequencing. Other common causes of liver disease were excluded by appropriate tests.

**Results:** Clinical and laboratory features are shown in the Table.

**Table:**

<table>
<thead>
<tr>
<th>CASE</th>
<th>CLINICAL PRESENTATION</th>
<th>IEF</th>
<th>GENOTYPE</th>
<th>THERAPY</th>
<th>12-mos FOLLOW UP</th>
</tr>
</thead>
</table>
| I 2-mos | **Hepatomegaly**  
**Hypertransaminasemia**  
AST x4.7 URL; ALT x3.2 URL  
**Cholestasis**  
GGT x1 URL; **BA 15.6 µmol/l**  
**A1AT:** 61.8 mg/dL | M3/? | Pi\(^*\)M1 Plowell | None | normalization of LFTs  
AST, ALT, GGT x1URL  
BA 6.0 µmol/L  
Fluctuation/Normalization of A1AT levels |
| II 1-mo | **Hepatomegaly**  
**Hypertransaminasemia**  
AST x4.9 URL; ALT x7.3 URL  
**Cholestasis**  
GGT x2.6 URL; **BA 60.7 µmol/l**  
**A1AT:** 67.9 mg/dL | M2/M2 | Pi\(^*\)M2 Mheerlen | UDCA 15 mg/kg daily | normalization of LFTs  
AST, ALT, GGT x1URL  
BA 7.4 µmol/L  
A1AT 70.4 mg/dL |
| III 4-mos | **Failure to thrive**  
**Hypertransaminasemia**  
AST x1.8 URL; ALT x 2 URL; GGT nl  
**A1AT:** 44.1 mg/dL | M1/S | Pi\(^*\)M1S | None | normalization of LFTs  
AST, ALT, GGT x1URL  
Fluctuation of A1AT (44.1-145 mg/dL) |

**Abbreviations:** A1AT, alpha 1 antitrypsin; ALT, alanine aminotransferase; AST, Aspartate aminotransferase; BA, Bile Acids; GGT, gammaglutamyl transpeptidase; LFTs, Liver function tests; Pi Protease inhibitor; UDCA, ursodeoxycholic acid
Conclusion: As reported for common allelic MS/MZ, also heterozygous rare allelic variants Mheerlen and Plowell may result in a transient early onset hepatopathy. The underlying pathomechanism may be explained in that the mutant proteins from these 2 rare allelic variants, although normal in size, amount and anti-elastase activity, are completely retained in hepatic cells, which also explains low A1AT plasmatic levels. A1ATD screening and characterization should be considered in similar cases. In fact, despite liver damage may spontaneously resolve, early detection of anti protease deficit is essential to start appropriate hepatopulmonary behavioral prevention.
Successful treatment of paediatric hepatitis C with direct acting antivirals in selected cases

Afrodite Psaros Einberg¹, Björn Fischler¹

¹Karolinska University Hospital, Clin-tec, Dep. of Pediatrics, Stockholm, Sweden

Objectives and study: Oral direct acting antiviral (DAA) treatment is not yet registered as treatment of hepatitis C virus (HCV) infection in children. The DAAs have revolutionised the treatment outcome in adults with HCV with almost 100 % sustained viral response (SVR) and very few side effects after only 12 weeks of treatment. According to Swedish guidelines, DAAs can be considered in children with severe liver disease or after transplantation. We have recently described the treatment outcome in a stem cell transplanted teenager with severe sickle cell disease, markedly high levels of HCV RNA and transaminases. He was given the combination of Sofosbuvir and Simeprevir, i.e. the only available treatment at that time. He eradicated his HCV infection after 12 weeks of treatment and had a sustained viral response (SVR) but developed severe lower leg oedema as a reversible side effect while treated, probably due to a pharmacological interaction (Fischler et al. Pediatr Infect Dis J. 2016; 35:708-10). We here report the subsequent treatment of another three HCV infected paediatric patients in our unit.

Methods: A retrospective description and analysis of three children that have undergone DAA treatment for HCV infection. Analysis was based on information in medical records.

Results: All three children were of male sex with mean age 14 years (range 11-17). Viral genotypes were 1a in two cases and 4c in one case. Treatment indications were other complicating diseases in two cases and fibrosis stage F2 in one case. For all three patients the combination of Sofosbuvir and Ledipasvir was used for 12 weeks. The doses recommended for adult patients were given. All patients had undetectable HCV RNA after 8 and 12 weeks of treatment and SVR at 3 months after stopping treatment. No side effects were reported.

Table:

<table>
<thead>
<tr>
<th>ID</th>
<th>Sex</th>
<th>Age (Years)</th>
<th>Weight (Kg)</th>
<th>Indication</th>
<th>Elastography (kPa)</th>
<th>Genotype</th>
<th>Viral Load (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Male</td>
<td>14</td>
<td>49</td>
<td>Liver transplantation</td>
<td></td>
<td>1b</td>
<td>1.20 E6</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>17</td>
<td>82</td>
<td>Fibrosis S2</td>
<td>9.8</td>
<td>1a</td>
<td>1.29 E6</td>
</tr>
<tr>
<td>3</td>
<td>Male</td>
<td>11</td>
<td>30</td>
<td>Ewing’s sarcoma</td>
<td>4.9</td>
<td>1a</td>
<td>3.68 E7</td>
</tr>
</tbody>
</table>

Conclusion: DAA treatment for hepatitis C seems to be as effective and safe in children as in adults. Simeprevir, which is metabolised by cytochrome P450 3A (CYP3A4) can cause side effects due to interaction and might be avoided in patients treated with other pharmacological substances that are also metabolised by the CYP 450 pathway.
The first study of Wilson’s disease prevalence in a Portuguese population

Bebiana Raquel Rodrigues Meireles de Sousa¹, Henedina Antunes²

¹School of Health Sciences of University of Minho, Gastroenterology, Oporto, Portugal
²Hospital de Braga, School of Health Sciences of University of Minho, Icvs/3b's and 2ca Braga, Paediatric Gastroenterology, Hepatology and Nutrition Unit, Braga, Portugal

Objectives and study: Wilson’s Disease (WD) is a rare autosomal recessive disorder responsible for an anomalous tissue deposition of copper. Global prevalence is estimated to be 1:40,000 although recent studies suggest possible underdiagnosis. There is an absence of studies regarding epidemiologic information of WD in Portugal. The primary goal of the study was estimating disease prevalence and incidence. Secondary goals focused on a descriptive analysis of the main clinical, pathological and biochemical characteristics of WD course in this population.

Methods: Study design was retrospective, and included WD patients of all ages, observed between 1995 and 2015, with a minimum follow-up of 3 months and confirmed to have been born in the Northern region of Portugal. Patients were identified through the use of the Portuguese National Health Service’s clinical coding system based on clinical data of thirteen Portuguese hospitals, liver biopsy histological assessment and hospital prescription records. Statistical analysis was conducted to establish potential clinical-analytical correlations through chi square, Mann-Whitney U, Friedman and Wilcoxon tests.

Results: We identified and collected clinical data on 94 WD patients, six of which were deceased. Prevalence of WD in the past 20 years was 1:37,000 with a current prevalence of 1 per 45,000 inhabitants and an incidence of 1 per million people/year. A pediatric age of presentation occurred in 55,8% with a median age at diagnosis of 16,6 years (12,3-20,8) and male gender in 53,2%. Average follow-up was 15,2±8,8 years. Predominant liver disease was the most common form of presentation in 54,8%, with 37,0% of these presenting with cirrhosis; mixed neurological/hepatic symptoms in 17,9% and predominant neurological presentation in 10,7%. Neurological symptoms were associated with a later disease onset (p=0,001) and higher presence of Kayser-Fleischer rings (p<0,001), detected in 27,0% of all patients. Liver transplant was accomplished in 23,9%. Regarding therapy, penicillamine was the most frequently used, with adverse reactions observed in 24,8% and trientine was used in 41,0% patients at some moment of the disease. A significant reduction in hepatic liver enzymes was observed 6 and 12 months after starting therapy (AST: p=0,002; ALT:p=0,002), which was not observed in urinary copper excretion.

Conclusion: This study constitutes a step further in a better comprehension of epidemiological, clinical and disease management of WD in the Northern Portuguese region, which appears similar to previously published works in other countries. Since more than half of WD patients were diagnosed at a paediatric age, efforts should be focused on development of tools directed to the establishment of an early diagnosis for a better disease management.
Salivary uric acid: a non-invasive diagnostic method of hepato-metabolic complications in obese children?

Federica Belmonte¹, Antonella Bisogno¹, Jacopo Troisi¹, Salvatore Neri¹, Francesca Marciano¹, Carmen Palladino¹, Olga Lausi¹, Salvatore Guercio Nuzio¹, Luca Pierri¹, Pietro Vajro¹

¹Department of Medicine and Surgery, University of Salerno, Pediatric Section, Baronissi, Italy

Objectives and study: Obesity represents one of the major causes of morbidity at all age groups including pediatrics, with a parallel high incidence of its complications, first of all metabolic syndrome (MetS) and Non-alcoholic Fatty Liver Disease (NAFLD). The objective of this study is to assess the diagnostic role of salivary uric acid (UA) for the non-invasive study of obesity related hepato-metabolic abnormalities in pediatric patients.

Methods: We recruited for our pilot case-control study 28 subjects [16 obese and 12 normal weight (NW) healthy controls] characterized on the basis of their medical history, clinical, anthropometric and laboratory data. MetS was defined as waist circumference >95th%ile; triglycerides > 150 mg/dl; Glucose > 100 mg/dl; systolic blood pressure > 95th%ile; HDL cholesterol < 40 mg/dl. Liver involvement defined on the basis of ultrasonographic liver brightness allowed to allocate patients into 2 groups: obese with ([St +], n=11) and without ([St -], n=5) hepatic steatosis. A saliva sample from each subject was collected by Salivette® and analyzed by gas chromathography-mass spectrometry to measure the UA levels.

Results: Serum and salivary UA levels showed a statistically significant correlation (r 0.16; p 0.03) and tended to be higher in obese pts compared to NW controls (4.8±1.4 vs 4.1±0.8 mg/dl and 158.2 ±15.2 vs 143.52±1.48 µM, respectively). Although UA did not show statistically significant differences between [St +] and [St -] patients, highest individual values were observed only in [St+]. Notably, UA values increased in both fluids proportionally to the number (n = 0,1,2,3) of MetS components (4.1±0.8; 4.3±1; 5±1.7 mg/dl, and 143.5±1.5; 154.1±17.5; 156.8±14.1; 161.9±15.7 µM, respectively in blood and saliva).

Conclusion: Our preliminary results indicate that salivary UA is a valuable surrogate of uricemia. Further and larger study are granted to confirm its value to individuate non-invasively obese children at risk of MS and fatty liver.
Psychiatric involvement in children with Wilson's disease treated early: are we missing something?

Giuseppe Ranucci¹, Martina Peluso¹, Giuseppe D'Andrea¹, Carmela Bravaccio¹, Raffaele Iorio¹

¹University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy

Objectives and study: Psychiatric involvement (PI) in Wilson’s disease (WD), despite being sneaky, is pretty relevant, with a prevalence of 30-100% among symptomatic patients. Missing data regarding PI in children with a liver disease at onset and treated for a long time. Furthermore, there is not any validated neuropsychiatric test that can identify the PI at pre-clinical stage.

Methods: We enrolled 18 children with a diagnosis of WD confirmed by liver histology or genetic analysis. Mean age was 14 ± 2.91 years old, with a mean age at the diagnosis of 6.16 ± 3.55 years and a mean treatment duration of 8 ± 4.73 years. Presentation was hepatic in 12 subjects (67%), while 6 patients (33%) were referred for family screening (presymptomatic). They didn’t have any neurologic involvement during the entire follow-up; in all brain magnetic resonance resulted negative. We consider three control groups matched for number, sex and age: (1) healthy subjects; (2) WD subjects with neurologic symptoms; (3) patients affected by another hepatic chronic condition without psychiatric disorders which is comparable to WD for daily drugs administrations and annual visits requested. Each patient was evaluated in a screening phase with a caregiver report of behavioral and emotional problems (CBCL) and with Raven’s Standard Progressive Matrices (SPM) to assess eventual cognitive disability. In a second phase, the patients who tested positive at CBCL scale were submitted to further evaluation using the semistructured diagnostic interview Kiddie Sads – Present and Lifetime Version.

Results: CBCL in case group resulted pathologic for half of the subjects, among whom 22% were not completely adherent to therapy. The CBCL test was pathologic or borderline: in 5 in the scale of anxious/depressed; in 5 in the scale of withdrawn; in 4 for somatic complaints; in 3 for the social problems; in 1 for thought problems; 1 for rule-breaking behaviors; 1 for aggressive behaviors. There’s no prevailing disorder (contingency analysis, p = 0.26, NS) depicting an heterogeneous spectrum of psychiatric manifestations. The K-SADS-PL was positive in 90 % of the analyzed patients, in the following areas: psychotic disorder (12.5%), panic disorder (12.5%), social anxiety (25%), ADHD (37.5%), oppositional defiant disorder (25%), conduct disorder (12.5%). In the 3 control groups CBCL was pathologic: in all neurologic WD patients, in none of healthy subjects and in 7% of subjects with other liver disease. ROC analysis showed a good accuracy of CBCL in identifying psychiatric involvement in WD children without neurologic involvement.

Conclusion: PI in children with WD without neurologic involvement in treatment for a long time seems quite prevalent, higher than in patients with other chronic liver disease. CBCL seems a good diagnostic tool to identify PI in WD children at a preclinical stage, with an important impact in the clinical practice.
Benign focal liver lesions in children: a diagnostic challenge!

Giusy Ranucci\textsuperscript{1}, Emilia Pirozzi\textsuperscript{1}, Gianfranco Vallone\textsuperscript{2}, Carmine Mollica\textsuperscript{2}, Raffaele Lorio\textsuperscript{1}

\textsuperscript{1}University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
\textsuperscript{2}University of Naples Federico II, Department of Advanced Biomedical Sciences, Naples, Italy

Objectives and study: Benign liver tumors (BLT) are generally considered common in adults but rare in children. Little information is available about the incidence of these lesions (hemangioma, adenoma, focal nodular hyperplasia -FNH, nodular regenerative hyperplasia –NRH, cysts) in children. Aim of this study was to describe the most frequently BLT diagnosed in children referred at a tertiary care liver unit and the diagnostic role of imaging. Furthermore, clinical, laboratory and radiological features of the pediatric patients with BLT were evaluated in order to identify predictive factors of evolution. To evaluate the accuracy of contrast-enhancement ultrasound (CEUS) to define the type of lesions in children.

Methods: A total of 55 children (29 girls; median age 5.5 years, range birth-16), diagnosed as affected by BLT, were retrospectively evaluated. The patients were recruited among all patients investigated for focal liver lesion between November 1995 and June 2016. Patients with malignant liver lesions were excluded. Number of lesions, their size, imaging characteristics, and background liver were recorded. Final diagnosis was assigned to each case based on pathology in the available cases and a combination of clinical features, serum \(\alpha\)-fetoprotein (AFP) level, imaging features, and follow-up in the remaining cases. A blinded radiologist analyze CEUS in 28 patients with a definitive diagnosis based on magnetic resonance.

Results: BLTs were distributed as follows: hemangioendothelioma in 12 (22\%) patients, hemangiomatosis in 14 (25\%) patients, mesenchymal hamartoma (MHL) in 6 (11\%) patients, focal nodular hyperplasia (FNH) in 8 (14\%) patients, nodular regenerative hyperplasia (NRHL) in 13 (24\%) patients, adenoma (HA) in 2 (4\%) patients. The type of BLT were clearly typed by ultrasound without contrast in 47 patients (85\%); while in 5 cases contrast-enhanced ultrasound (CEUS) for diagnostic definition was also required. Abdomen resonance (MRI) was performed in 28 (51\%) patients and in 20 of them hepatospecific contrast was used to achieve a proper diagnosis. Liver biopsy was performed in 11 (19\%) patients and in one case allowed an alternative diagnosis compared to diagnostic imaging. Computed-tomography (CT) with radiocontrast agents was performed in 8 patients but without adding additional information. CEUS showed a correlation with MRI in 94\% of studied cases. NRHL in 10 patients was related to other clinical conditions. INF was associated with high prevalence of metabolic syndrome abnormalities (p: 0.02).

Conclusion: Our study shows that CEUS may be most useful in optimizing US detection rate but its use remain off-label in childhood. MRI with hepatospecific contrast seems to be the most accurate test to make an appropriate diagnosis of FNH and also to clearly define a NRHL. INF seems to be related with metabolic syndrome.
HEPATOLOGY: Transplantation

H-eP-025

MDR3 deficiency mimicking Wilson disease: the importance of next generation sequencing based multi-gene panel analysis for definitive diagnosis

Mohammad Ali Shagrai1, Ali Syed Akhtar1, Dieter Clemens Broering2

1King Faisal Specialist Hospital and Research Centre, Pediatric Transplant Hepatology, Organ Transplant Centre, Riyadh, Saudi Arabia
2King Faisal Specialist Hospital and Research Centre, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia

Objectives and study: An autosomal recessive defect in the gene ABCB4 located on chromosome 7 that encodes for the Multidrug resistance class III P-glycoprotein (MDR3) results in clinical entity called Progressive Familial Intra-hepatic Cholestasis type 3 (PFIC3). Those affected usually present with high gamma glutamyl-transferase (GGT). The age at presentation varies from infancy to adulthood.

Wilson disease on the other hand is also an autosomal recessive disorder due to a mutation in the ATP7B gene that encodes for the copper-transporting P-type ATPase. A defect in this protein leads to excessive Copper accumulation in hepatocytes, also evidenced is low serum Ceruloplasmin level and high urinary copper excretion.

However, in cholestatic diseases such as MDR3 deficiency, primary sclerosing cholangitis and primary biliary cirrhosis we also find elevated hepatic copper content and biochemical profile similar to that found in Wilson disease. Hence making the diagnosis of these cholestatic disorders challenging. Here we present three such cases which were initially labeled as Wilson disease based on liver biopsy and biochemical profile but were later confirmed to have MDR3 deficiency based on genetic studies.

Methods and Results: Using next generation sequencing-based multi-gene panel for the first time to diagnose familial cholestatic diseases, in our retrospective cohort there were six patients (post liver transplant) with clinical and biochemical diagnosis of Wilson disease. Three of them were found to be negative for Wilson disease gene and instead had a homozygous ABCB4 gene mutation. These three patients were previously misdiagnosed as Wilson disease based on low serum Ceruloplasmin, high serum Copper and high Copper content on liver biopsy.

Conclusion: There are scattered case reports of patients with PFIC3 mimicking the biochemical profile similar to that found in patients in Wilson disease. Labeling such patients erroneously as Wilson disease exposes them to wrong management. Since the administration of chelation therapy has its own adverse effects, the correct diagnosis of PFIC3 is imperative to avoid the toxicities attributed to chelation therapy. Early diagnosis and timely intervention in patients with PFIC3 helps reverse the disease. Patients with PFIC3 are known to be at risk of hepatocellular carcinoma (HCC) which may be averted by early initiation of Ursodeoxycholic acid thus further increasing the need for timely correct diagnosis.

Studies have showed that patients with MDR3 deficiency have altered metabolism of Copper in the hepatocytes. Thus they have an overlap in the presentation with Wilson disease patients due to this alteration of Copper metabolism. MDR3 protein is predominantly expressed in the canalicular membrane of hepatocytes & is essential in transporting biliary phospholipids. Its dysfunction leads to exposure of the biliary epithelium to toxic bile salts which subsequently result in cholestasis, cholangitis and biliary cirrhosis.

Biochemical profile of low Ceruloplasmin, high urinary Copper and high Copper content on liver biopsy cannot be relied upon when making a definitive diagnosis of Wilson disease, doing so may lead to misdiagnosis which affects patient management. We emphasize the importance of confirming the diagnosis of Wilson disease and PFIC3 by genetic studies wherever possible since there is an overlap in the biochemical profile.
Sarcopenia in children with intestinal transplantation

Robert Hegarty 1, Pamela Allen 2, Annamaria Daganello 2, Maria Sellars 2, Jonathan Hind 1, Dhamyanthi Thangarajah 1

1King’s College Hospital, Paediatric Liver, GI and Nutrition Centre, London, United Kingdom
2King’s College Hospital, Department of Paediatric Radiology, London, United Kingdom

Objectives and study: Deficits in lean mass and muscle measures are well described in children with chronic disease e.g. childhood inflammatory bowel disease [1]. Sarcopenia is a poor prognostic biomarker in adults with advanced cancer, liver transplantation and in children with acute lymphoblastic leukaemia. [2-4]. Psoas muscle cross sectional area (PCA) has been shown to correlate with whole body muscle mass and can be measured from axial imaging [5]. Little is known about sarcopenia in children with intestinal transplantation (IT). The primary objective was to determine whether children who had IT show differences in total PCA when compared to healthy controls. The secondary objective was to investigate association of PCA and survival after IT.

Methods: A retrospective, case note review of children who had IT at a single centre since inception in 2009 to May 2016. Controls were identified from abdominal trauma series. Total PCA (mm²) was measured using direct techniques of magnetic resonance imaging or computed tomography at the level of the anterior superior iliac spine. To correct for body size, PCA index was derived for all subjects: PCA divided by height. PCA index was then described according to outcome. Statistical analysis was carried out using Social Sciences (SPSS) version 23.

Results: 16 patients (9 male) underwent IT at our centre. Post-transplant axial imaging was available for 12 (6 males), median age 6.2 [3.6 to 12.91] years patients in whom the diagnoses (n): Chronic intestinal pseudo-obstruction (3), gastrochisis (3), intestinal ischaemia (1), intestinal lymphangiectasia (1), volvulus (1), progressive familial intrahepatic cholestasis (1), Hirschsprung’s disease (1) and intestinal failure of indeterminate aetiology(1). One patient was excluded from analysis as she was a bilateral amputee.

Children who had IT had a significantly lower PCA and PCA index than controls; median PCA index (x10^-3 mm²) [IQR] in IT vs controls; 4.71[3.68 to 6.10] vs 9.55 [8.44 to 11.33], p<0.05. There was a trend toward higher PCA index in those who survived (n= 9) compared to those who did not (2).

Figure 1: PCA index in IT deceased versus alive
**Conclusion:** Children who underwent IT had sarcopenia of the psoas muscle in comparison to healthy controls. In IT patients who died there was a trend toward psoas muscle sarcopenia. This study adds to the evidence that body core muscle is consistently deficient in children with chronic disease and is the first to comment on children with IT. This small study provides the basis to develop PCA as a prognostic marker in children with transplantation.


Objectives and study: Sarcopenia, defined as loss of muscle volume, assessed by the measurement of psoas muscle surface area (PMSA) from cross sectional computed tomography (CT) imaging, is thought to be a physiologic correlate of frailty. Sarcopenia has been identified as a novel prognostic parameter to predict clinical outcomes in adult liver transplantation (LT). No reference values of PMSA exist for children. We hypothesized that determination of PMSA at both lumbar levels, L3/4 and L4/5 is feasible, and that children listed for LT have reduced PMSA.

Methods: Between 03/2013 and 12/2015, all available CT images from children (0-18y) with end stage liver disease (ESLD) listed for live donor LT (LDLT) who underwent an abdominal CT (as part of LDLT work-up) and a control group of age- and gender-matched healthy children (Control), obtained from an institutional Trauma Database, were reviewed. Children < 1y of age were matched 1:1 and children >1y of age 1:2 for further analysis. Total PMSA was determined for both intervertebral disc levels, L3/4 and L4/5, as the sum of the respective left and right PMSA in mm$^2$, for each patient. Quality control was performed by inter-observer correlation of two independent radiologists.

Results: In total16/31 subjects (LDLT) were available for further analysis. Of the 15 excluded children 3 children were falsely labeled as LDLT, for 7 children no age and gender match could be identified, 3 children had metabolic diseases, and in 2 CT scans were not completed. 25 healthy Controls (7 children <1.4 y and 18 children >1 y) were identified to match 1:1 and 2:1 respectively. The most prevalent diagnoses in the ESLD patients were biliary atresia (50%) and Alagille Syndrome (31%). Median PMSA was significant smaller in the ESLD group at lumbar level L4/5 median 505 mm$^2$ (IQR 339, 966) vs Controls 790 mm$^2$ (IQR 574, 1435) (p=0.0134) and lumbar level L3/4 median 394 mm$^2$ (IQR 276, 701) vs 646 mm$^2$ (IQR 439, 1105) (p= 0.0195) respectively. These results were independent to participants’ weight z-scores. Correlation of PMSA at both lumbar levels was excellent ($r^2$=0.92) as well as the inter-observer correlation ($r^2$=0.99)

Conclusion: In this pilot study, cross sectional area of the psoas muscle is significantly lower in children with ESLD compared to healthy age- and gender-matched controls. Hence we suggest that sarcopenia is an objective valid biomarker of frailty in children, independent to current anthropometric measures. The next step is to complete a reference database for PMSA in children to facilitate early identification of children who will benefit of pre-rehabilitation interventions, with the overarching goal of improving outcomes in paediatric liver transplantation.
Developing a transition service for liver transplant recipients - experience of Liver Centre in the UK

Marumbo Mtegha\textsuperscript{1}, Anokh Goodman\textsuperscript{2}, Lynne Henderson\textsuperscript{2}, Patricia McClean\textsuperscript{1}

\textsuperscript{1}Leeds Teaching Hospitals NHS Trust, Department of Paediatric Hepatology, Leeds, United Kingdom
\textsuperscript{2}Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Objectives and study: The Leeds Teaching Hospitals NHS Trust (LTHT) is 1 of 3 quaternary centres in the UK specialising in childhood liver disease. The department performs approximately 20 liver transplants per year.

The transition of patients from adolescence to adulthood is a challenging and complex process in which young people progress from a state of complete dependence to independence on the background chronic disease.

In a non-optimised setting; this transfer of care may be abrupt or delayed by an inappropriate extended stay in children’s services. This has the potential for loss from regular follow-up & adverse medical outcomes.

The National Institute for Clinical Excellence in the UK made proposals for professionals to implement transition as guided educational and therapeutic process with multidisciplinary working. It is on these recommendations that we at LTHT have modelled our transition service.

Methods: In the infancy of our liver service, transition was facilitated by 1 paediatric consultant & clinical nurse specialist (CNS) with interest in this area. There were no dedicated equivalent adult team members. Children aged 16 were reviewed in the same clinical setting as the adult patients.

Between 2009 and 2011, the adult & paediatric teams expanded their staffing to allow for a dedicated medical, nursing and support staff to take responsibility for these patients.

As of 2014, the transition team consists of the following permanent members:

2 Consultant Hepatologists (adult & paediatric), 2 Clinical Nurse Specialists (adult & paediatric)
a Young Persons’ Key Worker, Clinical Psychologist, Social Worker and Specialist Learning Mentor.

At present the transition pathway involves:

1. An Adolescent clinic Patients aged 11-16 years. Children are taken through a structured education programme by the Paediatric team.
2. An annual Pre-transition meeting between paediatric and adult medical team for medical and social handover of the 16 year olds to move to the adult service.
3. An annual Transition Clinic for patients discussed at the pre-transition meeting held in the Paediatric setting to introduce patients to the adult team.
4. A Young Adult Clinic attended from age 16 to 25 years of age prior to transfer to full adult clinical setting. This clinic is run by the adult team with the Young Person’s Key Worker and Paediatric CNS in attendance to provide continuity.

Results: The most readily measurable outcomes of post-transplant patients are graft loss and non-compliance to medical therapy. Our results are detailed in the table below.
Table:

<table>
<thead>
<tr>
<th></th>
<th>Year of Transition</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Number of patients transitioned</strong></td>
<td>38</td>
</tr>
<tr>
<td><em><em>Early death</em> following transition</em>*</td>
<td>5</td>
</tr>
<tr>
<td><em><em>Number with abnormal LFTs</em> due to n/c</em>**</td>
<td>9</td>
</tr>
<tr>
<td><strong>Median age at liver transplant</strong></td>
<td>14.4</td>
</tr>
</tbody>
</table>

LFTs = Liver function tests  
N/C = non-compliance  
Early Death = within 3 years

**Conclusion:** The preliminary results are encouraging in regard to negative outcomes in transplant patients following transition. We accept that at this stage that there are more factors contributing to this and that our numbers may be small. For future analysis, more detailed patient data will be needed.

Due to multidisciplinary team working and continuity of care, we are now able to collect these objective (higher education achievement, employment status) and subjective data (quality of life, service satisfaction).

This will provide us feedback to identify strengths & weaknesses within the service and give better understanding of our patients’ needs.
HEPATOLOGY: Transplantation

H-eP-029

Outcome of children with PFIC after living donor liver transplantation

Esra Polat1, Murat Zeytun2, Murat Kilic2, Latife Doganay3, Cigdem Anikan4

1Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
2Kent Hospital Organ Transplantation Center, General Surgery, Izmir, Turkey
3Kent Hospital Organ Transplantation Center, Pathology, Izmir, Turkey
4Memorial Atasehir Hospital Liver Transplantation Center, Pediatric Gastroenterology Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: Progresif familial intrahepatic cholestasis is uncommon causes of liver failure during childhood. Despite our understanding increased in disease pathogenesis, medical therapy may not prevent the development of end stage liver disease. The aim is to evaluate outcome of transplanted children with PFIC.

Methods: Patients data were collected from medical records and clinic charts. Patient demographics, clinical and laboratory data, surgical details, complications, and graft and patient survival are reviewed. Posttransplant immunosuppression consisted of a double regimen of tacrolimus and steroid. Statistical analysis was performed with SPSS version 16.0. Survival analysis was estimated using the Kaplan-Meier survival method. Numeric values are expressed as median and range unless otherwise stated.

Results: Between 2009 June -2016 September, 270 children underwent liver transplantation. Of the 62 children, 38 had PFIC type 2, 12 had PFIC type 1 and 11 had PFIC type 3. Median age at the transplantation, PELD and weight was 50 mos (3-77), 19 (-4-41), 9.2 kg (4-54), respectively. The indications of LT was liver failure (n=38), variceal bleeding due to portal hypertension (n=12), intractable pruritis (n=16), growth failure. Six of them underwent to partially internal biliary diversion prior to LT. Median followed up was 50 months (range3-77). Survival for 1, 2 and 6 years was 95 %, 95% and 95% respectively. One patient underwent retransplantation due to chronic rejection on posttransplant 31months. Posttransplant complications were infection (n=10), hemofagositic lymphohistiocytosis (n=3), PTLD and lymphoma (n=2), biliary problems (n=7), food allergy (n=8) and diarrhea (n=3). Two patients who developed low GGT cholestasis were successfully treated steroid and AntiCD-20 monoclonal antibody. Graft-biopsy specimens obtained during periods of such elevations did not show signs of both acute and chronic rejection. No donor had early or late postoperative complications.

Conclusion: PFIC is common indication for LT in our population. The outcome is promising. But we need to close follow up disease recurrence and extraintestinal involvement after transplantation.
Early liver transplantation or combined liver-kidney transplantation: what is the best solution for methylmalonic acidemia?

Samira Sissaoui1, Anais Brassier2, Christophe Chardot3, Carmen Capito3, Dominique Debray4, Muriel Girard4, Jean-baptiste Arnoux2, Pascale De lonlay5, Florence Lacaille6

1Hopital Necker Enfants Malades, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
2Necker-Enfants Malades, Metabolic Diseases, Paris, France
3Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Chirurgie Viscérale Pédiatrique, Paris, France
4Hopital Necker Enfants Malades, Unité D'hépatologie, Paris, France
5Hopital Necker Enfants Malades, Centre de Référence des Maladies Héréditaires du Métabolisme, Paris, France
6Necker-Enfants Malades, Gastroenterology-Hepatology- Nutrition, Paris, France

Objectives and study: Methylmalonic acidemia (MMA) is a rare autosomal recessive disorder of protein metabolism leading to death before the age of 7 in 80 % without intensive management. Surviving patients have a poor quality of life (QOL) due to recurrent hospitalizations for metabolic decompensations, intellectual disabilities, anorexia, and development of renal failure. The treatment is a severely restricted diet, usually with enteral feeding. In our unit, transplantation (Tx) has initially been considered for kidney failure, then for enzyme replacement therapy in the hope of improving the quality of life. Three types of Tx have been performed: kidney, liver or combined liver-kidney Tx. The aim of our study is to evaluate the results on mid- and long term.

Methods: We reviewed retrospectively the 13 children, all Mut0, who underwent Tx, their age, renal function, complications and protein intake before and after Tx.

Results: Seven children received a kidney Tx. The medium age at Tx was 9.7 years (5- 17), 4 were on dialysis. At 5 years follow up, the urinary MMA values had not changed from pre-Tx, renal failure had recurred in 4 cases. All children were still enterally fed. The protein intake increased by 44%. Five children underwent a combined liver-kidney Tx. One had a previous failing kidney Tx. All had a mGFR less than 30 ml/mn/1.73m2. Medium age was 14 years (6-19), with a medium of 1.5-year follow up. All of them were weaned from enteral feeding. The protein intake increased by 140 %, while urinary MMA decreased by 75 %. Complications included rejection and biliary problems were controlled. One patient developed axonal neuropathy, and myoclonus. One child received an isolated liver transplantation. With a follow up of 6 months, she increased her protein intake by 50%.

Conclusion: Early liver transplant has been proposed, and 22 cases reported, for prevention of neurological disabilities, improvement of QOL, and prevention or delay of renal failure. Combined liver-kidney Tx is mandatory if renal failure is severe. Tx has its own complications, does not abolish all neurological risks, and does not allow a totally normal diet. However the improvement of QOL in the patients with liver-containing Tx is encouraging for this disorder with such poor results on conventional treatment.
Hepatosplenic candidiasis in pediatric hematological malignancies

Miray Karakoyun1, Zuhal Sivis2, Burcu Akinci3, Akkiz Sahin3, Zumrut Sahbudak Bal4, Yesim Aydinok5, Deniz Yilmaz Karapinar5

1Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, Izmir, Turkey
2Tepecik Training and Research Hospital, Pediatric Hematology, Izmir, Turkey
3Ege University Medicine School, Pediatric Hematology, Izmir, Turkey
4Ege University Medicine School, Pediatric Infection Diseases, Izmir, Turkey
5Ege University Medicine School, Pediatric Hematology and Oncology, Izmir, Turkey

Objectives and study: Chronic disseminated candidiasis (also called hepatosplenic candidiasis [HSC]) is seen almost entirely in patients with hematologic malignancies who have just recovered from an episode of neutropenia. HSC occurs mostly in patients after profound and prolonged neutropenia, which is more often seen in patients with acute haematological malignancies while very few cases, some of which were not well documented, have been reported in patients who did not have leukemia or neutropenia. The incidence of HSC ranges between 3% and 29% in patients suffering from Acute Leukaemia.

Results: We report 3 cases of HSC occurring during a 7-year period: 1 was proven HSC, 2 were possible HSC. Our definition of cases was retrospectively based on 2008-revised EORTC/MSG study group diagnostic criteria for invasive mycoses. Of the 3 patients, only 1 patient with probable HSC had candidiasis with Candida parapsilosis. Two of our cases, the diagnosis relied only on imaging procedures showing hepatic or splenic nodules in haematological patients. None of the patients underwent live or spleen biopsy due to comorbidities.

Table: Characteristics of the patients

<table>
<thead>
<tr>
<th></th>
<th>Case 1</th>
<th>Case 2</th>
<th>Case 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age(months)</td>
<td>68</td>
<td>125</td>
<td>52</td>
</tr>
<tr>
<td>Gender</td>
<td>Male</td>
<td>Female</td>
<td>Female</td>
</tr>
<tr>
<td>Primary disease</td>
<td>Aplastic anemia</td>
<td>ALL(SR)</td>
<td>ALL(SR)</td>
</tr>
<tr>
<td>Duration of neutropenia <a href="days">&lt;500 neutrophils/mm3</a></td>
<td>226</td>
<td>36</td>
<td>-</td>
</tr>
<tr>
<td>Duration of profound neutropenia <a href="days">&lt;100 neutrophils/mm3</a></td>
<td>158</td>
<td>31</td>
<td>-</td>
</tr>
<tr>
<td>Candida spp.</td>
<td>C.parapsilosis</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Antifungal therapy</td>
<td>L-AMB, Caspofungin</td>
<td>Caspofungin, Voriconazole</td>
<td>Caspofungin, Posaconazole</td>
</tr>
<tr>
<td>AST/ALT (U/L)</td>
<td>12/16</td>
<td>19/22</td>
<td>23/25</td>
</tr>
<tr>
<td>GGT/ALP(U/L)</td>
<td>297/186</td>
<td>72/120</td>
<td>49/100</td>
</tr>
<tr>
<td>T.protein/Alb (g/dL)</td>
<td>5.7/2.5</td>
<td>5.1/2.9</td>
<td>6.6/2.9</td>
</tr>
<tr>
<td>Chemotherapy regimen</td>
<td>CSA</td>
<td>Induction</td>
<td>ARA-C</td>
</tr>
<tr>
<td>Infection site</td>
<td>Splenic</td>
<td>Hepato-splenic</td>
<td>Hepatic</td>
</tr>
<tr>
<td>HSC type</td>
<td>Probable</td>
<td>Possible</td>
<td>Possible</td>
</tr>
<tr>
<td>Delay of chemotherapy</td>
<td>Yes</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Attributable mortality</td>
<td>Yes</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusion: HSC is a rare and serious condition in children, mortality was 33% in our series but it was a small size study. Prolonged and profound neutropenia were detected in 2 of the three patients. All patients had a delay in receiving chemotherapy. Azoles can be used in the maintenance therapy.
(-)-Epigallocatechin-3-Gallate enhances poly I: C-induced interferon-lambda1 and contributes to HCV inhibition in hepatocytes

Yizhong Wang¹, Jieliang Li², Xu Wang², Ting Zhang¹, Wenzhe Ho²

¹Children’s Hospital of Shanghai, Department of Gastroenterology, Hepatology, and Nutrition, Shanghai, China
²Temple University Lewis Katz School of Medicine, Department of Pathology and Laboratory Medicine, Philadelphia, United States

Objectives and study: To investigate the effect of (-)-Epigallocatechin-3-gallate (EGCG) on poly I:C-triggered intracellular innate immunity against HCV in hepatocytes.

Methods: Cell culture HCV infectious model was generated by infection of HCV JFH-1 with a hepatoma cell line Huh7 (JFH-1-Huh7). HMW poly I:C and EGCG were used to stimulate JFH-1-Huh7 cells. Real time RT-PCR was used to detect intracellular gene mRNA expression, intracellular and extracellular HCV RNA level. ELISA was used to evaluate interferon (IFN)-λ1 for protein level in cell culture supernatant. And immunostaining was used to examine HCV core protein expression in Huh7 cells.

Results: Our recent study showed that HCV replication could impair poly I:C-triggered intracellular innate immune responses in hepatocytes. In the current study, we showed that EGCG treatment could significantly increase poly I:C-induced toll-like receptor 3 (TLR3), retinoic acid-inducible gene I (RIG-I), as well as IFN-λ1 expression in JFH-1-Huh7 cells. In addition, the supplement of EGCG increased the poly I:C-mediated antiviral activity in JFH-1-Huh7 cells at intracellular, extracellular HCV RNA and protein level. Further investigation of the mechanisms showed that EGCG treatment could significantly enhanced poly I:C-induced IFN-regulatory factor 9 (IRF-9) and several antiviral IFN-stimulated genes (ISG) expression, including ISG-15, ISG-56, myxovirus resistance A (MxA) and 2’-5’-oligoadenylate synthetase 1 (OAS-1), which are the key antiviral elements in IFN signaling pathway.

Conclusion: Our observations provide the experimental evidence that EGCG has the ability to enhance poly I:C-induced intracellular antiviral innate immunity against HCV replication.
SULT2A1 may alleviate liver fibrosis in biliary atresia

Kejun Zhou 1

1Department of Pediatric Surgery, Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Objectives and study: Liver fibrosis and cirrhosis develop dramatically in biliary atresia (BA). Cholestasis is severe in these infants. However, the detailed relationship between bile acid metabolism and liver fibrosis in BA is unclear.

Methods: We quantitatively measured major bile acids metabolism enzymes and bile acid profiles in livers of BA using multiple reaction monitor. Glycochenodeoxycholic acid 3-sulfate (GCDCA-3S) was further detected in urines of BA infants. Primary human hepatocytes were exposed to Glycochenodeoxycholic acid (GCDCA), taurochenodeoxycholic acid (TCDCA), and GCDCA-3S to study bile acids induced apoptosis.

Results: Bile salt sulfotransferase (SULT2A1) was found elevated in BA infants compared to normal control, and the levels in mild liver fibrosis patients were significantly higher than that in severe ones. Furthermore, we found liver expressions of SULT2A1 were negatively correlated with Collagen alpha-1(I) chain and Collagen alpha-1(IV) chain expressions. Bile acids profiling showed significantly higher content of total chenodeoxycholic acid in severe fibrosis infants. Trend decrease of GCDCA-3S was found in the urines of these infants. In vitro experiment also revealed that GCDCA-3S has significantly reduced apoptosis effect on primary hepatocytes.

Conclusion: SULT2A1 was increased in BA infants and its level was higher in mild fibrosis BA infants. SULT2A1 plays a protective role in liver fibrosis of BA.
To study the effect of room light on total micro-bilirubin values in vitro

Cheung Leung

Objectives and study: To study the effect of room light on total micro-bilirubin values in vitro

Methods: 417 capillary blood samples were collected with micro-tubes from jaundiced newborn infants at the nursery of Veterans General Hospital-Taipei. Samples were divided into 2 groups: 1. Room light group – 202 samples were placed on the desk in an office and irradiated with white fluorescent light from the roof in a distance 150 cm apart (spectral irradiance 425-475 nm=0.2µwatt/cm²/nm); 2. Dark group – 215 samples were placed in the dark. Total bilirubin values were checked with spectrophotometry at 0, 2, 4, 6, 24 and 48 hours after placing in different environments. The mean values obtained in 2 groups were analyzed with 2-way ANOVA with repeated measurement and Duncan’s multiple range test.

Results: There were significant decreases in bilirubin values of the room light group beginning at 6 hours (p<0.05), and there was no change of bilirubin values in the dark group.

Table: Mean values of total micro-bilirubin in different time groups

<table>
<thead>
<tr>
<th>Time(hours)</th>
<th>Room light group(mg/dL)</th>
<th>Dark group(mg/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>9.03±2.68</td>
<td>9.23±2.74</td>
</tr>
<tr>
<td>2</td>
<td>8.73±2.64</td>
<td>9.25±2.73</td>
</tr>
<tr>
<td>4</td>
<td>8.47±2.57</td>
<td>9.24±2.77</td>
</tr>
<tr>
<td>6</td>
<td>*8.12±2.66</td>
<td>9.20±2.78</td>
</tr>
<tr>
<td>24</td>
<td>*5.50±1.97</td>
<td>9.08±2.77</td>
</tr>
<tr>
<td>28</td>
<td>*3.33±1.66</td>
<td>8.73±2.76</td>
</tr>
</tbody>
</table>

*p<0.05

Conclusion: If blood samples are exposed to room light inevitably, it is safe to be checked within 4 hours. If immediate measurements are unavailable, the samples can be placed in a dark environment allowing the values to remain unchanged for 48 hours.
Clinical and endoscopy evolution of patients with intrahepatic portal hypertension after the first endoscopy screening for esophageal varices

Marina Adami¹, Carlos Kieling¹, Daltro Nunes¹, Renato Fagundes², Sandra Maria Gonçalves Vieira³

¹Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
²Universidade Federal de Santa Maria, Santa Maria, Brazil
³Universidade Federal Do Rio Grande Do Sul / Hospital de Clínicas de Porto Alegre, Pediatria, Porto Alegre, Brazil

Objectives and study: Evaluate the clinical and endoscopic evolution of patients with intrahepatic portal hypertension after the first endoscopic screening for esophagogastric varices (EGV).

Methods: We followed a historical cohort of patients with intrahepatic portal hypertension with no records of GI bleeding who underwent upper GI endoscopy screening for EGV. We recorded endoscopic findings related to the presence and characteristics of EGV. We classified the patients into two groups according to Conn’s classification, Group 1: no varices/Grade 1 and Group 2: Grade 2 or superior. We assessed the following outcomes: progression of varices size, rate of GI bleeding, liver transplantation or death.

Results: We follow-up 98 patients. We found VGE in 69.3% (78/98) of them. We classified 66 patients (67.3%) into Group 1, 33 of them with Grade 1 varices. We did not perform control endoscopy in 26 patients in Group 1. In this group, 19/40 (47.5%) patients presented enlargement of the varices in a mean time of 3.31±2.3 years. The GI bleeding rate for Group 1 was 1.5% (1/66). We allocated 32 patients (46%) into Group 2. In this group, 22 (68.7%) underwent to variceal band ligation as a primary prophylaxis (VBLPP). Upper GI bleeding rate in Group 2 was 13.6% (3/22) and 30% (3/10) for patients with and without VBLPP, respectively (p=0.35). During the follow-up, 28 patients underwent liver transplantation (12 for Group 1 and 16 for Group 2), and nine died with no transplantation (Seven in Group 1 and 2 in Group 2). Death and transplantation rates were 28.8% and 56.3%, respectively (p=0.01).

Conclusion: The upper GI bleeding rate in patients of the Group 1 was low in spite of the enlargement of the varices size. There was no significant difference in the GI bleeding rates in patients of Group 2 with or without primary prophylaxis. Group 2 presented transplantation and death rates significantly greater than Group 1.
Prevalence of liver disease in children with diabetes mellitus type 1 and correlation with metabolic control

Mirna Natalija Anicic, Lana Omerza, Duska Tjesic-Drinkovic, Irena Senecic-Cala, Nevena Kronic, Anita Spehar Uroic, Natasa Rojnic Putarek, Jurica Vukovic

1University Hospital Centre Zagreb, Zagreb, Croatia
2University Hospital Centre Zagreb, Zagreb School of Medicine, Pediatrics, Division of Pediatric Gastroenterology, Hepatology and Nutrition, Zagreb, Croatia

Objectives and study: Available data on prevalence of liver disease in children and adolescents with diabetes mellitus type 1 (DM1) are scarce. We have studied prospectively cohort of young DM1 patients in order to estimate the prevalence of liver involvement and compare our findings with measures of glycemic control.

Methods: The study group was simple cohort. Patients who regularly attended outpatient diabetic clinic were asked for consent on additional testing from the same blood samples which were drawn for their usual control visit purposes. Demographic data were collected from their registry. Office portable device was used for glycated hemoglobin (HbA1c) measurements. Patients with HbA1c ≤8.0% were considered as those with good metabolic control of DM1, and rest of them as suboptimally regulated patients. Liver enzymes as a marker of liver disease were considered elevated when both AST and ALT levels were at least two times above upper limit of normal. Abdominal ultrasound was added as a part of routine outpatient visit. Size of the liver, changes in echogenicity, and diffuse or focal involvement were evaluated. All the patients with increased aminotransferases levels and/or abnormal liver findings on initial visit were noted and if the findings were confirmed on subsequent visit within one month diagnostic work-up for liver diseases was scheduled.

Results: There were 46 children and young adults with DM1 (28 girls and 18 boys) throughout 3 months study duration. Their age ranged between 10-20 years, with a mean age of 15.4 years. The duration of DM1 was from 2-14 years, with mean duration of 6.6 years. Six out of 46 patients (13.04%) had elevated liver enzymes, and ten (21.73%) had changes on liver ultrasound. All patients with elevated aminotransferases (6/6) had pathological ultrasound finding. Twenty-one children (45.65%) had good glycemic control, and 25 (54.35%) had suboptimal glycemic control. In the group of suboptimally regulated patients 20% (5/25) had elevated aminotransferase compared to 4.76% (1/21) in the group with good glycemic control. Ten patients (4.6%) had abnormal liver ultrasound (hepatomegaly and hypoechochogenicity), 8 of them (32%) were in the suboptimally regulated group and 2 were in the well regulated group (9.52%). Statistical analysis using chi square test (p<0.05) showed that there was no statistical significance between glycemic control and elevated aminotransferase (p 0.126). There was also no statistical significance between glycemic control and ultrasound findings (p 0.065). The only statistical significance was found between aminotransferase levels and ultrasound finding (p 0.000001) which is quite understandable.

Conclusion: There is an important subset of young DM1 patients with signs of liver disease which cannot be attributed to any other cause but diabetes itself. Mechanisms which are leading to liver injury in patients with DM1 are more complex than it can be established by simply linking them to usual measurements of glycemic control as we have shown in our study. According to our data it can’t be considered as a part of spectrum of chronic diabetic complications because they all have well established link with poor metabolic control.
Liver size and gallbladder abnormalities in patients with extra hepatic portal vein obstruction

Maria Angela Bellomo-Brandao¹, Juliana Barreto¹, Gabriela Gomez¹, Flavia Justo¹, Roberta Alcantara¹, Adriana De Tommaso¹, Roberto Yamada¹, Gabriel Hessel¹

¹Faculty of Medical Sciences - University of Campinas, São Paulo, Brazil, Pediatrics, Campinas, Brazil

Objectives and study: The aim of the present study was to assess the changes in liver size and gallbladder ultrasonographic findings in patients with extrahepatic portal vein obstruction, and study the correlation between the presence of gallstones and reduced liver size. The extrahepatic portal vein obstruction (EHPVO) is a vascular disorder characterized by an obstruction of the extrahepatic portal vein, with or without involvement of the intrahepatic portal vein or splenic vein or superior mesenteric vein. In many studies, EHPVO is reported as a major cause of portal hypertension in pediatric patients. An abdominal ultrasonography allows evaluation of liver size and gallbladder abnormalities. Modifications in blood flow resulting from EHPVO have been associated with the decreased liver size, and this phenomenon could be related with an increased incidence of gallbladder varices and gallstones.

Methods: The study included 82 patients with EHPVO followed at university hospital. Ultrasonography was done using a Toshiba Power Vision 6000 with sectorial (3.75MHz) and linear (5MHz) transducers. References of normal liver size were based on tables established by Konus et al. The presence of gallstones, biliary sludge and gallbladder wall thickening (greater than 2.5mm) were investigated. Statistical analysis was performed using Chi-square and a 5% significance level was adopted.

Results: The average age at the moment of ultrasonographic evaluation was 14.5 years, with a median of 13.4 years; 65% (n=53) of subjects were male and 35% (n=29) female. Reduction in liver size was observed in 41.5% (n=34). The prevalence of gallbladder ultrasonographic findings was 73% (n=60) – gallbladder wall thickening/gallbladder varices being the most common finding (58.5% - n=48), followed by gallstone (14.5% - n=12), however 8 patients had both. In 4 cases, gallbladder was not assessed through ultrasonography due to previous cholecystectomy. No examination showed the presence of biliary sludge. In the group of patients with gallstones (n=12), 50% (n=6) presented reduced liver size and the same number had a normal liver size – no statistically significant difference was observed (p> 0.05). In the other hand, occurrence of gallbladder wall thickening / gallbladder varices were observed in 27 out of 34 patients with reduced liver size, establishing a statistically significant association (p<0.05).

Conclusions: In the present study, we observed a reduced liver size in almost half of patients with EHPVO, as well as a higher frequency of biliary lithiasis when compared with the general pediatric population. An association between reduced liver size and gallbladder wall thickening/gallbladder varices, but not with cholelithiasis, was observed. It is likely that the pathogenesis of gallstones is not related to decreased blood flow, which should be the main factor involved in liver reduction.
Congenital portosystemic shunt: a rare cause of cholestasis

Arzu Demir¹, Aytaç Yaman¹, Elçin Yıldız¹, Gulin Hizal¹, Burcu Berberoğlu Ateş¹

¹Ankara Child Health and Disease Hematology Oncology Training and Research Hospital, Paediatric Gastroenterology, Ankara, Turkey

Objectives and study: Congenital portosystemic shunt (CPSS) is a rare malformation (1:25 000/1:30 000 at birth) being associated with hepatic encephalopathy, pulmonary complications and liver tumors in older children and adults. Neonatal cholestasis occurs rarely as a complication of CPSS.

Methods: We report an infant with cholestatic jaundice owing to intrahepatic CPSSs which resolved spontaneously.

Results: A 41 days old male presented with jaundice. He was born fullterm with normal birth weight. Physical examination showed severe jaundice and 3 cm enlarged liver and spleen. Serum alanine aminotransferase (110 U/L N: 15-46) and aspartate aminotransferase activity were above normal. Total bilirubine was 24.62 mg/dL (N: 0.3-1.2) and direct bilirubine 22.88 mg/dL (N: 0-0.2) were elevated, prothrombine time was prolonged. Screening for galactosemia was positive falsely. Endocrine functions, viral serology and sweet chloride tests were all normal. Abdominal ultrasonography showed loculated dilatation in middle hepatic vein and tortious portal vein. Doppler ultrasonography showed intrahepatic shunts joining left portal branch to middle and left hepatic veins. Computerised tomography with contrast injection showed additionally a 12 mm sized vasculary malformation between left hepatic vein and shunt extending to left hepatic vein. Bilirubine levels normalized in 80 days. Control doppler ultrasonography showed spontaneous closure of the CPSSs.

Conclusion: Congenital portosystemic shunt should be searched in cholestatic infants. Intrahepatic shunts close spontaneously and recognition of congenital portosystemic shunt may prevent unnecessary investigations and treatment.
HEPATOLOGY: General Hepatology

H-P-009

Accuracy of the 2008 simplified criteria for the diagnosis of autoimmune hepatitis in paediatric population

José Vicente Arcos-Machancoses1, Cristina Molera Busoms2, Ecaterina Julio Tatis1, Victoria Bovo1, Jesús Quintero Bernabeu3, Javier Juamperez Goñi4, Vanesa Crujeiras Martinez5, Javier Martin de Carpi6

1Hospital Sant Joan de Déu, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
2Hospital Sant Joan de Déu, Unit for the Comprehensive Care of Pediatric Inflammatory Bowel Disease. Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
3University Hospital Vall D’Hebron, Paediatric Gastroenterology, Hepatology, Nutrition Support and Liver Transplantation, Barcelona, Spain
4Hospital Vall D’hebron, Paediatric Gastroenterology, Liver Transplantation and Nutritional Support Unit, Barcelona, Spain
5Hospital Clinico Universitario, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Santiago de Compostela, Spain
6Sant Joan de Deu Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain

Objectives and study: We hypothesized that the 2008 simplified diagnostic criteria for autoimmune hepatitis (AIH) are adequate during the childhood. In order to verify this, we aimed to study its accuracy, its clinical utility and the concordance of the clinical classifications based on this simplified system in comparison with the expert diagnosis based on the original criteria reviewed in 1999.

Methods: We selected a cohort of children under study for possible AIH through consecutive sampling with retro and prospective phases, in order to obtain the prevalence of cases within the group of differential diagnoses in a real clinical scenario. Study period from 2006 to 2017. As there isn’t a truly gold standard for AIH, we defined it through a modification of the classical criteria, that makes compatible liver histology and response to treatment necessary items. We included a wing for discrepant cases analysis to reduce possible false negatives. Validity indicators of the 2008 criteria for different cut-off points were obtained in an intention to diagnose approach: sensitivity (Se), specificity (Sp), likelihood ratios and predictive values (PV). Optimum cut-off point was estimated. We also calculated the area under the receiver operating characteristic curve (ROC) for the point system and for the diagnostic classification based on the optimal cut-off point. Clinical utility was assessed according to Pauker and Kassirer model. Concordance was studied with kappa statistic.

Results: Out of the 183 cases reviewed, 94 were AIH, showing a prevalence of 51.4%. The non-cases group included a variety of diagnoses like viral hepatitis, toxic hepatitis, Wilson's disease, acute cryptogenic hepatitis, primary sclerosing cholangitis, non-alcoholic steatohepatitis and others. Out of the AIH cases, 72.3% were females with a median age of 7.6 years old (range 1 -15 years). The majority of AIH were type 1 (84.0%). For the cut-off point of 6 in the 2008 simplified criteria (likely diagnosis according to the literature and also the optimal cut-off in our sample assigning a cost ratio of 1), a Se and a Sp of 70.2 and 95.5% were obtained respectively, with a 94.3% positive PV and a 75.2% negative PV. For 7 or more points, Se was 43.6%, Sp was 100%, positive PV was 100% and negative PV was 62.7%. The area under the ROC curve of the simplified criteria was 92.9%. For the classification model based on the optimal cut-off, the area under the curve was 82.9%. The kappa index with quadratic weighting for the pre-treatment concordance between the classical and simplified criteria (probable, definite and non-AIH) was 0.695, which indicates a good agreement. Moreover, therapeutic threshold calculated with utilities obtained from Manns (Hepatology. 2010;51:2193–213), was set in 56%, just between the prevalence and the positive predictive value, indicating that a positive result in the 2008 simplified criteria can justify starting the treatment in children under suspicion of AIH. Most classification errors were due to hypogammaglobulinemia, low autoantibody titres and to liver disease with cholestasis.

Vol. 64, Supplement 1, April 2017 657
Conclusion: The 2008 simplified criteria provide a moderate sensitivity for the diagnosis of AIH, but may play a role in indicating treatment in cases under suspicion, at children’s bedside with 6 or more points. Misdiagnoses were, in part, consequence of typical characteristics of paediatric AIH, which should be taken into account to propose specific criteria in children.
The autoimmune phenomena in paediatric chronic viral hepatitis

Irina Dijmarescu1, Daniela Pacurar2, Alexandra Moraru1, Dumitru Oraseanu2

1“Grigore Alexandrescu” Emergency Children’s Hospital, Paediatrics, Bucharest, Romania
2“Grigore Alexandrescu” Emergency Children’s Hospital and “Carol Davila” University of Medicine and Pharmacy, Paediatrics, Bucharest, Romania

Objectives and study: Autoimmune events have been reported in both paediatric and adult patients with chronic hepatitis B and C. Interferon treatment, which is widely used for this condition, has also been incriminated in inducing autoimmunity. We present an observational prospective study which aimed to evaluate the autoimmune phenomena associated to paediatric chronic hepatitis B and C. The research was conducted in the Paediatrics Department of “Grigore Alexandrescu” Emergency Children’s Hospital in Bucharest, Romania, between January 2013 and May 2016.

Methods: We included in the study a number of 114 patients, 92 with chronic hepatitis B and 22 with chronic hepatitis C. The subjects were divided in two groups - the first one consisted of patients who have received treatment and the second one of treatment-naive patients. Laboratory tests were performed in all patients. Autoimmune markers were pursued annually (cryoglobulins, circulating immune complexes, complement abnormalities, rheumatoid factor and non-organ specific autoantibodies - antinuclear antibodies, anti-smooth muscle antibodies, anti-liver kidney microsomal antibodies). We did not identify any clinically overt autoimmune manifestations, but 56 patients presented with serological evidence of autoimmunity at some point. SPSS Kaplan-Meier survival curves were used to evaluate the influence of treatment and period of time needed for the autoimmune phenomena’s occurrence in these patients.

Results: Fifty-two patients included in the study group have previously received treatment, out of which 26 were subsequently identified with autoimmune phenomena. Most of the patients have received Interferon, but some of those with chronic hepatitis B were treated with nucleosidic/nucleotidic analogues. Sixty-two of the patients were treatment-naive, out of which 31 presented autoimmune manifestations. We found that the longer the patient was chronically infected, the probability of identifying autoimmune manifestations increased. For patients who had received treatment this probability increase was slower in comparison to the group who has not yet been treated. At around 190 months, in the treatment group all patients presented with autoimmune phenomena, while at the same time in the non-treatment group the probability of the occurrence of an event was about 65%. The identified difference is statistically significant - Log Rank ($X^2 = 9.397$, df = 1, $p = 0.002$), Breslow ($X^2 = 10.454$, df = 1, $p = 0.001$), Tarone-Ware ($X^2 = 10.157$, df = 1, $p = 0.001$). The median for the time until the autoimmune manifestations occurred was 158 months in patients who had received treatment (with a 95% confidence interval between 123.27 and 192.72 months) and 71 months in treatment-naive patients (with a 95% confidence interval between 41.34 and 100.85 months).

Conclusion: Even though most of the patients had received Interferon, which is known to induce autoimmune events, our study shows that active infection may be a more important factor involved in triggering the autoimmune phenomena in paediatric patients with chronic hepatitis B and C.
**Objectives and study:** Treatment guidelines of children and adolescents with chronic hepatitis B (CHB) infection are still evolving. We aimed to analyze the status of our children with CHB at the present time to determine their eligibility for treatment in view of the recent ESPGHAN management guidelines for pediatric CHB.

**Methods:** This observational study included all children with CHB attending the Pediatric Hepatology Units at 2 centers. Inclusion criteria were: treatment-naive CHB infected children, aged 1-18 years, of both sex, provided they completed at least 12 months follow up. Children with co-infection with HCV, HDV or HIV or autoimmune hepatitis were excluded.

**Results:** One hundred and three children with CHB were enrolled. Their ages ranged between 1.5-18 years; 65% were males; 89% were born to HBsAg-positive mother. Fifty-one (49.5%) were immune tolerant, 28 (27.2%) were inactive carriers, 11 (10.7%) were immune active CHB and none had HBeAg-negative chronic hepatitis. Thirteen (12.6%) children had non-classic CHB status. Among immune active children who performed liver biopsy, only 2 were candidates for treatment.

**Conclusion:** Fifty percent of the studied children with CHB were in the immune tolerant phase, therefore children with CHB eligible for treatment represent a minority.
Sclerosing cholangitis in children: a promising medium-term follow-up

Federica Ferrari¹, Giusy Ranucci², Marina Alo¹, Fabiola Di Dato², Franca Viola¹, Salvatore Cucchiara¹, Raffaele Lorio²

¹Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Paediatrics, Rome, Italy
²University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy

Objectives and study: Sclerosing cholangitis (SC) is a chronic cholestatic liver disease and its diagnosis was increased in childhood. There are few data on paediatric features and long-term prognosis of SC.

Methods: We reviewed data of 45 patients under 18 years, diagnosed as SC in two referral centers, basing on biochemical, radiologic and/or typical histological findings.

Results: In our paediatric population (median age at presentation: 10.4 years; range 1.0-17.9) there was a prevalence of male sex (73.4%); 29 patients (64.4%) were asymptomatic at presentation and SC was suspected because of abnormal liver tests detection during a routine check-up in 16 patients or during a follow-up evaluation in 13 patients with inflammatory bowel disease (IBD). Among 16 symptomatic patients: 6 presented jaundice, 5 pruritus, 3 fatigue, 4 hepatomegaly and one splenomegaly. Radiologic imaging showed intrahepatic and extrahepatic involvement in 19 patients (42%); in 13 children (28%) only intrahepatic alterations were found. Isolated extrahepatic large duct involvement was rare (9/45). Liver biopsy, performed in 31 patients (68.8%), showed fibrosis of stage 1, 2 and 3 in 10 (32%), 10 (32%), and in 5 patients (16%), respectively. Five patients (16%) had cirrhosis at presentation. Ten patients (22.2%) with ipergammaglobulinemia and/or positive autoantibodies, without interface hepatitis, were classified as autoimmune SC. Twenty patients (44.4%) had IBD associated: ulcerative colitis (UC) in 17 (85%), and Crohn disease (CD) in 2 patients (10%), respectively. One patient (5%) showed a frame of unclassified IBD. Diagnosis of IBD was antecedent, contemporary or following in 5 (25%), 12 (60%), 3 (15%) patients, respectively. In 13 patients (28.8%) SC had not autoimmunity neither IBD. All patients were treated with ursodeoxicholic acid (UDCA) and about 26% of patients were taking also immunomodulators such as thiopurines or tacrolimus for IBD or autoimmune hepatitis. Serum AST, ALT, GGT levels significantly improved after one year on therapy in all patients. Five patients with SC and IBD-associated started vancomycin after a median time of 3.5 years from diagnosis. After a follow up time of 8.7 ± 5.6 years all patients were alive. In 4 children immunosuppressant was stopped; 26 (57.7%) patients continued only UDCA therapy; 2 (4%) patients stopped any therapy. During the follow-up time, 7 patients developed at least one liver-related complication such as oesophageal varices, cirrhosis with ascites and/or coagulopathy. Liver transplantation was performed only in 2 patients after a median time of 7 years from diagnosis of SC. Two patients required colectomy for refractory ulcerative colitis and they continued only UDCA therapy, without any complication.

Conclusion: In our paediatric study we found that 62% of children with SC had IBD and/or AIH/SC overlap. About 20% presented advanced fibrosis at diagnosis. After 9 years of follow-up, the patient survival free of liver transplantation was 95.5%.
Etiology, treatment and outcome of cholelithiasis in children

Maşallah Baran¹, Yeliz Cagan Appak¹, Gökhan Tümgör², Miray Karakoyun¹, Tunç Özdemir³, Gökhan Köylüoğlu³

¹Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, İzmir, Turkey
²Çukurova University Faculty of Medicine, Department of Paediatric Gastroenterology, Adana, Turkey
³Tepecik Training and Research Hospital, Department of Paediatric Surgery, İzmir, Turkey

Objectives and study: This study was intended to investigate the demographic characteristics and symptoms of children with cholelithiasis, the underlying etiology and gallstones’ response to ursodeoxycholic acid (UDCA) treatment.

Methods: 74 children with cholelithiasis who have followed at the outpatient clinic between September 2009 and June 2016 were recruited to the study. The patient’s gallstones were determined using ultrasonography (USG) and gallstones were classified on the basis of USG measurements. We retrospectively investigated demographic informations, presenting symptoms, laboratory findings, etiology and treatment outcome of children with cholelithiasis.

Results: Cases’ mean age was 7.4± 4.3 years (2 month- 17 years). The female:male ratio was 1.2:1. Average follow-up duration was 17± 17.1 months (2-82 months). Twenty-nine cases (39.2%) were asymptomatic. Abdominal pain was present in 38 cases (51.4%), nausea in 25(33.8%), vomiting in 21(28.4%), lack of appetite in 15(20.3%) and jaundice in 3(4.1). Analysis of case risk factors revealed a history of gallstones in the families of 14.9% cases. Acute pancreatitis was observed in two cases (2.7%), elevated transaminase in 10 cases (13.5%). We identified of etiology respectively; a history of total parenteral nutrition 17.6%, hemolytic disease 6.8%, choledochal cyst 4.1%, obesity %2.7, familial hyperlipidemia %4.1, prematurity %6.8, not identified etiology 28.4%. UDCA treatment was administered to all cases for an average of 9.7±7.2 months (2-24 months). Gallstones disappeared within 6 months after UDCA treatment in 22/74 cases (29.7%), within one year in 27/74 cases (36.5%). while no change was observed in 45/74 cases (60.8%). There was no response in children with hemolytic disease to UDCA treatment. Cholecystectomy was performed in 21 cases (28.4%).

Dimensions of gallstones and their responses to ursodeoxycholic acid treatment in Table.

Table. Dimensions of gallstones and their responses to ursodeoxycholic acid treatment

<table>
<thead>
<tr>
<th>Gallstone</th>
<th>UDCA treatment</th>
<th>Response to UDCA treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n (%)</td>
<td>n (%)</td>
</tr>
<tr>
<td>Gallstone larger than 1 cm</td>
<td>24 (32.4)</td>
<td>5 (20.8)</td>
</tr>
<tr>
<td>Multiple gallstones</td>
<td>25 (33.8)</td>
<td>7 (28)</td>
</tr>
<tr>
<td>Multiple millimetric gallstones</td>
<td>17 (23)</td>
<td>10 (58.8)</td>
</tr>
<tr>
<td>Bile sludge</td>
<td>5 (6.8)</td>
<td>5 (100)</td>
</tr>
</tbody>
</table>

Conclusion: UDCA treatment was especially effective in the first six months in our patients. UDCA treatment may particularly be considered before surgery in asymptomatic patients with no hemolytic disease.
Presentation and outcome of biliary atresia in Italy: the first report

Paola Gaio1, Enrico La Pergola2, matilde Pescarin1, Rosa Laverda1, Fabiano Dalla Valera1, Edoardo Rosellini1, Piergiorgio Gamba2, Giorgio Perilongo1, Mara Cananzi1

1Unit of Pediatric Hepatology, Dpt. of Woman and Child Health University Hospital of Padova, Padova, Italy
2Unit of Pediatric Surgery, Dpt. of Woman and Child Health, University Hospital of Padova, Padua, Italy

Objectives and study: Biliary atresia (BA) is a progressive inflammatory obliterative cholangiopathy affecting neonates and infants. Incidence varies from 1:20,000 live births in the Caucasian population to 1:5000 in Asiatic countries. No precise epidemiological data are available regarding most European countries and the Italian population. Though it is a rare disease, BA represents worldwide and in Italy the first cause of liver transplantation (LT) in children. The aim of the study is to report the characteristics at presentation and the outcome of patients diagnosed with BA in a tertiary referral centre for Pediatric Hepatology and Liver Transplantation in Italy.

Methods. The clinical charts of patients diagnosed and treated for BA from January 1990 to June 2016 at the Department of Woman and Child Health of the University Hospital of Padova, were retrospectively reviewed. The University Hospital of Padova is the main referral center for Pediatric Hepatology and Liver Transplantation in the North East of Italy. The following parameters were evaluated: demographic data, age at presentation and modality of referral, age at Kasai portoenterostomy (PE), Kasai efficacy defined as the normalization of total bilirubin level (< 20 umol/L) at 6 months after surgery; native liver survival and patient survival together with age at LT were also evaluated.

Results: From 1990 to 2016, 66 patients (M 26, F 40) were diagnosed with BA. 65 of 66 patients underwent Kasai procedure at a median age of 64 days (range 19-117 days) and only 1 patient was directly referred to LT due to old age (>7 months) along with decompensated cirrhosis. No significant differences were observed regarding age at diagnosis during the study period. The delayed diagnosis of BA in our population was mainly determined by a lack of recognition of the clinical signs of cholestasis (i.e. acholic stools, jaundice) by parents and primary pediatricians. 50% of children who underwent Kasai PE before 40 days of life, received the diagnosis of BA while admitted to our hospital for other medical conditions. Kasai PE resulted successful in 30% of patients. Native liver survival resulted equal to 46% and 40% at 5 and 10 years after Kasai PE. Overall patient survival resulted equal to 85% (56 subjects) at 10 years after diagnosis; among these subjects, 29 patients (52%) underwent LT at a median age of 19 months (range 5-191 months). 10 patients died: 4 on the waiting list for LT; 4 due to complications after LT; 1 due to a congenital cardiopathy associated to BA; 1 due to causes unrelated to liver disease.

Conclusion: This is the first study reporting the characteristics at presentation and the outcome of patients diagnosed with BA in Italy. With the limits of a retrospective study, we confirmed that BA in our geographic area is a rare disease with 2.5 new cases per year in a tertiary referral centre. In our population the diagnosis is frequently delayed mainly due to the lack of disease awareness in the medical and non-medical population and we have proven that this did not change during the 25 years study period. BA delayed diagnosis negatively influenced the efficacy of Kasai PE and the chances for native liver survival, indicating the need for screening and centralization policies in Italy.
Acholic stools: are parents and general pediatricians aware of the importance of this clinical marker of cholestasis?

Paola Gaio¹, Fabiano Dalla Valeria¹, Rosa Laverda¹, Enrico La Pergola¹, Matilde Pescarin¹, Piergiorgio Gamba¹, Giorgio Perilongo¹, Mara Cananzi¹

¹Unit of Pediatric Hepatology, Dpt. of Woman and Child Health University Hospital of Padova, Padova, Italy

Objectives and study: Biliary atresia is a progressive, fibro-inflammatory disorder of the biliary tree of unknown etiology. Worldwide delayed diagnosis is the main cause of poor outcome for these patients as jaundice and acholic stools are frequently unrecognized. In this study we wanted to investigate the capability of parents in identifying acholic stools and the degree of awareness upon this matter within a population of general pediatricians.

Methods: An iconographic test constituted of 6 pictures of real stools was developed to assess parents’ capacity in identifying cholic and acholic stools respectively as “normal” or “acholic”. An online questionnaire composed by multiple-choice questions was administered to a sample of general pediatrician working in north-east of Italy to assess their current clinical practice. We then proposed a stool color card (SCC) to parents and general pediatrician as a comparative tool to help identify pathologic stools.

Results: 80 parents were involved: 96.3% declared to be unaware of which color infant stools should be; without using the SCC only 17.5% were able to correctly identify all stool pictures. With the employment of a stool color card 82.5% of parents were able to correctly classify stool pictures as normal or acholic and this resulted statistically significant (p < 0.0001). 185 general pediatricians were involved: 54% declared to "seldom" or "never" directly evaluate stool color at pediatric visits. With or without the use of the SCC 89.8% of pediatricians correctly assessed all photos of the online questionnaire.

Conclusion: Parents are not able to correctly identify pathologic stools and general pediatricians rarely evaluate stool color at scheduled visits within the first months of life. These are the most reasonable causes of delayed diagnosis of biliary atresia in our Region. Awareness campaign and screening methods as stool color card could allow early and correct identification of cholestatic diseases in infants.
**Biliary atresia: the clinical course and outcome of patients at Red Cross War Memorial Children's Hospital, Cape Town, South Africa**

Lindsey Levin¹, Elizabeth Goddard¹, Ronalda De Lacy¹

¹Red Cross War Memorial Children's Hospital, Paediatrics, Cape Town, South Africa

**Objectives and study:** Biliary atresia (BA) is a progressive obstructive cholangiopathy of unknown aetiology, occurring during the perinatal period. If left untreated it rapidly progresses to hepatic fibrosis and cirrhosis, with death occurring within 2 years. It is the leading cause of end-stage liver disease in the paediatric population and remains the most common indication for paediatric liver transplantation in South Africa.

Despite a wealth of information from developed countries, very little information is available in Africa and other developing nations. This study aimed to describe the age of presentation, clinical course and outcome of infants presenting to Red Cross War Memorial Children's Hospital (RCWMCH) with BA.

**Methods:** A retrospective folder review was conducted on all patients with BA presenting to RCWMCH between January 2003 and December 2013. The main outcomes assessed were median time to presentation to tertiary services, clearance of jaundice post Kasai procedure (defined as bilirubin <20µmol/L) and 2- and 5-year overall survival (OS) and survival with native liver (SNL).

**Results:** The median age at presentation in the 80 cases reviewed was 70 days. Kasai procedure (KP) was performed in 62 (77.5%) patients at a median age of 68 days. 18 patients who presented late did not undergo KP. Clearance of jaundice was achieved in 39% of KPs. 13 patients underwent KP beyond 90 days with a success rate of 38%. 2- and 5-year SNL rates were 41% and 37.5% respectively with OS of 59% at 2-years and 56% at 5-years. Liver transplant was only performed in 12 of the 54 patients who showed progression to require transplantation.

**Table:**

<table>
<thead>
<tr>
<th>What is known</th>
<th>What is New</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Short-term clearance of jaundice has been achieved in 50-60% of cases in developed countries.</td>
<td>• Little information is available in the developing world.</td>
</tr>
<tr>
<td>• Emphasis has been placed on early recognition, referral and intervention to optimise outcome.</td>
<td>• This provides valuable insight into what is achievable in a resource limited setting.</td>
</tr>
<tr>
<td>• Previously 60 days was recommended as a cut off for performing KP, currently much debate exists around the benefits of performing late KP.</td>
<td>• A significant proportion of patients benefited from KP performed beyond 90 days.</td>
</tr>
</tbody>
</table>

**Conclusion:** Jaundice clearance post KP and SNL compared favourably with international figures, however, lower overall survival rates reflected lack of access to transplantation. Age at KP was not a predictor of poor outcome.
Effect of probiotics on cognitive findings in children affected by portal hypertension: a randomized, double-blind, placebo-controlled pilot trial

Valeria Casotti¹, Sara Giovannozzi¹, Ave Maria Biffi², Stefano Quadri², Lorella Caffi³, Mara Colusso⁴, Piero Amodio⁵, Lorenzo D’Antiga¹

¹Papa Giovanni XXIII Hospital, Paediatric Hepatology, Gastroenterology and Transplantation Unit, Bergamo, Italy
²Papa Giovanni XXIII Hospital, Neuropsychological Unit, Bergamo, Italy
³Papa Giovanni XXIII Hospital, Paediatric Neuropsychiatric Unit, Bergamo, Italy
⁴Papa Giovanni XXIII Hospital, Paediatric Surgery, Bergamo, Italy
⁵University of Padua, Department of Medicine, Padua, Italy

Objectives and study: Children affected by portal hypertension (PH), independently from the aetiology, may develop neurocognitive dysfunction (Minimal Hepatic Encephalopathy, MHE), due to the presence of portal systemic shunting. Several studies in adulthood have previously shown that probiotic treatment may improve MHE, by the modulation of gut microbiota. The present pilot trial was developed to evaluate the presence and degree of MHE in a group of children with compensated, anicteric PH and to evaluate the impact of a daily treatment with probiotics.

Methods: 18 patients (age range 4-17 Y, 4 M) where enrolled in a single Centre, with the following diagnosis, leading to confirmed PH: biliary atresia (n=10), portal thrombosis/portal cavernoma (n=3), autoimmune hepatitis/sclerosing cholangitis (n=2), congenital hepatic fibrosis (n=3). The children were randomized to receive placebo (treatment A) or a probiotic mixture composed by Streptococcus Thermophilus, Bifidobacteria and Lactobacilli (treatment B). At time 0 and after 14 (+/-1) weeks of treatment, the patients underwent the following examinations: biochemical analysis with blood ammonia measurement; Electroencephalogram (EEG) quantified by spectral analysis on P3-P4 derivations; extensive neuropsychological investigations. The protocol was approved by the Ethical Committee of the local hospital and was conducted according to the Helsinki criteria.

Results: Baseline clinical and demographic findings of patients receiving treatment A or B were comparable. 16 patients ended the study and no adverse effects were reported. With respect to baseline values (t0), at the end of the study (t1), no effect was found: 1) on blood ammonia (A: t0=39±13, t1=38±11 µmol/L, B: t0=39±10, t1=40±9 µmol/L, ANOVA interaction treatment x time: p=0.8), 2) on the mean dominant frequency of quantified EEG (A: t0=7.7±0.4, t1=7.9±0.4 Hz, B: t0=7.2±0.3, t1=7.6±0.3 Hz, ANOVA interaction treatment x time: p=0.7), as well as on psychometric tests. For simplicity, the block test (BT) and the phonemic fluency test (FFT) are reported (A: t0=8±1.9 and 104±8, t1=10±2.2 and 107±7 standardized scores, B: t0=7±1.3 and 93±6, t1= 10±1.5 and 96±6 standardized scores, respectively; ANOVA interaction treatment: p=0.9 and p=0.6).

Conclusion: In children with compensated, anicteric PH there was no clear evidence of MHE with the available biochemical, EEG and neuropsychological parameters; moreover, the effect of a probiotic treatment is negligible in this preliminary two-arm trial of 9 children each treated for 14 weeks.
NOTCH2 variants in children with cholestatic liver disease

Tassos Grammatikopoulos¹, Sandra Strautnieks¹, Melissa Sambrotta², Pierre Foskett¹, Maesha Deheragoda¹, Alex Knisely¹, Richard Thompson³

¹King's College Hospital, Institute of Liver Studies, London, United Kingdom
²King’s College London, Institute of Liver Studies, Division of Transplantation Immunology and Mucosal Biology, London, United Kingdom
³King's College Hospital, 1.Paediatric Liver, GI & Nutrition Centre 2. Institute of Liver Studies, Division of Transplantation Immunology and Mucosal Biology, King's College London, London, United Kingdom

Objectives and study: Mutations in JAG1 and NOTCH2 are reported in respectively 94% and about 1% of Alagille syndrome patients. We report eight cholestatic patients with novel and/or rare NOTCH2 variants.

Methods: After biliary atresia and α-1-antitrypsin deficiency were ruled out, cholestatic patients in whom clinical features and/or liver histology findings could not exclude AGS were assessed. NOTCH2 screening was performed as part of diagnostic next generation sequencing.

Results: Among 302 patients sequenced using a custom-designed cholestasis gene panel, heterozygous variants in NOTCH2 were identified in 8 (5 male) patients. Seven variants were missense changes. One was protein-truncating (Table). Median age at presentation was 5 weeks (range, 2wks-30yrs) with jaundice (7), hepatosplenomegaly (1), failure to thrive (4), pale stools (5), raised transaminases (7) and pruritus (2). Vertebral, ophthalmological and cardiac abnormalities were not identified in screened patients. Facial characteristics typical of AGS were identified in patient 1 and in his maternal grandmother who had the same genetic variant.

Liver microscopy showed lobular cholestasis (5), bile duct paucity (2), and fibrosis (3); cytokeratin 7, expressed in attenuated biliary radicles, was aberrantly expressed in hepatocytes (2). Abdominal sonography and magnetic resonance cholangiography showed bile duct irregularities (2), abnormal gallbladder (1) and renal cysts (1). Median serum bilirubin was 105 μmol/L [range, 5-227], AST 86 IU/L [31-319], ALT 90 IU/L [33-195], GGT 172 IU/L [27-389], albumin 38 g/L [35-30], creatinine 43 μmol/L [13-89], INR 0.98 [0.94-1.1] and cholesterol 3.89 mmol/L [1.9-5.1]. Patients 2 and 6 underwent liver transplantation before 1st birthday. Family histories included jaundice and gallstones in maternal grandparents (patient 3), heart murmur in mother (patient 2) and similar findings on liver biopsy in father (patient 6).

Table:

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Exon</th>
<th>Nucleotide change</th>
<th>Protein change</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3</td>
<td>c.271C&gt;T</td>
<td>p.Arg91Ter</td>
</tr>
<tr>
<td>2</td>
<td>34</td>
<td>c.6037C&gt;A</td>
<td>p.Pro2013Thr</td>
</tr>
<tr>
<td>3</td>
<td>28</td>
<td>c.5168A&gt;G</td>
<td>p.Asn1723Ser</td>
</tr>
<tr>
<td>4</td>
<td>21</td>
<td>c.3430A&gt;G</td>
<td>p.Ser1144Gly</td>
</tr>
<tr>
<td>5</td>
<td>21</td>
<td>c.3479A&gt;G</td>
<td>p.His1160Arg</td>
</tr>
<tr>
<td>6</td>
<td>25</td>
<td>c.4115G&gt;A</td>
<td>p.Arg1372Gln</td>
</tr>
<tr>
<td>7</td>
<td>4</td>
<td>c.731T&gt;C</td>
<td>p.Phe244Ser</td>
</tr>
<tr>
<td>8</td>
<td>34</td>
<td>c.6479A&gt;G</td>
<td>p.Tyr2160Cys</td>
</tr>
</tbody>
</table>
Conclusion: We report the identification of eight patients with cholestasis and variants in NOTCH2. We could find clinical features associated with AGS in only a minority of these patients. None met diagnostic criteria for AGS.
Do medical students have awareness of neonatal cholestasis and acholic stool?

Neslihan Gürcan Kaya¹, Sinan Sarı¹, Buket Dalgıc¹

¹Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey

Objectives and study: Neonatal cholestasis must always be considered in a newborn who is prolonged jaundice. Conjugated hyperbilirubinemia is never physiologic or normal. The most important condition in the differential diagnosis is biliary atresia (BA) and affected infants require a Kasai portoenterostomy ideally before the infant is 60 days old. Acholic stool is important for diagnosis of BA. Stool color cards published for promote the early diagnosis and treatment of BA. The aim of this study is evaluate awareness of medical students about neonatal cholestasis and acholic stool as a marker of BA.

Methods: A questionnaire was applied to class 4, 5 and 6 students during the 2015-2016 academic year of the Gazi University Faculty of Medicine. We excluded the students who do not have an internship in pediatrics. Five questions were asked to identify the prolonged jaundice and stool color card was shown to students to identify acholic stool as marker of the BA. The first five questions are about; describing prolonged jaundice in full-term infants, describing prolonged jaundice in pre-term infants, the first test to be done in infant with prolonged jaundice, biochemically definition of direct bilirubinemia, possible scenario for BA in a one month old infant, respectively. We asked have you ever seen acholic stool before and then showed by mixing nine-color stool color cards which used in Taiwan and modified by Canada (figure-1).

Results: Total 724 students accepted to fill out a questionnaire. Two hundred forty four was class 4, 237 was class 5 and 243 was class 6. The percentage of correct answers to the first 5 questions are; 57.8 %, 40.8 %, 65.2 %, 34.0 %, 23.7 % respectively. Sixty five percent of the students had never seen acholic stool before. There was no difference in the percentage of knowing acholic stool colors between the groups that had seen or had not seen acholic stool before. The percentage of correct answers to stool colors pictures are, 87.7%, 99.2%, 86.1%, 67.2%, 38.9%, 96.3%, 96.7%, 78.3%, 50.4% respectively (figure-1). The percentage of correct answers to the cholic stool colors and acholic stool colors are approximately over the 95% and 40-87% respectively. Acholic stool picture 1 and 3 are better known than other acholic stool pictures. Twenty two percent of the students answered correctly all of the stool colors.

Table: Figure-1

Conclusion: Early diagnosis of neonatal cholestasis is important. BA is associated with better prognosis if it is diagnosed before 60 days. As it was shown by the previous studies, the time of diagnosis might be shortened by stool card screening program. In our study we have shown that awareness of medical students about neonatal cholestasis and acholic stool is not sufficient.
Liver involvement in dengue infection at Thammasat University hospital

Sukkrawan Intarakho 1, Auchara Tangsathapornpong 1

1Thammasat University, Pediatrics, Pathum Thani, Thailand

Objectives and study: Liver involvement is a well-recognized feature associated with dengue infection. The liver injury ranges from asymptomatic transaminase elevation to fatal acute liver failure, especially in childhood. The primary objective is to describe the clinical manifestations and laboratory findings of liver involvement in children and adults with dengue infection.

Methods: A retrospective study was conducted among 765 patients (children and adults) with dengue infection who attended at Thammasat University Hospital which is a tertiary care hospital in Thailand from 2014 to 2015. Data were collected from medical charts and outpatient records.

Results: Of the 765 patients with dengue infection, including 255 (33.3%) children and 510 (66.7%) adults; 394 (51.5%) males and 371 (48.5%) females. The mean age was 23.5 years; range 2-77 years. Liver function test was performed in 172 patients, 23 children and 149 adults. Hepatomegaly is noted 39.13% in children and 5.37% in adults. Abnormal ALT and AST were represented in 82.6% and 78.3% of children, respectively. Mean ALT and AST were 248.9 (range 21-3584) and 614.5 (range 17-10590) U/L. The majority of children (69.5%) has mild elevation of transaminase (1-5 fold) and only two children (8.7%) have severe (>10 fold) elevation of transaminase. One of these two severe cases with underlying thalassemia has acute liver failure (prothrombin time >300 seconds) and succumbed. Regarding serum bilirubin, only 17.4% has increased serum bilirubin. In adult patients, abnormal ALT and AST were found in 85.2% and 93.9%, respectively. Mean ALT and AST were 204.8 (range 15-30516) and 325.9 (range 17-48565) U/L. Almost 85 in 149 (57%) has mild elevation of ALT. According to AST level, we found that 24.8% has severe (>10 fold) elevation while mild elevation was 50.3%. Acute liver failure in adults was 6% and all patients are not fatal.

Conclusion: Abnormal transaminase level is common in dengue infection of both children and adults. The majority of patient has mild elevation of transaminase and asymptomatic. Acute liver failure is uncommon, however this life-threatening complication is at greater risk among children.
Liver fibrosis and steatosis in children with chronic liver diseases - comparison between histology and transient elastography (Fibroscan)

Wojciech Janczyk1, Maciej Pronicki2, Wieslawa Grajkowska2, Piotr Socha1

1Children's Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
2Children’s Memorial Health Institute, Pathology, Warsaw, Poland

Objectives and study: Recently transient elastography (Fibroscan® Echosens, France) has been applied in many chronic liver diseases for reliable, non-invasive assessment of fibrosis and steatosis. We aimed to evaluate the degree of liver stiffness (fibrosis) and steatosis using Fibroscan in relationship to the extent and type of liver damage as assessed by liver histology in children with chronic liver diseases.

Methods: We included 33 children (15 females) with mean age 11.5yrs with chronic liver diseases (15-autoimmune hepatitis, 7-other hepatitis, 5-Wilson's disease, 6-others).

Liver biopsy was performed in all patients. Histology was described semiquantitatively e.g. modified NAFLD scoring system by Kleiner et al.: steatosis (0-3), fibrosis (0-4), inflammation (0-3) and necrosis.

At the same time all patients underwent Fibroscan examination with both: small (S2) and medium (M) probes to assess liver stiffness (E) and steatosis (Controlled Attenuation Parameter, CAP). The associations were tested with Spearman R test.

Results: On liver biopsy assessment the selected cohort of patients presented with variable fibrosis (grade 3-4 in 14 pts), mild steatosis (grade 1-2 in 8 patients), inflammation (grade 2-3 in 9 pts) and necrosis (1 pt).

Fibroscan showed slightly elevated liver stiffness 7.6kPa (4.8-14.3) (S2 probe) and 6.8kPa (5.2-14.3) (M probe). Patients presented with median steatosis (CAP) of 199dB/m (165-228) [median, lower, upper quartile].

Using statistical analysis we found strong correlation between liver fibrosis on histology and liver stiffness by Fibroscan: r=0.74 for S2 probe and r=0.66 for M probe respectively. Liver steatosis was also significantly related to CAP (r=0.5). Inflammation was inversely related to steatosis as assessed by CAP (r=-0.35).

Conclusion:

1. Liver stiffness assessed by both: small (S2) and medium (M) probes of Fibroscan® shows good correlation to liver fibrosis on histology in children with chronic liver diseases.
2. Liver steatosis measured by CAP reliably reflects degree of liver steatosis on histology.
Follow-up of liver steatosis and fibrosis in children with Wilson’s disease using transient elastography (Fibroscan)

Wojciech Janczyk, Maciej Dadalski, Piotr Socha

Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Liver involvement in children with Wilson’s disease ranges from simple steatosis, steatohepatitis to severe fibrosis. Pharmacological treatment is aimed to preserve liver function and improve patients’ clinical condition. Transient elastography (Fibroscan® Echosens, France) has been already applied in many chronic liver diseases for non-invasive assessment of liver stiffness/fibrosis and steatosis. We aimed to evaluate the change of liver stiffness/fibrosis and steatosis and selected laboratory markers of liver function over time in children with Wilson’s disease using Fibroscan.

Methods: We included 33 children (19 females) with mean age of 11.5yrs with Wilson’s disease, treated with either zinc or d-penicillamine. Patients with acute liver failure were excluded.

At the baseline and after a mean period of 1.5 yrs all patients underwent Fibroscan examinations with medium (M) probe to assess liver stiffness (E) and steatosis (Controlled Attenuation Parameter, CAP). Repeated laboratory liver function tests were performed at the same time. Wilcoxon test was used for statistical analysis.

Results: At the baseline, our patients presented with slightly elevated liver enzymes ALT-49.5U/I (27.5-69), AST-34.5U/I (25.5-45.5), GGTP-26U/I (19.5-35.5) and well preserved liver function INR-1.1 (1.05-1.16) [median, lower, upper quartile]. Initial Fibroscan examination showed normal median liver stiffness 4.4kPa (M probe) (4.0-5.4) and slightly elevated liver steatosis CAP-257dB/m (235-283) [median, lower, upper quartile].

After a period of 1.5 years we found decrease, but not statistically significant, in ALT, AST and INR in our patients. Only GGTP was significantly lower than the baseline results (p=0.02). Similarly we have not observed marked difference in liver steatosis (CAP) or liver stiffness by Fibroscan when compared baseline and repeated measurements.

Conclusion:

1. Liver stiffness/fibrosis and steatosis seem not to significantly improve in the short-term follow-up observation period of children with Wilson’s disease, as based on the Fibroscan measurements.
2. Transient elastography (Fibroscan®) can be easily used in children with Wilson’s disease for monitoring of liver stiffness/fibrosis and steatosis.
Cardiovascular risk assessment in children with biliary atresia and Alagille syndrome

Kamil Janowski¹, Łukasz Obyński², Piotr Czubkowski¹, Mieczysław Litwin², Aldona Wierzbicka³, Dorota Gliwicz², Krzysztof Kostewicz⁴, Piotr Socha⁴

¹The Children's Memorial Health Institute, Warsaw, Poland
²The Children's Memorial Health Institute, Department of Nephrology, Warsaw, Poland
³The Children's Memorial Health Institute, Department of Biochemistry, Radioimmunology and Experimental Medicine, Warsaw, Poland
⁴The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, The Children's Memorial Health Institute, Warsaw, Poland

Objectives and study: Chronic cholestatic liver diseases are associated with disturbed lipid metabolism, which potentially could influence cardiovascular (CV) risk. Nevertheless, limited data are available on the relationship between dyslipidemia and CV risk in children with cholestasis. The carotid intima-media thickness (cIMT) and pulse wave velocity (PWV) have been recognized as important parameters for CV risk stratification. The aim of the study was to evaluate the CV risk in children with biliary atresia (BA) and Alagille syndrome (AGS) by combined analysis of lipid metabolism, oxidative stress parameters, cIMT, PWV, obesity and hypertension in BA and AGS in relation to normal values.

Methods: We performed a prospective, single-centre study in children with BA and AGS. We investigated 18 patients with BA (aged 11,8 ± 6,1 years) and 16 patients with AGS (aged 11,9 ± 5,4 years) in whom anthropometric data, blood pressure measurements, lipid profiles as well as biomarkers of cholestasis, cIMT and PWV measurements (by oscillometric method) were performed. We present distribution as median with lower and upper quartiles. Both groups were compared by Mann-Whitney U test. Associations were tested with Spearman R test. P<0.05 was regarded to be statistically significant.

Results: In patients with AGS when compared with BA, we observed higher levels of urea, aminotransferases, markers of cholestasis, total cholesterol (TC) [236,5 mg/dl (197-336) vs 179 mg/dl (158-203), median (Q1-Q3), respectively], LDL cholesterol [166 mg/dl (119-209,5) vs 114,5mg/dl, (90-128)], apo B, TC/HDL cholesterol and LDL/HDL ratio. We observed increased TC (>190 mg/dl) in 13/16 and 8/18 pts (respectively in AGS and BA) and triglycerides (TG) (>150 mg/dl) in 4/16 and 0/18 pts. However, cIMT was increased only in 2 patients with AGS and in 6 with BA (≥95pc for age). No significant difference was detected in cIMT-SDS between both groups [AGS 0,83 (0,5-1,33) vs BA 1,5 (1-1,5)]. TC/HDL and LDL/HDL ratio correlated with cIMT in patient with BA, but no correlations between lipid profiles and cIMT could be found in AGS. PWV value was lower in patients with AGS compared with BA [respectively 4,5 m/s (4,3-5,1) vs 4,95 m/s (4,7-5,7), p=0,046]. 1 patient with AGS and 3 pts with BA had PWV SDS value above normal. In AGS, we found a negative correlation between LDL cholesterol and PWV and positive between TG and left ventricular mass index. We observed elevated blood pressure in 1/16 children with AGS and in 1/18 with BA (SBP or DBP ≥95pc for age).

Conclusion: Despite significant disturbances in lipid parameters only some children have increased intima-media thickness, still blood pressure in these patients is usually within the normal range. Thus, CV seems not to be significantly increased in children with BA or AGS. These findings should be further confirmed in larger cohorts of patients. The pathomechanism of AGS involving vessel structure requires caution in interpreting cIMT.

Ju Whi Kim¹, Kyung Jae Lee¹, Jin Soo Moon¹, Jae Sung Ko¹, Eun Joo Lee²

¹Seoul National University College of Medicine, Department of Pediatrics, Seoul, Korea, Rep. of South  
²Seoul National University Hospital, Department of Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Elevation of alanine aminotransferase (ALT) level is a surrogate marker of nonalcoholic fatty liver disease (NAFLD), the most common liver disorder in children and adolescents. The majority of studies of fatty liver in children have been in selected populations of the clinically obese or cross sectional design without time trends analysis. Study aims were to estimate the prevalence and time trends of elevated ALT in a general adolescent population and to identify leading risk factors for ALT elevation.

Methods: We analyzed data of adolescent participants (aged 10–18 years) in the Korean National Health and Nutrition Examination Survey 2001–2014, a representative sample of the general population in South Korea. Suspected NAFLD was defined by ALT elevation (>30 U/L) without hepatitis B surface antigen. In all statistical analyses, sampling weight and design based data were used.

Results: Elevated ALT was present in 5.3% (standard error: 0.3%) of the study population including adolescents participants (N=8455). No significant trend were found from 2001-2014 in elevated ALT prevalence among male and female adolescents. In multiple logistic regression analysis, independent associations with elevated ALT were found for sex (odds ratio [OR] male versus female 4.5; 95%CI, 3.3-6.2), obesity (OR 7.6; 95%CI, 5.3-11.0), and truncal obesity (OR 2.5; 95%CI, 1.8-3.5). In multiple regression analysis, sex, obesity, truncal obesity and house income levels were associated with log transformed ALT level.

Conclusion: In Korean adolescents, the prevalence of elevated ALT level was stabilized 2001 to 2014 in both gender adolescents group. This study revealed obesity, sex, truncal obesity and house income level are associated with pediatric NAFLD. Further investigations will be needed to found risk factors of pediatric NAFLD.
Long-term antiviral efficacy of tenofovir monotherapy compared to lamivudine monotherapy in children with nucleos(t)ide-naive chronic hepatitis B

Jae Young Choe1, Jungeun Kim1, Byung-Ho Choe1, Kyung Jae Lee2, Hye Ran Yang2, Jae Sung Ko2

1Kyungpook National University School of Medicine, Pediatrics, Daegu, Korea, Rep. of South
2Seoul National University College of Medicine, Department of Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Tenofovir disoproxil fumarate (TDF) has a higher genetic barrier to antiviral resistance and a more potent antiviral efficacy than lamivudine (LMV) in adult. The aim of the study was to compare the therapeutic efficacy of TDF with that of LMV in children and adolescents with nucleos(t)ide-naive chronic hepatitis B (CHB).

Methods: Seventeen patients (age; range 10.1~20.9 years, median ± SD 14.3±2.6) with chronic hepatitis B were first treated with TDF (TDF group), when confirmed to be in the immune-clearance phase. Pre-treatment hepatitis B virus (HBV)-DNA level was over 10^6 IU/mL. The TDF group was compared with the historical control group comprising 24 patients (age; range 8.0~15.2 years, median ± SD 12.9±1.9) treated with LMV. HBV-DNA titer decrement (>3 log10 IU/mL) was monitored after the initiation of each treatment, and compared. The treatment duration for HBV-DNA clearance (<357 IU/mL) was also compared as well as complete remission (HBeAg seroconversion and HBV DNA clearance). The follow-up period was 96 weeks.

Results: The mean duration for HBV-DNA titer decrement (>3 log10 IU/mL) was 14.8 weeks in all 17 patients (100%) of the TDF group, but was 14.5 weeks in only 19/24 patients (79.2%) of the LMV group. HBV DNA decrement (>3 log10 IU/mL) was achieved in 100% (17/17) in TDF group, but 62.5% (15/24) in LMV group (p=0.004) at 48 weeks after the initial of treatment. The HBV-DNA clearance (<357 IU/mL) in the TDF and LMV groups was as follows respectively: 64.7% (11/17) and 25.0% (6/24) at 12 weeks (p=0.011), 94.1% (16/17) and 50.0% (12/24) at 48 weeks (p=0.003), and 100% (14/14) and 54.2% (13/24) at 96 weeks (p=0.003). After initiation of the treatment, 2 of 17 patients (11.8%) of TDF group and 15 of 24 patients (62.5%) of LMV group were found to have an inadequate virologic suppression (>2000 IU/mL) at 24 weeks (p=0.001). Complete remission occurred in 38.5% (5/13) of HBeAg positive patients in TDF group and 28.6% (6/21) of LMV group at 96 weeks, without significant statistical difference.

Conclusion: Long-term TDF monotherapy showed a significantly more effective virologic response than LMV monotherapy in children with nucleos(t)ide-naive CHB.

Disclosure of interest: The authors (Choe BH, Ko JS) have been involved in the clinical trial sponsored by Gilead company as below;
A Randomized, Double-Blind Evaluation of the Antiviral Efficacy, Safety, and Tolerability of Tenofovir Disoproxil Fumarate Versus Placebo in Pediatric Patients with Chronic Hepatitis B Infection. (IRB No: 2012-04-021-053)

No patients in this study was overlapped with the patients enrolled in the global trial.
Investigation about clinical and pathologic relationships according to adult type and paediatric type of NASH in Korean children

Yong Joo Kim¹, Jung Min Yoon¹, Se Min Jang², Seung Sam Paik³

¹Hanyang University, College of Medicine, Paediatrics, Seoul, Korea, Rep. of South
²Keonyang University, College of Medicine, Pathology, Daejun, Korea, Rep. of South
³Hanyang University, College of Medicine, Pathology, Seoul, Korea, Rep. of South

Objectives and study: Nonalcoholic steatohepatitis (NASH) is defined by fatty liver with fibrosis, necrosis, and inflammation without obvious causes such as autoimmune hepatitis, viral hepatitis, or alcohol history. Histologically, NASH is divided into 2 groups, paediatric-type NASH and adult type NASH. Paediatric-type NASH is correspond to Type2 NASH and Adult-type NASH to Type1 NASH by Classification by Schwimmer et al. Strong steatosis, inflammatory cell infiltration in acinar zone 1 are histological features of Paediatric-type NASH, on the other hand, weak steatosis, inflammatory cell infiltration in acinar zone 3 are features of Adult-type NASH. Liver cirrhosis is present in both type. Generally, it is known that children have only paediatric-type NASH and overweight, boys are more common. Our objective is that identification whether adult-type NASH is seen in children and investigation of the difference of clinical characteristics according to histological type of NASH.

Methods: Liver biopsies were performed in 44 children of 7-15 years old in whom NASH was strongly suspicious, among them NASH was diagnosed in 38 children. We investigated anthropometry (Height, weight, BMI, Blood pressure), laboratory studies associated with NASH. Wilcoxon rank sum tests or t-test for continuous factors and Pearson’s chi-square or Fisher’s exact tests for categorical variables were used to assess which factors were significantly different between two groups.

Results: In 38 children, 21 patients were adult-type NASH, 17 patients were paediatric-type NASH. The age and severity of obesity were same in patients with type 1 and type 2 NASH. Boys were more than girls in both types fo NASH. Albumin (4.5±0.36 vs. 4.8±0.44, p=0.016) and hematocrit (40.1±3.2 vs. 42.6±2.44, p=0.013) showed a statistically significantly lower, but triglyceride (203.5 ± 100.65 vs. 139.2 ± 71.05, p=0.033) is significantly higher in adult type NASH rather than paediatric type. Insulin resistance - HOMA (5.85 ± 3.54 vs. 4.21 ± 2.88, p=0.15), Insulin resistance - QUICKI (0.16 ± 0.14 vs. 0.28 ± 0.23, p=0.21), Insulin sensitivity - FFA (5.85 ± 3.54 vs. 4.21 ± 2.88, p=0.15) were not show significant differences between two groups. Other clinical variables did not show statistically significant differences between the two types.

Conclusion: Not only paediatric-type NASH but also adult-type NASH were found in children. The classification according to the pathologic findings may not be set up between children and adults. Insulin resistance and insulin sensitivity are important to develop steatohepatitis, but do not seem to be pathogenic factors that determines the type of NASH. Fibrosis is essential in all patients with NASH, because of its association with risk of liver-related complications. Children with adult type NASH may have a more susceptibility to disease progression in early age. In our study, hematocrit, albumin, and triglyceride may be potential factors to predict pathologic types and disease progress.
HEPATOLOGY: General Hepatology

H-P-027

The effect of diet intervention on FCI of obese children with non alcoholic fatty liver disease

Ninung RD Kusumawati¹, Adriyan Pramono², Hartyanto Hartantyo³

¹Kariadi Hospital, Pediatric, Semarang, Indonesia
²Diponegoro University, Nutrition, Semarang, Indonesia
³Kariadi Hospital, Pediatrician, Semarang, Indonesia

Objectives and study: Non Alcoholic Fatty Liver Disease (NAFLD) is known as the most common in chronic heart disease in developing countries with prevalence of 10-24%. NAFLD can develop to hepatic fibrosis. Fibrosis Cirrhosis Index (FCI) is a non invasive parameter to evaluate hepatic fibrosis. Dietary restriction is considered as a first line management in high risk children with obesity. The objective of this study to identify the effect of low fat dietary intake at FCI level on NAFLD patients in Semarang, Indonesia.

Methods: An anthropometry (Body weight, Height, and BMI) assessment was done in 1247 Junior High School students. Forty obese children who met the inclusion criteria (abdominal US with NAFLD) were include in the study. Every subject was examined for laboratory test, and FCI. Twenty subjects were enrolled for intervention group and provided with low calorie diet and fat. The composition of intervention diet given was; total fat <25%, saturated fatty acid (SAFA) <10%, poly unsaturated fatty acid (PUFA) >10%, cholesterol <300mg/day, carbohydrate 55%, and protein 15-2%. Breakfast and dinner intake was composed by research team based on NAFLD low fat diet. The control group was 20 obese subjects of NAFLD without dietary intervention but low calorie diet intake and nutritional counseling. Food recall was conducted 3 days consecutively for 3 months. We measured the effect of intervention at week-12 and compared the FCI pre- vs. post-intervention.

Results: This research involved 70.6% male and 26.9 % female subject, with age proportion of 10-12 year old (n-8) and 13-15 year old (n=12). There was no significant difference between NAFLD grade 1 and grade 2 on FCI score. We could not identify a significant difference between NAFLD grade 1 and grade 2. There were significant differences for alkali phosphatase and IMT, however there was no significant difference on albumin, thrombocyte and FCI.

Conclusion: There was no significant difference on FCI before and post dietary intervention.
HEPATOLOGY: General Hepatology

H-P-028

Markers of systemic inflammation and insulin resistance in children with nonalcoholic fatty liver disease

Natalya Zavgorodnya1, Olha Lukianenko1

11"Institute of Gastroenterology of the National Academy of Medical Sciences of Ukraine", Pediatric Gastroenterology Department, Dnipro, Ukraine

Objectives and study: To establish the relationship between markers of systemic inflammation, insulin resistance and degree of liver steatosis in children with nonalcoholic fatty liver disease (NAFLD), assess the role of cytokines such as IL-6, IL-10 and TNF-alfa in pathogenesis of pediatric NAFLD. The study was conducted in 34 children with the average age of 11.73 ± 2.89 years. Patients were divided into four groups: a control group (S0) consisted of 21 patients without hepatic steatosis (61.8%), group S1 - 4 patients with 1 degree of steatosis (11.7%), group S2 - 4 patients with grade 2 steatosis (11.7%), group S3 - 5 patients with 3 degrees of steatosis (14.8%). All patients and their parents had given their agreement to participation in the study.

Methods: The presence and degree of hepatic steatosis were determined by transient elastography using «FibroScan®502-touch» with the measurement of controlled attenuation parameter (CAP). All patients underwent blood count analysis with determination of the erythrocyte sedimentation rate (ESR). We performed quantitative determination of interleukin-6 (IL-6), interleukin-10 (IL-10), tumor necrosis factor-alpha (TNF-α) concentration and insulin level with calculation of HOMA-IR.

Results: Obesity and overweight observed in 100% children with steatosis and in 47.6% of patients without steatosis (p<0.05). S3 group was characterized by higher average levels of white blood cells (95% CI 6.31-7.94) and erythrocyte sedimentation rate (95% CI 9.07-21.93) compared to other groups. ESR positively correlated with the levels of insulin and HOMA-IR. The level of insulin was significantly increased in groups with liver steatosis: group S1 – in 2.4 times, group S2 - in 2.8 times and S3 group - in 6.3 times compared to the control. All patients with steatosis (100%) had signs of insulin resistance, in 100% patients with steatosis HOMA-IR was higher than 75th percentile for normal subjects and gained a maximum value in S3 group. Maximum levels of TNF-α were at S3 group (1.8±0.8 pg / ml, p <0.05), which differed significantly from S0 group and other groups with steatosis. The level of IL-6 increased progressively with increasing steatosis degree, reaching maximum values in the group S3 (p <0.05) (S0 - 1.2±0.2 pg / ml, S1 - 1.55±0.3 pg / ml, S2 - 4.8±0.5 pg / ml, S3 - 6.1±0.5 pg / ml). Levels of IL-10 varied vastly: the minimum level was in S1 group that significantly distinguished from S0 group. The concentration of IL-10 reached maximum values in S2 group (9.5±1.1 pg / ml) and critically decreased in S3 group patients.

Conclusion: NAFLD in children is characterized by low-level systemic inflammation, which increases with the degree of steatosis. The maximum degree of steatosis is characterized by the elevation of such markers as ESR and proinflammatory cytokines. Pediatric NAFLD is characterized by imbalance pro- and anti-inflammatory cytokines with IL-6, TNF-α increase and IL-10 decrease due to hepatic steatosis progression associated with insulin resistance.
Primary prophylaxis of variceal bleeding in children with portal hypertension by variceal ligation is safe and as efficient as secondary prophylaxis

Julie Galand¹, Ley Delphine¹, Bakr Al Hussaini¹, Laurent Michaud¹, Dominique Guimber¹, Stephanie Coopman¹, Dominique Turck², Frédéric Gottrand¹

¹Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
²Chru, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases., Lille, France

Objectives and study: While primary prophylaxis of variceal haemorrhage by oesophageal variceal ligation (EVL) is recommended in adults with portal hypertension, it is still a matter of debate in children. The objectives of this study were to assess both safety and efficiency of EVL in children, in comparison to secondary prophylaxis.

Methods: Forty-seven patients with portal hypertension underwent at least one EVL in our tertiary centre from 1998 to 2016. Two children were not included because lost to follow-up; 45 patients were therefore included in this retrospective study.

Population was a priori divided in two groups: primary prophylaxis (P1) defined as use of EVL in children with grade 3 oesophageal varices and/or varices with red spot mucosa and no past history of bleeding; secondary prophylaxis (P2) defined as use of EVL to prevent recurrence of haemorrhage after a first episode of variceal bleeding. Clinical and endoscopic characteristics, treatment, episodes of bleeding as well as complications were recorded.

Results: Thirty patients were included in P1 (median age: 7.7 y, range: 1.2-18 y, 9 girls), and 15 in P2 (median age: 3.9 y, range: 1.5-14 y, 12 girls). Extra-hepatic portal vein obstruction was less frequent in P1 (6%) than in P2 (60%) (p<0.05). Median follow-up was 5.2 y (range: 0.1-12.8 y) in P1 and 4.0 y (range: 0.1-13.8 y) in P2 (NS). The use of associated treatments was not different between the two groups, including beta blockers and sclerotherapy.

Digestive haemorrhage occurred after the EVL program in 17% in P1 (4.67/100,000 person-year), and 27% in P2 (4.31/100,000 person-year) (NS).

Kaplan Meier analysis shows that actuarial survival without digestive haemorrhage was not different between the two groups.

Improvement (reduction of number and/or grading) and eradication (disappearance) of oesophageal varices was 92% and 16% in P1, and 88% and 20% in P2, respectively (NS). Adverse effects associated with EVL were observed in only two patients (all in P1): Enterobacter Cloacae septicaemia (n=1) and mild transient upper oesophageal sphincter stenosis (n=1).

Conclusion: Primary prophylaxis of variceal haemorrhage by EVL is safe and as efficient as secondary prophylaxis in children with portal hypertension.
Do patients with Crigler-Najjar type 2 always need a life-lasting treatment with phenobarbital?

Lorenza Matarazzo¹, Anna Gioachin², Alessandro Ventura³, Giuseppe Maggiore²

¹University of Trieste, Italy
²Department of Medical Science, University of Ferrara, Italy
³Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Paediatric Department, Trieste, Italy

Objectives and study: Crigler-Najjar type 2 (CN-2) is an autosomal recessive condition caused by mutations in UGT1A1 gene. In CN-2, uridine-di-phospho-glucoronosyl-transferase (UDPGT) enzyme activity is <10% of normal with a total serum bilirubin (TB) ranging from 6 to 20 mg/dl. Patients with CN-2 need a life-lasting treatment with phenobarbital due to a persistent risk of bilirubin encephalopathy.

Methods: We describe two brothers with an unusual CN-2 phenotype followed up respectively for 12 and 10 years.

Results: First patient was born at full term to non-consanguineous Italian parents. His medical history was remarkable for prolonged neonatal jaundice requiring phototherapy with a familial history of mild unconjugated hyperbilirubinemia in the mother. He was first seen at the age of 12 because of jaundice. Blood tests showed an increase of unconjugated bilirubin (TB 5.2 mg/dl, conjugated 0.56 mg/dl). Blood count, liver enzymes, haptoglobin, Coombs test and G6PDH activity were normal. Molecular analysis of UGT1A1 gene detected two heterozygous mutations (c.674T>G exon 1, c.1099C>T exon 4) and a heterozygous polymorphism (TA)7 of TATA box. He was followed up without treatment. At age fourteen, an acute and abrupt increase of his jaundice was observed with a TB of 18.15 mg/dl. No infections, fasting or stressful events were reported. Phenobarbital was administered with remarkable decrease of bilirubin (TB 1.83 mg/dl) but the therapy was discontinued after few days due to nausea and drowsiness. After two months a further increase of TB to 8.38 mg/dl was detected and phenobarbital was restarted. No further jaundice episodes occurred, and TB maximum values were of 2.74 mg/dl. Due to the unusually low total bilirubin levels for a patient with CN-2, phenobarbital was progressively discontinued after about 2 years of persistent treatment. He was strictly followed up for seven years with a good and stable clinical condition and a TB between 3.7-7.8 mg/d. The second patient is the 13 year-old brother of first patient. At the age of 3 he was screened for unconjugated hyperbilirubinemia with a TB of 2.76 mg/dl (conjugated 0.44 mg/dl). Molecular analysis confirmed the same mutations of the propositus. During the following 10 years a mild and persistent unconjugated hyperbilirubinemia was noticed (TB maximum value of 4.85 mg/dl) without acute episodes of jaundice. No treatment was proposed and he is on strict follow-up. Our patients’ UGT1A1 mutations have been previously described. The first (c.674T>G) was reported associated with a phenotype ranging from Gilbert and CN-2 syndrome when associated with (TA)7 promoter or frameshift mutations respectively. The second (c.1099C>T) was reported in a compound heterozygous patient with a mild CN-2 phenotype.

Conclusion: CN-2 has a wide range of clinical phenotypes and genetic variability involving UGT1A1 gene exons and promoter. Our report suggest that in mild CN-2 phenotype, as in our patients, treatment with phenobarbital may be “on-demand” once carefully instructed patients and parents to perform parenteral phenobarbital administration, with total bilirubin dosing, in case of evident increase of jaundice.
Liver disease and type 1 diabetes mellitus

Zuzana Michnova 1, Renata Szepoeva 2, Zuzana Havlicekova 3, Miriam Ciljakova 2, Peter Banovcin 3

1 Martin University Hospital and Jessenius Faculty of Medicine, Comenius University in Bratislava, Center for Diagnosis of Primary Immunodeficiencies, Department of Paediatrics, Martin, Slovakia
2 Martin University Hospital and Jessenius Faculty of Medicine, Comenius University in Bratislava, Department of Paediatrics, Martin, Slovakia
3 Martin University Hospital and Jessenius Faculty of Medicine in Martin, Comenius University in Bratislava, Center for Diagnosis of Primary Immunodeficiencies, Department of Paediatrics, Martin, Slovakia

Objectives and study: Liver plays important role in the regulation of carbohydrate metabolism. Type 1 diabetes mellitus (DM1) is one of the most frequent chronic metabolic diseases in children. Diabetes mellitus affects all organ systems including the gastrointestinal tract. According to the literature, the prevalence of hepatopathy in patients with DM1 ranges between 17-100 %, however, the majority of the studies were performed in adults. Non-alcoholic fatty liver disease and hepatic glycogenosis (Mauriac syndrome) are two most frequent liver diseases occurring as a consequence of diabetes mellitus, mainly resulting from inadequate compensation. We aimed to investigate levels of serum liver enzymes, liver profile and glycaemic control and to estimate the incidence of ultrasound changes of a liver in children with DM1.

Methods: We enrolled in the study 72 children with DM1 (29 boys, 40.27% and 43 girls, 59.72 %) who were hospitalized in 2015 at the Department of Paediatrics, University Hospital in Martin to perform control testing, adjust insulin therapy, or set an insulin pump for therapy. The median age was 13.92 years (IQR: 11.00–19.00 years). The average duration of diabetes in the population was 5.50 years (IQR: 2.00–8.50 years). All subjects underwent the panel of standard biochemical blood tests: fasting glucose level, fasting lipid profile, liver enzymes, creatinine, total bilirubin, glycated haemoglobin, C-peptide, microalbuminuria and ultrasonographic examination of the abdomen.

Results: Diabetes compensation was unsatisfactory, HbA1c was 10.19% (IQR: 6.50–16.40%). 23.61% patients were found out one or more liver abnormalities, hepatomegaly in 12.5 %, changes in echogenicity (hyperechoic appearance) of liver parenchyma in 11.11 % and liver enzymes elevation in 8.33 %. DM1 patients with abnormal hepatic ultrasound had significantly higher HbA1c (p= 0.05), fasting glucose level was increased, but not significantly (p=0.16), than those with normal findings. Mauriac syndrome was confirmed in 2 children by liver biopsy.

Conclusion: Hepatic abnormalities are frequent in paediatric patients with DM1 and they are usually related with long-term unsatisfactory metabolic control of the disease.
Single center experience in fulminant Wilson's disease

Şükrü Güngö¹, Mukkader Ayşe Selimoğlu¹, Fatma Ilknur Varol¹
¹İnönü University Faculty of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Malatya, Turkey

Objectives and study: Acute liver failure (ALF) due to Wilson’s disease (WD) responds to medical therapy poorly and is generally fatal without emergency liver transplantation (LT). Thus, more effective therapeutic strategies for these patients are needed. There is not any large pediatric case series of fulminant WD in the literature revealing treatment options and prognosis of those children. In the present study, we aimed to evaluate clinical and laboratory findings of 24 children with fulminant WD in comparison with other hepatic presentations, and to determine the effectiveness of plasmapheresis either as a cure or a bridge to LT.

Methods: Medical records of 24 consecutive cases of pediatric fulminant WD were evaluated retrospectively, focusing on the clinical, laboratory and treatment strategy findings in different clinical presentations.

Results: It was observed that while some laboratory (albumin, AST, alkaline phosphatase (ALP), total bilirubin, direct bilirubin, uric acid, white blood cell count (WBC), international normalized ratio (INR), total cholesterol, high density lipoprotein cholesterol (HDL), ammonia, 24 hour urinary copper and serum copper levels, AST/ALT ratio and AST/ALP ratio) were significantly different according to other hepatic presentations. Plasmapheresis was found being effective in reducing bilirubin and INR levels but also having potential for reducing Ca and Mg levels. Of patients who had plasmapheresis, four (30.7%) recovered without a need for LT and nine (69.2%) underwent LT. Of patients who had only medical treatment, six (54.6%) recovered without a need for LT and five (45.4%) underwent LT.

Table:
Laboratory findings of children with fulminant WD according to treatment regimens
M: Medical treatment group (11 children), M+PL: Medical treatment and plasmapheresis made group (13 children).

<table>
<thead>
<tr>
<th>Laboratory Value</th>
<th>Pretreatment</th>
<th>1st day</th>
<th>5th day</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>M+PL</td>
<td>p</td>
</tr>
<tr>
<td>AST</td>
<td>312.4</td>
<td>304.5</td>
<td>0.949</td>
</tr>
<tr>
<td>ALT</td>
<td>200.3</td>
<td>136.3</td>
<td>0.569</td>
</tr>
<tr>
<td>ALP</td>
<td>235.9</td>
<td>98.1</td>
<td>0.025</td>
</tr>
<tr>
<td>AST/ALT</td>
<td>2.1</td>
<td>6</td>
<td>0.006</td>
</tr>
<tr>
<td>AST/ALP</td>
<td>2.1</td>
<td>4.6</td>
<td>0.043</td>
</tr>
<tr>
<td>T.BIL</td>
<td>19.4</td>
<td>40.2</td>
<td>0.001</td>
</tr>
<tr>
<td>Albumin</td>
<td>2.7</td>
<td>2.4</td>
<td>0.394</td>
</tr>
<tr>
<td>WBC</td>
<td>9.3</td>
<td>15.9</td>
<td>0.017</td>
</tr>
<tr>
<td>INR</td>
<td>3.8</td>
<td>5.6</td>
<td>0.007</td>
</tr>
<tr>
<td>Ammonia</td>
<td>177.5</td>
<td>196</td>
<td>0.489</td>
</tr>
</tbody>
</table>

Conclusion: Other than well-known laboratory features of fulminant WD such as low ALP and low ALP/bilirubin values, we found that hypozincemia was more striking and hyperferritinemia was common, which might suggest their possible role in the development of a fulminant course in WD.

Vol. 64, Supplement 1, April 2017 682
also observed that plasmapheresis might have some benefits in some cases with fulminant WD, even leading to recovery, though LT is still the curative treatment for fulminant WD.
Liver copper concentration in differential diagnosis between presymptomatic Wilson disease and autoimmune hepatitis

Magdalena Naorniakowska¹, Maciej Dadalski¹, Piotr Socha¹

¹Children's Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Liver copper concentration is regarded to be a sensitive and specific diagnostic test in Wilson disease (WD). Concentrations above 250 µg/g dry weight have high Positive Predictive Value in adults, whereas concentrations below 50 µg/g practically exclude diagnosis of WD. Differential diagnosis of WD should include autoimmune hepatitis (AIH) with autoantibodies as one of the diagnostic criteria. However they can be positive in about 50% of WD patients. There is no data comparing specifically liver copper in children with WD and AIH.

Methods: 74 patients with WD diagnosed according to Ferenci score were the study group. 41 patients with AIH (diagnosis based on laboratory tests and liver biopsy) were the control group. They all have liver biopsy performed with liver copper measurement. Sensitivity and specificity were assessed for cutoff value of 250 µg/g and discriminant ability and optimal cutoff point were established with ROC curve analysis.

Results: Liver copper concentrations were 882; 626; 1124 [median, Q1, Q3] µg/g and 47,2; 28,37; 73 µg/g in the study and the control group, respectively. For cutoff point of 250 µg/g, the sensitivity was 0.96 (0.89; 0.99 [95% CI]) - 3 out of 74 patients had liver copper under 250 µg/g; and the specificity was 1 (0.91; 1) – all patients had liver copper below 250 µg/g. Area under ROC curve was 0.998. The optimal cutoff point for our groups was 304 µg/g with sensitivity 0.96 (0.89; 0.99) and specificity 1 (0.91; 1).

Conclusion: Liver copper concentration has high discriminant ability in differential diagnosis between presymptomatic WD and autoimmune hepatitis in children.
H- P-034

Etiology and prognosis of acute hepatic failure in children

Hoa Pham Anh Nguyen¹, Giang Thi Mai²

¹Vietnam National Hospital of Pediatric, Hepatology, Hanoi, Viet Nam
²Vietnam National Hospital of Pediatric, Hanoi, Viet Nam

Objectives and study: To study the etiology and prognosis of pediatric acute liver failure

Methods: The descriptive study of cases series 94 patients, who had acute failure as PALFSG

Results: Ninety-four children (55 males; median age: 10 months; Q1= 3 months–Q3= 4 years) were identified with acute liver failure based on criteria of PALFSG. Infants (44,7%) and young children (43,6%) were common age group. Median historical time 7 days (Q1= 4 days-Q3= 10 days). The etiologies were: metabolic disease (27,7%), infection (10,6%), drug-induced hepatotoxicity (6,4%), autoimmune hepatitis (4,3%), ischemic liver injury (3,2%) and indeterminate (47,9%). The statistical difference of etiology according to age groups was significant (p= 0,001). Poor prognosis, which was defined as liver transplantation or death within three months of admission, was 45,7%. Using ROC cut off for predictors of poor outcome was peak INR ≥ 4,2 with AUC = 0,74, sensitivity 72,1%, specificity 74,5%, positive predictive value 68,9%, negative predictive value 75,5%, p= 0,000

Conclusion: There are lot of etiology of acute hepatic failure still not define. INR ≥ 4,2 is one of predictor of poor prognosis
**A comparison between two causality assessment scales in Albendazole drug-induced hepatotoxicity**

Mihaela Claudia Nistor¹, Irina Dijmarescu², Andreia Florina Nita³, Luciana Zah¹, Daniela Pacurar⁴, Dumitru Oraseanu⁴

¹Grigore Alexandrescu Children’s Hospital, Paediatrics, Bucharest, Romania  
²“Grigore Alexandrescu” Emergency Children’s Hospital, Paediatrics, Bucharest, Romania  
³Grigore Alexandrescu Children’s Hospital and Carol Davila University of Medicine and Pharmacy, Paediatrics, Bucharest, Romania  
⁴“Grigore Alexandrescu” Emergency Children’s Hospital and “Carol Davila” University of Medicine and Pharmacy, Paediatrics, Bucharest, Romania

**Objectives and study:** Drug-induced liver injury (DILI) includes a variable clinical presentation forms, from asymptomatic patients with elevated liver enzymes to acute liver failure or chronic liver disease. DILI remains a diagnosis of exclusion and sometimes the diagnosis is difficult to establish. Two scores (RUCAM and Maria and Victorino scale) are used to objectively evaluate the probability of DILI. Albendazole, a frequently used antihelmintic is known for hepatotoxicity. In Romania it is widely used for supposed parasitic infections, often based on clinical criteria only. Our aim was to realise a comparison of these clinical scores for causality assessment in Albendazole induced hepatitis.

**Methods:** We performed a retrospective study in the Paediatric Department of „Grigore Alexandrescu” Emergency Children’s Hospital, between 1st of January 2009 and 1st March 2016. The data was collected by studying electronical and hardcopy records. After ruling out other causes of hepatitis we identified 18 patients with acute mild and moderate liver injury after Albendazole use for intestinal parasitoses. Hepatic biopsy was not necessary and the clinical evolution was good after non-specific symptomatic treatment. We assessed the causality by using two scales, RUCAM (Roussel Uclaf Causality Assessment Method) and Maria and Victorino (MV) scale, reffered to as the Clinical Diagnostic Scale (CDS).

**Results:** Both scores include the chronological criteria, course of the reaction, exclusion of other causes, rechallenge and previous information about hepatotoxicity. The elements that are different in RUCAM scale are risk factors and concomitant therapy, while the major addition of MV scale refers to extrahepatic manifestations.

In RUCAM scale the maximum value of the score ranges from 0 to 14 and the probability of the diagnosis was classified as “highly probable” (score >8), “probable” (6-8), “possible” (3-5), “unlikely” (1-2) or “excluded” (0).

The maximum value of the MV scale varies from -6 to 20, which corresponds to five probability degrees: “definite” (>17), “probable” (14-17), “possible” (10-13), “unlikely” (6-9), “excluded” (<6).

In our study the RUCAM scale showed a causal correlation between Albendazole intake and the liver injury event, highly probable in 2 cases, probable in 8 cases and possible in the other 8 cases.

MV score showed a definite causality in one case, probable in 6 cases, possible in 3 cases and unlikely in 8 cases. The score was lower in MV scale because of the lack of extrahepatic features in almost all cases (there were only 2 cases with peripheral eosinophilia). In the atypical cases, asymptomatic patients with elevated liver enzymes incidentally discovered or longer latency period the score dropped with 3 points, so was difficult to generate high scores and establish a good correlation.
Conclusion: The analysis of the scores indicated that RUCAM is a preferable instrument, showing a better discriminative power.

MV scale performs poor in atypical cases and is difficult to generate high scores and a good correlation.
**HEPATOLOGY: General Hepatology**

**H-P-036**

**Neonatal conjugated hyperbilirubinaemia and biliary atresia presenting before 14 days of life: observations from a single centre in Southeast Asia**

Fang Kuan Chiou¹, Fares Chedid², Ajmal Kader³

¹Kk Women's and Children's Hospital, Paediatric Gastroenterology, Singapore, Singapore
²Al Jalila Children's Specialty Hospital, Neonatology, Dubai, United Arab Emirates
³Al Jalila Children's Specialty Hospital, Paediatric Gastroenterology, Dubai, United Arab Emirates

**Objectives and study:** Conjugated hyperbilirubinaemia (CHB) in a neonate may be indicative of a serious hepatobiliary disorder such as biliary atresia (BA) or inborn errors of metabolism (IEM). As current guidelines recommend screening when jaundice is prolonged beyond 2 weeks, the true incidence and aetiology of CHB presenting before 14 days of life have not been well-defined. Published data suggest that diagnosis of serious conditions such as BA remains delayed in a significant proportion of infants and early detection within 14 days of life may lead to improved outcomes for these infants.

The primary objective is to define the aetiology and characteristics of CHB presenting in term infants within 14 days of life. The secondary objective is to describe the clinical course of infants diagnosed early with biliary atresia within 14 days of life.

**Methods:** Retrospective data collection was performed from medical records of consecutive term infants up to 28 days of age who presented with CHB at KK Women’s and Children’s Hospital in Singapore from 1 January 2010 to 1 January 2015. CHB is defined as conjugated bilirubin (CB) fraction greater than 15% of total bilirubin and CB greater or equal to 25µmol/L. Infants who had CHB detected within 14 days of life were categorised as ‘early-onset’ CHB (ECHB) group, while infants who presented with CHB at 15 – 28 days served as the comparator group and were referred to as ‘late-onset’ CHB (LCHB).

**Results:** Total of 117 term infants developed CHB during the neonatal period, 65 had ECHB and 52 had LCHB. Infants with ECHB were more likely to be clinically ill as compared to those with LCHB (80.0% vs 42.3%, p=0.000). In the subgroup of patients with ECHB who were clinically ill, 92.3% were due to secondary hepatic insult (Table), majority (87.5%) of whom had resolution of CHB without chronic liver disease. IEM made up 5.8% of this subgroup but was associated with 100% mortality in our series.

In well infants presenting with ECHB, the commonest cause was BA (61.5%). The indications for checking CB early in these well babies were suspected ‘bronze baby syndrome’ (38.5%), physician’s discretion (30.8%), antenatally detected hepatobiliary anomaly (15.4%) and non-specific gastrointestinal symptoms (15.4%). All of the infants with early presentation of BA proceeded to have an initial decline in total bilirubin levels while CB remained persistently elevated. None presented as an ill child or with pale stools at the outset.

**Table:**

<table>
<thead>
<tr>
<th>Aetiology</th>
<th>ECHB (N=65)</th>
<th></th>
<th>LCHB (N=52)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ill (N=52)</td>
<td>Well (N=13)</td>
<td>Ill (N=22)</td>
<td>Well (N=30)</td>
</tr>
<tr>
<td>Non-surgical Causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multifactorial liver injury</td>
<td>39 (75.0%)</td>
<td>0 (0)</td>
<td>18 (81.8%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Sepsis</td>
<td>9 (17.3%)</td>
<td>0 (0)</td>
<td>3 (13.6%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>Inborn errors of metabolism</td>
<td>3 (5.8%)</td>
<td>0 (0)</td>
<td>1 (4.5%)</td>
<td>0 (0)</td>
</tr>
<tr>
<td>CMV infection</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (6.7)</td>
</tr>
<tr>
<td>Idiopathic</td>
<td>0 (0)</td>
<td>5 (38.5)</td>
<td>0 (0)</td>
<td>21 (70.0)</td>
</tr>
<tr>
<td>Surgical Causes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biliary atresia</td>
<td>0 (0)</td>
<td>8 (61.5)</td>
<td>0 (0)</td>
<td>5 (16.7)</td>
</tr>
<tr>
<td>Choledochal cyst</td>
<td>1 (1.9%)</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td>2 (6.7)</td>
</tr>
</tbody>
</table>
Conclusions:

1. Real incidence of ECHB is unknown. However majority of the infants seem to have a non-hepatic aetiology for CHB.
2. In ill infants with ECHB, rare IEM are associated with high mortality. In the remaining infants, CHB is expected to resolve with supportive management.
3. BA is an important cause of ECHB in well-looking infants. In our series they did not present with pale stools and had improving total bilirubin levels initially.
4. Routine measurement of CB within the first 14 days of life may result in earlier detection of BA and other cholestatic liver diseases and potentially improve long-term outcomes.
Autoimmune hepatitis and other autoimmune associated disorders

Andreia Florina Nita1, Mihaela Claudia Nistor2, Alexandra Moraru3, Daniela Pacurar4, Dumitru Oraseanu4

1Grigore Alexandrescu Children’s Hospital and Carol Davila University of Medicine and Pharmacy, Paediatrics, Bucharest, Romania
2Grigore Alexandrescu Children’s Hospital, Paediatrics, Bucharest, Romania
3“Grigore Alexandrescu” Emergency Children’s Hospital, Paediatrics, Bucharest, Romania
4“Grigore Alexandrescu” Emergency Children’s Hospital and “Carol Davila” University of Medicine and Pharmacy, Paediatrics, Bucharest, Romania

Objectives and study: Several studies describe a variable rate of 7 to 21% of autoimmunity-related chronic inflammatory diseases in patients with autoimmune hepatitis (AIH). Concurrent immune disorders may mask the underlying disease leading to a delayed diagnosis and impact on long-term outcome. Worldwide there are few pediatric reports on this subject but lots of gaps in our knowledge. Due to a low prevalence prospective trials are not expected soon.

The objectives of this study were to identify patients diagnosed with AIH and AIH plus autoimmune associated disorders (AAD), to describe relationship (clinical and biochemical features) regarding onset and outcome and to identify any particularities and difficulties that may add to the knowledge on these rare entities.

Methods: We conducted a retrospective longitudinal descriptive population based study during 1st of January 2010-1st December 2016 in the Paediatric Department of “Grigore Alexandrescu” Children’s Hospital in Bucharest. We included 24 children diagnosed with AIH, out of which 11 were identified with other AAD. Cases were split into 2 groups: AIH with AAD and AIH without AAD. Diagnosis was established based on clinical, paraclinical (serological, biochemical) and histological studies after ruling out viral, metabolic and toxic etiology.

Results: Out of a total of 24 patients with AIH, 11 patients had AIH and different AAD as follows: 2 cases with AIH/Cholangitis overlap, 1 with AIH, Pancreatitis and Autoimmune thyroiditis, 1 case with AIH and Autoimmune haemolytic anemia (AHA), 3 cases with AIH and Medullary aplasia, 1 case with AIH overlap Wilson Disease and Medullary aplasia, 1 case with AIH and Ulcerative colitis and 2 cases with AIH and Celiac disease (CD). The age at diagnosis for AIH-AAD was distributed in 2 intervals: between 0 and 4 years 6 cases and 13-16 years 5 cases. Median age for AIH-AAD was 10 years, while for AIH without AAD was 7 years. Sex ratio was: 45.5 % females (F) and 54.5 % males (M) compared to 84.6%F:25.4%M for AIH without AAD. In AIH with AAD group, AIH was classified as: type I-1 case, type 2-1 case and unclassified (Cryptogenic chronic hepatitis) 9 cases while in AIH without AAD group, there were 10 cases type I and 3 type II. In 2 cases AAD (AHA and Ulcerative colitis) were diagnosed before AIH. All patients with AIH and Medullary aplasia were teenagers diagnosed with Medullary aplasia at 3-4 months after onset of AIH and the outcome was unfavourable, with deceases in short time in 3 cases. Two AIH-CD cases presented with symptoms of both affections; the outcome was favourable, both patients improved on diet without gluten. In AIH and AAD group 5 cases achieved remission after immunosuppressive therapy +/- diet. One patient (AIH/Cholangitis overlap) progressed to decompensated cirrhosis and underwent liver transplantation with a good response afterwards. Patient with AIH/AHA received Rituximab with a favourable response of AHA; in the follow-up he developed 2 episodes of marked hepatocytolysis and AHA. None of the patients from the AIH without AAD group have died.

Conclusion: One third of the total cases with AIH could not be classified according to International Autoimmune Hepatitis Group scoring system. Almost half of the patients (45%) with AIH were identified to have AAD. Sex ratio was inverted in favour of men compared to AIH without AAD sex distribution. Major therapeutic consequences resulted from AAD occurrence and the outcome was marked by the type of AAD.
**Objectives and study:** Extrahepatic biliary atresia (EHBA), the most frequent cause of liver transplantation during childhood, is a rare entity which is characterized by the obstruction or discontinuity of bile ducts. The aim of this study is to investigate the long term course of the patients with EHBA diagnosed and followed at one center.

**Methods:** Demographic, clinical, laboratory and diagnostic characteristics as well as prognostic factors and long term follow-up results of 81 biliary atresia patients treated between 1994-2014 at Hacettepe University Children’s Hospital Pediatric Gastroenterology, Hepatology and Nutrition Unit.

**Results:** Mean age at diagnosis was 73.1±4.7 days (median: 64 days). Male to female ratio was 1.53. Seventy-eight (96.3%) of the patients were operated. Mean age at operation was 76.8±4.7 (median: 72) days. Average follow-up duration was 3.5±1 years. Surgical success is found to be 60.5%. The only factor affecting surgical success is found to be the age at diagnosis younger than 60 days. Overall survival is found to be 66.2%.

The average age at diagnosis of the patients who are alive without complications is significantly lower than those who were dead (p=0.001). Among the eight patients followed up over 10 years, five had portal hypertension, gastroesophageal varices, hypersplenism, hepatopulmonary syndrome and malignancy. Univariate analysis revealed that good prognostic factors were the age at diagnosis lower than 60 days, age at operation lower than 70 days, initial ALT level lower than 81 IU/L, successful surgery; whereas the factors related to poor prognosis were the elevated prothrombin time (INR) at presentation, cirrhosis and/or fibrosis on the liver pathology. Successful surgery (p=0.016), presence of cirrhosis and/or fibrosis on the liver pathology (p=0.027) and prothrombin time (INR) at presentation (p=0.031) were the independent prognostic factors.

**Conclusion:** These findings lend support and add further dimensions to the previous literature. Considering the fact that early diagnosis and treatment is important for the outcome, initiating national screening programs, taking necessary precautions in order to prevent delayed diagnosis and referring biliary atresia patients to the experienced centers for operation are of great importance. Further long-term follow-up studies with larger cohorts may provide useful information regarding the optimal management of biliary atresia patients.
The association between white blood cell count and non-alcoholic fatty liver disease in pediatric obesity: results of the Beta-JUDO study

Katharina Paulmichl¹, Håkan Ahlström², Peter Bergsten³, Susanne Brunner⁴, Janne Cadamuro⁵, Marie Dahlbom⁶, Anders Forslund⁶, Joel Kullberg², Hannes Manell⁶, Jan Nasemann¹, Kirsten Roomp⁷, Kurt Widhalm¹, Fanni Zsoldos¹, Daniel Weghuber¹

¹Paracelsus Medical University, Department of Pediatrics, Salzburg, Austria
²Uppsala University, Department of Surgical Sciences, Radiology, Uppsala, Sweden
³Uppsala University, Department of Medical Cell Biology, Uppsala, Sweden
⁴Paracelsus Medical University, Laura Bassi Institute of Expertise - Therapep, Department of Pediatrics, Salzburg, Austria
⁵Paracelsus Medical University, Department of Laboratory Medicine, Salzburg, Austria
⁶Uppsala University, Department of Women’s and Children’s Health, Uppsala, Sweden
⁷University of Luxembourg, Clinical and Experimental Neuroscience, Luxembourg Centre for Systems Biomedicine (Lcsb), Esch-Belval, Luxembourg

Objectives and study: Non-alcoholic fatty liver disease (NAFLD) represents a major health issue in pediatric obesity. It has been associated to an elevated cardiovascular risk as well as insulin resistance and beta-cell dysfunction. The white blood cell count (WBC) is a well-established parameter of inflammation in clinical practice. Up to date, its relationship with pediatric NAFLD has not been assessed. Thus, the current study has examined this association in a large European pediatric obese cohort.

Methods: The Beta-JUDO (Beta-cell function in juvenile diabetes and obesity) study recruited 760 overweight as well as obese patients during 2012-2016 in two clinical centers in Austria and Sweden. The patients underwent elaborate clinical and laboratory phenotyping. NAFLD was defined biochemically (i.e. alanine aminotransferase or ALAT ≥ 24 IU/L; definition 1) and by assessing liver fat content (≥ 5%, definition 2) with magnetic resonance imaging. Participants diagnosed with alcoholic fatty liver disease, infectious and other metabolic causes of steatosis as well as acute signs of infection were excluded.

Results: Subject characteristics of both groups are presented as mean and standard deviation of the mean (Table 1.a. for NAFLD definition 1, Table 1.b. for definition 2). In the group using liver fat content WBC as well as high-sensitivity C-reactive protein (hs-CrP) were significantly elevated (p<0.01) in patients with NAFLD compared to non-NAFLD. In the other group defined using ALAT, WBC was significantly higher (p<0.05) in NAFLD patients, but hs-CrP was not significantly different compared to non-NAFLD, whereas TNF-alpha was significantly higher in NAFLD patients (p<0.01).
Table 1:

Table 1.a.: Subject characteristics – NAFLD vs. non-NAFLD according to liver fat content (≥5% vs. <5%).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (non-NAFLD/ NAFLD)</th>
<th>non-NAFLD (Mean ± SD)</th>
<th>NAFLD (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>89 / 99</td>
<td>13.97 ± 2.27</td>
<td>14.19 ± 2.32</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>89 / 99</td>
<td>38.2 %</td>
<td>65.7 %</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>88 / 99</td>
<td>1.99 ± 1.37</td>
<td>3.04 ± 0.56</td>
</tr>
</tbody>
</table>

Table 1.b.: Subject characteristics – NAFLD vs. non-NAFLD according to ALAT (≥24 IU/L vs. <24 IU/L).

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (non-NAFLD/ NAFLD)</th>
<th>non-NAFLD (Mean ± SD)</th>
<th>NAFLD (Mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>362/324</td>
<td>12.94 ± 2.92</td>
<td>13.48 ± 2.83</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>362 / 324</td>
<td>43.9 %</td>
<td>65.1 %</td>
</tr>
<tr>
<td>BMI-SDS</td>
<td>330/283</td>
<td>2.06 ± 1.44</td>
<td>3.00 ± 0.86</td>
</tr>
</tbody>
</table>

Conclusion: NAFLD is a major health issue in pediatric obesity and related to an elevated cardiovascular risk. This again is associated to subclinical inflammation, which can be diagnosed using various markers of inflammation. In our study we could show that NAFLD in pediatric patients is associated with an elevated WBC as sign of an inflammatory process.

Disclosure of interest: Katharina Paulmichl: no conflict of interest to disclose.
Håkan Ahlström: cofounder of and employed at Antaros Medical, Mölndal, Sweden.
Peter Bergsten: no conflict of interest to disclose.
Susanne Brunner: no conflict of interest to disclose.
Janne Cadamuro: no conflict of interest to disclose.
Marie Dahlbom: no conflict of interest to disclose.
Anders Forslund: no conflict of interest to disclose.
Joel Kullberg: cofounder of and employed at Antaros Medical, Mölndal, Sweden.
Hannes Manell: no conflict of interest to disclose.
Jan Nasemann: no conflict of interest to disclose.
Kirsten Roomp: no conflict of interest to disclose.
Kurt Widhalm: no conflict of interest to disclose.
Fanni Zsoldos: no conflict of interest to disclose.
Daniel Weghuber: no conflict of interest to disclose.
Use of Exome Aggregation Consortium data to identify pathogenicity of mutations and prevalence estimations in ultra-rare monogenic hepatic disorders

Jake Mann¹, Anna Carter², Patrick McKiernan³

¹University of Cambridge, Paediatrics, Cambridge, United Kingdom
²University College London, Medical School, London, United Kingdom
³Children’s Hospital of Pittsburgh of UPMC, Division of Gastroenterology, Hepatology and Nutrition, Pittsburgh, United States

Objectives and study: Identification of pathogenic mutations in ultra-rare conditions (those affecting <1/50,000) may be based on only a handful of exome sequences. Using small case series of a single ethnicity may result in incorrectly categorising a non-pathogenic polymorphism as a causative mutation. We aimed to demonstrate how large whole-exome databases may be employed to exclude polymorphisms as causative in rare paediatric liver diseases.

Methods: We searched MEDLINE, Online Mendelian Inheritance in Man (OMIM) database for ultra-rare (prevalence <1/50,000) paediatric, monogenic hepatic disorders. Conditions were then sorted into those primarily causing hepatocyte-mediated pathology. All reported pathogenic mutations were extracted from available literature, including ClinVar. Mutations were compared against population data (60,706 individuals) using the Exome Aggregation Consortium (ExAC) database (http://exac.broadinstitute.org) to classify mutations into: ‘congruous’, ‘borderline’, or ‘incongruous’ with the mutation’s population prevalence. Mutations were analysed through polyphen-2 and SIFT (Sorting Intolerant From Tolerant) to determine the pathogenicity of mutations. Combination of population allele frequency with method of inheritance allowed for estimation of prevalence.

Results: Database search yielded 98 ultra-rare paediatric monogenic conditions involving the liver. Mutations were analysed for 10 disorders that primarily affect hepatocytes, encompassing 190 mutations. From these, we found 175/190 mutations to be ‘congruous’, 8 ‘borderline’, and 7 as ‘incongruous’. For example, the suggested incidence of autosomal dominant polycystic liver disease type 2 was approximately 1/152 due to the high allele frequency (0.0033) of p.Glu568del mutation in SEC63. The calculated incidence of autosomal recessive infantile hypertriglyceridaemia was 1/26,000, from the p.Ile54Val mutation in GPD1 with an allele frequency of (0.0041).

Conclusion: These data illustrate how population-level whole-exome sequencing databases can be used to identify mutations that are more likely to be pathogenic in ultra-rare conditions and common. Several mutations may need to be re-classified as non-pathogenic. This process can be utilised by clinical genetics and genomics research to aid in correct identification of common mutations and to aid in the estimated prevalence of rare conditions.
Inflammatory myofibroblastic tumour of the biliary tract in a pediatric patient

Stephania Peña¹, Alejandra Calderon², Ana Maria Acevedo², Jacqueline Mugnier³, Felipe Ordoñez⁴

¹Instituto Nacional de Pediatría, Gastroenterology and Nutrition, Mexico City, Mexico
²Universidad de la Sabana, Pediatrics, Bogota, Colombia
³Fundación Cardioinfantil Instituto de Cardiología, Pathology, Bogota, Colombia
⁴Fundación Cardioinfantil Instituto de Cardiología, Gastroenterology and Hepatology, Bogota, Colombia

Objectives and study: To describe a case of inflammatory liver pseudotumor which required liver transplantation.

Methods: Case report

Results: A 10 years-old patient coursing with two months with jaundice, choluria, acholia, right hypochondrium abdominal pain. Imaging studies showed dilation of the intrahepatic biliary tract and amputation of the hepatic ducts. Serum studies showed direct hyperbilirubinemia, elevated transaminases and high alkaline phosphatase. Negative infectious profile and tumor markers. Percutaneous biopsy reported epithelial malignancy. Endoscopic retrograde cholangiopancreatography was performed, and no external stent placement was possible. The hepatobiliary and transplant surgery workgroup considered an obstruction of the bile hepatic ducts secondary to a benign tumor without resection option, being a candidate for liver transplantation. A cadaveric donor transplant was performed, during the procedure a nodule was found in the greater gastric curvature and was resected. In the histologic evaluation of the hepatobiliary lesion, myofibroblastic proliferation with estorifome pattern, IgG4 positive immunophenotype, smooth muscle actin, vimentin, H-Caldesmon, ALK-negative, compatible with inflammatory myofibroblastic tumor associated with IgG4 disease of the bile confluent was described. The gastric lesion was reported as a fibrous tumor positive for IgG4. Seven months after transplantation the patient has no evidence of relapse and receives immunosuppressive management.

Conclusion: IgG4-related liver inflammatory pseudotumor not associated with autoimmune pancreatitis should be considered as a differential diagnosis of liver tumors in children. The finding of the gastric tumor seems to correspond to the involution of a myofibroblastic tumor, probably prior to the biliary tumor.
Clinical and molecular characterization of patients with childhood-onset Wilson’s disease - a single center study

Ana Sánchez-Monteagudo1, Begoña Polo2, Vincenzo Lupo1, Isabel Sastre3, Irene Martínez3, Marina Berenguer Haym4, Carmen Espinós1

1Centro de Investigación Príncipe Felipe (Cipf), Unit of Genetics and Genomics of Neuromuscular and Neurodegenerative Disorders, Valencia, Spain
2La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
3Hospital Universitari i Politècnic La Fe, Department of Neurology, Valencia, Spain
4Hospital Universitari i Politècnic La Fe, Department of Gastroenterology, Valencia, Spain

Objectives and study: Wilson’s disease (WD) is an autosomal recessive disorder caused by mutations in the liver’s copper-transporter protein ATP7B, which results in an impaired biliary excretion of copper and its accumulation in many organs and tissues, mostly in liver and brain. Patients usually present with hepatic problems and some of them with neurological symptoms as well. Genetic testing allows for an early diagnosis and effective treatment and it should be performed in patients with clinical suspicions and to screen asymptomatic siblings. The aim of this study is to perform a clinical and molecular characterization of a cohort of WD patients from the Valencian Region (Eastern Spain; population: 4,932,906), with the purpose of improving clinical diagnosis and prognosis of these patients.

Methods: A clinical series of 10 paediatric (aged 6.86 ± 4.95 years) and 7 adult index cases with childhood-onset WD and in chelation therapy since clinical diagnosis (age at diagnosis 9.57 ± 2.76 years) retrospectively studied. All patients are supervised at the same referral center. Differential diagnosis based on routine tests (serum ceruloplasmin and free copper, 24h urinary copper) as well as other hepatic parameters and genetic studies. Neurological involvement was evaluated with the Global Assessment Scale (GAS) for WD. Genetic analysis of ATP7B included the study of the promoter, coding exons and its flanking intronic regions by Sanger sequencing, and the detection of large deletions and duplications by multiplex ligation-dependent probe amplification (MLPA) analysis.

Results: Genetic diagnosis was achieved in 9 cases; only one mutation was detected in 4 cases; and no candidate mutations were identified in 4 cases. The most common mutations in our cohort were p.M645R, (17.6% of the alleles), and p.Q111X, (11.8% of the alleles), both in compound heterozygous status with other rare disease-causing variants. In all cases, clinical presentation was hepatic. Interestingly, some adult patients (aged 36.14 ± 10.38) present with neurological signs (tremor, dystonia and parkinsonism) in recent evaluations.

Conclusion: The genetic studies performed in our cohort contribute to improve knowledge about the clinical variability appreciated in them. Despite of chelation therapy, in some cases neurological signs persist. An in-depth clinical assessment is relevant in order to establish if these manifestations are really due to the presence of copper deposits in brain.

Funding: Fundació Per Amor A L’Art.
**Gamma glutamyl transferase activity in infants: what is breastfeeding role?**

Giusy Ranucci¹, Chiara Vitiello¹, Francesco Nunziata¹, Antonietta Giannattasio¹, Maria Immacolata Spagnuolo¹, Raffaele Lorio¹

¹University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy

**Objectives and study:** Serum gamma glutamyl transferase (GGT) is the main cholestatic marker in children. GGT activity depends largely from genes, but a lot of factors and conditions (hepatic and extrahepatic) may influence its values. GGT is higher in neonatal care intensive unit (NICU) patients. No studies have been conducted in healthy infants. It has not been clarified if feeding patterns in the first months of life may influence GGT activity.

**Methods:** We enrolled 180 infants (92 males) followed from January 2014 and January 2016 at the reference perinatal infections unit of University Federico II of Naples, for an history of perinatal TORCH exposition but with a final diagnosis of “non infected”. As exclusion criteria we considered: APGAR score below 7, any other liver, systemic or genetic conditions, infections in the first months of life, NICU admission, birth weight below 2.5 Kg, presence of mother diseases during gestational period. We retrospectively analyzed all available serum parameters including GGT, AST, ALT, total bilirubin (TB) and ferritin (FE) and their trend in the first year of life (first determination/basal 0-2 months of age; second determination 2-4 months; third determination 11-12 months). For the analysis we considered three group of patients: infants fed breast milk (BF), infants fed breast milk plus formula (MF), infants fed formula (FF).

**Results:** Mean basal GGT levels (mean age 36 days) was 66.7 UI/L (range 6-259 UI/L). GGT was significantly higher in BF group than FF (p: 0.043). In all groups GGT levels decreased progressively over time (p<0.01). Basal ALT and AST values were not different among three groups and they did not modify over time. Basal TB levels resulted significantly higher in BF patients (p:0.018), with levels that decreased over time. We found a direct correlation between GGT and TB values (R: 0.04). Basal FE levels resulted higher in BF patients than FF (p:0.018), with a significant reduction over time in all patients. GGT activity seemed linearly related to FE levels (R:0.02). GGT activities resulted slightly higher in males, but this finding was not significant. Type of delivery did not influence GGT activity.

**Conclusion:** In the first months of life GGT limits of normal are higher in healthy infants than adults. GGT seems influenced by the type of feeding and in particular breast milk induces positively GGT, BT and FE levels. The link between these parameters and breast milk has to be clarified.
**HEPATOLOGY: General Hepatology**

H-P-044

**Biliary features in children with autoimmune hepatitis**

Antonio Marseglia¹, Andrea D'Adda¹, Aurelio Sonzogni², Lisa Licini², Paolo Brambilla³, Michela Bravi¹, Valeria Casotti⁴, Lorenzo D'Antiga⁴

¹Paediatric Hepatology, Gastroenterology and Transplantation, Hospital Papa Giovanni XXIII, Bergamo, Italy
²Liver Pathology, Hospital Papa Giovanni XXIII, Bergamo, Italy
³Department of Radiology, Hospital Papa Giovanni XXIII, Bergamo, Italy
⁴Papa Giovanni XXIII Hospital, Paediatric Hepatology, Gastroenterology and Transplantation Unit, Bergamo, Italy

**Objectives and study:** The clinical and histological features of Autoimmune hepatitis (AIH) in children are commonly associated with abnormalities of the biliary tree that can be demonstrated at cholangiography, making a picture overlapping with sclerosing cholangitis (SC), defined autoimmune sclerosing cholangitis (ASC). Primary sclerosing cholangitis (PSC) in children is much less common. AIH and ASC are also referred to as autoimmune liver disease (AILD). In this study we aimed at re-evaluating the liver biopsies performed at presentation in children with AILD to see whether histological biliary involvement may distinguish AIH from ASC.

**Methods:** We reviewed retrospectively the medical records of paediatric patients with AILD (AIH or ASC) between 2003 and 2015. Patients with a diagnosis of PSC or secondary SC were excluded from the study, as well as those in whom either histology or cholangiography was not available. All patients underwent a liver biopsy at presentation before the treatment start. The histology slides were retrieved and reviewed blindly and independently by two expert liver pathologists. Inflammation and fibrosis were evaluated and graded according to the Ishak score. In order to better characterize the biliary involvement, we built a detailed score expanding a previously reported grading system adopted for PSC in adults (Ludwig J. Am J Surg Pathol 1989;13 Suppl 1;43-9).

**Results:** 20 children with AIH (median age 10.7 years, 16 female) and 9 with ASC (10.1 years, 6 females) were compared. AST, ALT, GGT, Bilirubin, ALP, AST/ALP, INR and immunoglobulin levels, autoantibodies type and titres did not differ. All patients had interface hepatitis, more prominent in ASC, although not reaching statistical significance. Fibrosis score was 2.7 vs 2.4 (p=NS), inflammation 7.3 vs 8.6 (p=NS), biliary score 6.1 vs 6.8 (p=NS) in AIH and ASC respectively. Bile duct inflammation was more prominent in ASC (p=0.04), but bile duct injury was present in all 29 patients. Periductular fibrosis was observed in 10/20 AIH patients.

**Conclusion:** Our study shows that in children AIH and ASC at diagnosis are indistinguishable on histological ground, since both share the presence of biliary features on liver biopsy. Cholangiography remains the only tool to differentiate AIH from ASC in children. Further studies on larger groups of patients and with longer follow up are required to better understand the determinants of biliary involvement and its progression in paediatric AILD.
**HEPATOLOGY: General Hepatology**

H-P-045

**Predictors of outcome in patients with neonatal hepatitis**

Almida Reodica¹, Randy Urtula¹, Maria Estela Nolasco¹

¹Philippine Children's Medical Center, Section of Pediatric Gastroenterology, Hepatology and Nutrition, Quezon City, Philippines

**Objectives and study:** Very few studies on neonatal hepatitis (NH) prognostication are available in Asia. This current research was undertaken to augment the lack of information locally by determining factors that affect outcome in patients with NH.

**Methods:** All patients with jaundice before 4 months old not associated with biliary obstruction seen from July 2013 to February 2014 at a pediatric tertiary hospital in Quezon City, Philippines were recruited in this prospective cohort study. 3 visits were done 3 months apart where baseline data, nutritional status, complications, bilirubin, alanine amino transferase (ALT), international normalized ratio (INR) and albumin were evaluated to determine significant associations with poor outcome.

**Results:** Fifty subjects with NH participated in the study. The population had a slight male predominance, majority having idiopathic NH (88%). The 1st visit showed majority had malnutrition (56%), bilirubin levels >3mg/dl (100%) ALT >3 times normal (70%), albumin >35mg/dl (56%) and INR <1.5 (94%). Forty four percent of the subjects had poor outcome by the 6th month follow-up with majority of complications coming from third spacing of fluids (73%), and gastrointestinal bleeding (59%). Age of onset of jaundice, bilirubin levels and ALT had no association with outcome. The factors that are significantly associated with complications and mortality are nutritional status, albumin, and INR.

**Conclusion:** The predominant cause of NH is idiopathic with a slight male predominance, and with a majority having malnutrition. Early laboratory results in NH show evidence of liver injury with impaired excretory function but intact synthetic liver capacity. The factors that are significantly associated with complications and mortality are severe malnutrition, low albumin and elevated INR. These factors could be used to determine which patients need closer monitoring in anticipation of complications as well as to develop a scoring system to predict NH prognosis.
Seronegative autoimmune hepatitis: search and treat strategy

Ignacio Ros¹, Lorena Lahilla¹, María Luisa Baranguan¹, Ruth García Romero¹,
Eduardo Ubalde Sainz¹, Jose Miguel Martinez de Zabarte¹, Monica López Campos¹

¹Miguel Servet Children's Hospital, Pediatric Gastroenterology and Nutrition Unit, Zaragoza, Spain

Objectives and study: Recently, a paper describing children with seronegative Autoimmune Hepatitis (snAIH) has been published (Maggiore G et al. Dig Liver Dis. 2016). This is described as a similar condition to the classic autoimmune hepatitis (cAIH) but the autoantibodies are absent and the serum gamma globulins can be normal, although the histological features are compatible with an autoimmune hepatitis.

Our objective was to review the children of our Paediatric Gastroenterology Unit, diagnosed with idiopathic chronic liver disease in whom the biopsy showed advanced fibrosis or cirrhosis, to rule out the possibility of an undiagnosed snAIH, and to treat them if necessary.

Methods: We reviewed 4 cases of idiopathic liver cirrhosis, in which other possibilities had been excluded: Infectious, celiac, thyroid, metabolic or neuromuscular diseases, drug-induced or neoplastic disorders or alph-1 antitrypsin deficiency. The autoantibodies were negative and the cAIH diagnosis had not been proposed by the pathologist.

Results: After discussing with the pathology team, they suggested the diagnosis of snAIH in two out of the four cases. We describe data, treatment and outcomes of these two cases diagnosed with snAIH.

Case 1 was a 12-year old boy that presented with elevated liver enzymes detected 3 years before, without any known cause and being asymptomatic. Case 2 was a 6-year-old girl, diagnosed with celiac disease 3 years before, that showed elevated liver enzymes prior to celiac diagnosis, and she was following a gluten free diet since the diagnosis of celiac disease

Both cases had normal serum gamma globulins concentration, and no specific autoantibodies or blood diseases. The liver biopsy review showed cirrhosis and plasma cell infiltration, interface hepatitis in case 1 and necrosis in case 2. No “rosette” formation was observed.

After assessment of this findings, snAIH diagnosis was suggested, so oral prednisone treatment (2 mg/kg/day) was initiated, being later gradually decreased to 2.5 mg every 48 hours, and azathioprine was added (1 mg/kg/day), being afterwards gradually increased to 2.5 mg/kg/day.

Three months after the beginning of the treatment, liver enzymes were normal in both cases (Table).
**Conclusion:** In our experience the histology review with the pathologist searching for snIAH led to a new diagnosis and allows an effective treatment for these patients.

As the snIAH has been described in children, currently it is mandatory to assess this diagnosis in patients with idiopathic liver enzyme alterations and advanced fibrosis or cirrhosis.

To perform a proper diagnosis and treatment of the snIAH is highly recommendable in order to avoid progression of liver disease.

<table>
<thead>
<tr>
<th></th>
<th>Before liver biopsy</th>
<th>Beginning of the treatment</th>
<th>Three months after</th>
<th>Six months after</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Case 1</strong></td>
<td><strong>AST (U/L)</strong></td>
<td>62-325</td>
<td>89</td>
<td>31</td>
</tr>
<tr>
<td></td>
<td><strong>ALT (U/L)</strong></td>
<td>100-430</td>
<td>163</td>
<td>58</td>
</tr>
<tr>
<td><strong>Case 2</strong></td>
<td><strong>AST (U/L)</strong></td>
<td>80-630</td>
<td>82</td>
<td>26</td>
</tr>
<tr>
<td></td>
<td><strong>ALT (U/L)</strong></td>
<td>90-820</td>
<td>93</td>
<td>22</td>
</tr>
</tbody>
</table>
Paritaprevir/Ritonavir/Ombitasvir plus Rivabirin in a child with hepatitis C virus infection

Ignacio Ros¹, María Luisa Baranguan¹, Ruth García Romero¹, Eduardo Ubalde Sainz¹, Sara Feo Ortega¹, Monica López Campos¹, Jose Miguel Martinez de Zabarte¹

¹Miguel Servet Children's Hospital, Pediatric Gastroenterology and Nutrition Unit, Zaragoza, Spain

Objectives and study: Direct-acting antiviral (DAA) medications have been approved and have shown a high response without important side effects in adult patients. Currently their use in children has not been approved and few data about security and efficacy is available. Our objective is to describe the outcome of a child treated during 12 weeks with a DAA drug.

Methods: Our patient is a 12-year old child diagnosed with genotype 4 Chronic Hepatitis C infection due to vertical transmission. He had been followed in another centre and received treatment with Peg-Interferon 2b plus rivabirin (PEG-IFN/RBV) when he was 6 years old during 12 weeks without response.

When he moved to our city (January 2016), we found liver enzyme alteration (Table) and a nodular enlarged liver in the ultrasound study. The liver stiffness measured by transient elastography (Fibroscan device®) was 21 KPa related to severe fibrosis (F4). A liver biopsy showed mild inflammatory activity, moderate chronic hepatitis and cirrhosis. After discussing with the family, a DAA treatment was requested to the hospital drugs committee for off-label use. Following the American Association for the Study of Liver Diseases (AASLD) recommendations for adult patients with HCV genotype 4 infection who have compensated cirrhosis, in whom prior treatment with PEG-IFN/RBV has failed, we proposed for our 45 kilograms child a daily fixed-dose combination of PrO; paritaprevir (150 mg)/ritonavir (100 mg)/ombitasvir (25 mg) and ribavirin for 12 weeks.

Results: The request was approved and the patient received PrO plus ribavirin 600mg during 12 weeks, without developing any side effects. The VHC real time polymerase chain reaction value was not detectable after the treatment, and all the laboratory tests became normal (Table).

Table:

<table>
<thead>
<tr>
<th></th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
<th>AFP ng/ml</th>
<th>Bile acids mmol/l</th>
<th>HCV PCR (IU/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Week 0</td>
<td>159</td>
<td>113</td>
<td>105</td>
<td>127</td>
<td>6064299</td>
</tr>
<tr>
<td>Week 12</td>
<td>39</td>
<td>25</td>
<td>4</td>
<td>12</td>
<td>Not detected</td>
</tr>
</tbody>
</table>

Conclusion: The use of PrO plus ribavirin in a child with compensated cirrhosis secondary to chronic HCV genotype 4 infection after failing PEG-IFN/RBV treatment was safe and effective.

The clearance of the HCV led to a rapid improvement in hepatic function in our patient
Antibiotics induce remission in pediatric PSC-AIH overlap syndrome allowing corticosteroid-free therapy

Pauline Sambon¹, Varma Sharat¹, Mina Komuta², Philippe Clapuyt³, Etienne Sokal⁴

¹Cliniques Universitaires Saint-Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
²Clinique Universitaire St Luc, Pathology, Brussels, Belgium
³Cliniques Universitaires Saint-Luc, Pediatric Radiology Unit, Brussels, Belgium
⁴Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Objectives and study: Concomitant presence of autoimmune hepatitis (AIH) and primary sclerosing cholangitis (PSC) is labelled as AIH-PSC overlap syndrome or autoimmune sclerosing cholangitis (ASC). Treatment of AIH with corticosteroids and azathioprine; and of the PSC component with ursodeoxycholic acid (UDCA) is the standard practice. Antibiotics are increasingly being shown to have benefit in PSC but their role in paediatric ASC is not well evaluated. We investigated the response to oral antibiotics as initial or subsequent therapy in children with ASC.

Methods: Patients diagnosed with ASC on basis of biochemical, liver biopsy and radiology findings were included. They received metronidazole or vancomycin for 14 days [10-220] either at diagnosis (i.e. initial therapy) or during their maintenance period. When antibiotics were administered as initial therapy, steroid free induction regime was adopted. In children during the maintenance phase antibiotics were administered if they had not achieved biochemical remission with their standard treatment of steroids, azathioprine and UDCA. The outcome parameters to assess the efficacy of antibiotics were achievement of biochemical remission and additionally steroid avoidance when given in the initial therapy.

Results: Ten children with ASC were included, of which 6 received oral antibiotics (4 metronidazole, 2 vancomycin) at diagnosis and 4 received metronidazole during the maintenance period. All patients showed a significant decrease in their AST (-55%, p=0.005), ALT (-84%, p=0.003) and GGT (-53%, p=0.003), without significant difference across the two groups. All six children in the initial therapy group did not need corticosteroids and continued to be in remission until last follow up duration of 400 days [216-888]. Among the four children administered antibiotics in the maintenance phase, two showed biochemical remission and steroids could be tapered; while two did not show any benefit. There was transient biochemical relapse after stopping antibiotics in one responder, for which they were restarted and continued until last follow up while continuing to be in remission.

Conclusion: We demonstrate the benefit of antibiotics in ASC by achieving steroid free treatment when given at diagnosis as induction regime. When given in the maintenance phase they assist in achieving long term biochemical remission in an otherwise uncontrolled ASC.
Novel AKR1D1 gene mutation in two Colombian patients with congenital defect of bile acid synthesis type 2

Alfredo Santamaría¹, María Elsy Sepúlveda-Hincapié², Patricia Ruiz Navas², Catalina Ortiz², Ana Cristina Ortiz¹, Juan Camilo Pérez Cadavid², Jorge Hernán Montoya¹, Beatriz Helena Aristizabal², Carolina Baquero Montoya²

¹San Vicente Fundación, Medellín, Colombia
²Hospital Pablo Tobón Uribe, Medellín, Colombia

Objectives and study: Bile acid synthesis defects (BASD) are uncommon genetic disorders leading to persistent cholestasis in infants. The associated liver diseases may be life threatening, and are treatable usually by replacement of deficient primary bile acids. To date, the few reported cases of BASD have been described in Europe, Asia and North America, none in Latin America. Most of the described patients have deficiency of 3β-hydroxy-Δ5-C27-steroid dehydrogenase [3β-HSD / HSD3B7] and less than 10 patients Δ4-3-oxosteroid-5β-reductase [Δ4-3-oxoR / AKR1D1]. Here, we report on two Colombian patients with cholestasis from the first months of life, in whom elevated 3-oxo-Δ4 bile acids in urine by gas chromatography–mass spectrometry was detected as well as a homozygous de novo mutation in AKR1D1.

Methods: Patient 1, is a 9 months of age Colombian girl, who from the first month of life presented progressive jaundice with liver dysfunction, diarrhea due to malabsorption of fat, coagulopathy, hepatomegaly and a fine tremor in the extremities. Basic biochemical tests including GGT as well as liver biopsy were initially taken. Subsequently, urine bile acids analysis by gas chromatography-mass spectrometry (GC-MS) was performed and whole exome sequencing.

Patient 2, is a 10 months of age Colombian girl, who from the first month of life presented progressive jaundice with liver dysfunction and hepatomegaly. Basic biochemical tests including GGT as well as liver biopsy were initially taken. Subsequently, urine bile acids analysis by GC-MS was performed and whole exome sequencing.

Results: Both initial biochemical tests showed increase in AST and ALT with prolongation of coagulation times and a normal GGT. The liver microscopic findings included giant cell transformation and wide fibrotic bands at portal areas. Urine bile acids using GC-MS demonstrated absence of allo cholic acid with an increase of oxo bile acids, typical of Δ4-3-oxosteroid-5β-reductase deficiency. Whole exome sequencing demonstrated a de novo homozygous mutation in AKR1D1 (c.332T>C; p.Leu111Pro).

Conclusion: The description of these two cases confirmed the presence of patients with BASD, Δ4-3-oxosteroid-5β-reductase deficiency, in Latin America, expanding the clinical spectrum as well as the reported mutations in AKR1D1.
The significance of supportive treatment by selective plasma exchange in children with liver failure

Nilüfer Ülkü Şahin¹, Derya Altay², Taner Özzür¹, Ayşegül Otuzbir³, Ali Gü³, Tanju Başarır Özkan¹

¹Uludag University Faculty of Medicine, Department of Pediatric Gastroenterology, Bursa, Turkey
²Fırat University Faculty of Medicine, Pediatric Gastroenterology, Elazığ, Turkey
³Uludag University Faculty of Medicine, Bursa, Turkey

Objectives and study: Acute liver failure is defined as an occurrence of liver failure within weeks and/or months in people without pre-existing liver disease knowledge. While in the neonatal period metabolic diseases are in the forefront, in older children infections, drugs and toxins take the first place.

Methods: Cases applied within the last two years with a liver failure, performed therapeutic and bridge aimed selective plasma exchanges were included in the study.

Results: Thirteen patients under follow up with an acute liver failure were included in the study. Six of the patients were female and 7 of them were male. The ages of our patients ranged from 18 months to 17 years. Two of our patients were diagnosed with autoimmune hepatitis, 1 of them with obstructive hepatitis, 4 of them with toxic hepatitis and 6 of them with decompensated Wilson’s disease. Average selective plasma exchanges of our patients were initialized in between 24 to 72 hours of their hospital stay. In average, 1 to 10 cycles of selective plasma exchange were performed on our patients. Baseline values of our patients were in between; total bilirubin: 1.8- 52.4 mg/dl, direct bilirubin: 1.15-25.8, AST: 71-19061 İÜ/L, ALT: 51-8819 İÜ/L, PT : 11.0-22.8 seconds, PT%: 19.2-98, INR: 1.04-5.9, Ammonia: 54-424 mg/dl, Albumin: 2.9-5.4 mg/dl. Hospital leave values of our patients were in between; total bilirubin : 0.31-28.8 mg/dl, direct bilirubin: 0.16-18.9, AST: 21-515 İÜ/L, ALT: 25-513 İÜ/L, PT : 11.2-21.0 seconds, PT%: 12.3-92, INR: 1.01-5.15, Ammonia: 49-158 mg/dl, Albumin: 3.1-4.3 mg/dl. In overall, a progress in the laboratory values of patients, complete recovery especially on the ones with acute liver failure resulting from toxic reasons was observed.

Conclusion: As selective plasma exchange can be performed as a bridge treatment until liver transplantation process in patients without pre-existing liver disease knowledge but with a decompensated chronic liver disease resulting from infections or toxic substance intake, it can also lead to complete recovery in patients without any previous liver disease but developed acute liver failure as a result of toxic substance ingestion.
Therapeutic experience in children with congenital portosystemic shunt from Turkey

Sinan Sarı1, Ali Harman2, Koray Akkan3, Aydı̇n Dalgı̇ç4, Fatih Boyvat2, Baran Önal2, Erhan Ilgıt3, Buket Dalgı̇ç1

1Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
2Başkent University, Radiology, Ankara, Turkey
3Gazi University, Radiology, Ankara, Turkey
4Gazi University, General Surgery, Ankara, Turkey

Objectives and study: Congenital portosystemic shunts (CPS) are uncommon abnormalities of the portal venous system resulting in the diversion of portal blood away from the liver to the systemic venous system. CPS may lead to severe complications such as cholestasis, hepatic encephalopathy, hepatopulmonary syndrome and tumors. In here we describe the clinical and imaging features of six children with CPS in our clinic.

Methods: The diagnostic imaging and medical records for children with CPS were retrieved and evaluated in our institution.

Results: Six patient (two females, four males) was diagnosed as CPS. The age at diagnosis ranges from 30 months to 16 years. The patients presented with hepatic encephalopathy (2), hepatopulmonary syndrome (1), portopulmonary hypertension (2). CPS was detected in one patient incidentally. The portosystemic shunt was extrahepatic (5) or intrahepatic (1). Portosystemic shunts were closed by endovascular methods in 3 children and surgically in 1 patient. Shunt closure resulted in restoration of intrahepatic portal flow in all, with complete regression or stabilization of pulmonary, cardiac and neurological complications. The results are summarized in Table.
### Table:

<table>
<thead>
<tr>
<th>Patient no.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>F</td>
<td>M</td>
<td>M</td>
<td>F</td>
<td>M</td>
<td>M</td>
</tr>
<tr>
<td>History</td>
<td>Vertebral malformation</td>
<td>Congenital cardiac abnormality</td>
<td>Cholestatic jaundice at neonatal period</td>
<td>Cholestatic jaundice at neonatal period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Presentation</td>
<td>Incidentally</td>
<td>Growth retardation</td>
<td>PPH</td>
<td>HE</td>
<td>FNH</td>
<td>HPS</td>
</tr>
<tr>
<td>Age at diagnosis, year</td>
<td>2.5</td>
<td>9</td>
<td>2.5</td>
<td>14</td>
<td>6</td>
<td>11</td>
</tr>
<tr>
<td>Type of shunt</td>
<td>End-to-side between PV and IVC</td>
<td>End-to-side between right PV and IVC</td>
<td>End-to-side between PV and IVC</td>
<td>End-to-side between PV and IVC</td>
<td>End-to-side between PV and IVC</td>
<td></td>
</tr>
<tr>
<td>PP after occlusion test, mmHg</td>
<td>None</td>
<td>20</td>
<td>26</td>
<td>14</td>
<td>22</td>
<td>55</td>
</tr>
<tr>
<td>Treatment</td>
<td>None</td>
<td>Radiological closure with covered stent in IVC</td>
<td>Radiological closure with covered stent in IVC</td>
<td>Surgical closure in one step</td>
<td>Radiological closure with Amplatzer plug</td>
<td>Surgical closure in two step was planned</td>
</tr>
<tr>
<td>Follow-up time after closure</td>
<td>-</td>
<td>4,5 years</td>
<td>4,5 years</td>
<td>8 months</td>
<td>2 months</td>
<td>-</td>
</tr>
</tbody>
</table>

F, female; M, male; PP, portal pressure; PV, portal vein; IVC, inferior vena cava; HE, hepatic encephalopathy; HPS, hepatopulmonary syndrome; PPH, portopulmonary hypertension; FNH, focal nodular hyperplasia

**Conclusion:** Congenital portosystemic shunt should be kept in mind in differential diagnosis of the patients with neonatal cholestasis, encephalopathy, and cyanosis. Closure of shunt by radiological or surgical is successful treatment method in CPS.
Use of thiopurine metabolite levels in children with autoimmune hepatitis

Elias Jahjah1, Oren Ledder2, Orit Pappo3, Raffi Lev-Tzion2, Ami Ben Ya'acov1, Eyal Shteyer2

1Shaare Zedek Medical Center, Pediatric Gastroenterology Institute, Jerusalem, Israel
2Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel
3Hadassah Medical Center, Department of Pathology, Jerusalem, Israel

Objectives and study: The mainstay of treatment for autoimmune hepatitis (AIH) is prolonged immunosuppression, usually achieved by corticosteroid induction with sustained azathioprine (AZA) maintenance. Measurement of AZA metabolites is widely used in the treatment of inflammatory bowel disease but is not well established in AIH. This study aims to report a single center real life experience of the use of AZA metabolites in children with AIH.

Methods: 6-thioguanine (6-TGN) and 6-methyl-mercaptopurine (6-MMP) levels were measured in children treated with AZA for AIH. Parameters of biochemical and histological inflammation were assessed in relation to drug metabolite levels.

Results: Seventeen children (59% female; mean age 10.4 years, range 1-15 years) were included in the study. Of 21 metabolite measurements, 13 were taken at time of liver biopsy. Only four children had elevated liver enzymes, of which 3 had low 6-TGN. Of the whole cohort, 15 children had signs of biochemical or histological inflammation, of which 11 (73%) had low levels of 6-TGN as opposed to one (25%) of children with no sign of inflammation. In some children with low 6-TGN levels, adjustment of AZA dose improved inflammation and prevented steroids treatment.

Conclusion: Most children with evidence of inflammation had low AZA metabolite levels were low and underwent dose adjustment. AZA metabolite monitoring in pediatric AIH is useful in identifying patients who are receiving inadequate immunosuppression according to current recommended doses. Further, larger prospective studies are needed to corroborate our findings.
Infections in children and adolescents with cirrhosis due to biliary atresia: frequency and involved agents

Joel Stefani¹, Bruna Enzveiler¹, Sandra Maria Gonçalves Vieira², Camila Smid¹, Carlos Kieling³, Carolina Mariano da Rocha⁴

¹Universidade Federal Do Rio Grande Do Sul / Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
²Universidade Federal Do Rio Grande Do Sul / Hospital de Clínicas de Porto Alegre, Pediatria, Porto Alegre, Brazil
³Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
⁴Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil

Objectives and study: The aim of this study is to identify the features of first infections in children with the diagnostic of cirrhosis due to Biliary Atresia (BA) admitted in a tertiary hospital, the patients’ age at the moment of diagnosis of infection, the etiological agents, the spectrum of acquisition of infection, and the outcome of the clinical condition.

Methods: It is a cross-sectional study that included patients between six months and eighteen years old admitted from January 1999 to February 2015 at Hospital de Clínicas de Porto Alegre (HCPA). Clinical and epidemiological data were assessed from electronic medical records from Pediatric Gastroenterology unit. Three classifications to the spectrum of acquisition of infections were predetermined as follows. Nosocomial infection (NI): infection that occurs 48 hours after the patient is admitted; Health-Care Associated Infection (HAI): infection during the first 48 hours of hospitalization with one of the following criteria: (1) hospitalization ≥ two days or surgery in the prior six months, (2) outpatient care in the prior 30 days or (3) residency in nursing home or a long-term care facility; Community Infection (CI): the one that does not meet the criteria above. The study was approved by the HCPA Research Ethics Committee under protocol number 16-0207.

Results: Seventy-six patients met the inclusion criteria. Two patients were excluded due to incomplete historical records. The median age at the time of infection diagnostic was eight months. The infection frequency was 89.2% (66/74). Regarding the spectrum of acquisition, we noticed: NI = 30.3%, HAI = 54.5%, CI = 15.2%. The most common diagnostics were bronchopneumonia (27%), upper airway infection (15%), spontaneous bacterial peritonitis (12%) and cholangitis (12%). Klebsiella pneumoniae (10.6%) and respiratory syncytial virus (5.1%) were the most prevalent pathogens. In 51% of infections, no pathogens were identified. Death due to infection occurred in 13.6% of the patients.
Table:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Count</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amigdalitis</td>
<td>1</td>
</tr>
<tr>
<td>ORS</td>
<td>3</td>
</tr>
<tr>
<td>Sepsis</td>
<td>4</td>
</tr>
<tr>
<td>Other</td>
<td>8</td>
</tr>
<tr>
<td>UTI</td>
<td>5</td>
</tr>
<tr>
<td>SBP</td>
<td>8</td>
</tr>
<tr>
<td>Cholangitis</td>
<td>8</td>
</tr>
<tr>
<td>UAI</td>
<td>10</td>
</tr>
<tr>
<td>BCP</td>
<td>18</td>
</tr>
</tbody>
</table>

UTI: Urinary tract infection; SBP: Spontaneous bacterial peritonitis; UAI: Upper airway infection; BCP: Bronchopneumonia.

Conclusion: The frequency of infection in the studied population was high and has been associated to mortality. It is clear that this specific population is more sensitive to infectious processes, not only because of an impaired immune system, but also due to this group of patients frequently attending health care units for other reasons, increasing exposure to pathogens. Early detection, appropriate treatment and immunization might change this reality. The authors declare have no conflicts of interest.
Do we miss liver steatosis in obese children? Application of fibroscan in obese/overweight children increases detection of steatosis

Sebastian Więckowski1, Wojciech Jańczyk1, Aleksandra Byczyńska2, Agata Kozłowska2, Anna Świąder-Leśniak3, Mieczysław Szalecki2, Piotr Socha4

1Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
2Children’s Memorial Health Institute, Endocrinology and Diabetology, Warsaw, Poland
3Children’s Memorial Health Institute, Laboratory of Anthropology, Warsaw, Poland
4Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: At present NAFLD detection is based on ultrasound (US) and elevated levels of ALT. Still, US has limited sensitivity. Fatty liver seems to be common in children with overweight/obesity, but is detected in a small percentage of children based on US and assessment of ALT. The aim of our study was to find out whether overweight/obese children in whom primarily liver steatosis excluded have features of fatty liver measured by Fibroscan®. Recent studies in pediatric population assessing hepatic steatosis compared liver biopsy and Fibroscan® with option Controlled Attenuation Parameter (CAP) found that optimal threshold to detect steatosis CAP > 225 dB/m. Liver stiffness measurement (E) values using Fibroscan® haven’t been established yet in this population.

Methods: We used Fibroscan® with CAP for more precise assessment of hepatic steatosis and stiffness of the liver in 3 groups of patients matched for age (ag 8-20 years). We analyzed 42 patients with obesity and non-alcoholic fatty liver disease-NAFLD (steatosis detected by US and elevated ALT level), 40 patients with simple obesity (qualitative exclusion of steatosis by US using Saverymuttu criteria and with normal ALT levels) and 30 healthy controls with normal BMI. Exclusion criteria in all groups were: diabetes (type 1 and 2) and arterial hypertension for group with simple obesity. For group comparison we used Mann-Whitney U test and for association-Spearman R test.

Results: There were no differences in age among groups: median age in children with simple obesity was 14.3 (range 8.8-18.5), in NAFLD – 13.8 (range 9.8 – 19) and in control group – 13.8 (range 8.5-20.5). Liver stiffness (E) measured by Fibroscan® was statistically higher (p<0.05) in NAFLD group (median E=5.4 kPa) compared to controls (median E=4.3 kPa) and compared to the group with simple obesity (median E=4.0 kPa). The median steatosis measured by CAP in NAFLD group was significantly higher-300 dB/m(range 186-393) than in patients with simple obesity - 247.5 dB/m(range 100-349) and controls – 195 dB/m(range 100-273)(p<0.05). Still, CAP was also significantly higher in simple obesity compared to controls. CAP values correlated with age only in the NAFLD group (R=0.5), whereas CAP was significantly related to liver stiffness(E) in children with simple obesity (R=0.33). 35/42 (83.3%) patients with NAFLD and 29/40 (72.5%) patients with simple obesity received CAP>225 db/m using Fibroscan®, which are regarded to be diagnostic for NAFLD.

Conclusion:
- Fibroscan® can detect liver steatosis in obese children in whom fatty liver was primarily excluded based on normal ultrasound and ALT measures. Liver steatosis seems to be commonly associated with obesity in children.
- Liver steatosis is significantly higher in patients primarily diagnosed to have NAFLD compared to those with simple obesity and lean controls.
Portal hypertension in cystic fibrosis-related liver disease is a non-cirrhotic portal hypertension due to obliterative venopathy

Peter Witters¹, Louis Libbrecht², Tania Roskams³, Christiane De Boeck⁴, Lieven Dupont⁴, Marijke Proesmans⁴, François Vermeulen⁴, Geert Maleux⁵, Diethard Monbaliu⁶, Jacques Pirenne⁶, David Cassiman⁷

¹University Hospitals Leuven, Paediatric Gastroenterology, Hepatology and Nutrition, Leuven, Belgium
²Katholieke Universiteit Leuven, Liver Research Facility, Leuven, Belgium
³University Hospitals Leuven, Pathology, Leuven, Belgium
⁴University Hospitals Leuven, Cf Center, Leuven, Belgium
⁵University Hospitals Leuven, Radiology, Leuven, Belgium
⁶University Hospitals Leuven, Abdominal Transplant Surgery, Leuven, Belgium
⁷University Hospitals Leuven, Gastroenterology and Hepatology, Leuven, Belgium

Objectives and study: Cystic fibrosis-related liver disease (CFLD) is theoretically caused by inspissated bile and small bile duct obstruction leading to focal biliary fibrosis and cirrhosis with ultimately the development of portal hypertension (PHT). However, CFLD patients present with PHT in the absence of end-stage liver disease. Moreover, biliary pathology is often not clinically/biochemically evident. Therefore, we investigated whether CFLD-related PHT could be a vascular disease, more specifically non-cirrhotic PHT (NCPH).

Methods: We studied 8 patients with CFLD. In 4 patients with PHT we performed transjugular biopsies and hepatic venous portal gradient (HVPG) measurements. Additionally in 5 explant livers were closely reviewed the histology.

Results: In 4 patients, PHT was diagnosed because of esophageal varices (>grade 2, bleeding in 2 patients), abdominal venous collaterals, splenomegaly and/or ascites. MELD-scores were low (range 6-9) and none had hepatic encephalopathy. Liver tests were below 1.5x upper limit of normal. HVPG was 4-9mmHg in all, thus well below the cut-off for clinically significant PHT. Given the absence of portal vein thrombosis, this is consistent with presinusoidal portal hypertension. On histology, none of them had cirrhosis, while vascular changes as in NCPH leading to portal hypertension were found.

We subsequently analysed 5 the explant livers of patients with PHT (MELD range 7-12). There was no cirrhosis, only mild to moderate fibrosis (F2-F3) or incomplete septal cirrhosis (n=2). The most striking changes were: obliteratorive venopathy with absence of portal vein branches or fibrosis and calcification of the lumen (also sometimes visible on abdominal imaging). Paraportal shunt vessels and sinusoidal dilatation were prominent as signs of portal hypertension.

Conclusion: CFLD-related PHT is not due to a biliary cirrhosis but corresponds to vascular damage as in NCPH. This observation can open new avenues in the management of CFLD.
Drop out of obese children in different care settings: presence of NAFLD complications tends to improve compliance

Olga Lausi¹, Marina Tripodi¹, Luca Pierri¹, Federica Belmonte², Antonella Bisogno¹, Salvatore Guercio Nuzio¹, Pietro Vajro¹

¹Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi, Italy
²Department of Medicine and Surgery, University of Salerno, Pediatric Section, Baronissi, Italy

Objectives and study: Drop out represents a challenge for the management of obesity and obesity related complications, including NAFLD. Here we aimed to characterize predictors of and reasons for drop out in a tertiary care-based clinic vs. the family pediatrician (FP) setting.

Methods: a] Review of clinical records of 99 obese children (45 with NAFLD) aged 8-14 years seen at an academic setting (AS) between 2012 and 2016 + family questionnaires on barriers to compliance.
b] Access to 3 FPs’ database to identify obesity prevalence, management and drop out + survey with 9 FPs focusing obesity diagnosis and barriers to treatment.

Results: In the AS, >50% of children did not return at all for follow up after the 1st visit (Non Completers, NC). Absence of NAFLD (and -marginally- of parental obesity + female gender) was found more frequently associated with drop out, independent from BMI and waist circumference (WC) values (p NS), as shown in the Table. Only 9 (8 with NAFLD) of 64 NC and Partial Completers (patients unseen for an average of 8 months since their last visit), accepted to be re-visited after having been recontacted for a free of charge visit. Inadequate screening for hepato-metabolic risk (57.9% for hypertransaminasemia; 12,4% for NAFLD) and scarce referral to secondary/tertiary care settings (3%) despite personal poor outcomes emerged as a main critical issue in the FP setting. According to the survey, FPs competence and preventive efforts do collide with their lack of sufficient time for these patients and the underestimation of the problem by households. Those were felt as the principal reason of drop out (30% in their setting, with 52,3 % females, and 19 % NAFLD complicated obesity).

Table:

<table>
<thead>
<tr>
<th>FEATURES</th>
<th>COMPLETERS</th>
<th>PARTIAL</th>
<th>NON COMPLETERS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>TOTAL (N= 13)</td>
<td>PARTIAL (N= 30)</td>
<td>(N= 56)</td>
</tr>
<tr>
<td>Females (%)</td>
<td>38.4</td>
<td>36.6</td>
<td>53.5</td>
</tr>
<tr>
<td>Baseline BMI z score (mean +/- SD)</td>
<td>3.0 +/- 0.93</td>
<td>3.2 +/- 0.99</td>
<td>3.2 +/- 1.57</td>
</tr>
<tr>
<td>WC (cm &gt; 95%ile) (mean +/- SD)</td>
<td>17.8 +/- 12.96</td>
<td>19.5 +/- 8.29</td>
<td>19.9 +/- 14.63</td>
</tr>
<tr>
<td>NAFLD complicated obesity (%)</td>
<td>84.6</td>
<td>53.3</td>
<td>32.1</td>
</tr>
<tr>
<td>Parental complicated obesity (%)</td>
<td>38.4</td>
<td>30.0</td>
<td>26.6</td>
</tr>
<tr>
<td>Obese parents (%)</td>
<td>53.9</td>
<td>33.4</td>
<td>35.8</td>
</tr>
</tbody>
</table>

Conclusion: Drop out affects weight management results in both academic and general pediatric settings. A diagnosis of NAFLD at baseline appears to improve compliance. Efforts to identify factors predicting poor compliance since the first visit are necessary to individuate those obese children requiring a more tailored management to avoid drop out.
**Growth and bone health in children following liver transplantation**

Faris Alkhalil, Rana Bitar, Amer Azaz, Hisham Natouri, Noora Almuraikhi, Mohamad Miqdady

1Sheikh Khalifa Medical City, Paediatrics, Abu Dhabi, United Arab Emirates

**Objectives and study:** Children with liver transplantation are achieving very good survival and so there is now a need to concentrate on achieving good health in these patients and preventing disease. Immunosuppressive medications have side effects that need to be monitored and if possible avoided. Glucocorticoids and calcineurin inhibitors are detrimental to bone and mineral homeostasis in addition steroids can also affect linear growth. Steroid sparing regimes in renal transplant children has shown to improve children's height.

We aim to review the growth and bone health of children post liver transplant by measuring bone mineral density (BMD) using dual energy X-ray absorptiometry (DEXA) scan and assessing if there is a clear link between poor growth and impaired bone health and use of long term steroids.

**Methods:** This is a single centre retrospective Cohort study, we reviewed the medical notes of children (0-16 years) who underwent a liver transplantation between November 2000 to November 2016 and currently being followed at our centre.

**Results:** 39 patients were identified (25 males and 14 females), the median transplant age was 2 years (range 9 months - 16 years). Four patients received a combined transplant, 2 kidney and liver transplant and 2 received a liver and small bowel transplant.

The indications for transplant included, Biliary Atresia (31%), Acute Liver failure (18%), Progressive Familial Intrahepatic Cholestasis (15%), transplatable metabolic disease (10%), TPN related liver disease (8%), Primary Hyperoxaluria (5%), Hepatocellular carcinoma (3%) and other causes (10%).

36 patients (95%) were on a calcineurin inhibitor (34 patients were on Tacrolimus and 2 on Cyclosporin). The other two patients were on Sirolimus. Low dose long-term steroids was used in 21% of the patients.

A considerable proportion of the patients had poor growth. 15% were below the 3rd centile for weight for age and 21% were below the 3rd centile for height for age. Most of our patients with poor growth were not on long term steroids.

49% of patients had a DEXA scan post transplantation. 21% of these children had low bone mineral density, one patient had met osteoporosis criteria with a vertebral fracture. Most of our patients with impaired bone health were not on long term steroids.

20% of the patients who did not undergo a DEXA scan developed long bone fractures and 50% of them were on long term steroid use which may suggest impaired bone health in these patients.

**Conclusion:** The incidence of impaired bone health, although studied in limited number of patients; was high. Early recognition and treatment should be instituted to avoid fractures and improve bone health. Many of the patients were below the 3rd centile for weight and height however there was no clear relationship between steroid use and impaired bone health, reduced weight and reduced linear height.
Overseas liver transplantation in children: One centre experience

Faris Alkhalil1, Rana Bitar1, Amer Azaz1, Noora Almuraikhi1, Hisham Natouri1, Mohamad Miqdady1

1Sheikh Khalifa Medical City, Paediatrics, Abu Dhabi, United Arab Emirates

Objectives and study: Paediatric liver transplantation is the most widely accepted treatment for end stage liver disease. Many children requiring liver transplantation don’t have access to a liver transplant unit in the country they live in and travel to overseas specialist centres for treatment. Their long-term subsequent post transplant care, however, tends to take place in their home country. This may influence the success of transplantation. The outcome and long term survival of these children has not been reviewed previously. In the United Arab Emirates (UAE) there is no liver transplant service for children. Patients travel to overseas transplant units for transplantation. However, almost all pre and post liver transplant patient care takes place in Sheikh Khalifa Medical City (SKMC); the main paediatric hospital in the UAE with an established paediatric gastroenterology unit.

We aim to review children living in the UAE who underwent liver transplantation looking at the diagnosis, country of transplant, type of transplant, immunosuppressive treatment, complications and outcome including long term survival and graft survival.

Methods: This is a single centre retrospective cohort study. We reviewed the medical notes of children (0-16 years) who underwent a liver transplantation outside the UAE from November 2000 to November 2016 and are followed up in SKMC.

Results: 39 patients were identified (25 males, 14 females). The median transplant age was 2 years (range 9 months - 16 years). 4 patients received a combined transplant, 2 kidney and liver transplant and 2 received a liver and small bowel transplant.

The indications for transplant included, Biliary Atresia (31%), Acute Liver failure (18%), Progressive Familial Intrahepatic Cholestasis (15%), transplantable metabolic disease (10%), TPN related liver disease (8%), and other causes (18%).

33% of patients had their transplant in the United Kingdom, 15% in India, 10% in the United States of America, 10% in Germany, 8% in Korea, 5% in France, And other countries (20%) 64% of the patients received a living related donor transplant (LRDT), 33% were cadaveric. All patients going to Germany, France, and most going to the USA received a cadaveric liver. However, most patients receiving a liver transplant in the UK and India received a LRDT. Tacrolimus was the main immunosuppressant used. 56% of patients were on monotherapy, 36% were on double immunosuppression, and 8% were on triple immune suppression.

Complications included chronic rejection 13%, hypertension 10%, Post-Transplant Lymphoproliferative disease 8%, end stage renal disease 8%, portal hypertension 5%, portal vein thrombosis 5%, hepatic artery thrombosis 2%, non-Hodgkin’s lymphoma 2%, and biliary stricture 2%. The overall survival rate was 92%. There were 3 deaths, and all were due to sepsis. Only one patient had a graft failure shortly after transplant.

Conclusion: Our patients received liver transplantation in multiple overseas centres. The overall indications and complications of liver transplantation in this group of patients were similar to already published reports. Despite being managed in a non transplant centre; the overall survival rate was high. This suggests that performance of liver transplantation in overseas centres with subsequent post transplant care in home country can be safe and can carry a good survival. Sepsis was the main cause of death. This highlights the need for timely and aggressive treatment of infection in these patients.
Cytomegalovirus viremia in the first post liver transplant year in children

Mohamed Barr¹, Aly Akhtarul Hassan², Laszlo Szonyi², Talal Algoufi²

¹King Faisal Specialist Hospital and Research Centre, Pediatric Transplant Hepatology, Organ Transplant Centre, Riyadh, Saudi Arabia
²King Faisal Specialist Hospital and Research Center, Organ Transplant Center, Pediatric Liver Transplant, Riyadh, Saudi Arabia

Objectives and study: infection with CMV in immune-compromised transplant patients is associated with enhanced immune suppression leading to opportunistic infection, increased risk of graft loss, and significant morbidity and mortality. At the beginning of the first post-transplant year, immunosuppression is at its peak, and is then gradually tapered. There are multiple studies demonstrating the effectiveness of prophylactic antiviral medications in reducing the incidence and severity of CMV disease in adult transplant recipients. This study aims at analyzing the risk of CMV viremia during the first year post liver transplant in children, with correlation to ganciclovir and valganciclovir prophylaxis.

Methods: a retrospective review was done for 156 pediatric liver transplants done in King Faisal Specialist Hospital and Research Center, Riyadh, between 2011 and 2014. For these children, pretransplant CMV status was reviewed including CMV serology and CMV quantitation. Inclusion criteria were; children who had negative pretransplant CMV IgM serology, undetectable pretransplant CMV load, immediate post-transplant 14 days 5 mg/kg/day IV ganciclovir prophylaxis, followed by 100 days of oral valganciclovir, and had positive CMV load during the first post-transplant year.

Results: A total of 73 cases (n=73, 46.8%) had post-transplant CMV viremia. Children who met the inclusion criteria were 19 cases (n= 19, 26%). During the first 90 days post-transplant, Early-onset viremia was detectable in (n=11, 15%) children, after a mean post-transplant duration (34.6 ± 20.6) days, with a mean CMV load (22936 ± 57820). Between 91-180 days post-transplant, early post-prophylactic viremia was detectable in (n=4, 5.5%) children, after a mean post-transplant duration (139.8 ± 28.1) days, with a mean CMV load (21545 ± 23124). Between 181-365 days post-transplant, late-postprophylactic viremia was detectable in (n=4, 5.5%) children, after a mean post-transplant duration (272.3 ± 34.7) days, with a mean CMV load (2095 ± 1970).

Conclusion: There is increased risk of CMV viremia during the first post-transplant year in children. Early-onset CMV viremia was common in the study population, in spite of prophylactic 14-day course IV ganciclovir, followed by 100-day course of valganciclovir. Such high CMV load could be attributable to the relatively high degree of immunosuppression during the early post-transplant period. Early post-prophylactic viremia was significantly high and comparable to the early-onset viremia. During this period, still higher serum levels of immunosuppressive medications are needed, in addition to the continuous steroid coverage over the first six months post-transplant.
ABCB11 mutations diagnosed by next generation sequencing (NGS): phenotypic correlation and the role of NGS in personalized medicine

Mohammad Ali Shagrani¹, Mohamed Barr¹, Dieter Clemens Broering²

¹King Faisal Specialist Hospital and Research Centre, Pediatric Transplant Hepatology, Organ Transplant Centre, Riyadh, Saudi Arabia
²King Faisal Specialist Hospital and Research Centre, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia

Objectives and study: Mutations in ABCB11 gene, encoding bile salt export protein (BSEP), are inherited in an autosomal recessive pattern. Deficiency of BSEP is a known genetic disorder in Saudi Arabia, enhanced by the predominance of consanguineous marriage. The BSEP is a member of the adenosine triphosphate-binding cassette (ABC) superfamily and P-glycoprotein/multidrug resistance (MDR/ABCB) subfamily of transporters, in the hepatocyte canalicular membrane. Deficiency of BSEP results in failed secretion and intra-hepatocyte accumulation of conjugated primary bile acids (bile salts). Infants affected with the progressive form of BSEP deficiency (progressive familial intrahepatic cholestasis type II; PFIC II), present with jaundice, failure to thrive, pruritus, malabsorption, and high serum bile salts. Most patients ultimately need orthotopic liver transplantation with considerable risk for HCC (hepatocellular carcinoma).

Methods: Using next-generation sequencing (NGS)-based multi-gene panel which designed, tested and validated at King Faisal Specialist Hospital & Research Centre.

Results: Mutations in ABCB11 gene were evident in fifteen patients (n=15, 22.7%), most patients (n=10, 66.6%) manifested below one year of age, others (n=5, 33.3%) presented later on. Most patients were from consanguineous parents (n=13, 86.67%), and had positive family history of similar disease (n=10, 66.7%). Patients presented with jaundice (n=15, 100%), hepatomegaly (n=11, 73.3%), splenomegaly (n=10, 66.7%), itching (n=10, 66.7%) coagulopathy (n=3, 20%), failure to thrive (n=3, 20%), and ascites (n=2, 13.3%). All patients had normal GGT at presentation (mean 32.4 U/L ± SD 9.4). High pre-transplant serum bile acids (mean 304.96 ± SD 135.8) could be retrieved for some patients (n=9, 60%). Twelve patients (n=12, 80%) underwent liver transplantation, others (n=3, 20%) are still not transplanted. One non-transplanted patient (n=1, 6.7%) recently developed hepatocellular carcinoma (HCC). Of the twelve post liver transplant patients, a brother and a sister (n=2, 16.7%) developed recurrence of the primary disease. Both had truncated mutations in ABCB11 gene, with complete pretransplant deficiency of BSEP. They were successfully treated with advanced protocols.
**Conclusion:** Mutations in ABCB11 are significantly remarkable in our patient population, and are significantly transmitted by consanguinity. The spectrum of BSEP deficiency phenotype is widely variable; mostly presenting in the first year of life as an early progressive disease demanding liver transplantation, to a slowly progressive disease allowing patients to reach puberty and even adulthood. Jaundice is a universal finding, followed by hepatomegaly, splenomegaly, and itching. Normal GGT and high serum bile acids are characteristic findings. Truncated mutations in ABCB11 gene are a risk factor for post-transplant recurrence of the primary disease.
**HEPATOLOGY: Transplantation**

H-P-061

**Pediatric liver allograft health with normal liver function test, 10 years after liver transplantation: all is not well!!!**

**Saista Amin**

1Kokilaben Ambani Hospital,, Pediatric Hepatology, Mumbai, India

**Objectives and study:** To evaluate the liver histology in children with normal tests of liver functions and radiology, 10 years after liver transplant; study conducted at Kings college hospital, London.

**Methods:** 62 children, 10 years after liver transplant with normal liver functions (AST, ALT, GGT, Bilirubin, Albumin) who consented for liver biopsy, were studied prospectively. Incidence and risk factors for abnormal graft histology were also evaluated.

**Results:** Of the 62 children (32 male), age being between 11 and 25 years, median age was 14 (+/- 2 years), at the time of biopsy. 53 children had abnormal histology (fibrosis/steatosis/both). On Ishak staging stage 3 and 4 fibrosis was found in 23 (43.5%) children. 11 (20.7%) had stage 1 fibrosis, 17 (32%) with stage 2. Recipient related risk factors evaluated were episodes of acute rejection, biliary and vascular complications, CMV infection, de novo autoimmune hepatitis and PTLD. Donor related risk factors evaluated were age, sex, CMV status, graft steatosis. Both donor and recipient risk factors were comparable with normal and abnormal histology groups.

**Conclusion:** Normal liver biochemistry does not reflect graft histology. Hence a caution has to be observed while predicting allograft health without liver biopsy.
Liver transplantation does not impact the renal function outcome in Alagille syndrome

Tanguy Demaret¹, Sharat Varma², Yelena Vainilovich¹, Ugur Halac¹, Diana El Bizri¹, Jérome Ambroise³, Isabelle Scheers⁴, Xavier Stephenne⁵, Francoise Smets⁵, Etienne Sokal⁴

¹Cliniques Universitaires Saint-Luc, Gastro-Entérologie et Hépatologie Pédiatrique, Brussels, Belgium  
²Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium  
³Université Catholique de Louvain, Center for Applied Molecular Technologies, Bruxelles, Belgium  
⁴Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium  
⁵Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Pediatric Gastroenterology and Hepatology Unit, Brussels, Belgium

Objectives and study: Alagille syndrome (AS) is an autosomal dominant multi-systemic disorder caused by pathogenic variants in JAG1 and NOTCH2. Characteristic findings include hepatic involvement with bile duct paucity and 20-50% eventually need a liver transplantation. Post-LT Tacrolimus induced nephropathy is well recognised and 40% of AS patients have an underlying renal anomaly. In the current study we analysed the impact of LT and Tacrolimus on the evolution of renal function (RF) in children with AS.

Methods: Retrospective study including 50 children that satisfied 3 of 5 major Alagille syndrome criteria and under regular follow-up at our centre between 1984 and 2016. Clinical, biochemical and radiological data were collected at similar time points of follow-up among the transplanted and non-transplanted children. The time points were at diagnosis or at LT and after 1-2 years, 2-3 years, 3-5 years, 5-7 years and 7-10 years of follow-up. The RF was estimated by glomerular filtration rate (eGFR) using the updated Schwartz formula. The RF outcomes of children with AS having undergone LT were compared with those without LT and also with children having undergone LT for non-AS related indication but without associated nephropathy.

Results: 28 of 50 (56%) included AS children underwent LT and were compared with 77 children transplanted for non-AS indications. Mean eGFR post-LT in AS patients and non-AS patients were 93.8 mL/min and 143.2 mL/min, respectively (difference: 49.4 mL/min, p<0.0001). Among children with AS mean eGFR observed in those who did not receive LT was 87.9 mL/min, -5.9 mL/min compared to those who received LT though this was statistically insignificant (p=0.32). Presence of renal ultrasound abnormalities was correlated to RF impairment in AS patients, with or without LT: -14.6 mL/min (98.5 mL/min vs 83.9 mL/min, p=0.03) and -40.9 mL/min (97.8 mL/min vs 56.9 mL/min, p<0.0001), respectively.

Conclusion: Post-LT renal function outcomes are significantly worse in children with AS being the primary disease. Among the children with AS, the RF outcome is not worse after LT.
Ectopic jejunal varices due to extrahepatic portal vein obstruction in a post liver transplant child treated by percutaneous portal vein stenting

Jaswinder Kaur¹, Anand Gupta¹, Nishant Wadhwa¹

¹Sir Ganga Ram Hospital, New Delhi, India, Pediatric Gastroenterology, Hepatology and Liver Transplant, New Delhi, India

Objectives and study: Here, we report a case of ectopic jejunal variceal bleeding due to extrahepatic portal vein obstruction in a post transplant child that was treated successfully by percutaneous portal vein stenting

Methods: 3 months female child presented at our centre with cholestasis. Liver biopsy done was suggestive of extrahepatic biliary atresia with cirrhosis. Child was given nutritional support and supplements and prepared for liver transplant. Live donor left lateral segment liver transplant was done at 8 months of age. Child remained stable afterwards and was continued with immunosuppression. At 5 years of age, child presented with persistent malena requiring packed cell transfusion. Upper GI endoscopy done was normal, there were no esophageal varices. Lower GI endoscopy done was also normal. CT angiography done was suggestive of ectopic jejunal varices (multiple collaterals along the wall of the hepaticojejunostomy loop) and a collateral joining the portal venous confluence suggestive of extrahepatic portal venous obstruction. Interventional radiologist’s consultation was taken. Under general anaesthesia, splenic vein was punctured through splenic parenchyma, portovenogram was done and it showed complete obstruction of extrahepatic part of portal vein. Multiple collaterals were seen in the jejunal wall filling the portal vein distally. Guide wire was threaded through the splenic vein but it could not be negotiated through the extrahepatic portal vein obstruction. Percutaneous portal vein puncture was done and wire was passed through the obstructed segment of the portal vein and a metallic stent of 10mm x 6mm was placed across the obstruction. Post stenting, portovenogram showed no filling of jejunal collaterals. Child gradually improved, malena stopped within 24 hours and child was discharged.

Results: Jejunal varices are an uncommon manifestation of portal hypertension and are rarely symptomatic. Jejunal varices are associated with portal hypertension, which may be due to cirrhosis or extrahepatic portal venous obstruction. Ectopic varices most commonly develop at sites of tissue adhesion in patients who have previously undergone abdominal surgery. Mostly jejunal variceal bleeding has been treated surgically. Non-surgical treatment options may include porto-caval shunt, endoscopic sclerotherapy, embolization and balloon dilatation.

Conclusion: Jejunal varices can occur and cause significant bleeding in children with portal hypertension especially in children who had undergone some abdominal surgery. Percutaneous portal vein stenting can be a modality of choice in treatment of extrahepatic portal vein obstruction.
Post-liver transplantation follow-up over 17 years for mild Zellweger spectrum disorder and additional cases

Tanguy Demaret¹, Sharat Varma², Xavier Stephenne³, Francoise Smets⁴, Isabelle Scheers⁵, Lionel van Maldergem⁶, Raymond Reding⁷, Etienne Sokal⁸

¹Cliniques Universitaires Saint-Luc, Gastro-Entérologie et Hépatologie Pédiatrique, Brussels, Belgium
²Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Brussels, Belgium
³Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
⁴Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Pediatric Gastroenterology and Hepatology Unit, Brussels, Belgium
⁵Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium
⁶Centre Hospitalier Régional Universitaire de Besançon, Centre de Génétique Humaine, Besançon, France
⁷Clinique Universitaire St Luc, Pediatric Liver Transplantation and Surgery, Brussels, Belgium

Objectives and study: Mild Zellweger spectrum disorder, also described as Infantile Refsum disease, is attributable to mutations in PEX genes. Its clinical course is characterized by progressive hearing and vision loss, and neurodevelopmental regression. Supportive management is currently considered the standard of care, since plasmalogens supplementation, low phytanic acid diet, cholic acid, and docosahexaenoic acid have not shown clinical benefits. Liver transplantation (LT) was shown to correct levels of circulating toxic metabolites, partly responsible for chronic neurological impairment, with LT survival currently being >95%.

Methods: We reviewed medical records of the three patients having undergone LT for mild ZSD in our institution.

Results: One patient died after LT, while the other two displayed significant neurodevelopmental improvement on both the long- (17 years post-LT) and short-term (9 months post-LT) follow-up. We documented a sustained improvement in the biochemical profile, with a complete normalization of plasma phytanic, pristanic and pipecolic acid levels. This was associated with improved clinical evolution, puberty achievement, as well as stabilization of hearing and visual functions, and neurodevelopmental status, which has enabled the older patient to lead a relatively autonomous lifestyle on the long-term. The psychomotor acquisitions have been remarkable. Specially seen in comparison to their affected siblings who did not undergo LT and exhibited a poor neurological outcome with severe disabilities.

Conclusion: Based on our short- and long-term follow-up experience, we speculate that LT performed before the onset of severe sensorineural defects in mild ZSD, enables partial metabolic remission and improved long-term clinical outcomes.
Liver transplantation in propionic acidemia

Cristina Molera1, Jesús Quintero Bernabeu2, Javier Juampérez Goñi3, Silvia Meavilla4, Susana Redecillas Ferreiro5, Óscar Segarra2, Javier Martin de Carpi6, Ramon Charco7

1Hospital Universitari Sant Joan de Déu, Comprehensive Unit of Complex Hepatology and Pediatric Liver Transplantation, Barcelona, Spain
2University Hospital Vall D’Hebron, Paediatric Gastroenterology, Hepatology, Nutrition Support and Liver Trasplantation, Barcelona, Spain
3Hospital Vall D’Hebron, Paediatric Gastroenterology, Liver Transplantation and Nutritional Support Unit, Barcelona, Spain
4Hospital Universitari Sant Joan de Déu, Paediatric Gastroenterology, Hepatology and Nutrition Section, Barcelona, Spain
5Hospital Vall D’Hebron, Nutrition Unit, Barcelona, Spain
6Sant Joan de Deu Hospital, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
7Hospital Universitari Vall D’hebron, Hepatology and Liver Transplantation Department, Barcelona, Spain

Objectives and study: Despite optimal medical treatment and strict low protein diet, the prognosis of Propionic Acidemia (PA) patients is generally poor. Some studies have report benefits of Liver Transplantation (LT), minimizing the risk of metabolic decompensations and improving their nutrition and quality of life. We aim to report our experience with LT in the management of PA patients.

Methods: We retrospectively analyzed all pediatric LT performed in PA patients in our center. Patient data were obtained by reviewing inpatient and outpatient medical records and our transplant database. The diagnosis of PA was made by mutation analysis and low propionyl-CoA carboxylase activity in the cultured fibroblasts in all cases.

Results: Four patients (2 male) with PA received a LT in our center at a mean age of 5.2 years (2.9-7.5). Despite severe protein restriction (median protein intake of 0.72 mg/Kg/day; 0.56-0.8 mg/Kg/day), all patients presented a suboptimal pre-LT metabolic control (urine methylcitrate and serum propionylcarnitine median levels of 360 mmol/L; 252-506mmol/L and 75 mmol/mL; 90-65 mmol/mL, respectively). All patients were fed using a PEG (3) or a nasogastric tube and used ammonia-lowering agents pre-LT. The indications for LT were frequent metabolic decompensations (3) and elective management (1). Two patients received a whole liver graft and two patients a living-donor transplantation. All children were alive without any need of re-transplantation. Two patients presented hepatic artery thromboses which were solved by interventional radiologist approach (1 stents 1 angioplasty balloon dilatation). After the LT, none decompensations were observed. Patients were fed orally without any supportive feeding or lowering-ammonia agents. Despite patients still follow a controlled low-protein diet, the total protein intake was greater with a median of 1.4 mg/Kg/day (0.86-1.5 mg/Kg/day). All patients presented a better but not normal metabolic control with a decline in the urine methylcitrate and serum propionylcarnitine levels at 1 year post-LT (median of 86 mmol/L; 26-140mmol/L and 18.3 mmol/mL; 22-12 mmol/mL). All patients presented non progression or improvement of their neurological status using the Griffiths Mental Development Scale score pre-LT and 1 year post-LT. The median follow-up was of 2.1 years (0.31-3.2 years).

Conclusion: LT could be a good treatment option for patients with PA improving their metabolic control and quality of life.
Cystatin C estimates glomerular filtration rate in liver transplanted children more accurately than creatinine

Emil Bluhme¹, Silvia Malenicka², Ulla Berg³, Björn Fischler⁴, Antal Nemeth⁵, Carl Jorns⁶

¹Medical Faculty, Karolinska Institutet, Stockholm, Sweden
²Astrid Lindgren Children’s Hospital, Karolinska University Hospital Huddinge, Paediatric Gastroenterology, Hepatology and Nutrition, Stockholm, Sweden
³Karolinska Institutet, Stockholm, Sweden
⁴Dept. of Pediatrics, Karolinska University Hospital, Clintec, Stockholm, Sweden
⁵Karolinska University Hospital, Alb Childrens’ Hospital, Paediatric Gastroenterology, Hepatology & Nutrition, Stockholm, Sweden
⁶Karolinska University Hospital Huddinge, Division of Transplantation Surgery, Stockholm, Sweden

Objectives and study: Impaired renal function in liver transplanted (LT) children is a recognized problem. To accurately monitor glomerular filtration rate (GFR) is imperative in order to detect declining renal function. GFR can be estimated via serum creatinine (eGFR_{crea}) or plasma cystatin C (eGFR_{cyst}), or measured by inulin or iohexol clearances (mGFR_{iohex}). The aim of this study was to compare eGFR_{crea} and eGFR_{cyst}, respectively, to mGFR_{iohex} in a cohort of LT children.

Methods: Data from 94 children, LT between 1984 and 2015, with median age at transplantation 4.1 years (0.4-17.6), and a total of 334 concomitant measurements of all three markers - plasma cystatin C, serum creatinine, and iohexol clearance – obtained between 2007 and 2015 was analysed. Accuracy, precision, and bias of GFR calculated via cystatin C-based equation CAPA (Caucasian, Asian, paediatric, and adult cohorts; eGFR_{cyst}), creatinine-based revised Schwartz estimate formula (eGFR_{crea} <18y), and MDRD (Modification of Diet in Renal Disease Study; eGFR_{crea} >18y) equation, respectively, was assessed in comparison to that of mGFR_{iohex} (ml/min/1.73m²). To minimize the risk of over representation of individual variations cluster bootstraping was used in calculation of the confidence intervals.

Results: The correlation coefficient for comparison to mGFR_{iohex} was 0.549 for eGFR_{crea} (CI 0.388-0.682) and 0.698 for eGFR_{cyst} (CI 0.595-0.786). There was a trend of spreading out in higher and lower GFR which was more pronounced for eGFR_{crea}. Median percentage difference (i.e. accuracy) for eGFR_{crea} was 21% (CI 18-25) and for eGFR_{cyst} 13% (CI 11-14.5). For eGFR_{cyst} 88.6% of the measurements were within the 30% error margin compared to 67.4% of the eGFR_{crea}. The precision (i.e. lower values indicating a smaller spread of the difference) for eGFR_{crea} was 28.71 (CI 24.22-32.57) and for eGFR_{cyst} 22.74 (CI 19.02-28.24). For eGFR_{crea} the absolute difference (i.e. bias) was 16.20 (CI 13.19-20.60) and for eGFR_{cyst} -0.15 (CI -3.32-2.84) ml/min/1.73m². All these differences between eGFR_{cyst} and eGFR_{crea} were more pronounced in a subgroup analysis of 36 patients turning older than 18 years during the study period, where eGFR_{crea} was calculated from the MDRD formula.

Conclusion: eGFR_{cyst} was significantly more accurate and less biased than eGFR_{crea} when compared to mGFR_{iohex} in our study population. Our findings support the use of eGFR_{cyst}, calculated via the CAPA equation, in LT children.
Characteristics of invasive fungal infections in paediatric liver transplant recipients

Yehonatan Pasternak¹, Shiri Rubin¹, Efi Bilavski², Yael Mozer – Glassberg³, Elhanan Nahum⁴, Eran Rom², Liat Ashkenazi-Hoffgong⁵

¹Schneider Children’s Medical Center of Israel, Department of Pediatrics A, Petach Tikva, Israel
²Schneider Children’s Medical Center of Israel, Department of Pediatrics C, Petach Tikva, Israel
³Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach-Tikva, Israel
⁴Schneider Children’s Medical Center of Israel, Pediatric Intensive Care Unit, Petach Tikva, Israel
⁵Schneider Children Medical Center, Petach Tikva, Israel

Objectives and study: Invasive fungal infections post-liver transplantation are an important cause of morbidity and mortality; however data in the paediatric population are scarce. Knowledge accrued regarding epidemiology and risk factors can contribute toward devising rational antifungal prophylactic and treatment strategies. The objective of this study was to investigate the incidence and predictors of invasive fungal infections in paediatric liver transplant recipients in the early post-transplantation period

Methods: The electronic medical records of all paediatric patients, who underwent liver transplantation at Schneider Medical Center between January 2004 and December 2014, were analyzed. Data included patient demographics, clinical and laboratory parameters, microbiological studies and outcome. Patients diagnosed with invasive fungal infection were compared to their counterparts.

Results: Nine invasive fungal infections cases were identified amongst 81 liver transplant recipients (11.1%), with the majority occurring in the first month after transplantation. Candida species were responsible for 8 cases (89%), in which candidemia was diagnosed in 3 cases, urinary tract infection in 2 cases and abdominal abscess in 2 cases. One case of invasive mucormycosis was diagnosed. Significant risk factors for invasive fungal infection were a living donor (78% vs. 26%, p<0.01), recipient of multiple blood products transfusions during transplantation (12 vs. 7.6, p<0.01), prolonged hospitalization period (82.6 vs. 41.4 days, p=0.02) and pediatric intensive care unit hospitalization period (40.5 vs. 14.6 days, p<0.01), prolonged use of indwelling intravenous catheter (18.1 vs. 10.3 days, p<0.01), prolonged intravenous antibiotic treatment (61.5 vs. 15.5 days p<0.01), and pulse steroid treatment. There were no cases of fungal-infection-related mortality.

Conclusion: Invasive fungal infections are a significant early infectious complication among children post liver transplantation. Antifungal prophylaxis should be considered in high-risk patients in the early post transplantation period. Future prospective studies are needed to evaluate the efficacy of a targeted anti-fungal prophylaxis approach.
Quality of life in long term survivors of paediatric liver transplant for biliary atresia: a multicenter study

Mar Miserachs1, Agnieszka Bakula2, Joanna Pawlowska3, Loreto Hierro4, Carmen Macarena5, Lorenzo D’Antiga6, Valeria Casotti7, Imeke Goldschmidt8, Dominique Debray9, Muriel Girard10, Valérie McLin11, Anthony Otley12, Ulrich Baumann13, Vicky Lee Ng14

1The Hospital for Sick Children, Division of Gastroenterology, Hepatology and Nutrition. Transplant and Regenerative Medicine Centre, Toronto, Canada
2Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
3The Children’s Memorial Health Institute, Warsaw, Poland
4“la Paz” University Hospital, Paediatric Liver Service, Madrid, Spain
5Hospital Infantil Universitario La Paz, Madrid, Spain
6Hospital Papa Giovanni XXIII, Paediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy
7Papa Giovanni XXIII Hospital, Paediatric Hepatology, Gastroenterology and Transplantation Unit, Bergamo, Italy
8Hannover Medical School, Division of Pediatric Gastroenterology and Hepatology, Children’s Hospital, Hanover, Germany
9Hôpital Bicêtre, Paris, France
10Hopital Necker Enfants Malades, Unité D’hépatologie, Paris, France
11University Hospitals Geneva, Pediatrics, Geneva, Switzerland
12Iwk Health Centre and Dalhousie University, Nova Scotia, Canada
13Medizinische Hochschule Hannover, Paediatric Gastroenterology and Hepatology, Hannover, Germany
14The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: Biliary atresia (BA) is the commonest indication for paediatric liver transplant (LT), with excellent long-term patient and graft survival world-wide. Optimizing durable outcomes for this patient population can be enhanced by understanding health-related quality of life (HRQoL) concerns. This study aimed to i) evaluate HRQoL in long-term survivors of children who underwent LT for BA and ii) explore the relationship between HRQoL with patient demographic and medical variables.

Methods: We conducted a cross sectional study at 7 different paediatric LT centres in Canada or in the ChilSFree/EPLTN network program. Validated paediatric disease-specific (Paediatric Liver Transplant Quality of Life, PeLTQL) and generic (Paediatric Quality of Life Inventory, PedsQL™) HRQoL tools were administered to BA children (current age 8-12 years) who underwent LT before the age of two years. Their parents completed the corresponding, validated parent-proxy tools. Total scores range between 0 and 100 for both PeLTQL and PedsQL™, with higher scores indicating better HRQoL. Correlations between the measures were examined. Patient demographics and medical variables were also reviewed.

Results: A total of 64 (female 54%, median age 9.77 (range 8.05-12) years, BA subjects 6 or more years after LT were included. Strong correlation was seen between PeLTQL and PedsQL™ scores (r=.61, p<0.0001) and between patient-reported and parent-reported PeLTQL scores (r=.71, p <0.0001) (Table 1). Total PedsQL and PeLTQL scores were not statistically different between different language speaking populations (Polish, Italian, Spanish, German, French and English). Higher total PeLTQL scores were seen in subjects on immunosuppression monotherapy (60.9%, 100% on tacrolimus, n=39) compared to patients on dual or multiple therapy (n = 23; PeLTQL Total Score 78.4±12.9 vs 68.5 ±18.5, p= 0.03).
**Table 1.** Patient- and parent-reported total and domains scores

<table>
<thead>
<tr>
<th></th>
<th>Patient (median, range)</th>
<th>Parent (median, range)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n=62</td>
<td>n=63</td>
</tr>
<tr>
<td><strong>PeLTQL Total Score</strong></td>
<td>77.8 (26.9-96.6)</td>
<td>79.4 (51.9-100)</td>
</tr>
<tr>
<td>Future Health Subdomain score</td>
<td>83.3 (8.3-100)</td>
<td>85.9 (50-100)</td>
</tr>
<tr>
<td>Coping &amp; Adjustment Subdomain score</td>
<td>71.8 (31.2-93.7)</td>
<td>71.8 (37.5-100)</td>
</tr>
<tr>
<td>Socio-Emotional Subdomain score</td>
<td>80.5 (30.5-100)</td>
<td>77.7 (41.6-100)</td>
</tr>
</tbody>
</table>

**Conclusion:** HRQoL scores were not different in BA patients in receipt of paediatric LT across six different language-speaking populations, suggesting similarity of broader determinants of health issues. Ongoing work is targeting better understanding of the impact of immunosuppression requirements on HRQoL.
Clinical relevance of routine liver biopsies after paediatric liver transplantation

Sinja Ohlsson1, Bianca Hegen1, Denisa Pilic1, Simone Kathemann1, Alexander Dechêne2, Hideo Baba3, Peter Friedrich Hoyer1, Elke Lainka2

1University Hospital Essen, Clinic for Paediatric II, Essen, Germany
2University Hospital Essen, Clinic for Gastroenterology and Hepatology, Essen, Germany
3University Hospital, Institute of Pathology, Essen, Germany

Objectives and study: Routine liver biopsies as invasive diagnostic procedures after liver transplantation are performed in clinically inapparent patients. Aim of this study was to evaluate the clinical and prognostic relevance of routine liver biopsies after paediatric liver transplantation.

Methods: A retrospective analysis of 84 biopsies in 63 children who underwent liver transplantation was performed and the association of laboratory and clinical parameters was measured. Children were separated into four groups (I= biopsy in 1st year after LTX, n= 9; II= 2nd-5th year, n= 27; III= 6th-10th year, n= 15; IV= > 10th year, n= 12). 21 children underwent a second routine liver biopsy in the course of their treatment. In 43 biopsies an additional transient elastography (fibroscan) was performed.

Results: A histopathologically proven stage of fibrosis (Metavir) ≥ 2 was diagnosed in 33% (21/63) of the routine biopsies. No major differences between the groups were detected (I= 22%, II= 33%, III= 40%, IV= 33%). In children with a second routine biopsy (n=21) which was performed on average four years after the 1st biopsy, the stage of fibrosis decreased in 14% of patients whereas 76% showed a steady and 10% a progressive stage. Inflammatory activity (Desmet) ≥ grade 1 was detected in 52% (33/63) of patients (I= 66%, II= 66%, III= 26%, IV= 42%) indicating an unspecific inflammatory reaction. Clinical consequences like modification of the immunosuppressive medication, start of an antiproliferative treatment, improvement of bile flow or performance of an indicative biopsy were drawn in 19% (12/63) of the cases. No peri-interventional complications occurred in 84 routine biopsies. No association between laboratory parameters (liver synthesis parameters, transaminases and bilirubin, virology or autoantibodystatus) and the stage of fibrosis or the inflammatory activity could be shown. Using transient elastography (fibroscan), in 77% (33/43) the stage of fibrosis could be detected in consistency with the histopathological diagnosis with a deviation of +/- one stage. Correlation coefficient between liver elasticity in transient elastography and histopathological stage of fibrosis was 0,87.

Conclusion: Invasive routine liver biopsies seem to play an important role in the evaluation of liver transplants especially within the first 10 years after transplantation. None of the laboratory parameters could sufficiently predict the histopathologically proven stage of fibrosis or inflammatory activity. By using noninvasive transient elastography only the evaluation of the stage of fibrosis was possible. In our cohort results of routine liver biopsies led to clinical consequences in almost 1/5th of the patients. Regarding the complication rate (0%), therefore performance of invasive routine liver biopsies seemed reasonable. Nevertheless it is necessary to implement innovative non-invasive immunological biomarkers for individual follow-up after paediatric liver transplantation.
Evaluation of cardiovascular risk in children after liver transplantation

Dolóresz Szabó¹, Dorottya Szentpáli¹, Laszlo Szonyi², Antal Dezsőfi¹

¹Semmelweis University, First Department of Pediatrics, Budapest, Hungary
²Organ Transplant Center, Riyadh, Saudi Arabia

Objectives and study: The risk of development of cardiovascular (CV) diseases and metabolic syndrome in children after liver transplantation (LTx) is higher than in the normal population. The decrease of arterial elasticity, hypertension, increased body-mass index (BMI) and other metabolic alterations related to the side effects of immunosuppressive therapy may further increase morbidity and mortality. Pulse wave velocity (PWV) is a non-invasive tool to assess CV risk.

We prospectively measured PWV and some metabolic parameters in children after LTx.

Methods: We enrolled 22 (10 males, mean age: 11.95 year±2.27) children after LTx. The mean time after LTx was 8.1 year (1-11.5). Sixteen children were on tacrolimus, 5 on cyclosporine and 1 on sirolimus based immunosuppressive therapy. PWV was measured using a non-invasive portable tonometer for determining arterial pressure wave and pulse wave velocity (PulsePen®). At the time of the measurement we obtained laboratory parameters (serum total cholesterol, HDL-cholesterol, triglyceride, ALT, albumin, INR), performed oral glucose tolerance test (OGTT), 24-hour ambulatory blood pressure monitoring (ABPM) and calculated BMI. For calculation of PWV, ABPM, BMI age and gender corrected z-scores were used. Homeostasis model assessment of insulin resistance (HOMA-IR) considered normal below 2.5. Laboratory parameters showed non normal distribution. Statistical analysis was made by Spearman rank correlation and Pearson correlation analysis.

Results: Based on our data the average PWV z-score was −0.42, the average ABPM systolic and dyastolic z-scores value were −0.59 and -0.61, respectively. The average of the ABPM's 50 percentiles was 108/66 Hgmm. Total and HDL-cholesterol (median 3.6 mmol/l; 1.9 mmol/l), triglycerides (0.9 mmol/l), albumin (44 g/l), ALT (17.5 U/l) and INR (1.17) median values were in normal range. Based on the results of OGTT HOMA-IR indexes were calculated, which were increased in 13% of patients. The average BMI and BMI z-score were 18 and 0.2, respectively. Three out of 20 had BMI z-score<2 SD, which indicated thinness. Only one patient had obesity (BMI z-score>2 SD), 4 patients were overweight (BMI z-score between 1-2 SD). Correlation analysis resulted moderate negative correlation between total cholesterol and PWV (Spearman’s rho=−0.44), time from LTx and PWV (Pearson correlation=−0.28).

Conclusion: We did not observe any significant difference in the arterial wall stiffness in patients after LTx compared to healthy age matched children. Moreover, based on the result of correlation analysis it seems so that arterial elasticity has been slightly improved slightly in time. To clarify these findings further follow-up of patients is necessary. There were no significant differences in metabolic parameters, however, carbohydrate metabolism should be closely monitored.
Efficacy and safety of a probiotic-mixture for the treatment of infantile colic: a double-blind, randomized, placebo-controlled clinical trial

Maria Elisabetta Baldassarre¹, Manuela Capozza¹, Valentina Rizzo¹, Silvio Tafuri¹, Antonio Di Mauro², Nicola Laforgia¹

¹“Aldo Moro” University of Bari, Department of Biomedical Science and Human Oncology, Bari, Italy
²University of Bari “Aldo Moro”, Neonatology and Neonatal Intensive Care Unit, Department of Biomedical Science and Human Oncology, Bari, Italy

Objectives and study: Infantile colic is a frequent problem in neonates and infants, which causes parental distress and medical effort. Recent evidences suggest that infantile colic is associated with low-grade systemic inflammation and gut microbiota alterations. Manipulation of the gut microbiota with probiotic supplementation seems to play a preventive measure and a therapeutic role in colic management. Aim of this study was to investigate the effectiveness and the safety of a probiotic-mixture (containing Lactobacillus plantarum DSM 24730, Streptococcus thermophilus DSM 24731, Bifidobacterium breve DSM 24732, Lactobacillus paracasei DSM 24733, Lactobacillus delbrueckii subsp. bulgaricus DSM 24734, Lactobacillus acidophilus DSM 24735, Bifidobacterium longum DSM 24736, Bifidobacterium infantis DSM 24737 and currently sold under the brand Vivomixx® in Continental Europe and Visbiome® in USA and Canada) for the treatment of infantile colic in breastfed infants, compared with placebo.

Methods: A randomized, double blind, placebo-controlled trial was conducted involving exclusively breastfed infants with colic, randomly assigned to receive a probiotic-mixture or placebo for 21 days.

A structured diary on gastrointestinal events in newborns, such as number of minutes of inconsolable crying per day, number of regurgitation episodes per day, number of bowel movements per day and stool consistency, was given to parents. Diaries, infants’ anthropometrics and type of adverse events were monitored weekly. The trial was registered to Clinicaltrial.gov at number: NCT01869426.

Results: 59 exclusively breastfed infants completed the 3 weeks of probiotic-mixture (n.28) or placebo (n.31) treatment.

Infants given probiotic-mixture showed a significant reduction in average daily episodes of fussing at the end of treatment period, compared with those receiving placebo (6,5±9,1 vs 12,7±12,7; p=0,01). Also average minutes of crying per episode on day 21 is shorter compared with infants given placebo (34,3±36,7 minutes vs 65,8±50,2 minutes; p=0,009).

Total average minutes of inconsolable crying per day throughout the study were significantly shorter among colic infant in the treatment group compared with those of placebo group and reached statistical significance at the end of treatment period (214,8±338,3 minutes vs 710,4±716,0 minutes; p=0,00).

No differences between groups are collected regarding infants’ anthropometric data, number of regurgitation episodes per day, number of bowel movements per day and stool consistency (p>0.05). No adverse events were reported related to the study intervention.

Conclusion: Administration of a probiotic-mixture for the treatment of infantile colic is safe and significantly reduces minutes of inconsolable crying per day in exclusively breastfed infants with colic.
Objects and study: Recent reviews have once again highlighted the poor predictive values of estimating caloric requirements with calculations. It is further recognised that patients with chronic disease and altered body compositions are most likely to have the biggest range of error. The caloric requirements of non-ambulatory patients with severe neurological impairment are very poorly investigated making clinical decision on how much to deliver difficult. There are limited studies comparing true resting energy expenditure (REE) measured by indirect calorimetry (IC) with predictive equations such as FAO/WHO/UNO. The Oxford predictive equation predates these studies and its validity is yet to be assessed in this specific group. It has been proposed the Oxford equation may prove to be the most accurate and generalizable predictive equation due to its design. Our aim was to compare REE measured by IC with the Oxford equation for BMR.

Methods: Patients were identified from the nutrition team complex case load and dietetic referrals between January and November 2016. Patients were included if they were non ambulatory (GMFCS 5 or equivalent), exclusively artificially fed and had neurological impairment. Preparation and collection of data from IC followed standard recognised guidelines and values of RQ between 0.67-1.3 were used as markers of validity of the measurement.

Results: 5 patients were identified. The Oxford BMR equation overestimated the REE in all patients by a median of 46.7% (range 5.2%-47.2%).

Table:

<table>
<thead>
<tr>
<th>Subject</th>
<th>Age (years/months)</th>
<th>BMI Centile</th>
<th>Resting energy expenditure (Kcals)</th>
<th>Difference between measured and predicted (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Measured (IC)</td>
<td>Predicted (Oxford)</td>
</tr>
<tr>
<td>1</td>
<td>6y /4m</td>
<td>&lt;0.4</td>
<td>736</td>
<td>777</td>
</tr>
<tr>
<td>2</td>
<td>7y /7m</td>
<td>&gt;91st</td>
<td>518</td>
<td>969</td>
</tr>
<tr>
<td>3</td>
<td>8y /2m</td>
<td>&gt;25th</td>
<td>534</td>
<td>1005</td>
</tr>
<tr>
<td>4</td>
<td>8y /10m</td>
<td>&gt;98th</td>
<td>649</td>
<td>1230</td>
</tr>
<tr>
<td>5</td>
<td>15y /4m</td>
<td>9th</td>
<td>806</td>
<td>1241</td>
</tr>
</tbody>
</table>

Conclusion: In our group of patients with severe neurological impairment and exclusive reliance on artificial feeding, the Oxford equation markedly overestimated the REE. Notably 2 patients had a BMI centile >91st suggesting historical excess caloric delivery (the practical worry in this group). This comparison data is of concern as when resting energy expenditure is estimated rather than measured (which is most common in clinical practice) the risk and impact of overfeeding is increased. IC can assist in better estimating caloric needs in this vulnerable group.
Does gastrostomy tract length change with the child growth?

Rachel Leshem Namedar, Yael Adler, Batia Weiss

Background: The number of disabled children with long term gastrostomy tube feeding has increased as a result of increase in life expectancy. Most parents prefer the skin level “button” which allows a better function. The button is placed after measuring the length of the tract created through the skin, abdominal wall and stomach wall. Accurate estimation of the stoma tract length is important to prevent gastric ulcer formation and/or skin damage. The children are followed at the gastrostomy- tube clinic, to ensure that the length of the tube is appropriate for the child’s growth. A length increase of over 0.2cm requires a tube exchange. Our long standing observation shows that the tube length is almost unchanged during the child’s growth and development.

Aims: To examine the predicting factors for change of gastrostomy tract length during follow-up.

Methods: A retrospective chart review of 82 patients under 18 years of age, followed by attendant nurses at the gastrostomy-tube clinic between January 2000 and August 2016. All patients had a Mic Key gastrostomy. Clinical, demographic and anthropometric data and measurements of the gastrostomy tract over time were retrieved from the patients’ charts and body mass index (BMI) was calculated. An increase of tube length of 0.2 cm was considered significant.

Results: 82 patients (41 males), aged 0.5-18 years (mean 4.97± 5.05) with at least 2 measurements of the gastrostomy tract length during follow up, were included. The mean follow-up was 2.45 years with a range of 0.5-10 years and the number of tract measurements was 204.

A significant change in tube length of ≥ 0.2 cm was found in 15 patients. The factors related to increase in the tract length were: 1. the time elapsing between the first and the second measurements: 3.9 ± 2.2 years and 2.1± 2.4 years in patients with and without gastrostomy tract elongation, respectively (p=0.012). 2. A shorter tract length in the first measurement was associated with tract elongation: 1.5 ±0.3 cm and 1.9 ± 0.6 cm, in patients with and without tract elongation, respectively (p=0.012). Other factors including age at tube insertion, gender, BMI, or concomitant fundoplication had no influence on change of tube length during follow-up.

Conclusions: Elongation of gastrostomy-tube length with age occurs in less than 20% of children during follow-up. The factors predicting tract elongation are the time duration since tube insertion and a short initial tract length. Tract elongation is uncommon in the first 2 years after tube insertion. Therefore, there is no need for measurements of the tract and gastrostomy tube change for at least 2 years after insertion.
Clinical and financial benefits of a Nutritional Support Team

Tracey Johnson¹, Michelle Butcher², Haidee Norton¹, Amanda Scott³, Adam Henderson³, Theo Wong⁴, Sue Protheroe⁵

¹Birmingham Children's Hospital, Dietetics Department, Birmingham, United Kingdom
²Birmingham Children's Hospital, Nutritional Care, Birmingham, United Kingdom
³Birmingham Children's Hospital, Pharmacy, Birmingham, United Kingdom
⁴Birmingham Children's Hospital, Gastroenterology, Birmingham, United Kingdom
⁵Birmingham Children's Hospital, Paediatric Gastroenterology, Birmingham, United Kingdom

Objectives and study: The evidence-based standard for optimal nutritional support is the multidisciplinary team (MDT) approach of a Nutrition Support Team (NST). The NST at Birmingham Children's Hospital was devolved in 2007 and audit raised concern regarding lack of competence in prescribing, inappropriate use of PN, inadequate monitoring, high wastage and over and under provision of nutrition. The NCEPOD Report (1) and Chief Pharmacists Report (2) recommended national standards in nutritional care needed to be improved and all children on PN should have access to a competent MDT. A pilot study between 2012-2013 confirmed the risk and showed reduction in PN usage and wastage. The business case was accepted in 2014 to fund the NST. The aim of the study was to assess improvements in clinical care and financial benefits before and after the inception of the NST.

Methods: The impact of the NST on patient care was assessed by review of biochemical monitoring, nutritional status and intake compared to an audit carried out in 2008 and educational strategies. Financial impact was assessed from total PN usage, standard bag usage and PN wastage before and after implementation of the NST.

Results: >60% patients met their Estimated Energy Requirement and gained weight at an appropriate rate compared to only 38% meeting the EER and 26% gaining weight at an appropriate rate in 2008. Improvements in biochemical monitoring were seen. New educational strategies included the development of a Moodle providing support for staff to achieve competencies in the prescription of PN, a PN study day and a parent information leaflet. Between 2012-2015 there has been a 20% reduction in the number of total PN bags/year resulting from avoiding inappropriate use of PN and achievement of good nutritional status in an appropriate time frame. Standard bag usage has increased from 6% to 15% without compromising nutritional intakes. The combined cost saving is estimated at £144,000/year. Wastage has fallen from 5% to 3% amounting to an additional cost saving of approximately £19,000/yr.
Conclusion: PN is a safe and effective treatment but management of children receiving PN requires a high level of knowledge and expertise. The interventions of the NST have resulted in sustained improvement in clinical care and cost savings.

References

1. A Mixed Bag: A report by the National Confidential Enquiry into Patient Outcome and Death (2010)

2. Improving practice and reducing risk in the provision of parenteral nutrition for neonates and children: A report from the Paediatric Chief Pharmacists 2011
Introduction of solids in infants with short bowel syndrome

Tamara Farrell\textsuperscript{1}, Jackie Falconer\textsuperscript{1}, Krishna Soondrum\textsuperscript{2}

\textsuperscript{1}Chelsea and Westminster Hospital, Nutrition and Dietetics, London, United Kingdom
\textsuperscript{2}Chelsea and Westminster Hospital, Paediatric Gastroenterology, London, United Kingdom

Objectives and study: In the current literature, there is minimal evidence available outlining ideal timing and type of food introduction for infants with short bowel syndrome. A previous unpublished audit conducted by Elaine Buchanan (presented at ESPGHAN 2007) showed variable practice for introducing solids in short gut infants across the United Kingdom (UK). Varying practices across the UK and the rest of the world led to a decision to audit present practice.

The objectives of the audit were to determine:

2. Current first and second line formula choice in infants with short bowel syndrome, when breast milk is not available.

Methods: A literature review was conducted using ‘EMBASE, CINAHL, PUBMED’ to determine the current evidence available, for introduction to solids, formula choice and allergy testing in short gut infants. A short survey, created with Survey Monkey, was emailed to ESPGHAN and BSPHGAN allied health professional members, as well as individual gastroenterology dietitians across multiple centres. The survey incorporated 10 questions (multiple choice or free text) pertaining to the above objectives. Survey responses were collected over an 11 week period, from 19\textsuperscript{th} April to 4\textsuperscript{th} July 2016. Results were collated in August 2016.

Results: A total of 36 survey responses were received, from 35 different children’s hospitals across the UK, Europe, Israel, United Arab Emirates, South Africa and Australia.

Introduction to solids and food exclusions: The majority of respondents (58%) state their weaning and food exclusion practice would be different, depending on length/quality of bowel remaining. Only 11% have a guideline for introducing solids in short gut infants, however 33% have a guideline for food reintroductions/challenges post food exclusions. All respondents would aim to introduce solids between four and six months; however timing for introducing solids would also depend on tolerance of enteral feeds. Eighty nine percent of respondents would routinely exclude one or more foods during weaning; the most common food exclusions were dairy (39%) or four food exclusion (dairy/egg/wheat/soya), 28%. Twenty five percent reported avoidance of other carbohydrates/foods such as sugar, lactose, fruit and fibre.

Formula choice: If breast milk is not available, as a first line feed, the majority of respondents choose extensively hydrolysed (89%) and 11% choose whole protein cow’s milk formula. As a second line feed choice, most respondents choose amino acid (72%), while 19% choose extensively hydrolysed, 6% modular, and 3% whole protein cow’s milk formula.

Allergy testing: The vast majority of centres (89%) did not carry out any allergy testing during weaning; while 6% undertake specific IgE testing.

Conclusion: There is some consensus between centres in the UK and worldwide on first line feed choice and timing for introducing solids, however clear differences were noted, particularly for second line formula choice, and routine food exclusions. This is a complex patient group where individual assessment is required; however there is a clear need for consensus statements for introducing solids and feed choice in short gut infants.
Change in plasma atherogenic index after 1-year intervention based on Mediterranean diet in obese children

Carlotta Lassandro¹, Marta Brambilla¹, Sara Vizzuso¹, Benedetta Mariani¹, Giuseppe Banderali¹, Elvira Verduci¹

¹San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy

Objectives and study: The Atherogenic Index of Plasma (AIP) may predict the risk of cardiovascular disease (CVD) in adults, reflecting the relationship between protective and atherogenic lipoprotein and being associated with the size of pre- and anti-atherogenic lipoprotein particle. The aim of this study was to evaluate the effect of a 12-month lifestyle intervention on the risk of cardiovascular disease.

Methods: A cohort of 125 Caucasian obese children aged 6-15 years (61 boys and 64 girls) was recruited. BMI z-scores were calculated. Fasting blood samples were analysed for lipids, insulin and glucose, at baseline and at the end of intervention. Homeostatic model assessment of insulin resistance (HOMA-IR), to evaluate liver insulin resistance, triglyceride glucose (TyG) index, reflecting mainly muscle insulin resistance, quantitative insulin sensitivity check index (QUICKI), to detect insulin sensitivity, and HOMA-β%, to evaluate pancreatic β-cell function, were calculated. The triglycerides/HDL ratio was calculated. The AIP was calculated: (Log [Triglycerides/HDL]). Educational sessions based on the promotion of a normocaloric Mediterranean diet and of at least 60 min moderate-to-vigorous-intensity physical activity daily were held at the San Paolo Hospital, Milan, Italy. A Mediterranean diet pyramid for the pediatric age was developed “ad hoc” on the basis of the Mediterranean diet pyramid for adults. Written educational brochures were given to the parents, including general nutritional advice, food choice lists, the Mediterranean diet pyramid for the pediatric age, and recommended average servings for principal food categories, according to updated Italian Dietary Reference Values. Statistical significance of longitudinal variations was tested by the Student’s t test for paired data or the Wilcoxon test, and adjustments were made for age, sex, baseline BMI z-score and Tanner stage.

Results: At the end of intervention children (n=118) showed lower [mean (SD)] BMI z-score than recruitment [2.89 (0.86) vs 3.41 (0.95), P<0.0001]. Reduction of daily energy intake and macronutrient redistribution towards the recommended range were observed. At the end of the intervention children showed lower HOMA-β% [245.84 (131.53) vs 332.74 (291.60); P=0.043], TyG index [vs 8.08 (0.44) vs 8.33 (0.50); P<0.001] and increased QUICKI [0.33 (0.03) vs 0.33 (0.03); P=0.025]. After 1-year intervention children also showed lower total cholesterol [158.54 (31.66) vs 164.14 (29.82) mg/dL; P=0.023], triglycerides (83.98 (38.38) vs 109.71 (54.87) mg/dL; P<0.001*) levels, lower triglycerides/HDL ratio [1.80 (1.12) vs 2.49 (1.64); P<0.001] and atherogenic index 0.19 (0.23) vs 0.32 (0.27); P<0.001], and increased HDL cholesterol (50.30 (10.33) vs 48.02 (9.76); P<0.001). A reduction of AIP index > 50% of the baseline value was observed in 38 (32.2%) children.

Conclusion: To our knowledge this study is the first intervention study that evaluated the atherogenic index in a paediatric population and found that it decreased after 12-month intervention based on promotion of Mediterranean diet.
Scottish home parenteral nutrition longitudinal point prevalence suggest a dramatic rise over the last 3 years

Iain Chalmers¹, Paul Henderson¹, Christina Mcguckin², Catherine Paxton¹, David Goudie³, David Mitchell¹, Shyla Kishore⁴, Diana Flynn⁵, Andrew Barclay⁵

¹Royal Hospital for Sick Children, Paediatric Gastroenterology, Edinburgh, United Kingdom
²Royal Hospital for Children, Paediatric Gastroenterology, Glasgow, United Kingdom
³Raigmore Hospital, Paediatrics, Inverness, United Kingdom
⁴Royal Aberdeens Childrens Hospital, Paediatric Gastroenterology, Aberdeen, United Kingdom
⁵Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Glasgow, United Kingdom

Objectives and study: Longitudinal data on home parenteral nutrition (HPN) are usually published by single centres of excellence with inherent recruitment bias. Previously published UK-wide point prevalence data suggest that the rise in HPN prevalence is accelerating (1). However these data have not been republished since 2012 and more recent surveys are incomplete. We aim to present longitudinal, collaborative, Scottish HPN epidemiological data (representing 7.4% of the UK population <16yrs), which has been uniquely accrued since 2003.

Methods: HPN prevalence and basic demographic data were prospectively collected annually from 2003-2010 by the Scottish HPN managed clinical network (SMCN), and subsequently through the SSPGHAN nutrition group in 2012, 2015 and 2016. Population data for Scotland from the National Records of Scotland provided population figures for children aged <16 years. Trend analysis was performed for the 2 epochs 2003-08 and 2009-16 using Poisson regression. Data were extrapolated to the entire UK population using publicly available data. Statistics were performed in Rv3.1.1.

Results: HPN point prevalence has increased from 9 cases in 2003 to 24 cases in 2016. Diagnoses in 2016 were: short bowel syndrome 13 (54%), neuromuscular disease 9 (38%) and enterocyte disorders 2 (8%). Scottish HPN point prevalence is currently 26.3/1,000,000 population at risk. Epoch analysis revealed a significant increase in point prevalence from 7.1/1,000,000 (95% CI 5.1-9.7) to 17.2/1,000,000 (95%CI 13.6-21.5) from 2003-2008 to 2009-2016 (p=0.006)(Figure 1). Extrapolating for the UK in 2016, data would suggest a total of 324 prevalent HPN cases

Table:
Conclusion: We present longitudinal, collaborative, Scottish HPN epidemiological data. Due to the unique close working practices of the SMCN and SSPGHAN nutrition group, we can be uniquely confident of complete case ascertainment. A secular trend in increasing neuromuscular disease was noted, this may reflect increased survival (2) or case recognition, but also the expansion of indications for HPN within neuro-disability. Given the insights provided by Scottish epidemiology, rejuvenation of UK-wide HPN epidemiology is a research priority. The sharing of such data is important for informing patients and the planning of services on a regional and national basis.

2. Barclay and Henderson JPGN 2016 62(3):363-4
Diet and micronutrient status in 0-2 years old children with cow’s milk protein allergy

Janne Anita Kvammen¹, Rut Anne Thomassen¹, Mari Borge Eskerud², Jarle Rugtveit¹, Christine Henriksen³

¹Oslo University Hospital, Department of Paediatric and Adolescent Medicine, Oslo, Norway
²Lovisenberg Dioconal Hospital, Department of Internal Medicine, Clinical Nutrition, Oslo, Norway
³University of Oslo, Faculty of Medicine, Department of Nutrition, Institute of Basic Medical Sciences, Oslo, Norway

Objectives and study: To study diet and micronutrient status in cow’s milk protein allergic (CMPA) children 0-2 years of age.

Methods: An observational cross-sectional study was performed at Oslo University Hospital from January 2014 until May 2015. Fifty-seven CMPA children 0-2 years of age (70% participation) were included. A 3-day food record was collected. Blood samples were analysed for total homocysteine (tHcy), vitamin B12, iron parameters, vitamin 25-OH-D and zinc. Subgroup analyses were done on different feeding patterns according to weaning stage; mainly breastfed (mBF); receiving less than 50 % of their estimated energy requirement from food, partially breastfed (pBF) and weaned.

Results: Median age was nine (6-12) months and 54 % were boys. More than half of the children (57 %) were breastfed; 24 % mBF and 33 % pBF. The mBF were significantly younger than the pBF and weaned children. Most children, 69 %, used a hypoallergenic formula. Complementary foods were introduced at median age four months, and no later than seven months. The median time on milk-free diet before enrollment was 17 weeks. Vitamin B12 depletion, assessed by plasma t-Hcy > 6.5 µmol/L, were detected in 39 % of participants; 62 % of mBF, 50 % of pBF and 17 % of the weaned. Plasma t-Hcy was significantly higher in the mBF children compared to the weaned and the pBF. Serum vitamin B12 was significantly lower in mBF children compared to the weaned. Serum vitamin B12 < 250 pmol/L was found in 14 % of participants; 31 % of mBF, 17 % of pBF and 5 % of weaned children. Dietary intake (except for breast milk content) of vitamin B12 and iron were lower than recommended levels for mBF children. For pBF B12 intake was adequate, but iron intake was lower than recommended. For weaned children intake of B12 and iron were as recommended. Iron deficiency (s-ferritin < 12 µg/L) was found in 12 % of participants; 15 % of mBF, 17 % of pBF and 9 % of weaned children. Anemia (Hb < 10.5 g/dL) was present in 9 % of participants; 15 % of mBF and 11 % of pBF. None of weaned CMPA children had anemia. All participants had normal s-folate. Vitamin D deficiency was not present, and 91 % had serum 25-OH-D values > 50 nmol/L. Medium vitamin D intake was 13.2 µg/d included dietary supplements, significantly higher than 5.3 µg/d from foods. Zinc deficiency (s-zinc < 10 µmol/L) was found in 7 % of the participants. Zinc intake from foods other than breast milk, was lower than recommended levels for mBF and pBF children.

Conclusion: CMPA children 0-2 years of age were at risk of B12 depletion, especially if mBF. Iron deficiency was a problem, while vitamin D status was adequate. Zinc deficiency was present in some children. Ensuring weaning foods rich in vitamin B12 and iron seems appropriate. Vitamin D, 10 µg/d, as a dietary supplement seems appropriate. Monitoring micronutrient status can be considered in clinical practice. Further research and larger studies on micronutrients are necessary to improve clinical practice and ensure health in the first 1000 days for both CMPA and healthy infants.

Disclosure of interest: Janne Anita Kvammen and Rut Anne Thomassen: Conflict; speakers fees for lectures paid by Nutricia
Comprehensive analysis of the nutritional profile of gluten-free products as compared to their gluten-containing counterparts

Sandra Martínez-Barona¹, Jaquim Calvo Lerma¹, Victoria Fornes², Paula Crespo Escobar³, Esther Donat⁴, Carmen Ribes Koninckx⁴

¹Instituto de Investigación Sanitaria La Fe, Valencia, Spain
²Instituto de Investigacion Sanitaria La Fe, Unidad de Bioestadística, Valencia, Spain
³Hospital Universitari i Politecnic La Fe, Valencia, Spain
⁴La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

Objectives and study: Gluten free-diet is the life-long therapy for patients with Coeliac Disease (CD). This supposes the exclusion of staple foods coming from gluten containing cereals from the daily dietary intake. In order to tackle this gap, a wide range of gluten-free products (GFP) is available in the market, which mimic the physical and organoleptical characteristics of their gluten-containing counterparts (GCC) with the only difference that the raw materials for their elaboration have replaced the forbidden cereals, mainly by corn or rice flour and potato starch. The elimination of the gluten, however, supposes a great technological challenge since this protein is the responsible for the tridimensional structure conferred to the food matrices. This cannot be achieved by any other ingredient, but a similar palatability and texture in the GFP can be obtained by the addition of other ingredients. Thus, the different elaboration process may lead to a different nutritional profile between these two groups of products. Therefore, the aim of the present study was to assess the nutritional composition of the GFP as compared to their GCC.

Methods: A total number of 654 GFP from 25 brands and 655 GCC from 29 brands were selected. Nutritional facts information was obtained from the labeling of the products, which according to the Spanish legislation, include Energy (kcal), protein (g), carbohydrates (g), sugar (g), fat (g), saturated fatty acids (g) and fibre, for the vast majority of the food products. According to the role in the diet, each food item was assigned with a food group: bread, roll bread, bread toast, bread bun, pasta, flour, breakfast cereal, biscuits, pastries, pizza, snacks, ready meals, battered and ice-cream. A linear regression model was used to explain differences in nutritional composition between GFP and GCC for each food group.

Results: Overall, the GFP had a slightly higher energy content than their GCC. The main difference in terms of nutrients was the protein content of GCC which in some of the food groups was two to three times higher than the content in the GFP, especially in the case of flours, breads, pasta and pizza (p<0.0001). Total carbohydrates profile of both type of products was similar, but when referring to sugar, gluten-free breads had a significantly higher content (p<0.001). Heterogeneity was found in the case of lipid content: whilst it was significantly higher in some GFP like breads (p<0.001), some products had a similar amount for example biscuits and pastries, or even some GCC such as flour, snacks and battered had a higher lipid content than their GCC. A similar pattern was observed in the case of saturated fatty acids. With the exception of pasta, breakfast cereal and snacks, GFP had an equivalent or a higher content of fibre.

Conclusion: In the light of the results of the present study we conclude that GFP cannot be considered as substitutes for their GCC. The assessed food products that may have a greater impact in the diet of a CD patient, like bread and pasta, differ from their GCC in terms of protein, sugar and fat. We identify the need for a reformulation of the GFP with more healthy raw materials and ingredients and encourage the food industry to innovate the recent advances in this field.
Dietary manipulation of the healthy human and colitic murine gut microbiome by CD-TREAT diet and exclusive enteral nutrition; a proof of concept study

Vaios Svolos1, Richard Hansen2, Umer Ijaz3, Christopher Quince4, David Watson5, Adel Alghamdi6, Asker Brejnrod7, Cecilia Ansalone8, Simon Milling8, Daniel Gaya9, Richard Russell2, Konstantinos Gerasimidis10

1University of Glasgow, Human Nutrition, School of Medicine, College of MVls, Glasgow Royal Infirmary, Glasgow, United Kingdom
2Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
3University of Glasgow, Glasgow, United Kingdom
4Warwick Medical School, University of Warwick, Warwick, United Kingdom
5Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom
6Strathclyde Institute of Pharmacy and Biomedical Sciences, University of Strathclyde, Glasgow, United Kingdom
7University of Copenhagen, Department of Biology, Copenhagen, Denmark
8Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom
9Department of Gastroenterology, Glasgow Royal Infirmary, Glasgow, United Kingdom
10University of Glasgow, Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, Glasgow Royal Infirmary, Glasgow, United Kingdom

Objectives and study: The extensive modulation of gut microbiome in children with Crohn's disease (CD) treated with exclusive enteral nutrition (EEN) offers clues about EEN's potential mode of action; but also on the development of novel therapies through dietary manipulation of the gut microbiota. This proof of concept study compared the effect of a novel 'ordinary' food-based diet (CD-TREAT diet) and EEN on healthy human and colitic murine gut microbiota.

Methods: A)Healthy adults followed two experimental diets for 7 days with a 15 day wash out period in between; EEN and CD-TREAT, an "ordinary" food diet which has similar nutrient and food ingredient composition to EEN (e.g. fibre, gluten, lactose content and fatty acid composition). Participants were randomly allocated to start with EEN or CD-TREAT first. Fresh faecal and urine samples were collected before and after each dietary intervention and 16s rRNA sequencing, untargeted faecal and urine metabolomics (using LC-MS) were performed; B)10-month-old HLA-B27 and HLA-B7 transgenic rats received EEN, CD-TREAT diet or regular rat chow for 4 weeks. Faeces were collected at baseline, 1, 2, 3 and 4 weeks post treatment initiation. Gut contents, ileal and colonic tissue were harvested at sacrifice. Disease activity was quantified by blinded histological scores and gut microbiota metabolic activity was measured by faecal short chain fatty acids (SCFA) quantification.

Results: A) 100 faecal and urine samples were collected from 25 healthy subjects. During EEN and CD-TREAT gut bacterial community structure (using Operational Taxonomy Units) significantly changed after both EEN (R-squared=0.14501, p-value=0.001) and CD-TREAT (R2=0.05016, p-value=0.003) and shifted towards the same direction. EEN's and CD-TREAT's impact on 3% OTU community structures was strongly correlated (Adjusted R-squared=0.3755, p-value<2.2e-16). Similarly, untargeted faecal metabolomics revealed a strong correlation between the changes during EEN and CD-TREAT (Pearson's R=0.31, p-value<10^-14). B) 100 faecal samples were collected from 12 HLA-B27 and 8 HLA-B7 adult transgenic rats. Both dietary interventions increased the body weight of the HLA-B27 rats [Median(IQR)%weight change, EEN: +9.2(+6.5,+12.4) vs CD-TREAT: +15.7(+10.4,+17.7) vs Control: -2.1(-2.7,-0.3)] and decreased the weight of caecum and colon contents [Median(IQR) gut contents weight(g), EEN: 1(0.6,1.2), 0.1(0.0,0.26) vs CD-TREAT: 2.1(1.8,2.9), 0.5(0.3,0.7) vs Control: 3.5(3.1,5.2), 0.7(0.4,1.4)]. Faecal concentration of total SCFA, acetic, propionate decreased while iso-butyric and isocaproic increased during both dietary interventions [AMedian µmol/g, EEN: -324, -271, -44.8, +4.7, +2.2 vs CD-TREAT: -354, -292, -56.2, +3, +1.5]. Histopathology scores revealed that both dietary interventions benefited moderately ileal but not colonic inflammation.
**Conclusion:** We have developed an "EEN composition alike" food based diet which induces similar effects on gut microbiome with EEN. This proof of concept study supports a subsequent pilot trial in people with active CD.
Dietary bovine and human milk oligosaccharides and their combination influence body composition in the young pig

Marcia Monaco¹, Mei Wang¹, Anna Dilger², Jose Manuel Ramos Nieves³, Jonas Hauser³, Jian Yan⁴, Ryan Dilger², Sharon Donovan¹

¹University of Illinois, Food Science & Human Nutrition, Urbana, United States
²University of Illinois, Animal Sciences, Urbana, United States
³Nestle Research Center, Lausanne, Switzerland
⁴Nestlé Nutrition R&D, King of Prussia, United States

Objectives and study: Milk glycans, including free oligosaccharides, are increasingly recognized as drivers of microbiota development and gut health, with the potential to impact growth. Human milk oligosaccharides (HMO) are characterized by a high degree of fucosylation and low sialylation, while bovine milk oligosaccharides (BMOS) are predominantly sialylated. The objective of this study was to determine the influence of dietary bovine milk oligosaccharides (BMOS) – a mixture of multiple oligosaccharides from cow’s milk, human milk oligosaccharides (HMO) [2’fucosyllactose (2’FL) and lacto-N-neotetraose (LNnT)], or a combination of the two on piglet growth and body composition.

Methods: Beginning at 2 d of age, 48 vaginally-derived male piglets were randomized (n=12 per diet) to receive one of four diets formulated to contain: control (CON) [0 g/L HMO + 0 g/L BMOS, Purina ProNurse milk replacer], BMOS [CON + 6.5 g/L BMOS], HMO [CON + 1.5 g/L of 2’FL + LNnT combined (2:1 ratio)], or HMO + BMOS [CON + 6.5 g/L BMOS + 1.5g/L of 2’FL + LNnT combined (2:1 ratio)]. All diets were supplemented with lactose to equalize the added carbohydrate to 8 g/L. Body weights (BW) were measured daily, and body circumference and crown-rump length measurements were taken on 2 and 32 d of age. Proximate analysis was conducted on soft tissue to determine its composition. All outcomes were subjected to a 2-way ANOVA to assess the main effects of HMO and BMOS as well as their interaction. Data are expressed as Mean±SE and statistical significance was defined as p ≤ 0.05 and trends defined as 0.05 < p ≤ 0.10.

Results: Randomization assured that all treatment groups had similar mean BW (1.83 kg ± 0.04) at the beginning of the study. Overall BW gains were comparable, but tended to be lower for animals supplemented with HMO (p=0.07). When analyzed weekly, BW gain was higher (p < 0.03) during week 4 of the study (d 23-30) in the combined HMO+BMOS group than any other group. However, total BW gain, body circumference and crown-rump length did not differ among the groups. In BMOS-supplemented animals, lipid % of soft tissue was decreased (p≤0.05) and lean % increased (p≤0.05) compared with HMO+BMOS animals, but did not differ from CON and HMO. HMO-supplemented animals tended (p=0.06) to have lower soft tissue lipid % and higher lean % than HMO+BMOS.

Conclusion: Dietary oligosaccharides impacted piglet growth with HMO+BMOS promoting faster growth and greater lipid accumulation than HMO and BMOS alone, but similar to CON piglets. Further research is warranted to determine if these effects are due to a greater quantity or synergistic effect of oligosaccharides. On-going analyses are assessing effects of dietary HMO and BMOS on gut microbial populations and possible associations with the observed differences in growth. This project was funded by Nestlé Nutrition Research.

Disclosure of interest: Jose Manuel Ramos Nieves is an employee of Nestle Nutrition Research
Jonas Hauser is an employee of Nestle Nutrition Research
Jian Yan is an employee of Nestle Nutrition Research
Ryan N Dilger has received grant funding and consulted for Nestle Nutrition Research
Sharon M. Donovan has received grant funding and consulted for Nestle Nutrition Research
A new lipid composition for infant nutrition enhances cholesterol absorption and reduces endogenous cholesterol synthesis in a piglet model

Peter Jones1, Elizabeth Babawale1, Fabiana Bar-Yoseph2, Yael Richter2, Shane Rutherfurd3

1University of Manitoba, Manitoba, Canada
2Enzymotec, Migdal Haemek, Israel
3Massey University, Riddet Institute, Palmerston North, New Zealand

Objectives and study: Human breast milk is believed to provide the optimal nutrition for infants. Consequently, commercial infant formulas are formulated to mimic the composition of human milk as best as practicable. Human milk is rich in cholesterol which is necessary for infant growth and development as it is a crucial component of the lipid bilayer present in cell membranes, is a necessary precursor for steroid hormone and bile acids synthesis, and plays a key role in lipoprotein synthesis and metabolism. Furthermore, studies suggest that the high concentrations of cholesterol in human milk are related to its protective effect on cardiovascular risk at adulthood. In contrast, infant formulas, which commonly contain vegetable oils as their fat source, possess lower cholesterol concentrations. Moreover, vegetable oils also contain plant sterols (phytosterols) that are structurally similar to cholesterol and inhibit cholesterol absorption. The latter potentially results in early programming of higher endogenous cholesterol synthesis with long term effects on cholesterol metabolism and cardiovascular risk. However, the combined actions of cholesterol and phytosterol in infant formulas on cholesterol trafficking have not be examined. The aim of the present study, therefore, was to investigate the impact of reducing dietary phytosterols on cholesterol metabolism using the neonate piglet as a model for human infant.

Methods: Thirty two 1 week old male piglets were randomly allocated to one of four infant formulas with combinations of cholesterol and phytosterol content based on their concentrations in human milk and in commercial infant formulas (cholesterol concentration of 80 or 20mg/l and phytosterol concentrations of 9mg/l or 90mg/l respectively). Blood samples were collected after 21 days of feeding and analysed for total cholesterol as well as endogenous cholesterol synthesis precursors (desmosterol, lathosterol and lanosterol). In addition samples of small intestine and liver were analysed for sterols.

Results: No differences were observed in growth or food consumption across treatment groups. Circulating cholesterol concentrations were higher (P<0.05) in the animals fed the formula with high cholesterol and reduced phytosterol concentrations (124.1±4.7 mg/100ml), compared to the control group animals fed regular infant formula with high phytosterol and low cholesterol concentrations (103.8±6.3 mg/100ml). Reducing the phytosterols levels (low phytosterol low cholesterol group, 111.5±6.1 mg/100ml) or increasing the cholesterol levels (high phytosterol high cholesterol, 115.1±6.2 mg/100ml) did not reveal significant difference compared to the control. Moreover, the changes in circulating cholesterol in the animals fed formula with high cholesterol and reduced phytosterol concentrations were also accompanied by reductions (P<0.05) in the concentrations of cholesterol precursors in plasma and in liver, compared to the control animals fed regular infant formula with high phytosterol and low cholesterol concentrations and the animals fed infant formula with high phytosterol and high cholesterol concentrations.

Conclusion: The results suggest that reducing phytosterol concentrations in cholesterol-enriched infant formulas may facilitate better cholesterol absorption and reduce endogenous cholesterol synthesis which may in turn have long term benefits via the early programming of cholesterol metabolism.

Disclosure of interest: Yael Richter and Fabiana Bar-Yoseph are Enzymotec employees
The study was funded by Enzymotec Ltd., Israel.
Long-Chain polyunsaturated fatty acids and extensively hydrolyzed casein induce browning in a UCP-1 reporter mouse model of obesity

Liufeng Mao1, Marieke H. Schoemaker2, Yan Zhong3, Tim T. Lambers2, Eric A.F. Van Tol2, Tao Nie1, Donghai Wu1

1Guangzhou Institute of Biomedicine and Health, Gibh, Chinese Academy of Sciences, Guangzhou, China
2Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands
3Mead Johnson Pediatric Nutrition Institute, Shanghai, China

Objectives and study: The prevalence of childhood obesity and related problems is rising globally. In the present study, the browning inducing effects of LCPUFAs (ARA+DHA) and milk-derived bioactive peptides (extensively casein hydrolysate, eCH) were investigated in a unique UCP1-luciferase knock-in mouse reporter model. Their potential to program functional adipose tissue and support metabolic flexibility under an obesogenic challenge later in life was also assessed.

Methods: Male Ucp1+/LUC mice (4 weeks old) were fed standard chow or standard chow supplemented with ARA+DHA, hydrolyzed casein diet, or hydrolyzed casein+ARA+DHA diet for 8 weeks. Mice were switched to high-fat diet (HFD) with or without ARA+DHA, or eCH, or a combination thereof for another 12 weeks. In vivo and ex vivo luciferase activity was assessed across the study and in adipose tissues by imaging or luciferase assay respectively. Browning-related protein and genes expression was done using Western blot, RT-qPCR (PGC1a, PRDM16, UCP-1) and immunohistochemistry (UCP-1). Systemic and adipose inflammation (IL1β, TNFα by ELISA and RT-qPCR) as well as metabolic flexibility (glucose & insulin tolerance tests, plasma risk factors and adipokines) were assessed.

Results: Nutritional interventions reduced body weight gain and adipose tissue weight against high fat diet. Also ARA/DHA, the eCH or the combination thereof induced UCP-1 expression in adipose tissues both prior and during HFD exposure as well as increased PGC1a, PRDM16 expression versus HFD. In the 3 intervention groups, systemic and adipose tissue inflammation were beneficially impacted. Nutritional interventions improved metabolic flexibility as shown by improved glucose tolerance and enhanced insulin sensitivity versus control and HFD groups and attenuated plasma levels of TG, TC, FFA, insulin, leptin, resistin, FGF21, ALT and AST and increased levels of adiponectin versus the HFD group.

Conclusion: Early nutritional intervention with ARA/DHA, eCH and their combination can attenuate HFD-induced obesity. Their impact on stimulating browning activity already early in life as well as limiting inflammation might be the underlying mechanisms for these detected effects.

The relationship between serum lauric acid and hippocampal choline metabolites is partially mediated by hippocampal dihomo-gamma-linolenic acid in the young pig

Austin Mudd¹, Rosaline Waworuntu², Brian Berg², Sharon Donovan³, Ryan Dilger⁴

¹University of Illinois, Piglet Nutrition & Cognition Laboratory, Urbana, United States
²Mead Johnson Pediatric Nutrition Institute, Evansville, United States
³University of Illinois, Food Science & Human Nutrition, Urbana, United States
⁴University of Illinois, Animal Sciences, Urbana, United States

Objectives and study: Fatty acids are critical for growth and development of the neonate, and the brain is especially susceptible to their presence or absence. There is interest in understanding the mechanisms whereby circulating fatty acids influence brain development. Moreover, relatively little research has explored medium chain fatty acids (MCFA), specifically, in this context. Therefore, the objective of this exploratory study was to identify novel relationships whereby circulating MCFA levels modulate hippocampal metabolites.

Methods: Beginning at 2 d and continuing until 30 d of age, 24 vaginally-derived male piglets were provided custom milk replacer formulated to meet piglet nutrient requirements. At 30 d of age, piglets underwent magnetic resonance spectroscopy (MRS) procedures to quantify metabolite concentrations in the hippocampus. Following MRS, samples from the right hippocampus and serum were harvested from pigs at 31 d of age for lipidomic profiling. Linear regressions were used to assess the relationship between serum MCFA and hippocampal MRS metabolites, as well as between serum MCFA and hippocampal FA. Subsequently, a mediation model was used to investigate whether the relationships between serum MCFA and hippocampal MRS metabolites were mediated by hippocampal FA. A bootstrapping method drawing 5,000 samples with replacement from the dataset was implemented to estimate a sampling distribution (95% confidence interval) for the indirect and direct mediation effects.

Results: The mediation analysis revealed that hippocampal free dihomo-γ-linolenic acid (FA-20:3n6) partially mediated the relationship between serum free lauric acid (FA-12:0) and brain glycerophosphocholine plus phosphocholine (GPC-PCh). First, increased levels of serum FA-12:0 related to decreased levels of hippocampal FA-20:3n6 (P = 0.011). Second, increased levels of serum FA-12:0 related to decreased brain GPC-PCh (P = 0.002). We observed a significant (P < 0.05; 95% CI: -0.245 to -0.019) indirect path of the mediation (i.e., effect of serum FA-12:0 though hippocampal FA-20:3n6 on brain GPC-PCh). Additionally, the direct path (i.e., effect of serum FA-12:0 on brain GPC-PCh, accounting for hippocampal FA-20:3n6) was also significant (P < 0.05; 95% CI: -0.435 to -0.012). Therefore, hippocampal FA-20:3n6 partially mediated the relationship between serum FA-12:0 and brain GPC-PCh.

Conclusion: The results from this study indicate that the levels of circulating FA-12:0 may be related to hippocampal metabolism of previously unrelated complex fatty acid moieties. Future research should test for direct effects of altering circulating FA-12:0 on these metabolites and any associated roles in brain development and functions.

Disclosure of interest: This project was funded by Mead Johnson Nutrition.
Vitamin D supplementation is associated with decreased serum lipid levels in young Swedish children: a double blind randomized clinical intervention trial

Inger Ohlund1, Torbjörn Lind1, Olle Hernell1, Sven-Arne Silfverdal1, Pia Karlsland-Akeson2

1Umeå University, Clinical Sciences, Pediatrics, Umeå, Sweden
2Department of Pediatrics, Lund University, Malmö/Lund, Sweden

Objectives and study: To evaluate the impact of a vitamin D supplementation on vitamin D status and serum lipid levels in Swedish children.

Methods: In this prospective, double-blinded, randomized, food-based intervention study, 5 to 7-year old, fair and dark skinned children received a daily vitamin D supplement of 25 µg, 10µg or placebo (2µg) during 3 winter months. Levels of serum 25-hydroxy vitamin D, (S-25(OH) D), total cholesterol (TC), high-density lipoprotein cholesterol (HDLC), low-density lipoprotein cholesterol (LDLC), apolipoprotein A1 (ApoA1) and apolipoprotein B (ApoB) were analyzed. Body mass index (BMI) was calculated from measured height and weight and converted to z-scores. All data were collected at baseline and follow-up after 3 months.

Results: Of 206 included children, 189 fulfilled the blood sampling at the follow-up visit. Overweight and obesity were observed in 15 and 5 percent, classified as BMI-z score ≥ 1 and ≥2, respectively. At follow-up, TC, LDLC, and ApoB decreased significantly among those supplemented with 25 µg, both over time (P<0.001) and compared to the other groups (P<0.05) (Table 1). A linear regression analysis of the impact of BMI on vitamin D status at follow up, adjusted for skin color and study site, revealed that children with higher total vitamin D intake (β 1.1, P=0.001), lower baseline levels of 25(OH) D (β -0.44, P=0.001) and lower BMI z-score (β -0.192, P=0.015) had a higher increase of S-25(OH) D after the intervention period.

Table: Changes of serum 25-hydroxy vitamin D and serum lipid levels from baseline to follow-up in preschool children who received different doses of vitamin D3 or placebo during 3 winter months.

<table>
<thead>
<tr>
<th></th>
<th>Intervention 25 µg (n=77)</th>
<th>Intervention 10 µg (n=69)</th>
<th>Control 2 µg (n=35)</th>
<th>P-value for difference between groups3</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline1</td>
<td>Follow up1,2</td>
<td>Baseline1</td>
<td>Follow up1,2</td>
</tr>
<tr>
<td>S-25(OH)D3 (nmol/L)</td>
<td>58 (21)</td>
<td>82 (17) ***</td>
<td>57 (17)</td>
<td>70 (15) ***</td>
</tr>
<tr>
<td>TC (mmol/L)</td>
<td>4.4 (0.60)</td>
<td>4.2 (0.59) ***</td>
<td>4.2 (0.63)</td>
<td>4.2 (0.64) *ns</td>
</tr>
<tr>
<td>LCLC (mmol/L)</td>
<td>2.47 (0.47)</td>
<td>2.35 (0.47) ***</td>
<td>2.30 (0.56)</td>
<td>2.29 (0.59) *ns</td>
</tr>
<tr>
<td>HDLC (mmol/L)</td>
<td>1.54 (0.35)</td>
<td>1.49 (0.34) *ns</td>
<td>1.50 (0.35)</td>
<td>1.44 (0.33) *ns</td>
</tr>
<tr>
<td>ApoA1(g/L)</td>
<td>1.45 (0.21)</td>
<td>1.40 (0.22) *ns</td>
<td>1.40 (0.21)</td>
<td>1.39 (0.21) *ns</td>
</tr>
<tr>
<td>ApoB (g/L)</td>
<td>0.74 (0.13)</td>
<td>0.70 (0.12) *ns</td>
<td>0.70 (0.14)</td>
<td>0.69 (0.15) *ns</td>
</tr>
</tbody>
</table>

1Values are mean and SDs, 2Paired samples T-test, ***P<0.001 and *P<0.001 were significantly different from baseline, and *ns not significantly different from baseline within groups. 3 ANOVA repeated measures, P-value for differences between intervention group 25 µg and control group are reported.
Conclusion: Vitamin D supplementation of 25 µg per day during 3 months resulted in decreased serum lipids in 5 to 7-year old Swedish children. Children with lower BMI responded with higher increase in S-25(OH) D concentration.

Keywords: Nutrition, supplements, Serum 25-hydroxi vitamin D₃, Intervention study

None of the authors declare any conflicts of interest
Fetal versus maternal genetic variants influencing neonatal vitamin D status

Ketil Stordal1, Karl Mårild2, German Tapia3, Margaretha Haugen2, Sandra Rinne Dahl4, Arieh Cohen5, Marika Lundqvist6, Benedicte Lie6, Lars Stene2

1Norwegian Institute of Public Health, Oslo, Norway
2Norwegian Institute of Public Health, Child Health, Oslo, Norway
3Norwegian Institute of Public Health, Dept. of Epidemiology, Oslo, Norway
4Oslo University Hospital, Aker Hormone Laboratory, Oslo, Norway
5Statens Seruminstitut, Copenhagen, Denmark
6Oslo University Hospital, Laboratory of Genetics, Oslo, Norway

Objectives and study: Maternal 25-hydroxyvitamin D (25OHD) is transferred across the placenta. The role during fetal life is unclear, but severe deficiency may impact the developing fetal skeleton, and possibly other health outcomes in the infant. Several genetic polymorphisms influence vitamin D status in adults. To our knowledge, the relative importance of maternal and fetal genetic variants in determining newborn vitamin D status has not been studied before. We therefore aimed to study genetic and environmental determinants of vitamin D status in the newborn.

Methods: We randomly selected 578 mother and child dyads from the prospective Norwegian Mother and Child Cohort study. Maternal samples were taken around week 18 of pregnancy and 1-2 days after delivery, and cord blood samples collected at birth. Concentrations of 25OHD (sum of 25OHD2 and 25OHD3) and vitamin D-binding protein (DBP) were assayed, and the molar ratio of 25-OHD: DBP calculated as a proxy for the free fraction of 25OHD. We genotyped for 11 previously described single nucleotide polymorphisms (SNPs) from 5 genes in the mother and newborn. Then we calculated a vitamin D deficiency genetic risk score (GRS) for the 5 SNPs with the best prediction of vitamin D, based on the literature. The proportion of variance explained (R2) was estimated for each of the studied exposures.

Results: Mean 25-OHD was 35.2 nmol/l (SD 19.1) in cord blood compared to 59.4 nmol/l (SD 24.1) in mid-pregnancy and 49.5 nmol/l (SD 25.0) in maternal post-delivery samples. DBP concentrations in cord blood were half the levels of maternal post-delivery samples (2.7 vs 5.5 mmol/l). Thus, the molar 25OHD:DBP ratio was higher in cord samples compared to maternal post-delivery samples (13.7 vs 9.9). The maternal post-delivery and neonatal levels were closely correlated (Spearman’s rho=0.77, p<0.001).

The single most important environmental factor for neonatal vitamin D was the month of birth, with a peak in August of 49.2 and 23.8 nmol/l at nadir in April (R2 for season by quarterly intervals = 0.159). After adjusting for seasonal variation, maternal intake from foods and supplements in quartiles (2.8 nmol/l increase per quartile, R2 0.030) and maternal pre-pregnancy BMI (3.7 nmol/l decrease per category, R2 0.024) were significant predictors, whereas maternal origin and smoking were not.

In further analyses adjusted for season, we found the strongest genetic association for a polymorphism in the GC gene (rs2282679, 4.9 nmol/l per allele for the child [R2=0.033], 2.6 nmol/l per maternal allele [R2=0.0070]). We also found significant association with rs12785878 in the DHCR7 gene (3.5 nmol/l per child allele [R2=0.017], 2.3 nmol/l per maternal allele [R2=0.0052]). Child GRS accounted for 0.029 of the variation in fetal concentrations, and maternal GRS for 0.0087 of the variation. With child GRS and maternal GRS in the regression model, only fetal GRS was associated with neonatal 25-hydroxyvitamin D (change 1.7 nmol/l per risk allele).

Overall, season, child genotype, maternal intake and pre-pregnancy BMI could explain 24.9% of the total variation in cord blood 25-hydroxyvitamin D.

Conclusion: While maternal dietary intake of vitamin D was confirmed to predict neonatal vitamin D status, we showed for the first time that the fetal genotype (GC, DHCR7, CYP2R1, CYP24A1, CYP27B1) was more important than that of the mother.
NUTRITION: Neonatal and infant nutrition

N-O-018

Impact of the lipid quality of infant formula on brain function in an artificially reared rat offspring model: effects of dairy lipids and supplementation in DHA and ARA

Nacima Aidoud1, Charlotte Baudry2, Pascale le Ruyet2, Bernadette Delplanque3, Cyrielle Garcia4, Lucie Arnoux5, Dominique Darmaun6, Samantha Fernandez7, Benjamin Guillot1, Claudine Antona8, Brigitte Nicolini9, Noelle Masotti9, Martin Jean-Charles10

1Amu, Nutrition, Marseille, France
2Lactalis R&d, Nutrition, Retiers, France
3Inserm, Orsay, France
4Agrocampus Ouest, Nutrition, Rennes, France
5Aphm, Pediatry, Marseille, France
6Nantes University, Inra, Umr 1280, Imad, Crnh Ouest, Nantes, France
7Amu, Cerimed, Marseille, France
8Inra, Nutrition, Marseille, France
9Amu, Animal Facility, Marseille, France
10Inra1260/Inserm1060, Nutrition, Marseille, France

Objectives and study: After birth, the brain of the infant is still immature. This makes it sensitive to the quality of the nutritional intakes of long-chain polyunsaturated fatty acids (LC-PUFA). The objective of this study was to evaluate the impact of the lipid quality of infant formulas on the composition and function of rat brain at weaning.

Methods: This study was carried out on a model of artificially reared neonatal rats fed for day 5 until weaning (day 21) with formulas providing: vegetable fat only (VF) or a vegetable fat and milk fat (VMF) mixture, supplemented or not in DHA and Arachidonic acid (ARA) (2: 1). A group of sham-gastrostomized suckling rat pups was used as a physiological reference.

At the time of withdrawal, we evaluated (i) brain functional activity via the incorporation of the 18Fluoro-D-glucose (FDG) radiotracer by positron emission tomographic imaging (PET sc), (ii) the fatty acids and whole lipid composition of the brain by lipidomics approaches, (iii) gene expression by transcriptomics, and epigenetics modifications (miR expression and total genome methylation) at the cerebral level.

Results: At weaning, brain and red blood cells (RBC) DHA levels were statistically similar in rats fed milk-fat based formulas in the lactating period, irrespective of DHA+ARA supplementation, but remained lower than sham controls. Brain and RBC DHA levels in rat fed with VF formulas reached those found in rat fed VMF formulas only when DHA+ARA were added to VF. ARA content remained unaffected by any treatments. Interestingly, a combination of 3 RBC fatty acids with a PLS algorithm accurately predicted brain DHA levels. Adding DHA+ARA in the formulas increased ceramides species and free cholesterol in the brain. Cerebral functional activity estimated through FDG PET Sc imaging was similar to shams when the pups were supplemented with DHA + ARA (VF or VMF). However, in the presence of DHA + ARA, the VMF matrix in formulas favored activation of the cerebellum over the hippocampus when compared to a VF matrix. (P<0.05). Concerning the transcriptome, approximately 1600 genes were modified by the lipid quality of the diets. DHA+ARA supplementation normalized the gene expression profile only when added on the plant basis (VF). Comparatively the VMF formula alone generated an expression profile similar to Sham controls. The genes whose expression were modified by the formulas were associated to several functional clusters including cell signaling and/or neuronal activity and cell division / differentiation. This was also accompanied by changes in epigenetic markers with the VF formula alone, such as some miR, as well as the methylation rate of the genome which was increased with that formula.
Conclusion: These results on cerebral functioning and development using a unique experimental model of artificially reared neonatal rats and mimicking the situation of the human bottle-fed newborn confirmed the interest of supplementing formulas with DHA (+ ARA?), although this could appear less critical on formulas made with a milk-fat background. Our algorithm predicting brain DHA using 3 RBC fatty acids could be worth testing in other animal models and human. Adding DHA+ARA in formulas seemed to modify the lipid profile beyond that of DHA content in the brain, such as ceramides species and cholesterol. Functional impact needs to be sought. Finally, the impact on the genome methylation rate suggests a resilient long-term effect, particularly with the VF formula alone.

Disclosure of interest: nacima aidoud is a recipient of a lactalis group fellowship which partially funded the study the study directed by jean-charles martin was partially funded by the lactalis group.
Bile salt dependent lipase has effects on intestinal adaptation in rats with massive small bowel resection

Linxi Qian¹, Wei Cai²

¹Shanghai Institute for Pediatric Research, Shanghai, China
²Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Pediatric Surgery, Shanghai, China

Objectives and study: Intestinal adaptation is important for the short bowel syndrome (SBS) patients. Recently, growing evidence has suggested that bile salt dependent lipase (BSDL) not only has the lipolytic activity, but also the antiviral, immune-modulating and pro-proliferative activities. The purpose of this study was to investigate the effects of BSDL on intestinal adaptive growth and gut barrier function in a rat model of SBS.

Methods: Twenty-four male Sprague-Dawley rats were randomly divided into three experimental groups (n=8 per group): sham group (rats underwent bowel transection and reanastomosis), SBS group (rats underwent 80% bowel resection), SBS-BSDL group (rats underwent 80% bowel resection and were orally administered 0.04 g/kg BSDL per day). The animals were weighed daily. The intestinal morpho-histochemical changes (villus height, crypt depth, enterocyte proliferation, and enterocyte apoptosis) and intestinal barrier function were determined 14 days after the operations. Meanwhile, the expressions of Wnt signaling molecules in enterocytes were also analyzed by immunohistochemistry and Western blot.

Results: The body weight of the SBS-BSDL group showed significant increases from postoperative day 5 to day 14, in comparison to that of the SBS/untreated group. The rats treated with BSDL had significantly greater villus height, crypt depth, and enterocyte proliferation in their residual intestines, as compared to the sham-control group and the SBS/untreated group. The recovery of intestinal barrier function was promoted and the expressions of tight-junction proteins were increased in the SBS rats treated with BSDL. Furthermore, the data indicated that the proadaptive activities of BSDL might be mediated via Wnt signaling.

Conclusion: These observations suggested that enteral BSDL supplementation promoted intestinal adaptive growth and barrier repairing by activating Wnt signaling pathway in SBS rats.
Phosphatidylserine enriched with DHA promotes structural and functional brain development in a preterm pig model

Randal Buddington¹, Jeffrey Sable², Viktor Chizhikov³, Ariel Gilert⁴, Yael Richter⁴

¹University of Memphis, School of Health Studies, Memphis, Tn, United States
²Christian Brothers University, Department of Behavioral Sciences, Memphis Tn, United States
³University of Tennessee, Department of Anatomy and Neurobiology, Knoxville Tn, United States
⁴Enzymotec, Migdal Haemek, Israel

Objectives and study: Neurodevelopment is compromised in 40-50% of preterm infants. It is evident from decreased cerebellar size and corresponds with increased risk of intellectual, sensory, and developmental disabilities. We tested if brain development of preterm pigs would benefit from feeding milk replacer supplemented with a novel phosphatidylserine conjugated to omega-3 fatty acids enriched with DHA (PS-DHA). Functional development was evaluated using event-related brain potentials (ERP) recorded the day of delivery and postnatal days 2, 5, and 10 in response to pairs of tones with specific emphasis on the N1 component which is associated with attention and encoding of information into sensory memory. Structural development was assessed at postnatal day 10 by weight, cerebellum immunohistochemistry, and magnetic resonance imaging (MRI) scans.

Methods: Preterm pigs delivered at 92% term (day 105 of 115 day gestation) were fed milk replacer supplemented with or without (control) PS-DHA (1.9gr/L; 0.23 gr/(Kg*day)). Term pigs euthanized at day 0 served as an additional control. ERPs were recorded in response to pairs of 50-ms tones at days 0, 2, 5, and 10 to evaluate functional development. Preterm pigs were euthanized at postnatal day 10 (term equivalent) and analyzed for total brain and cerebellar weight, Pax6+ granule progenitors in the cerebellar external granule cell layer and MRI (DTI of white and gray matter regions as well as T2 relaxation imaging) as indicators of structural development.

Results: Survival was higher for preterm pigs fed milk replacer with PS-DHA. Growth was similar.

Functional development: N1s in both groups became larger and earlier with development. Amplitudes were largest on Day 5, but were more mature on Day 10. Across days, the N1 peak amplitude for the second tone was larger for the control group compared with the PS-DHA group (P = 0.038) suggestive of enhanced maturation of inhibitory networks in the PS-DHA supplemented group.

Structural development: Control preterm pigs at term equivalent age had lower brain (P=0.01) and cerebellar (P=0.03) weights than term pigs. PS-DHA supplementation for 10 days increased total brain (P=0.14) and cerebellar weight (P=0.006) compared to control preterm pigs, and significantly increased Pax6+ granule progenitors in the cerebellar external granule cell layer (~150% vs control, P<0.05). MRI Fractional anisotropy (FA) values were significantly higher for PS-DHA compared to control pigs in the corpus callosum and the right internal capsule (P<0.05) suggestive of enhanced myelination in white matter. T2 values were significantly higher in PS-DHA supplemented compared to control pigs in most of the regions.

Conclusion: The increased brain and cerebellar growth, higher densities of granule cells, enhanced myelination of white matter, and reduced N1 amplitude to the second tone (ERP) suggest that PS-DHA supplementation may enhance functional and structural development of the preterm brain. The increased survival is indicative of other possible benefits. These results warrant clinical studies to investigate potential benefits of feeding PS-DHA supplemented formula to preterm infants.

Disclosure of interest: the study was funded by Enzymotec Ltd., Israel.
Prof. Randal Buddington - the study was funded by Enzymotec Ltd., Israel.
Prof. Jeffery Sable - the study was funded by Enzymotec Ltd., Israel.
Prof. Viktor Chizhikov - the study was funded by Enzymotec Ltd., Israel.
Dr. Gilert Ariel - the study was funded by Enzymotec Ltd., Israel.
Dr. Richter Yael - the study was funded by Enzymotec Ltd., Israel.
Infant serum and breast milk leptin infant-mother pairs 4 months after birth

Belén Pastor-Villaescusa1, Maria Grunewald2, Olaf Uhl3, Christian Hellmuth3, Renata Auricchio4, Gemma Castillejo5, Ilma Korponay-Szabo6, Isabel Polanco6, Carmen Ribes Koninckx8, Luisa Mearin9, Berthold Koletzko3, Hans Demmelmaier3

1Institute of Nutrition and Food Technology “José Mataix”, University of Granada. CiberPhysiopathology of Obesity and Nutrition (Ciberobn), Department of Biochemistry and Molecular Biology II, Granada, Spain
2Dr. von Hauner Children’s Hospital, Ludwig-Maximilians-University, Division of Metabolic and Nutritional Medicine, Munich, Germany
3Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
4University “federico ii”, Department of Translational Medical Science, Section of Paediatrics, and European Laboratory for Food-Induced Disease (Eliid), University of Naples Federico II, Italy, Naples, Italy
5Hospital Universitario Sant Joan de Reus, Pediatric Gastroenterology Unit, Reus, Spain
6Heim Pál Children’s Hospital, Celiac Disease Center, Budapest, Hungary
7La Paz University Hospital, Dept. of Pediatric Gastroenterology and Nutrition, Madrid, Spain
8La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
9Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands

Objectives and study: Breast-feeding is recommended as the optimal mode of infant feeding. Leptin is an anorexigenic hormone associated with body weight and sex in adults, especially in females. The variable leptin concentrations in human milk (HM) might affect growth of breast-fed infants. The objective of our study was to explore relationships between HM leptin, infant serum leptin and infant anthropometry with special consideration of infant sex.

Methods: We included 144 mother infant dyads of PreventCD, a multicentre, randomised, double-blind, intervention study on the effect of gluten introduction on the risk to develop celiac disease. Infant weight and length were measured at the age of four months and maternal anthropometry before pregnancy was self-reported. Leptin concentrations were determined by enzyme-linked immunosorbent assay (R&D Systems) in HM and infant serum samples also collected at the age of four months. Student’s t-test was applied for group comparisons and relationships were determined with correlation analyses. Log transformation was performed when necessary. Corresponding non-parametric tests were applied, if normal distribution could not be assumed. The study was conducted according to the Declaration of Helsinki and registered at Current Controlled Trials (ICTRP CTRP NTR890).

Results: Infant serum leptin concentration was significantly higher in female than in male infants (3523 pg/ml ± 1799 vs. 2784 pg/ml ± 1467; P=0.004). HM leptin concentration was clearly lower than infant serum leptin (142.8 pg/ml ± 128.1 vs. 3179 pg/ml ± 1688, P<0.001) and not different for male (n=66) and female infants (128.4 pg/ml ± 94.6 vs. 156.8 pg/ml ± 150.3, P=0.495). Only female infants showed significant correlations between serum leptin and weight (r=0.403, P =0.001) and BMI Z-score (r=0.443, P<0.001). Concentration of HM leptin showed a weak correlation with infant serum leptin in girls (r=0.335, P=0.049), but no correlation in boys. However, adjustment of serum leptin for infant BMI led to insignificant correlations for boys and girls. HM leptin was positively correlated with maternal pre-pregnancy weight (61.72kg ± 10.14) and body mass index (21.98kg/m² ± 3.31) with r=0.403 (P=0.001) and BMI Z-score (r=0.325, P=0.009), respectively. Infant serum leptin was significantly higher in exclusively breast fed (EBF) infants (n=116) compared to partially formula fed infants (3320 pg/ml ± 1733 vs. 2544 pg/ml ± 1496; P=0.024). Serum leptin was correlated with infant BMI Z-score in EBF infants (r=0.325, P=0.001), but not in partially breast fed infants (r=-0.001, n.s.). Neither in the total studied population nor in any of the tested subgroups significant associations between HM leptin and infant anthropometry were found.
Conclusion: The positive association between HM leptin and serum leptin in the subgroup of girls and the higher serum leptin in EBF infants might agree with the hypothesis that HM leptin may be absorbed by the infant, but other factors might as well explain these findings. At the age of four month no influence of HM leptin on infant growth could be detected. The relationship of serum leptin with infant weight gain and BMI observed in female but not in male infants suggests sexually dimorphic relationships between feeding mode and growth. This finding emphasises the importance of the consideration of sex for the elucidation of determinants of early growth.

(Funded by the European Commission and others; PreventCD Current Controlled Trials number, ISRCTN74582487).
CoMiSS score and the response to cow’s milk free diet in infants and children

Giorgio Ottaviano¹, Chiara Armano¹, Letizia Fumagalli¹, Chiara Luini¹, Silvia Salvatore¹

¹University of Insubria, Varese, Italy

Objectives and study: The diagnosis of Cow’s milk allergy (CMA) is still challenging particularly in infants and in non-IgE mediated cases. To increase awareness of primary health care providers, the Cow’s Milk-related Symptom Score (CoMiSS) has been recently developed. A score ≥12 has been suggested as a cut-off able to define select infants who can benefit from a cow’s milk free diet (CMFD) and/or at risk of CMA. The aim of this study was to assess the accuracy of CoMiSS score.

Methods: Since January 2016 we prospectively and consecutively enrolled all infants and toddlers referred to our hospital for a cow’s milk (CM) oral challenge because of suspected CMA or intolerance (CMI). CoMiSS was scored according to author’s instructions at starting of CMFD and at challenge. Additional clinical symptoms were considered. Skin prick test for CM protein and prick by prick for CM were also performed. All patients were submitted to a standardised (according to published recommendations) oral open challenge in our hospital with a direct observation of at least 4 hours. A telephone interview recorded the delayed reactions and whenever unclear a clinic recall was organized. Rate of positivity, positive (PPV) and negative predictive value (NPV) were calculated.

Results: Overall 40 children (median age 9 months, range 3-41 months) have been currently recruited. At first evaluation, on CM, median CoMiSS score was 10 (range 4-21) and score ≥12 was found in 17 (42.5%) patients. All except 2/40 patients (CoMiSS 5 and 9) reported major improvement (>50% reduction of the score) with complete resolution (score = 0) of symptoms in 18/40 (45%) patients on CMFD. PPV and NPV of CoMiSS were 100% and 9%, respectively. Failure to thrive, bloody stools, feeding and sleeping problems were additional symptoms reported. At the challenge CoMiSS score was negative (<12) in 38/40 (95%) patients. CMFD included extensive hydrolyzed or elemental formulas based on the severity of initial presentations (blind to the CoMiSS score). CMFD was administered for a median of 5 months (range 1-12 months) before the challenge. Ten patients presented positive allergy tests. Oral challenge was positive in 6/40 with immediate reactions in 4 (all with positive allergy tests and initial CoMiSS>12) and delayed reaction in the other two (both with negative allergy tests, one with CoMiSS 10 and the other with CoMiSS 14).

Conclusions: Our findings support the use of CoMiSS score as a helpful tool to select infants who can benefit from CMFD. Elimination diet is related to a reduction of CoMiSS score even in patients with negative allergy tests. However, further clinical validations of CoMiSS score are needed to overcome our selection bias, to identify the best cut-off value and/or additional symptoms to be considered.
Iron supplements to low birth weight infants lower systolic blood pressure at 7 years of age - results from a randomized controlled trial

Staffan Berglund¹, Josefine Lindberg¹, Björn Westrup², Mikael Norman³, Magnus Domellöf¹

¹Umeå University, Department of Clinical Sciences, Pediatrics, Umeå, Sweden
²Karolinska Institutet, Department of Women's and Children's Health, Division of Neonatology, Stockholm, Sweden
³Karolinska Institutet, Department of Clinical Science, Intervention and Technology, Pediatrics, Stockholm, Sweden

Objectives and study: Low birth weight (LBW; ≤2500 g) is associated with iron deficiency in infancy and high blood pressure (BP) later in life. The objective of this study was to investigate the effect of iron supplementation to LBW infants on mid-childhood BP.

Methods: In a randomized double-blinded controlled trial, 285 marginally LBW (2000-2500 g) infants were included at two Swedish centres between May 2004 and November 2007. The infants were randomized to placebo, 1, or 2 mg iron/kg/day, from six weeks to six months of age. In secondary analyses at the age of seven years, systolic BP (SBP), diastolic BP (DBP), and the prevalence of children having a BP within the hypertensive range (>90th percentile), were compared between the groups.

Results: BP was analyzed by intention to treat in 189 children. When combining the iron supplemented groups in covariate adjusted analyses, SBP in LBW children who had received iron supplementation in infancy was significantly lower than in those un-supplemented. Multivariate logistic regression showed that iron supplementation in infancy reduced the odds of having a SBP within the hypertensive range at seven years of age. For DBP, there were no significant differences between the intervention groups.

Conclusion: Iron supplementation (1 or 2 mg/kg/day) in marginally LBW infants lowered their systolic BP at seven years of age. This novel observation suggests that the increased risk of hypertension observed in children and adults born small might be reduced with early micronutrient interventions. Furthermore, the results generate a novel hypothesis regarding the mechanisms behind early programming of cardiovascular risk.
NUTRITION: Neonatal and infant nutrition

N-O-024

The power of breastmilk: a study of the impact on the infant metabolism

Christian Hellmuth¹, Hans Demmelmaier¹, Olaf Uhl¹, Luisa Mearin², Renata Auricchio³, Gemma Castillejo⁴, Ilma Korponay-Szabo⁵, Isabel Polanco⁶, Maria Roca⁷, Sabine Vriezinga², Katharina Werkstetter⁸, Berthold Koletzko⁹, Franca Kirchberg⁹

¹Dr. von Hauner Children's Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
²Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
³University “federico II”, Department of Translational Medical Science, Section of Paediatrics and European Laboratory for Food-Induced Disease (Elfid), University of Naples Federico II, Italy, Naples, Italy
⁴Hospital Universitari Sant Joan de Reus, Urv, lipv, Dept. of Pediatric Gastroenterology Unit, Reus, Spain
⁵Heim Pál Children’s Hospital, Celiac Disease Center, Budapest, Hungary
⁶La Paz University Hospital, Dept. of Pediatric Gastroenterology and Nutrition, Madrid, Spain
⁷Instituto de Investigación Sanitaria La Fe, U. Enfermedad Celiaca e Inmunopatología Digestiva, Valencia, Spain
⁸Dr. von Hauner Children’s Hospital, LMU Munich, Division of Pediatric Gastroenterology and Hepatology, Munich, Germany
⁹Dr. von Hauner Children’s Hospital, University of Munich Medical Center, DIV. Metabolic and Nutritional Medicine, München, Germany

Objectives and study: Compared to infant feeding, breastfeeding is beneficial for both mothers but especially for their offspring when it comes to infections and reduction the risk of childhood obesity. Underlying mechanisms or biochemical changes are poorly understood and need to be clarified to improve infant nutrition interventions. The aim of this study was to analyse the relation between maternal breast milk (BM) composition and infant metabolism.

Methods: 250 mother/infant pairs from the European cohort for the study of coeliac disease (CD) PreventCD were studied. Maternal BM samples collected at month 1 and month 4 after birth were analysed for macronutrients (fat, protein) as well as fatty acid composition and hormones (insulin, IGF-II, adiponectin, leptin). The corresponding blood serum samples of 4-month old infants were analysed with an LC-MS/MS based metabolomics platform for phospholipids, acylcarnitines, and amino acids. Associations between BM component and infant metabolites were analysed with spearman correlation (S) and linear mixed effect models (LM) with BM compound as independent variable, adjusted for infant sex, breastfeeding status (exclusively BF yes/no), and the infant’s age when blood sample was taken. Batch number and study centre were included as independent random intercepts. P-values were corrected for multiple testing by dividing the p-value with number of metabolites (Bonferroni correction).

Results: 183 metabolites were quantified in infants aged 4 months. We found no differences in composition of infant metabolites according to later CD development or maternal human leukocyte antigen status. Interestingly, month 1 BM protein content - but not month 4 - was strongly associated with lyso-phosphatidylcholines (LPC) 14:0 in the infant blood serum at 4 month of age (Rs=0.302, pLM=0.007). No associations between BM protein content and serum amino acids were found, neither at month 1 of month 4. Total fat content in BM and polar serum lipids concentrations in the infants were not associated, but the relative composition of BM fatty acids were associated to polar lipids in the serum of the infants aged 4 months. Particularly, month 1 and month 4 middle- and odd-chain fatty acids composition in BM were significantly related to middle- and odd-chain fatty acid containing serum LPCs and sphingomyelins in the in the infant plasma (Rs=0.318-0.579, pLM<0.05), while only month 4 20:5n-3 and 22:6n-3 percentages in BM were significantly associated to LPC 22:6 (Rs=0.472, pLM=7.56×10-3; Rs=0.506, pLM=5.74×10-5, respectively) and alkyl-linked PC (Rs=0.391-0.449, pLM<0.05) in infant serum. Other polyunsaturated fatty acids and hormones showed only weak or no positive association with serum metabolome.
Conclusion: The composition of BM seems to have only a small influence on the infant’s metabolome at 4 months of age. We speculate that the amount of BM intake has a more important influence on the infant’s metabolome and that infants may adjust their BM intake according to BM composition. However, especially serum LPC are affected by BM fatty acid composition and, most surprisingly, BM protein content in early lactation. LPC 14:0 was the most influenced serum metabolite by BM protein content and was found to be positively associated to growth and obesity risk. Thus, LPC 14:0 might be a key metabolite not only reflecting BM protein intake in infants but also relating high protein content in BM or infant formula to childhood obesity risk.
Bifidobacterium animalis subsp. lactis HN019 protects against respiratory tract infections in Chinese infants

James Dekker1, Leiming Xu2, Qian Hong3, Sheng Xiaoyang4

1Fonterra Research and Development Centre, Nutrition, Palmerston North, New Zealand
2Xinghua Hospital, School of Medicine, Shanghai, China
3Anhui Medical University, Hefei, China
4Shanghai Xinhua Hospital, Shanghai, China

Objectives and study: While a variety of probiotic strains are currently used for infant formula, the efficacy of each strain must be shown to justify its inclusion in the infant diet. To explore the benefits to infant health of probiotic bacteria, a double-blind, placebo-controlled clinical trial was conducted in Chinese infants that compared two established probiotic strains.

Methods: The study enrolled 192 healthy infants aged 6 to 12 months, who were divided into three groups: one group (n=64) received daily a follow-on formula without probiotics (control); a second group (n=64) received the follow-on formula with 106 CFU/g Bifidobacterium animalis subsp. lactis HN019 (HN019, DR10™); while a third group (n=64) received the formulae with 106 CFU/g Lactobacillus rhamnosus HN001 (HN001, DR20™). The intervention period was for 12 weeks over the winter period. The primary study endpoint was physician-confirmed bacterial or viral respiratory infections, while secondary endpoints included requirement for antiviral or antibiotic treatments, hospitalization, stool frequency and consistency, and parentally-reported (i.e. unconfirmed) infections.

Results: Over the 12-week intervention period, 6 infants had confirmed respiratory tract infections in the control group, compared to no cases in the HN019 group (p=0.03), and only 2 cases in the HN001 group (p = 0.28). Similarly for parentally-reported infections, 16 cases were reported in the placebo group, compared with 6 in the HN019 group (p=0.02), and 9 in the HN001 group (p=0.12). No infants in the HN019 group were prescribed antibiotics or antivirals, compared with 3 in the HN001 group and 7 in the control group. The probiotic follow-on formulae were well tolerated and no formulae-related adverse events were reported. No cases of diarrhoea were reported in any of the infants over the 12-week study period, and no differences in stool frequency or stool characteristics were reported. Faecal samples were collected from infants at the end of the treatment period. PCR analysis for the probiotic species showed that B. lactis was detected at higher rates in infants that received HN019, while HN001-related L. rhamnosus strains were detected at similar rates across all three groups.

Conclusion: In conclusion, a comparison of two established probiotics when added to follow-on formulae showed that although HN001 showed non-significant trends toward infant health benefits, HN019 showed superior performance, with statistically-significant reduction in physician-confirmed respiratory infections, parentally-reported infections, and antibiotic/antiviral use in Chinese infants aged 6 to 15 months.

Disclosure of interest: Dr James Dekker - Study supported by Fonterra, employer of Dr James Dekker
Prof Xu Lei Ming - None
Prof Hong Qian - None
Prof Sheng Xiao Yang - None
**NUTRITION: Neonatal and infant nutrition**

N-O-026

**Retinol status in mother-infant pairs from Midwest USA: is it a good indicator of vitamin A sufficiency in clinical practice?**

Corrine Hanson¹, Elizabeth Lyden², Jeremy Furtado³, Mariana Schumacher⁴, Matthew Van Ormer⁵, Elizabeth McGinn⁶, Kara Weishaar⁶, Caleb Cave⁶, Rebecca Johnson⁶, Ann Anderson Berry⁷

¹University of Nebraska Medical Center, Medical Nutrition Education, Omaha, United States  
²University of Nebraska Medical Center, College of Public Health, Omaha, United States  
³Harvard University, Boston, United States  
⁴Unmc, Pediatrics/Medical Nutrition, Omaha, United States  
⁵University of Nebraska Medical Center, Omaha, United States  
⁶Unmc, Pediatrics, Omaha, United States  
⁷University of Nebraska Medical Center, Pediatrics, Omaha, United States

**Objectives and study:** Evaluate vitamin A status based on WHO guidelines in a population of pregnant women and their newborns from Midwest USA. Vitamin A deficiency is one of the most prevalent nutritional public health problems in many developing countries, however industrialized nations are assumed to be vitamin A sufficient. Deficiency of vitamin A is associated with significant infectious morbidity and mortality in infants and children. Serum retinol (SR) levels have been traditionally used to evaluate vitamin A status. The World Health Organization (WHO) has defined criteria for vitamin A status, as measured by retinol concentrations. Serum concentrations of $\leq 0.7$ nmol/L are considered vitamin A deficient, and a cutoff value of $\leq 1.05$ nmol/L has been used to identify those with inadequate vitamin A stores. As newborns are dependent on a maternal supply of vitamin A, they represent a population who may be susceptible to vitamin A deficiency.

**Methods:** Samples of maternal and infant cord blood were collected on 189 mother-infant pairs at delivery. Concentrations of were measured using high-performance liquid chromatography. Descriptive statistics were calculated and Independent sample t-tests were used to compare retinol measures between racial groups. The prevalence of vitamin A insufficiency and inadequacy was determined based on WHO cut-off levels of serum retinol. P<0.05 was considered statistically significant.

**Results:** Serum retinol levels by category of deficiency are shown in Table 1. Less than half (48.6%) of mothers had adequate SR levels ($>1.05\mu$mol/L), while the majority (98.3%) of newborns were insufficient or deficient. In terms of race, non-whites had a higher risk of being classified as deficient or insufficient when compared to whites (p=0.03); 62.5% of mothers with SR levels $<0.70\mu$mol/L were non-white. Birth weight percentile ranking showed a trend toward statistical significance between SR categories (p=0.06). No positive correlation between maternal and cord levels of retinol was found.
Table 1: Prevalence of Vitamin A deficiency and insufficiency

<table>
<thead>
<tr>
<th></th>
<th>Infants (n = 189)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severely Deficient (&lt;0.35 µmol/L)</td>
<td>14 (7.6)</td>
<td></td>
</tr>
<tr>
<td>Deficient (0.35-0.70 µmol/L)</td>
<td>138 (72.8)</td>
<td></td>
</tr>
<tr>
<td>Insufficient (0.70-1.05 µmol/L)</td>
<td>34 (17.9)</td>
<td></td>
</tr>
<tr>
<td>Adequate (&gt;1.05 µmol/L)</td>
<td>3 (1.7)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>Mothers (n = 189)</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Severely Deficient (&lt;0.35 µmol/L)</td>
<td>1 (0.7)</td>
<td></td>
</tr>
<tr>
<td>Deficient (0.35-0.70 µmol/L)</td>
<td>18 (9.3)</td>
<td></td>
</tr>
<tr>
<td>Insufficient (0.70-1.05 µmol/L)</td>
<td>78 (41.4)</td>
<td></td>
</tr>
<tr>
<td>Adequate (&gt;1.05 µmol/L)</td>
<td>92 (48.6)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** The prevalence of vitamin A deficiency and insufficiency based on WHO retinol levels in this population was higher than expected in a developed nation, with discrepancies based on race. Vitamin A status may be an unrecognized health disparities issue in the United States. Specific cut-off levels of SR during pregnancy for optimal outcomes need to be better established.

Corrine Hanson, Elizabeth Lyden, Jeremy Furtado, Marina Schumacher, Matt VanOrmer, Elizabeth McGinn, Kara Weishaar, Caleb Cave, Rebecca Johnson, Ann Anderson Berry
NUTRITION: Neonatal and infant nutrition

N-O-027

Infant feeding practices in Poland. The 2016 PITNUTS Study

Halina Weker¹, Marta Barańska¹, Agnieszka Riahi¹, Małgorzata Strucińska¹, Małgorzata Więch¹, Agnieszka Bzikowska¹, Grażyna Rowicka¹, Hanna Dyłąg¹, Witold Klemarczyk¹, Hania Szajewska², Agnieszka Bzikowska³

¹Institute of Mother and Child, Nutrition Department, Warsaw, Poland
²The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
³Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: A number of scientific organisations, including ESPGHAN, have developed recommendations for infant feeding. However, even if the best evidence-based guidelines are available, these guidelines do not necessarily lead to adherence to recommendations. Little is known about the feeding practices across Central and Eastern Europe. We aimed to assess the infant feeding practices in Polish infants aged 5 to 12 months and to determine how closely they compare with the current recommendations.

Methods: A national cross-sectional study was conducted in Poland from May to July 2016. Parent-child pairs were selected by a systematic, nationwide, random sampling technique. Feeding practices were evaluated by a questionnaire survey of the parents of the studied children, conducted by professional pollsters trained in dietary issues related to infants. Additionally, information on socioeconomic status/maternal education level and sources of knowledge on infant feeding were collected.

Results: A total of 447 infants were included. Among them, 8% of the infants were exclusively breastfed at the age of 6 months, and 54% continued breastfeeding at the age of 6 months. In contrast to the current recommendations, complementary feeding was introduced before 5 months of age in 61% of the infants. In 30% of the infants, complementary feeding was introduced between 5 and 6 months of life. Of the included infants, 51% received snacks between meals, and 30% received meals with the addition of salt. Earlier introduction of complementary feeding was less likely in the infants of mothers with a higher level of education (OR 0.48, 95% CI 0.36 to 0.64). Mothers who declared knowledge of recommendations and guidelines on infant nutrition less often introduced complementary feeding before their infants were 5 months of age (OR 0.6, CI 0.40 to 0.90). Place of family residence and their economic status were not significantly associated with earlier introduction of complementary foods into the infant’s diet.

Conclusion: This national cross-sectional study carried out in Poland showed that a substantial portion of parents of infants do not follow current recommendations. More educational efforts are required to increase the awareness and/or the adherence to current guidelines.

Disclosure of interest: The study was supported by a research grant from Nutricia Foundation Poland.

Vol. 64, Supplement 1, April 2017 763
Neurodevelopmental outcome at 2.5 years in very preterm infants randomised to receive two different parenteral nutrition regimens at birth: the SCAMP nutrition study

Colin Morgan1, Sam Parry1, Maw Tan2

1Liverpool Women's Hospital, Neonatology, Liverpool, United Kingdom
2Alder Hey Children's Hospital, Neurodisability, Liverpool, United Kingdom

Objectives and study: We have previously shown that increasing parenteral protein and energy intake using a Standardised, Concentrated with Added Macronutrients Parenteral (SCAMP) nutrition regimen ameliorates early head growth failure in very preterm infants (VPI) (1). The effect was greatest in infants less than 27 weeks gestation. Head circumference (HC) is correlated with brain volume and later neurodevelopmental outcome. We hypothesised that a SCAMP nutrition regimen would improve neurodevelopmental outcome.

Aim: To compare neurodevelopmental outcome at 2-3.5 years in VPI randomised to receive SCAMP nutrition (12% glucose, maximum 3.8g/kg/day protein/lipid) or a control standardised, concentrated PN regimen (10% glucose, maximum 2.8g/kg/day protein/lipid).

Methods: The double-blind study (ISRCTN: 76597892) received ethical approval. Control PN was started within 6 hours of birth. VPI (stratified into 24-26 and 27-28 weeks gestation) were randomised to either start SCAMP or remain on the control regimen. Maximum intakes were achieved after day 4. The consent process included neurodevelopmental assessment (Bayley III) all performed (blinded) by MT or SP between 2 and 3.5 years corrected gestational age. The raw scores of each subtest are converted to scaled and composite scores. A composite score of 100 is equivalent to normative mean. The combined score is a cognitive/language average validated to offer comparison with the Mental Developmental Index. 1SD below the mean (85) has been validated as the level that is associated with significant neurodisability.

Results: The original study randomised 150 infants to SCAMP (n=74) and control (n=76) groups respectively. Bayley III assessments were performed in 38/60 SCAMP survivors and 41/63 control survivors. Table 1 summarises the composite score data for all infants, the 24-26 week stratum and the percentage of infants scoring 50-85 in each subtest (lowest possible score 50).

Table: Mean (sd) Bayley III composite scores in SCAMP versus control groups

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Age (mths)</th>
<th>Cognitive</th>
<th>Language</th>
<th>Motor</th>
<th>Combined</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCAMP: All infants (38)</td>
<td>29.2 (3.7)</td>
<td>87 (15)</td>
<td>81 (18)</td>
<td>79 (13)</td>
<td>84 (15)</td>
</tr>
<tr>
<td>Control: All infants (41)</td>
<td>30.0 (3.9)</td>
<td>81 (14)</td>
<td>76 (17)</td>
<td>76 (15)</td>
<td>78 (14)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.49</td>
<td>0.08</td>
<td>0.11</td>
<td>0.38</td>
<td>0.09</td>
</tr>
<tr>
<td>SCAMP: 24-26 wks (15)</td>
<td>28.9 (3.4)</td>
<td>85 (17)</td>
<td>75 (20)</td>
<td>74 (15)</td>
<td>80 (18)</td>
</tr>
<tr>
<td>Control: 24-26 wks (16)</td>
<td>30.3 (3.5)</td>
<td>75 (16)</td>
<td>67 (13)</td>
<td>69 (18)</td>
<td>71 (13)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.32</td>
<td>0.11</td>
<td>0.25</td>
<td>0.44</td>
<td>0.14</td>
</tr>
<tr>
<td>SCAMP: score 50-85 (%)</td>
<td>29.2 (3.7)</td>
<td>11 (29)</td>
<td>16 (42)</td>
<td>21 (55)</td>
<td>11 (29)</td>
</tr>
<tr>
<td>Control: score 50-85 (%)</td>
<td>30.0 (3.9)</td>
<td>18 (47)</td>
<td>29 (71)</td>
<td>27 (66)</td>
<td>21 (51)</td>
</tr>
<tr>
<td>p-value</td>
<td>0.49</td>
<td>0.17</td>
<td>0.013*</td>
<td>0.36</td>
<td>0.07</td>
</tr>
</tbody>
</table>

Conclusion: This study showed evidence of improved neurodevelopmental outcome with SCAMP versus control regimens. The pattern of improvement is consistent with the previously published head growth data.

References
Breastfeeding and symptoms of dyslexia in children and adolescents

Marie Standl1, Gerd Schulte-Körne2, Joachim Heinrich1

1Institute of Epidemiology I, Helmholtz Zentrum Munich – German Research Center for Environmental Health, Neuherberg, Germany
2Klinik für Kinder- und Jugendpsychiatrie, Psychosomatik und Psychotherapie, Munich, Germany

Objectives and study: Breastfeeding is generally highly recommended, but recent reports have raised doubts on the evidence of the WHO recommendation of exclusive breastfeeding for six months or four months to prevent obesity, obesity related disorders in adulthood, allergies and neuro-behavioural disorders. Dyslexia is one of the most common neuro-behavioural disorders in childhood, with prevalence rates up to 10% depending on diagnostic criteria and region. Apart from the genetic background involving many genes, as for other complex diseases, and the familial aggregation, the etiology is not completely understood. Although the impact of breastfeeding on a broad spectrum of neuro-behavioural disorders is extensively (and controversially) discussed, no single study has investigated the association between breastfeeding and reported symptoms of dyslexia later in life so far. Therefore, the aim of this study is to analyze the association between breastfeeding and symptoms of dyslexia prospectively using data from two large population-based birth cohorts in Germany.

Methods: Within the two ongoing German multicenter birth cohorts GINIplus and LISAplus, information on reading/spelling problems and difficulties were collected at the 10 and 15 year follow-ups. Parents answered the question whether their child presented reading/spelling problems as well as reading/spelling disorders. Here we used the combined answers to reading/spelling problems or disorders. Breastfeeding data during the first six months of life were collected at the 6-months survey in LISAplus and the 1-year survey in GINIplus. Breastfeeding was defined as exclusive breastfeeding for at least the first four months of life. Thus, data from 4242 children aged 10 years and 4285 adolescents aged 15 years, respectively, could be included in this analysis. Logit models were adjusted for sex, age, cohort, study center, parental education, birth weight, maternal smoking during pregnancy, BMI at follow-up and parental psychopathology.

Results: Reading/spelling problems or difficulties were reported for 11.1% and 10.0% of the subjects aged 10 and 15 years, respectively. Exclusive breastfeeding for at least the first four months of life were reported in 57.6% of all subjects. The majority of the cohort members (66.1%) have a high educational background, while for only 6.8% of the subjects both parent have less than 10 schooling years. Exclusive breastfeeding for at least the first four months of life was statistically significantly associated with lower adjusted odds ratios for reading/spelling problems or difficulties at age 10 years (aOR 0.75, 95%CI (0.59-0.95), p<0.05), while the association attenuated (0.82 (0.66-1.03), p=0.09) at age 15 years.

Conclusion: Exclusive breastfeeding for at least the first four months of life might be a protective factor for dyslexia, although residual confounding cannot be ruled out so far.
Assessment of paediatric malnutrition: results from an international survey on current clinical practice and barriers

Koen Huysentruyt1, Jessie Hulst2, Feifei Bian3, Philip Arthur3, Bashar Alhashash4, Titia Vanderstelt5, Raanan Shamir6, Melinda White7, Rafael Galera Martinez8, Ana Moráis9, Aydan Kansu10, Konstantinos Gerasimidis11

1Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
2Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
3Royal Hospital for Sick Children, University of Glasgow, Human Nutrition, School of Medicine, College of Medicine, Veterinary and Life Sciences, Glasgow, United Kingdom
4Royal Hospital for Sick Children, University of Glasgow, Glasgow, United Kingdom
5Royal Hospital for Sick Children, University of Glasgow, Human Nutrition, School of Medicine, College of Medicine, Veterinary and Life Sciences, Glasgow, United Kingdom
6Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
7Lady Cilento Children's Hospital, Department of Dietetics and Food Services, Brisbane, Australia
8Hospital Torrecárdenas, Servicio de Pediatría, Almeria, Spain
9"LA Paz" University Hospital, Pediatric Nutrition AND Metabolic Diseases, Madrid, Spain
10Ankara University School of Medicine, Paediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
11University of Glasgow, Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, Glasgow Royal Infirmary, Glasgow, United Kingdom

Objectives and study: A lack of international consensus for the definition and assessment of paediatric malnutrition may lead to under-recognition of the problem in clinical practice. This survey aimed to 1) investigate which measurements health professionals consider the most important for the assessment of paediatric malnutrition; 2) identify barriers for routine nutritional screening/assessment; 3) explore differences across countries.

Methods: A web-based questionnaire survey was sent out to paediatric gastroenterologists (MD) and dieticians (RD) in seven countries (the Netherlands, Belgium, UK, Australia, Israel, Spain and Turkey). The survey was distributed via the local professional associations in participating countries.

Results: In total, 693 responders (Australia: n=89; Belgium: n=34; Israel: n=126; the Netherlands: n=73; Spain: n=139; Turkey: n=79; UK: n=153) completed the survey; 45% were MD and 55% RD with a different distribution of professions across countries (p<0.001). MD’s and RD’s had respectively a median of 15 (10;25) and 9 (3;14) years’ experience in paediatrics. The majority worked in a tertiary (51%) and/or district general hospital (33%), with differences noted across countries. A total of 588 responded to the question regarding screening and assessment in routine clinical practice. Of these, 43 (7%) did not routinely screen for malnutrition (this was most prevalent in Australia (16%) and the least (0%) in The Netherlands; difference across countries: p=0.012). Differences were noted across countries in the way malnutrition is evaluated in routine clinical practice. Assessing weight changes was done most frequently overall (85%; most frequently in Israel (93%), least frequent in Australia (70%), p=0.004), followed by plotting weight for age (80%), weight for height/BMI (77%) and height for age (77%) on growth charts. The WHO charts were used by 60%, national growth charts by 36% and a combination of both by 12%; 17% used the CDC charts or national growth charts from another country. Body composition was routinely assessed by only 20% of the respondents (50% of the Spanish, followed by 13% of UK respondents, all other countries ≤10%, p<0.001). Only 3% routinely used disease-specific growth charts. Overall, screening tools were used by 23 % (Belgium, the Netherlands and UK: 40-50%, other countries ≤15%, p<0.001); the most popular tools were STRONGkids, PYMS and STAMP. Functional tests (e.g. grip strength) or energy levels were assessed by a minority of the respondents (14%) and was significantly (p=0.008) more frequently done in Israel (24%) and Australia (17%). Blood parameters such as inflammatory markers (31%), nutritional markers (51%) and micronutrients (43%) were assessed significantly (p<0.02) different across countries. Considering the most commonly perceived barriers for routine nutritional evaluation, low
staff awareness on the role of nutrition on patient care (47%), lack of local policy or guidelines to screen for malnutrition (33%), lack of time (33%) and lack of dieticians to intervene (33%) were found most often, although differences existed across countries.

**Conclusion:** Assessing changes in weight, and plotting weight for age were the most frequently proposed ways to assess paediatric malnutrition; body composition was recommended the least. Half of the respondents perceived low staff awareness and one-third a lack of local guidelines as barriers for the routine evaluation of the nutritional status.
Clinical significance of pediatric nutritional screening tool in hospitalized children with burn injuries

Ky Young Cho¹

¹Hallym University College of Medicine, Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Nutritional support has been the cornerstone of management in burned children at risk of malnutrition. However, in our knowledge, there were no studies of nutritional risk screening in children with burn injuries. We assessed the nutritional risks in hospitalized children with burn injuries and its relationship with clinical outcomes using 3 popular pediatric nutritional screening tools [the Screening Tool for Risk of Impaired Nutritional Status and Growth (STRONG_kids), the Pediatric Yorkhill Malnutrition Score (PYMS), and the Screening Tool for the Assessment for Malnutrition in Pediatrics (STAMP)].

Methods: This prospective, cross-sectional study was conducted in 100 children aged 3 months to 16.5 year old from October 2015 to November 2016 in a regional burn center. Two physicians assessed the nutritional risks, which were compared with anthropometric measures, burn severity and clinical outcomes. We evaluated the agreement of nutritional risks between 3 screening tools and between two observers.

Results: The anthropometric measures (weight for age, height for age, weight for height, and body mass index for age) and burn severity (minor, moderate, and major type in American Burn Association’s Grading System) were not significantly different between high, moderate and low risk group in 3 screening tools. Children categorized as high risk (STRONG_kids: 16%, PYMS: 40%, and STAMP: 28%) had significantly longer length of hospital stay, delayed wound re-epithelization, longer course of antibiotics, greater hospital expenses, higher rates of infectious complications, and greater weight loss than those who categorized as moderate and low risk (STRONG_kids: 84% and 0%, PYMS: 14% and 46%, and STAMP: 10% and 62%, respectively) (P< 0.001). The agreement between 3 tools were moderate or good strength (kappa; between STRONG_kids and PYMS: 0.5, between PYMS and STAMP: 0.8, between STRONG_kids and STAMP: 0.6) The agreement between two observers were moderate strength (kappa; STRONG_kids: 0.6, PYMS: 0.5, and STAMP: 0.6, P=0.000).

Conclusion: This study showed that the identification and classification of malnutrition risk varied among 3 screening tools. However, hospitalized burned children with high nutritional risks had poor clinical outcomes in all tools. The data obtained could not recommend the use of one in 3 screening tools for clinical practice. The pediatric universal nutritional screening tool is needed to improve the outcomes of management in children with burn injuries.
Changes in dietary intake and functional abdominal pain disorders during adolescence

Carla Harris¹, Katharina Werkstetter², Irina Lehmann³, Andrea von Berg⁴, Dietrich Berdel⁴, Tamara Schikowski⁵, Carl Peter Bauer⁶, Marie Standl⁷, Joachim Heinrich⁸, Sibylle Koletzko⁹

¹Institute of Epidemiology I, Helmholtz Zentrum München, German Research Centre for Environmental Health, Neuherberg, Germany
²Dr. von Hauner Children's Hospital, LMU Munich, Division of Pediatric Gastroenterology and Hepatology, Munich, Germany
³Ulz - Helmholtz Centre for Environmental Research Leipzig, Department of Environmental Immunology, Leipzig, Germany
⁴Marien-Hospital, Wesel, Germany
⁵Iuf - Leibniz Research Institute for Environmental Medicine (Iuf), Düsseldorf, Germany
⁶Fachklinik Gaißach, Zentrum für Chronische Erkrankungen, Gaißach, Germany
⁷Institute of Epidemiology I, Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany
⁸Institut für Epidemiologie I, Helmholtz Zentrum München - Deutsches Forschungszentrum für Gesundheit und Umwelt, German Research Center for Environmental Health, Munich/Neuherberg, Germany
⁹Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany

Objectives and study: Functional abdominal pain disorders (FAPD), are a common cause of chronic abdominal pain in children and adolescents. Certain foods are perceived to exacerbate symptoms, and hence a role of diet in the aetiology of FAPD has been suggested. In addition, children suffering from FAPD may change their dietary intake. Prospective epidemiological studies could help provide better insight. We therefore aim to assess the association between changes in dietary intake and FAPD during adolescence.

Methods: Children participating in the GINIplus and LISAplus birth cohort studies with complete data on dietary intake, symptoms of FAPD, and covariates, were included (N=432). Dietary intake was assessed by means of a food frequency questionnaire (FFQ) at ages 10 and 15 years. Intakes of 15 food groups (fruit, vegetables, starchy vegetables, whole grains, refined grains, egg, meat, fish, nuts, dairy, butter, margarine, oil, sugar-sweetened foods and caloric drinks), fat, carbohydrate and protein, were converted into percentages relative to total daily energy intake (%EI), and changes in dietary intakes were calculated as the difference in %EI from age 10 to age 15 years. Self-reported symptoms of FAPD were assessed at age 15 years by the validated age-appropriate questionnaire created as part of the Rome III process. Children fulfilling the different criteria for either of functional dyspepsia, irritable bowel syndrome, abdominal migraine or functional abdominal pain, were considered to suffer from a FAPD (yes;no). Associations of changes in dietary intake with FAPD were assessed using binary logistic regression (binary-reduction method), adjusting for sex, study, region, parental education, pubertal stage, BMI, exact age, sedentary behaviour, total caloric intake and dietary intake at age 10 years.

Results: Increasing caloric drinks and total carbohydrate intakes from age 10 to age 15 years, was associated with a higher probability of having a FAPD at age 15 years [adjusted OR=1.05, 95% CI=(1.01;1.09) and 1.07 (1.01;1.13), respectively for an increase of 1%EI]. On the other hand, increasing protein and fat intakes from age 10 to age 15 years, was associated with a lower probability of having a FAPD [0.85 (0.72;0.98) and 0.94 (0.88;0.99), respectively].

Conclusion: Although a causal relationship between dietary intake and FAPD cannot be inferred from this study, these findings suggest that dietary changes from childhood to adolescence might play a role in the development of FAPD.
NUTRITION: Nutrition and health outcomes

N-O-033

Prevalence of hepatic steatosis measured by CT scan in paediatric accidental trauma victims in Ontario

Jasbir Dhaliwal¹, Govind Chavhan², Paul Wales³, Eberhard Lurz¹, Simon Ling⁴, Marialena Mouzaki⁴

¹Hospital for Sick Children, Department of Pediatrics, Division of Gastroenterology, Hepatology and Nutrition, Toronto, Canada
²Hospital for Sick Children, Department of Paediatric Radiology, Toronto, Canada
³Hospital for Sick Children, Department of Paediatric Surgery, Toronto, Canada
⁴The Hospital for Sick Children, Division of Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: Non-alcoholic fatty liver disease (NAFLD) is the most common cause of liver disease in children. NAFLD is typically diagnosed in the context of obesity, as excess adiposity and insulin resistance contribute to fat deposition within the liver. More recently the concept of ‘lean NAFLD’ has emerged, suggesting that a proportion of patients with NAFLD are not obese. (1) To determine the prevalence of hepatic steatosis (HS) on computer tomography (CT) scan in a cohort of previously healthy children and adolescents who are victims of accidental trauma, and (2) the association between HS and subcutaneous adipose tissue.

Methods: Retrospective review of data from the Sickkids trauma database (from 2004 to 2015). Inclusion criteria: previously healthy children ages 1-17yr having undergone an abdominal CT scan as a part of routine trauma assessment. Exclusion criteria: Involvement of spleen and/or liver in the injury, known metabolic condition, concurrent use of medications that could predispose to HS. Anthropometrics and baseline demographics were collected. Steatosis was defined as a liver spleen attenuation index (L/S AI) of <0.8. Subcutaneous adipose tissue (SAT) was defined as the distance from the skin to the body musculature, and measured at the midpoint from the iliac crest to the umbilicus bilaterally, at the level of umbilicus. The mean of the two measurements was calculated. Statistical analyses were performed using two-tailed t test and Pearson’s correlation coefficient, with Graphpad Prism 7.

Results: A total of 140 children (61% male) were included in the analyses with a mean (±SD) age of 7 (±4) years. The mean weight z score was 0.47 (±0.98); 5% had a weight z-score ≥2. HS on imaging was found in 22 patients (16%), including 14% of those with weight z-score <2. There was no significant difference in the SAT between males and females (9.5±1.1 vs 6.5±0.9; p=0.07). SAT was significantly different in those with vs. without HS (12.5 ± 2.9 vs 7.1±0.6; p<0.01). There was an inverse correlation between SAT and L/S AI (r=-0.3, p<0.01) (Fig 1).
Conclusion: HS is highly prevalent in this cohort of previously healthy children in Ontario. We found an association between HS and subcutaneous adipose tissue. Larger population based studies are needed to investigate the prevalence of HS in children across Canada.
High fat meal, systemic inflammation and glucose homeostasis in obese children and adolescents

Anita Morandi\textsuperscript{1}, Elena Fornari\textsuperscript{1}, Francesca Opri\textsuperscript{2}, Massimiliano Corradi\textsuperscript{1}, Mara Tommassi\textsuperscript{1}, Riccardo C. Bonadonna\textsuperscript{3}, Claudio Maffeis\textsuperscript{1}

\textsuperscript{1}University Hospital of Verona, Pediatric Diabetes and Metabolic Disorders Unit, Verona, Italy
\textsuperscript{2}University Hospital of Verona, Verona, Italy
\textsuperscript{3}University of Parma, Aoi of Parma, Ospedale Maggiore, Parma, Italy

Objectives and study: The relationships between dietary fat, IL-6 and glucose homeostasis are poorly understood. We aimed to assess in obese children and adolescents whether i) IL-6 is associated with glucose homeostasis; ii) a fat meal ingestion is associated with lypopolysaccharide (LPS) translocation; and iii) acute LPS translocation and chronic LPS exposure are associated with IL-6 and glucose homeostasis.

Methods: Twenty obese children/adolescents (9-17 years old, 11 boys) were recruited at the Centre for Pediatric Obesity of Verona, Italy. They underwent a standard OGTT and, 7-14 days later, a fat meal test. IL-6 and two markers of LPS exposure and translocation, LPS-binding protein (LBP) and soluble CD14 (sCD14), were measured before and in the 5 hours after the ingestion of an ice-cream supplemented with sunflower oil and extra-virgin olive oil (fat=69% of energy, SFA/MUFA/PUFA=31.5%/35%/33.5%). There were assessed: i) correlations between IL-6 and glucose homeostasis (HOMA-IR, Matsuda-index, raw and adjusted insulin secretion: AUCinsulin/glucose and Matsuda-index * AUCinsulin/glucose, respectively); ii) incremental AUCs (iAUCs) of IL-6, LBP and sCD14 during the meal test; and iii) correlations of basal IL-6, LBP, sCD14 and their iAUCs with each other and with glucose homeostasis.

Results: IL-6 correlated with HOMA-IR ($r=0.61[0.24-0.82]$, $p=0.013$), the Matsuda-index ($r=-0.53[0.12-0.78]$, $p=0.03$) and AUCinsulin/glucose ($r=0.53[0.12-0.78]$, $p=0.034$). IL-6 did not change after meal ingestion, whereas LBP and sCD14 decreased significantly (iAUCs= -451.8[-699 - -203] and -21 335[-36 908 - -5 762 ], respectively), indicating LPS translocation. LBP, sCD14 and their iAUCs did not correlate with IL-6 or glucose homeostasis.

Conclusion: IL-6 is associated with insulin sensitivity in obese children/adolescents. A high-fat meal with a balanced content of SFA/MUFA/PUFA produces LPS translocation but does not stimulate IL-6 or impair glucose homeostasis in obese youth.
The clinical efficiency of fish-oil emulsion to improve parenteral nutrition-associated liver disease in children with intestinal failure

Nan Wang¹, Ying Wang¹, Weihui Yan¹, Lina Lu¹, Yijing Tao¹, Wei Cai²

¹Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Clinical Nutrition, Shanghai, China
²Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Pediatric Surgery, Shanghai, China

Objectives and study: Long-term parenteral nutrition (PN) is required in children with intestinal failure. Parenteral nutrition-associated liver disease (PNALD) is one of the complications of parenteral nutrition, including cholestasis, cholelithiasis, or even liver cirrhosis, liver failure, and it can be seriously life-threatening. Pathogenesis of PNALD is still not clear, which may be related to intravenous fat emulsion of soybean oil, and a number of studies have found that fish oil riching in omega-3 polyunsaturated fatty acids can reverse parenteral nutrition-associated liver disease. We performed a retrospective study to observe if fish-oil lipid emulsion can improve parenteral nutrition-associated liver disease in children with intestinal failure.

Methods: Twelve patients (6 males and 6 females) with long-term parenteral nutrition were enrolled in this study. The changes of parenteral nutrition, enteral nutrition and liver function (TBA, ALT, AST, AKP, GGT, Tbi, Dbi) were observed before and after the treatment of fish oil lipid emulsion.

Results: The average duration of PN was 77 days before using fish oil lipid emulsion. The average PN calorie was 45.3 ± 17.0 kcal/kg/d, EN calorie was 29.1±17.2 kcal/kg/d, the dose of lipid emulsion was 1.3 ± 0.4g/kg/d, amino acid dose was 2.1 ± 0.5g/kg/d, carbohydrate dose was 6.2 ± 2.9g/kg/d before using fish oil lipid emulsion. After the treatment, the average dose of lipid emulsion was 1.0 ± 0.6g/kg/d, amino acid was 1.4 ± 0.7g/kg/d, carbohydrate was 4.7 ± 3.1g/kg/d, PN intake was 33.3 ± 19.5 kcal/kg/d, EN intake was 64.3 ± 37.9 kcal/kg/d. After 26±16 days of ω-3 fish oil lipid emulsion treatment, the level of ALT,AST,GGT were significantly decreased.

Table: The changes of liver function before and after the treatment of fish oil lipid emulsion

<table>
<thead>
<tr>
<th></th>
<th>Before</th>
<th>After</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBA</td>
<td>10.8 (2.7-17.9)</td>
<td>6.2±5.3</td>
<td>.0803</td>
</tr>
<tr>
<td>ALT</td>
<td>180±126</td>
<td>31 (25-61)</td>
<td>.0021</td>
</tr>
<tr>
<td>AST</td>
<td>150±77</td>
<td>62 (42-78)</td>
<td>.0008</td>
</tr>
<tr>
<td>AKP</td>
<td>315 (209-350)</td>
<td>240±139</td>
<td>.0522</td>
</tr>
<tr>
<td>GGT</td>
<td>169±135</td>
<td>52 (23-82)</td>
<td>.0059</td>
</tr>
<tr>
<td>Tbi</td>
<td>10.3 (5.4-25.7)</td>
<td>11.0±7.0</td>
<td>.2510</td>
</tr>
<tr>
<td>Dbi</td>
<td>2.7 (1.5-14.9)</td>
<td>1.9 (1.0-7.3)</td>
<td>.2734</td>
</tr>
</tbody>
</table>

TBA, total bile acid, µmol/L; ALT, alanine aminotransferase, IU/L; AST, aspartate aminotransferase, IU/L; AKP, alkaline phosphatase, IU/L; GGT, γ-glutamyltransferase, IU/L; Tbi, total bilirubin, µmol/L; Dbi, direct bilirubin, µmol/L.

Conclusion: ω-3 fish oil lipid emulsion can improve parenteral nutrition-associated liver disease (PNALD). Fish oil lipid emulsion may be an effective treatment for parenteral nutrition-associated liver disease, but its mechanism remains to be elucidated.
Acquisition of oral feeding skills in preterm infants born <32 weeks

Zahra Khan¹, Cornelia Sitter¹, Berndt Urlesberger¹

¹Medical University of Graz, Division of Neonatology, Graz, Austria

Objectives and study: In preterm infants, attainment of safe oral feeding skills is an important milestone. American Academy of Paediatrics has provided guidelines for hospital discharge of high risk neonates. According to these guidelines, prior to discharge, it is recommended that preterm infants establish competent oral feeding by breast or bottle, without cardiorespiratory compromise. The ideal time to introduce oral feeds has yet to be established. Research is needed to clarify multiple issues surrounding the topic of the initiation of oral feeding in the NICU. The aim of current study was to identify the time point regardless of the GA (at birth) when attainment of full oral feeding is possible.

Methods: A prospective cohort study was conducted including preterm infants born <32 weeks entering the NICU during 1-year-time period. Feeding performance and anthropometric parameters were recorded during hospital stay. Infants were divided in two groups on the basis of Gestational Age (GA): <28 weeks (Extremely preterm infants (EPI); ≥28 weeks (very preterm infants (VPI). To assess individual feeding performance, important time points were defined regarding tube feeding phase and oral feeding phase. Tube feeding phase included days to reach full enteral nutrition (FEN) and oral feeding phase included transition from gavage feeding to oral/suck feeds i.e. (i) 10% oral feed, (ii) 50% oral feed, (iii) 100% orally fed, (iv) ad libitum feeds

Results: All preterm infants successfully acquired oral feeding skills before discharge and were discharged on ad libitum feeds. EPI (n = 24) compared to VPI (n = 47) showed significantly different feeding performance during both tube feeding and oral feeding phase. EPI needed more time to reach FEN than VPI (19 vs 8 days). Attainment of full oral feeding skills was also late in EPI vs VPI.(see table). We found significantly lower weight increment in EPI group as compared to VPI group during 10-100% oral feeds period.
Table:

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total Sample (mean ± SD)</th>
<th>VPI (mean ± SD)</th>
<th>EPI (mean ± SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA at Birth (weeks)</td>
<td>28.45 ± 2.3</td>
<td>29.9 ± 1.10</td>
<td>25.6 ± 1.17</td>
</tr>
<tr>
<td>Birth weight (g)</td>
<td>1186 ± 428</td>
<td>1390 ± 376</td>
<td>786 ± 150</td>
</tr>
<tr>
<td>Days to reach FEN</td>
<td>11 ± 7</td>
<td>8 ± 3</td>
<td>19 ± 8</td>
</tr>
<tr>
<td>GA at FEN-10% oral feeds (weeks)</td>
<td>33 ± 1.56</td>
<td>32 ± 0.92</td>
<td>34 ± 2.06</td>
</tr>
<tr>
<td>GA at 10%- 50% oral feeds (weeks)</td>
<td>34.4 ± 2.24</td>
<td>33.7 ± 1.06</td>
<td>35.9 ± 3.11</td>
</tr>
<tr>
<td>GA at 50%-100% oral feeds (weeks)</td>
<td>35.3 ± 2.32</td>
<td>34.6 ± 1.11</td>
<td>36.9 ± 3.16</td>
</tr>
<tr>
<td>GA at 100% - ad libitum feeds (weeks)</td>
<td>36.01 ± 2.34</td>
<td>35.1 ± 1.04</td>
<td>38.0 ± 2.87</td>
</tr>
<tr>
<td>GA at Discharge (weeks)</td>
<td>37 ± 2.72</td>
<td>35.9 ± 1.25</td>
<td>39.1 ± 3.5</td>
</tr>
<tr>
<td>Weight at Discharge (g)</td>
<td>2560 ± 503</td>
<td>2400 ± 447</td>
<td>2087 ± 543</td>
</tr>
</tbody>
</table>

Conclusion: Before discharge, successful oral feeding skills can be acquired in very preterm infants regardless of GA at birth. However, the time point of attainment of full oral feeding was significantly later in EPI compared to VPI. During transition phase mean weight gain per day was lower in the EPI compared to VPI. These findings suggest careful monitoring of growth parameters is required during transition phase to oral feeding.
Tracking dietary patterns between 1 and 8 years of age in a cohort of children from five European countries


Universitat Rovira i Virgili, Iispv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
Hospital Universitari de Tarragona Joan XXIII, Servei de Pediatria, Tarragona, Spain
Von Haunersches Kinderspital, Centre Division of Metabolic and Nutritional Medicine, Munich, Germany
Dr. von Hauner Children's Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
The Children’s Memorial Health Institute, Department of Neonatology and Neonatal Intensive Care, Warsaw, Poland
Children's Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
University Children's Hospital Queen Fabiola, Ulb, Brussels, Belgium
Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia
University of Western Australia, School of Population Health, Perth, Australia

Objectives and study: Evidence suggests that childhood dietary patterns may persist into adulthood and determine adult health. It is therefore important to identify when key dietary patterns are established. The present works aims to describe dietary patterns and their tracking between 1 and 8 years of age in a cohort of children from 5 European countries (Germany, Belgium, Italy, Poland and Spain).

Methods: A 3 day food diary was collected 1, 2, 3, 4, 5, 6 and 8 years of age. Foods recorded in the diaries were allocated to one of 27 major food groups. Exploratory factor analyses (EFA) with varimax rotation was performed using all food group intakes (g/day) to identify major dietary patterns at each age. Factors (dietary patterns) explaining the maximum variance in food intakes were selected. Each child received a z-score for each identified dietary pattern. For each pattern, a stability (tracking) coefficient [B (95% CI)] was calculated from 2 to 8 years using a general estimated equation regressing baseline dietary pattern z-score on later z-scores.

Results: Please copy and paste the corresponding text here.

Table: At age 1 year (n=827, 15% variance explained), two dietary patterns were identified. One was labelled as Core Foods Dietary Pattern (CORE) and the other was labelled as Low Quality Fats and Sugars (F&S). Main foods positively loading for CORE were vegetables, potatoes, fish, olive oil, white and red meat, and negatively loading were ready-to-eat infant products, added sugars and confectionary. Main foods positively loading for F&S were saturated spreads, soft cheese, added sugars, fruit juices and confectionary, and negatively loading were olive oil, fish and cow’s milk. At ages 2 (n=703, 13% variance explained), 3 (n=514, 14% variance explained), 4 (n=482, 13% variance explained), 5 (n=436, 14% variance explained) and 8 years (n=393, 16% variance explained), similar CORE and F&S patterns were consistently identified in addition to a high protein sources dietary pattern (PROT) in which milk, flavoured milks, fish, eggs, white meat, processed meat, potatoes and olive oil loaded positively at all ages and processed cereals and fresh fruits loaded negatively a several timepoints. Figure 1 shows factor loadings (the ten loading highest per pattern) for the 3 patterns at 2 years as an example.

Tracking coefficients from 2 to 8 years were 0.36 (95% CI: 0.30, 0.41) for CORE, 0.61 (95% CI: 0.56, 0.67) for F&S and 0.50 (95% CI: 0.44, 0.56) for PROT. Fifty percent of the children in the highest quartile for CORE z-score and 42% in the lowest quartile for CORE z-score at 2y were in the same quartiles at 8y; 69% of the children in the highest F&S and 40% in the lowest F&S quartiles at 2y were...
at the same quartiles at 8y; and 50% of the children in the highest PROT and 33.3% in the lowest PROT quartiles at 2y were at the same quartiles at 8y.

**Conclusion:** At one year, when children have not completely finished their complementary feeding, 2 dietary patterns (CORE and F&S) were identified. Afterwards, three patterns (CORE, F&S and PROT) were consistently identified at 2, 3, 4, 5 and 8 y. Healthy dietary patterns in children achieved at 2 years (as shown by highest CORE and lowest F&S quartiles) track moderately to 8 years. Children with a high score for a dietary pattern characterized by added sugars and low quality fats at age 2, tend to have the same dietary characteristics at 8y.

Figure 1. Factor loadings (the 10 foods with the highest factor loadings) for the three dietary patterns at 2 years.
Breastfeeding and infant hospitalisation for infections: large cohort- and sibling analysis

Ketil Stordal¹, Karen Marie Lundeby², Anne Lise Brantsæter³, Margaretha Haugen⁴, Britt Nakstad⁵, Nicolai A. Lund-Blix⁶, Lars Stene⁶

¹Norwegian Institute of Public Health, Oslo, Norway
²Oslo University Hospital, Child Health, Oslo, Norway
³Norwegian Institute of Public Health, Environment, Oslo, Norway
⁴Norwegian Institute of Public Health, Child Health, Oslo, Norway
⁵Institute of Clinical Medicine, University of Oslo, Campus Akershus University Hospital, Oslo, Norway
⁶Norwegian Institute of Public Health, Chronic Diseases, Oslo, Norway

Objectives and study: Breastfeeding may protect against infections, but optimal duration of breastfeeding remains controversial. WHO recommends exclusive breastfeeding for the first 6 months and continuation of breastfeeding if possible until 24 months age. We aimed to study the association between duration of full and any breastfeeding and infections during the first 18 months of life.

Methods: The Norwegian Mother and Child Cohort Study (MoBa) is a prospective pregnancy cohort study, which recruited expecting mothers giving birth from 2000-2009. We analysed data from the full cohort (n=70 511) and sibling sets (n=21 220) with parental report of breastfeeding and infections. The main outcome measures were the relative risks for hospitalisation because of infections during the first 18 months by age at introduction of complementary foods, and by duration of any breastfeeding.

Results: In the cohort, 14% of the children were fully breastfed the first six months of life; 80% still received breastmilk at six months and 39% at 12 months. Of breastfed children who received complementary foods at 4-6 months of age, 7.3% were hospitalised compared to 7.7% of those receiving complementary foods after 6 months (adjusted relative risk [RR] 0.95, 95% CI 0.88-1.03). We found some evidence for an overall association between longer duration of full breastfeeding and lower risk of hospitalisations for infections during the first 6 months (per month of full breastfeeding; aRR 0.98, 95% CI 0.97-1.00). This was driven by a higher risk among infants given complementary formula from birth, with no association found for solid foods.

Higher risk of hospitalisation was observed in those breastfed six months or less (10.0%) compared to ≥12 months (7.6%, adjusted RR 1.22, 95% CI 1.14-1.31), but with similar risks for 6-11 months (8.2%, adjusted RR 0.97, 95% CI 0.91-1.03) versus ≥12 months.

Matched sibling analyses showed non-significant associations and were generally weaker compared with the cohort analyses.

Conclusion: Our results support the recommendation to breastfeed beyond 6 months, but do not indicate that infections requiring hospitalisation differs by introduction of complementary foods at 4-6 compared to after 6 months. Infants breastfed longer than 12 months had similar risks of infections as compared to those breastfed 6-11 months, indicating no added beneficial effect of breastfeeding beyond 12 months for protection against infections.
Human milk peptides differentiate between the preterm and term infant more than across lactational stages

Kelly Dingess¹, Marita de Waard², Sjef Boeren³, Jacques Vervoort³, Tim T. Lambers⁴, Hans van Goudoever⁵, Kasper A. Hettinga¹

¹Wageningen University, Dairy Science and Technology Group, Wageningen, Netherlands
²Emma Children’s Hospital-Academic Medical Center, Pediatrics, Amsterdam, Netherlands
³Wageningen University, Laboratory of Biochemistry, Wageningen, Netherlands
⁴Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands
⁵Vu University Medical Centre, Paediatrics, Amsterdam, Netherlands

Objectives and study: Donor human milk (DHM) is the preferred source of nutrition for preterm infants if mothers own milk is not available. DHM is usually of a late lactational stage (LS) and may not provide adequate nutrients for the preterm infant. Therefore, understanding of the compositional differences between term and preterm human milk (HM) at varying LS is of importance. Peptides are an understudied component of HM. It has been well documented that total milk protein is higher in preterm than term milk, and overall decreases throughout lactation. We therefore hypothesised that the endogenous peptide profiles, peptide functionality, and the enzymes responsible for these peptides would be different in preterm and term milk across LS.

Methods: A total of 29 HM samples from the Dutch Human Milk Bank were used for total protein, peptide analysis, peptide functionality and enzyme prediction. Three groups were included in the assessment, preterm late LS, term early and term late LS. Gestational age (GA) groups were defined as preterm (24-34 wks gestations) and term (≥35 wks gestation). LSs were determined to be either early (16-36 days postpartum) or late (55-88 days postpartum). Total protein was assessed by Pierce Protein BCA Assay Kit. Peptides were extracted from skim milk samples by trichloroacetic acid precipitation and analyzed by LC-MS/MS. Data analysis for parent proteins (proteins from which peptides were identified) and peptides was done using Maxquant software. Statistical analysis was done using ANOVA and two-sided t-tests; all statistics were done with STATA and Perseus. PeptideRanker was used to assess likelihood of peptide bioactive functionality. EnzymePredictor was used to assess predicted enzymes.

Results: Total protein concentrations between the preterm late and term early LS groups were significantly different (p<0.04). There were 9 different parent proteins identified, but no significantly different parent proteins by GA or LS. A total of 902 peptides were identified, of which the majority were from the parent proteins β-casein, αs1-casein, polymeric immunoglobulin receptor, osteopontin and κ-casein. There were significant differences in peptide profiles based on GA (59 differing sequences; p<0.05), LS (37 differing sequences; p<0.05) and the interaction of GA and LS (5 differing sequences; p<0.05). Only two of these differing peptides had significant odds of having known bioactive functionality. Enzyme prediction analysis determined that the most likely enzymes responsible for the cleavage of the identified HM peptides were plasmin, a trypsin-like enzyme and cathepsin D.

Conclusion: HM peptides did not significantly differ at the parent protein level based on GA or LS; however, the peptide profiles themselves were significantly different. Further research should be done to assess functionality of these peptides, and to better understand their role in infant health outcomes such as gut and immune development.

Disclosure of interest: Tim T. Lambers, Conflict with: Mead Johnson Nutrition
Nasogastric versus orogastric route of feeding in preterm 32 weeks neonates: a prospective randomized open label controlled study

Naveen Gupta¹, Syed Zia¹, Rekha Mittal², Shyam Kukreja³, Chetnanand Jha¹

¹Max Superspeciality Hospital, Patparganj, Delhi, Neonatology, Delhi, India
²Max Super Speciality Hospital, Patparganj, Delhi, Pediatric Neurology, Delhi, India
³Max Super Speciality Hospital Patparganj, Delhi, Pediatrics, Delhi, India

Objectives and study: Primary Objective: To compare the frequency of Bradycardia defined as HR < 100/min and Desaturation defined as SpO2 < 85% in preterm hemodynamically stable preterm neonates (≤32 weeks gestational age) not requiring any respiratory support fed by orogastric tube as compared to nasogastric tube.

Study Site: Level III Neonatal Intensive Care Unit, Max Superspeciality Hospital, Patparganj, Delhi, India

Study Design: Prospective, Randomized, Open Label, Controlled study.

Study Duration: October 2015 to June 2016

Methodology

Material & Methods: Eligible population was enrolled after taking informed consent. Adverse events were recorded by bedside nurse if monitor gave alarm for desaturation (< 85%) or bradycardia (<100/min) with regular wave forms. Events were recorded till the time tube remain in situ which was considered as 1 feeding tube insertion episode (FTIE). Since duration of tube stay may vary in nasogastric and orogastric group, no of episodes/hr were compared. To demonstrate 50% reduction in adverse events in orogastric tube as compared to nasogastric group we needed 80 feeding tube insertion episodes in each group considering an α error of 0.05 and β error of 0.2. 2 stratas were made of <30 weeks (Group 1) and ≥ 30 weeks (Group 2) gestation. Block randomization was done in block size of 4.

SPSS 20 version was used for statistical analysis.
**Results:**

- **Assessed for Eligibility** (n = 50)
  - Excluded (n = 29)
    - Sepsis, NEC, IVH (n = 8)
    - Severe congenital malformation (n = 2)
    - Transfer to other hospital (n = 5)
    - Early death (n = 4)
    - Did not give consent (n = 10)
  - Enrolled (n = 21)
    - 160 Feeding tube insertion episodes in these babies

- **Stratification**
  - Gestational Age < 30 weeks
    - Randomization (n = 80)
      - Nasogastric (n = 40)
        - CPAP – 4
          - Ventilated - 2
        - Completed episodes (n = 34)
      - Orogastric (n = 40)
        - CPAP – 0
          - Ventilated - 2
        - Completed episodes (n = 38)
  - Gestational age ≥ 30 weeks
    - Randomization (n = 80)
      - Nasogastric (n = 40)
        - CPAP – 1
          - Ventilated - 0
        - Completed episodes (n = 39)
      - Orogastric (n = 40)
        - CPAP – 0
          - Ventilated - 0
        - Completed episodes (n = 40)

*Figure 1 – Trial Flow of the study: included, excluded and enrolled babies.*
Mean Gestational age was 29.3±2.3 weeks and Birth weight was 1112±450 grams. Mean gestational age and birth weight was 29.07±1.6 weeks and 1180±296 grams respectively. Median age of enrollment was 16 days with range from 2-38 days. There were total 609 bradycardia episodes and 647 desaturation episodes. In Group I (<30 weeks) episodes of bradycardia (p = 0.003 with 95%CI (0.027-0.132) and desaturation per hour (p = 0.000 with 95%CI (0.078-0.205) were significantly increased in nasogastric as compared to orogastric group. In Group 2 (≥30 weeks) there was significant increase in desaturation per hour in nasogastric group (p = 0.007 with 95%CI 0.008 – 0.048) but no difference was noticed in episodes of bradycardia per hour (p = 0.107 with 95%CI -0.004 – 0.04). Group 3 (Group 1 + Group 2) also showed statistically significant increase in adverse events per hour in nasogastric group (p value 0.001 and 0.000 respectively). No differences were observed in secondary outcomes in form of duration of stay or displacement of tube.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Nasogastric tube group (n = 40)</th>
<th>Orogastric tube group (n = 40)</th>
<th>P value (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Group 1 (&lt;30 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia episodes/hour</td>
<td>0.158±0.150</td>
<td>0.078±0.071</td>
<td>0.003* (0.0274 – 0.1325)</td>
</tr>
<tr>
<td>Desaturation episodes/hour</td>
<td>0.1927±0.179</td>
<td>0.051±0.093</td>
<td>0.000*(0.078-0.205)</td>
</tr>
<tr>
<td><strong>Group 2 (≥30 weeks)</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia per hour</td>
<td>0.116±0.051</td>
<td>0.098±0.048</td>
<td>0.107 (-0.004 – 0.04)</td>
</tr>
<tr>
<td>Desaturation per hour</td>
<td>0.124±0.049</td>
<td>0.095±0.042</td>
<td>0.007* (0.008 – 0.048)</td>
</tr>
<tr>
<td><strong>Group 3 (Group 1 + 2) ie. Primary outcome</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradycardia per hour</td>
<td>0.137±0.011</td>
<td>0.088±0.06</td>
<td>0.001*(0.020-0.077)</td>
</tr>
<tr>
<td>Desaturation per hour</td>
<td>0.158±0.135</td>
<td>0.073±0.075</td>
<td>0.000*(0.05-0.119)</td>
</tr>
</tbody>
</table>

**Conclusion:** Since episodes of bradycardia and desaturation were significantly higher in nasogastric group we recommend orogastric route as feeding method of choice in hemodynamically stable preterm babies ≤ 32 weeks gestation.
**NUTRITION: Neonatal and infant nutrition**

N-O-041

**Oropharyngeal breastmilk administration in extreme prematurity reduces gram negative sepsis and feed intolerance**

Deepa Hariharan¹, Ganesh Veluswami², Lavanya Balasubramanian², Velmurugan Kannappan²

¹Sooriya Hospital, Neonatology, Chennai, India
²Sooriya Hospital, Chennai, India

**Objectives and study:** Late-onset sepsis is a major cause of morbidity and mortality in extreme prematurity. Breastmilk, especially colostrum, secreted by mothers of premature infants is rich in biofactors such as lactoferrin. However, premature infants do not get the immunostimulatory benefits of breastmilk on oropharyngeal-associated lymphoid tissue, as they are kept nil oral or fed by nasogastric tubes for a few weeks. We hypothesized that early oropharyngeal administration of own mothers milk will improve outcomes in extreme prematurity. The aim of the study was to determine the effects of early buccal delivery of breastmilk on late-onset sepsis in extremely premature infants. The study was conducted in a busy referral NICU in India with >1000 high-risk admissions per year.

**Methods:** Infants with birth weight < 1250g, gestation <32 weeks admitted during the 6 month study period (June to December 2016) were given expressed breastmilk delivered on the buccal mucosa from 6 hours of age. A volume of 0.2 ml of milk was delivered with a syringe on the buccal mucosa (0.1ml on each side of the mouth) every 6 hours, till 30 weeks corrected GA or initiation of oral feeds (study group, n= 56). The control group comprised historical matched controls (for gestation and weight) admitted during the preceding 6 months (n= 56). Feeding regimen (starting on day 1, advance by 25ml/kg/day, fortification at 50ml/kg/day, maximum feed of 180ml/kg/day), objective definition of feed intolerance (bilious NG aspirate or prefeed abdomen girth increase confirmed by neonatologist ) and use of expressed breastmilk were similar in both periods, with no major changes in protocols. Surfactant, caffeine, ventilatory and inotrope use, PDA closure and protocols for central venous access were similar. Outcomes studied were episodes of feed intolerance needing NPO for >48h, NEC stage II or III(Bell's criteria read by radiologist), late-onset bacteremia, time to reach full feeds, and death.

**Table:**

<table>
<thead>
<tr>
<th>Study</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>56</td>
</tr>
<tr>
<td>Mean BW (g)</td>
<td>970± 23</td>
</tr>
<tr>
<td>Mean GA (weeks)</td>
<td>28.7 ± 0.4</td>
</tr>
<tr>
<td>Number of infants needing ventilator +/- inotrope support</td>
<td>25</td>
</tr>
<tr>
<td>Transient feed intolerance episodes</td>
<td>28</td>
</tr>
<tr>
<td>Late-onset sepsis (gram negative rods)</td>
<td>4</td>
</tr>
<tr>
<td>Stage 2/3 NEC</td>
<td>1</td>
</tr>
<tr>
<td>Average time to full feeds (days)</td>
<td>17.5</td>
</tr>
<tr>
<td>Death</td>
<td>2</td>
</tr>
</tbody>
</table>

* p<0.05 , No adverse events noted due to buccal delivery of milk
**Conclusion:** Early oropharyngeal breastmilk administration is feasible, safe and associated with lower incidence of feed intolerance and nosocomial sepsis in extreme prematurity. Implementation of this will be a cost-effective practice to improve outcomes in Indian NICUs.
Complications of gastrojejunal feeding- a single centre experience

Fiona Cameron¹, Michelle Brooks¹, Hazel Duncan², Diana Flynn¹, Vikki Garrick¹, James Andrews³, Gregor Walker³, Andrew Barclay¹

¹Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Glasgow, United Kingdom
²Royal Hospital for Children, Department of Nutrition and Dietetics, Glasgow, United Kingdom
³Royal Hospital for Children, Department of Paediatric Surgery, Glasgow, United Kingdom

Objectives and study: Jejunal feeding is becoming more common within paediatric complex enteral nutrition (CEN) as an alternative to gastric feeding in those with poor feed tolerance. There is a paucity of information on complications associated with the various devices available and a lack of clinical experience with their use, particularly outside of paediatric gastroenterology. The aim of this study was to examine the frequency and types of complications associated with gastrojejunal (GJ) feeding within our CEN service from 01.01.2013 to 31.10.2016.

Methods: All patients within the Complex Enteral Feeding clinic at the Royal Hospital for Children were included. Patients were identified using the CEN database and confirmed through case note review. Basic demographics were collected including: age, gender, underlying medical conditions and reason for gastrojejunal feeding, type of device, complications and outcome of GJ feeding.

Results: 38 patients were identified, 8 excluded (1 non jejunally fed and 7 not under the CEN service), 22/30 (73%) were male. The most common underlying reason for GJ feeding was neurological impairment: 10 cerebral palsy, 8 developmental delay and 6 underlying neurological syndromes. Other conditions included GI dysmotility in 5, short gut in 3, complex cardiac disease in 3 and gastroesophageal reflux in 15. The most common reasons for GJ feeding were: vomiting in 18, poor weight gain/failure to thrive in 11 and poor enteral feed tolerance in 6.

Fourteen patients (47%) had Corflo™ inserted as a primary device (16Fr with 6Fr jejunal extension), 10 (33%) had a gastrojejunal button (14Fr or 16Fr) and 6 (20%) had a primary Freka™ device (15Fr with 9Fr jejunal extension). In those with Corflo™ the most common complication was blockage of the device occurring in 8/14 compared with 2/10 with a GJ button and none with a Freka™. 4/14 had their device blocked at least once (2 Corflo™ and 2 GJ button), 2/14 (both Corflo™) blocked twice, 3/14 (all Corflo™) blocked 3 times and 1/14 blocked their Corflo™ device on 4 occasions. The other most common complication was dislodgement of the device occurring in 19/30 patients requiring reinsertion up to four times, 11/19 Corflo™ and 8/19 GJ button. Other complications included disconnection of the device, GJ button twisted on itself and problems with end connectors.

At the study end 13/30 remained jejunally fed although 3/13 proceeded to formal Roux-en-Y jejunostomy, 2/13 had witzel jejunostomy and 8/13 still had a GJ device. 12/30 were de-escalated to gastric feeding, 2/12 underwent fundoplication and one patient died of an undiagnosed neurological condition. Two patients were nil enterally due to underlying disease.

Conclusion: Complications of GJ feeding are common leading to a significant burden on the MDT as well as families in managing them. In our single centre experience, Corflo™ devices blocked and dislodged more frequently than other devices despite significant input from the MDT. Consequently, we have changed our practice to use Freka™ devices as our primary GJ device give the unacceptable rate of complications observed with other devices. Further multi centre collaboration is needed to determine if these results are applicable to other centres using gastrojejunal devices.
Anaemia in children receiving home parenteral nutrition

Elena Cernat¹, Tania Ahmad², Susan Hill³, Anna Hughes³, Jutta Koeglmeier³

¹King's College Hospital, Paediatric Liver, Gi and Nutrition Centre, London, United Kingdom
²Great Ormond Street Hospital, Paediatric Gastroenterology, London, United Kingdom
³Great Ormond Street Hospital for Children, Paediatric Gastroenterology, Division of Nutrition, Intestinal Failure and Rehabilitation, London, United Kingdom

Objectives and study: Children receiving long term Home Parenteral Nutrition (HPN) are at risk of developing iron-deficiency anaemia. Causative factors are inadequate absorption of enteral iron due to underlying gastrointestinal pathology, recurrent venopuncture and limited ability to add iron to the PN bag.

The aim of this study was to determine the incidence of iron deficiency anaemia in paediatric HPN patients and to establish what treatment symptomatic children received.

Methods: Data was collected retrospectively from children receiving HPN at a large tertiary referral centre over a 12 months’ period (December 2014 - December 2015) and 41 patients were identified. Blood test including full blood count (FBC), Ferritin and C reactive protein was done at least 3 times for each patient in the follow-up period. The liver tests were checked at the beginning and at the end of the study. The number of blood transfusions and iron infusions was registered.

Results: 41 HPN patients (61% females) were identified during the studied interval. The median age at the beginning of the study was 7 years 8 months [IQR 2 years 10 months to 10 years 4 months] and the median duration of home PN at the beginning of the study was 2 years 7 months [IQR 1 years 2 months to 5 years 3 months].

The indications for home PN were an underlying motility disorder in 51% of the cases, enteropathy in 29% of the cases and short bowel syndrome in 20% of the cases. 73% of the patients received oral/enteral feeds but none received oral iron supplements. The average amount of iron added to the PN bag was 0.45 µmol/kg. At the beginning of the study, 5% had severe anaemia, 54% moderate anaemia, 24% mild anaemia, and 17% had a normal haemoglobin (Hb) as per World Health Organization recommendations. On repeat testing, 10% had severe anaemia, 51% had moderate anaemia, 20% had mild anaemia and 19% had normal Hb. At the end of the study, 5% of the patients had severe anaemia, 51% had moderate anaemia, 17% had mild anaemia and 27% had normal Hb.

Iron deficiency anaemia (microcytic, low ferritin and iron) was most commonly seen. Information about blood transfusions/iron infusions was available in 40 of the cases – 46% of them received blood transfusions and 29% iron infusions.

The patients who received oral/enteral feeds or had more than 0.5 µmol/kg of iron added to the PN didn’t had a significant lower grade of anaemia at the end of the study. Children who received iron infusions didn’t have significantly higher rate of improved haemoglobin compared with the ones who received blood transfusions (50% vs. 33%, p=0.657) and didn’t have significantly higher difference in haemoglobin (g/L) compared with blood transfusions after the treatment (0.5 [-11.5 to 8] vs. -6 [-17 to 8], p=0.506).

From the group of children who had transfusion/infusion, the ones who had infusions had significantly higher rate of normal liver function compared with the one who had transfusions.

Conclusion: Iron deficiency anaemia, most commonly in the moderate severity range, is common in children receiving home PN. Many patients still receive blood transfusions if symptomatic. Intravenous iron may be a good alternative to prevent anaemia. Treatment guidelines are required to advice when and how much iron should be prescribed.
Dietary intakes, nutritional issues and bone health in neurologically impaired children

Elena Crehuá-Gaudiza¹, Mónica García-Peris², Beatriz Padilla³, Paula Grattarola³, Carmen Jovani-Casano⁴, Cecilia Martínez-Costa⁵

¹Hospital Clínico Universitario, Pediatrics, Valencia, Spain
²Hospital Lluis Alcanyís, Pediatrics, Xàtiva, Spain
³Instituto de Investigación Sanitaria Incliva, Hospital Clínico Universitario de Valencia, Valencia, Spain
⁴Hospital General, Pediatrics, Castellón, Valencia, Spain
⁵University of Valencia, Pediatrics, Valencia, Spain

Objectives and study: Inadequate dietary intake is one of the major contributors to poor nutritional status and altered growth in neurologically impaired children. Our aim was to analyze dietary intakes, nutritional status and bone mineral density (BMD) in children presenting moderate-severe neurological diseases.

Methods: A prospective observational multicentre study was conducted in children with moderate-to-severe neurological impairment (equivalent to Gross Motor Function System Classification, GMFCS III-V). Several clinical parameters were analyzed: anthropometric measures (calculating z-score for age and sex according to WHO references), type of feeding and dietary intake, biochemical analysis and lumbar spine BMD measured with dual-energy X-ray absorptiometry (DXA, measures were converted to age and gender normalized z-scores). Nutrient intakes were assessed by means of a three-day food diary applying DietSource junior® software. The study plan was approved by the Hospital's Ethics Committee.

Results: Seventy-two children (aged 2-16 years) were recruited. Primary diagnosis included 49 cases of cerebral palsy, 7 of genetic disorders, 4 of neuromuscular diseases and 12 other diagnoses. Most of these patients presented severe GMFCS. 20 patients received feeding by gastrostomy tube. Average of z-score were: -2.53 (SD 1.55) for weight, -2.51 (SD 1.71) for height, -1.26 (SD 1.80) for body mass index -BMI-, -0.87 (SD 1.23) for arm circumference, -0.28 (SD 1.1) for tricipital skinfold, and +0.01 (SD 0.79) for scapular skinfold. 50% of sample exhibited adequate energy intake according to age, gender and physical activity level (Dietary Reference Intakes -DRIs-), while 32% had excess energy and 18% showed evidence of an energy deficit. Considering total energy intake, protein intake contributed a mean of 17.6% of calories (SD 5.1), fats 31.2% (SD 7.5) and carbohydrates 51.3% (SD 7.3). Low intake of calcium, phosphorus, magnesium, zinc and iron was common even in those receiving nutritional supplements. No differences were found in terms of dietary intake when comparing gastrostomy and non-gastrostomy fed children. Serum concentrations of calcium, phosphorous and magnesium appeared to be normal in all of them. However, vitamin D and zinc deficiency were detected in 42% and 17% of cases respectively. A large percentage of children (46%) had low BMD (z score less than -2).

Conclusion: It was common to observe nutritional alterations among the patients included in this study. Despite the deficits observed in the intake of energy and nutrients, calcium-phosphoric metabolism remained normal at biochemical level, while vitamin D was often low. BMD was altered in almost half of the cases whose aetiology is probably not only related to nutritional factors.

The authors declare no conflicts of interest.
Nutritional interventions in children with asthma as significant factors with impact on asthma control

Gheonea Cristian¹, Carmen Elena Niculescu¹, Nedelcută Ramona Mihaela², Ligia Georgeta Stanescu²

¹University of Medicine and Pharmacy of Craiova, Pediatrics, Craiova, Romania
²Hospital Philanthropy, Pediatrics, Craiova, Romania

Objectives and study: There is an increasing body of evidence that obesity augments the risk of asthma in children, and may also influence exacerbations and asthma severity and thus, asthma control. Current guidelines suggest the implementation of nutritional interventions as useful components of case management in asthmatic children. We performed a study to evaluate the impact of nutritional status and interventions on asthma control in children.

Methods: Children with asthma (n = 92, 51 boys, age 11.2±4.6 yrs.) attending a Regional Centre for Paediatric Asthma were included. Nutritional status evaluation was performed using anthropometrical indices (i.e. based on current NCHS/WHO growth reference curves) body mass index (BMI), and then nutritional interventions were customized by a dedicated nutritionist. One-to-one interventions were administered. The validated Childhood Asthma Control Questionnaire was used as a composite marker to assess asthma control. Multivariable linear regression was performed.

Results: Overall, boys with normal weight had better asthma control (OR 3.43; 95%CI 1.27-6.95; p = 0.004), whereas no significant differences were registered in girls. Nutritional intervention provided a three-fold increase in scoring at the asthma control questionnaire (from 6.8 ± 6.9 to 21.4 ± 8.5) in the obese boys group. Among demographic factors, children with an above the average family financial status (OR 2.84; 95%CI 1.18-4.80; p = 0.002) had better asthma control whereas neither urban nor rural setting of the families, nor the educational level of the parents/caregivers had a predictive value for asthma clinical outcome at the studied group.

Conclusion: Non-obese boys had better asthma control, while customized nutritional interventions significantly improved the clinical outcome at the studied group. Data collected support the recommendation that promotion of healthy nutrition and access to professional coaching for patients and their families/caregivers on nutritional interventions should be included in individual action plans for children with asthma.
Food allergy: immunophenotypes in predicting the development of tolerance to cow's milk

Svetlana Makarova¹, Maria Petrovskaya¹, Leila Namazova-Baranova¹, Irina Zubkova¹

¹Federal State Autonomous Institution "Scientific Center of Children's Health" of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Objectives and study: To determine immunophenotypes of FA and evaluate their role in predicting developing tolerance to cow's milk protein (CMP) in early age children with FA.

Methods: The prospective observational study included children with FA (n = 153) aged from 1 to 18 months. Blood samples were taken to determine sIgE and sIgG4 to CMP and its fractions and to goat's milk twice - before elimination diet and after 6-12 months of elimination diet and oral food challenge procedure with CMP. sIgE were detected using the UniCAP method, and sIgG4 using ELISA.

Results: According to the results of oral food challenge procedure with CMP, performed after 6-12 months of elimination diet, 50.3% children became tolerant to CMP, of which 42 developed tolerance by the end of the first year (54.5% of all children who developed tolerance), and 35 by the end of the 2nd year (45.5% of all who developed tolerance). During evaluation of immunological markers, taken, before elimination diet, we determined 4 immunophenotypes. We found that tolerance to CMP developed in 97.9% of patients with 'sIgE \leq 0.7 kUA/l and sIgG4 3+' immunophenotype, and in 90.1% of patients with 'sIgE >0.7 kUA/l and sIgG4 3+' immunophenotype. Thus, these results indicate a high probability of development of tolerance to CMP after 6 months of elimination diet in children with these immunophenotypes. In contrast, 19.2% of patients with 'sIgE \leq 0.7 kUA/l and sIgG4 0-2+' immunophenotype, and none of the patients with 'sIgE >0.7 kUA/l and sIgG4 0-2+' immunophenotype became tolerant after after 6-12 of the elimination diet (p<0.05). Thus, these results seem to provide unfavorable evidence regarding the development of food tolerance.

Conclusion: Different immunophenotypes of FA can be successfully used as an evaluation tool for predicting the development of tolerance to CMP in early age children.
**NUTRITION: Clinical nutrition**

N-eP-006

**Quality improvement initiative: monitoring and supplementation of fat soluble vitamins in infants following Kasai portoenterostomy**

Inez Martincevic¹, Beth Haliburton¹, Binita M. Kamath², Vicky Lee Ng³, Simon Ling³, Marialena Mouzaki³

¹The Hospital for Sick Children, Clinical Nutrition, Toronto, Canada
²The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada
³The Hospital for Sick Children, Division of Gastroenterology, Hepatology and Nutrition, Toronto, Canada

**Objectives and study:** The nutritional management of infants with biliary atresia (BA) following Kasai portoenterostomy (KPE) is not protocolized. The aim of this quality improvement initiative was to review the nutritional management and outcomes of BA infants following KPE at the Hospital for Sick Children in an effort to develop institutional nutritional care guidelines.

**Methods:** Single center, retrospective chart review of patients with confirmed BA and KPE performed at our institution between January 2010 and December 2015. Patients with other concurrent liver disease were excluded. Data were collected from different time points: time of KPE (C0), third clinic visit post KPE (C3) and at 1 year of age (C12). Data for patients listed for transplantation were collected until time of listing. Data collection included: fat soluble vitamin (FSV) levels specifically serum retinol (vitamin A), serum 25-hydroxycholecalciferol (vitamin D), serum α-tocopherol (vitamin E) levels; as well as FSV supplementation dosing and type. Biochemical data was collected ±2 weeks of the clinic visit. Statistical analyses were performed using Stata MP v13.0.

**Results:** 30 (40% male) patients underwent KPE. Median age at KPE was 69 (22-105) days. Mean age at C3 and C12 was 149±35 and 360±31 days, respectively. Serum FSV levels were not available at all clinic visits. At C0, 67% (20/30) of patients had serum vitamins A and D, and 60% (18/30) had serum vitamin E levels drawn. At C3, 63% (19/30) had serum vitamin D and 43% (13/30) serum vitamins A and E taken. At C12, 50% (15/30) of patients had been listed for transplant. Of the patients not listed, serum vitamin D was reported for all, whereas serum vitamin A and E levels were available for 80% (12/15). The proportion of FSV deficiency is shown in Figure 1a. All serum FSV levels improved from C0 to C12 (p<0.05) but a significant proportion of patients remained deficient in vitamins A and D at C12. Vitamin A was prescribed as palmitate in increments of 1500 international units (IU) pre-2015 and 750 IU post, due to manufacturing changes. Vitamin D was prescribed as cholecalciferol in 400 or 1000 IU increments. Vitamin E was prescribed as dl-α-tocopherol in increments of 50 or 400 IU. The mean daily supplement dose for all FSV increased over time and is shown in Figure 1b.
Conclusion: In the absence of nutritional care guidelines for BA infants post KPE, FSV levels were not measured consistently. FSV deficiency was prevalent at time of KPE and improved significantly with supplementation. By 1 year of age, low serum retinol levels persisted despite supplementation; an average vitamin D dose of approximately 2500 IU/day was not sufficient to prevent vitamin D deficiency in more than a third of patients; and vitamin E deficiency was not noted. Accurate assessment of FSV status was limited by inconsistent monitoring practices, missing documentation of FSV supplementation, and lack of available serum retinol binding protein levels to better define vitamin A deficiency. The development of nutritional care guidelines in this population may help to improve monitoring of FSV levels and correct deficiencies.
Therapeutic role of improvement of dietary pattern in children and adolescents with NAFLD

Joanna Neuhoff-Murawska¹, Andrzej Mięgoc¹, Aldona Wierzbicka², Wojciech Janiczyk³, Agnieszka Biliska⁴, Jolanta Olkowska⁵, Ewa Samocik⁶, Joanna Gromadzka-Ostrowska⁷, Piotr Socha⁸

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology and Nutrition Disorders, Warsaw, Poland
²The Children's Memorial Health Institute, Department of Biochemistry, Radioimmunology and Experimental Medicine, Warsaw, Poland
³Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
⁴Medical Faculty, University of Rzeszów, Medical Faculty, University of Rzeszów, Rzeszów, Poland
⁵University School of Medicine, Pediatric, Endocrinology, Diabetes Silesian, Katowice, Poland
⁶Medical University, Pediatric, Gastroenterology, Allergology, Białystok, Poland
⁷Warsaw University of Life Sciences, Warsaw, Poland
⁸Children's Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Weight loss seems to play the crucial role in therapy of NAFLD. There is growing evidence, that also diet composition may play a role: like decrease intake of fructose, iron, saturated fatty acids, n-6 fatty acids. In our study we focused on dietary patterns evaluated among children with NAFLD who improved in regard of liver involvement without loss weight

Methods: 26 boys aged 13,53 ± 2,6 y, suffering on NAFLD, from four centers underwent 6 months of dietary intervention, the aim of which was slow weight loss (0.5 kg per week). At the beginning and end of the study we evaluated the following parameters: body weight, height, BMI, BMI Z score, waist circumference, WHR, WHtR, fatty liver by ultrasound in scale Saverymuttu, ALT, AST, GGTP activity. At the same points of time we compared also the consumption of main groups and sub-groups of food and we calculated daily nutrient intake with Energia.FFQ program in regard of: energy, water, protein, total fat and fatty acids, carbohydrates, minerals, vitamins.

Results: We did not find a difference in body weight, BMI, BMI Z score, waist circumference and waist, WHR and WHtR between the baseline and end results in the study group despite caloric restrictions, nevertheless we noticed decreasing ALT [75,5 (37-157)U/l vs 51,5 (26-132)U/l, median (lower-upper quartile)], GGTP [38 (14-118)U/l vs 32,5 (16-87)U/l] activity and echogenicity on ultrasound according to Saverymuttu [1,5 (0,5-3) vs 1(0-3)].

At the beginning and after six months there were differences in consumption of soft drinks: 327,5 (278-1000) ml/d vs 116(0-357)ml/d, juices: 60(2-203)ml/d vs 2(0-203)ml/d, fruits and their products: 213(4-769)g/d vs 103(0-412)g/d, cereals: 299(109-625)g/d vs 274(122-407)g/d including white bread: 85(0-300)g/d vs 12(0-270)g/d and baked sweet: 19(0-85)g/d vs 4(0-17)g/d, sugar and confectionery: 50(1-156)g/d vs 30(2-60)g/d, cheeses: 58(1-250)g/d vs 27(1-100)g/d and fast food: 6(0-40)g/d vs 0(0-80)g/d, (p<0,05). Consumption of rye bread increased: 12(0-140)g/d vs 84(0-230)g/d, (p<0.05). As consequence some nutrients intake decreased: water: 2438(1117-7124)ml/d vs 2204(995-6966)ml/d, total protein: 87(34-199)g/d vs 62(38-136)g/d, total fat: 95(25-197)g/d vs 70(39-137)g/d, cholesterol: 297(86-760)mg/d vs 211(127-575)mg/dl, iron: 13(6-43)mg/d vs 10(6-20)mg/dl, sodium: 4270(1931-9217)mg/d vs 3283(1520-6146)mg/d. Intake of fiber (g/1000kcal) increased from 9(6-18)g/1000kcal vs 13(8-19)g/1000kcal, % energy from monounsaturated and polyunsaturated fatty acids was rising: 13(7-17) vs 14(8-20) and 4(3-11) vs 6(7-9) % of energy intake, respectively, (p<0,05).

Conclusion: Improvement of dietary pattern by eliminating excess of: protein, fat, cholesterol, fructose, iron and increasing of fiber and unsaturated fatty acids intake may play the role in treatment of NAFLD among children and adolescents even without weight loss.
Short-term vitamin D3 supplementation in children with neurodisabilities: comparison of two delivery methods

Francesca Penagini\textsuperscript{1}, Barbara Borsani\textsuperscript{1}, Katia Maruca\textsuperscript{2}, Valeria Giosia\textsuperscript{1}, Stefania Bova\textsuperscript{3}, Massimo Mastrangelo\textsuperscript{3}, Gian Vincenzo Zuccotti\textsuperscript{2}, Stefano Mora\textsuperscript{2}

\textsuperscript{1}V. Buzzi Children's Hospital, University of Milan, Department of Paediatrics, Milan, Italy
\textsuperscript{2}San Raffaele Scientific Institute, Laboratory of Paediatric Endocrinology, Milan, Italy
\textsuperscript{3}V. Buzzi Children's Hospital University of Milan, Paediatric Neurology Unit, Milan, Italy

Objectives and study: Children with neurodisabilities are at increased risk of vitamin D deficiency as a result of several factors including oropharyngeal dysphagia, poor appetite, inadequate sun exposure and treatment with anti-epileptic drugs. We hypothesized that a buccal spray formulation containing micro-sized droplets of vitamin D\textsubscript{3} could be superior to oral delivery in this population of children due to rapid and complete absorption by the oral mucosa.

Methods: Twenty-four children with neurodisabilities and vitamin D deficiency (25OHD $\leq$ 20 ng/mL) aged 5-17 years (M:F ratio 10:14) were enrolled at the “V. Buzzi” Children’s Hospital, University of Milan, Italy. All patients were randomized to receive vitamin D supplementation as either buccal spray 800 IU/daily ($n=12$) or oral drops 750 IU/daily ($n=12$). Supplementation occurred during winter (from November 2015 to March 2016) and lasted for 3 months. At completion of the study a satisfaction questionnaire was administered. The following scores were assigned: 0=not satisfied at all (the child totally refused the supplementation), 1= quite dissatisfied (the child took the supplementation with difficulty), 2= quite satisfied (the child took the supplementation but reported poor palatability), 3= completely satisfied (the child took the supplementation without any reported problems). Blood was collected at baseline and at the end of the study for dosage of 25-hydroxy vitamin D (25OHD), parathyroid hormone (PTH), calcium, phosphate and two markers of bone metabolism: C-terminal telopeptide of type I collagen (CTX) as marker of bone resorption and bone specific alkaline phosphatase (BAP) as marker of bone formation. Comparison between data at baseline and after 3 months in the two intervention groups were performed.

Results: After 3 months of supplementation both groups had a statistically significant increase in 25OHD concentration ($t=10.5; P<0.0001$). The differences between baseline and final PTH measurements were not significant in the group receiving oral drops, while it reached significance in the group on buccal spray ($t=-2.1; P=0.05$). Markers of bone formation and resorption did not change significantly in both groups, likely due to the low vitamin D dose and the short supplementation period of observation, unable to determine significant changes in bone turnover. Evaluation of patients’ compliance to the vitamin D\textsubscript{3} supplementation demonstrated a non-significant difference between the two groups, while satisfaction of the prescribed supplementation resulted to be significantly higher in patients using the spray compared to oral drops group (54.5% score 2 and 45.5% score 3 in oral drops group vs. 8.3% score 2 and 91.7% score 3 in spray group, $P=0.027$). Palatability issues were reported only in oral drops group.

Conclusion: Vitamin D\textsubscript{3} supplementation with buccal spray and oral drops are equally effective in short-term treatment of vitamin D deficiency in a population of children with neurodisabilities. Buccal spray has been found to be more acceptable by the patients. This may be an important issue when long-term supplementation or chronic treatment is necessary.
Short bowel syndrome: a 16-year single-center experience in 156 patients

Bruna Perrella¹, Eli Nader², Cecile Lambe³, Cécile Talbéc⁴, Bénédicte Pigneur⁵, Florence Lacaille⁶, Hélène Lengline³, Catherine Poisson⁴, Amélia Rocha¹, Christelle Alliot¹, Frank Ruemmele², Virginie Colomb⁵, Yves Aigran¹, Christophe Chardot⁶, Olivier Goulet²

¹Hôpital Necker-Enfants Malades, Department of Pediatric Gastroenterology-Hepatology-Nutrition, Paris, France
²Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
³Necker-Enfants Malades, Gastroenterology-Hepatology-Nutrition, Paris, France
⁴Hôpital Necker-Enfants Malades, Pediatric Gastroenterology, Hepatology and Nutrition, Paris, France
⁵Hôpital Necker-Enfants Malades, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
⁶Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Chirurgie Viscérale Pédiatrique, Paris, France

Objectives and study: Short Bowel Syndrome (SBS) is the leading cause of Intestinal Failure (IF) in children requiring Home Parenteral Nutrition (HPN). This 16-year study evaluates the complications and prognosis factors of SBS patients managed by a single expert center.

Methods: SBS pediatric patients referred to HPN between January 1st 2000 and December 31st 2015 were classified into 3 groups: type 1: end jejunostomy, type 2: jejuno-colic anastomosis and type 3: jejuno-ileal anastomosis. The level of PN dependency [by using the index Non Protein Energy Intake (NPEI)/Resting Energy Expenditure (REE) by Schofield formula], outcomes, complications, growth, pubertal onset were analyzed.

Results: For the 156 children, the underlying diseases were necrotizing enterocolitis (NEC) (22.40%), midgut volvulus (21.80%), gastrochisis (20.50%), extensive Hirschsprung’s disease (EHD) (16.00%), intestinal atresia (15.40%), or other events (3.90%). Weaning off was achieved in 79 patients (50.70%), after 2.20 ± 1.70 years of PN. Intestinal Transplantation (ITx) was performed in 13 patients (8.30%) after 4.20 ± 1.30 years of PN. At the end of the study period, 63 patients (40.40%) were still on HPN for 5.3 ± 3.7 years. Only one patient with cystic fibrosis and liver cirrhosis deceased. By Cox regression analysis, the following anatomical characteristics are independent prognosis factors of PN duration: length of remnant bowel, presence of an ostomy, ileo-caecal valve (ICV) resection, colon resection. Citrulline plasma levels correlate with the ratio NPEI/REE. Overall rate of catheter related sepsis was 1.2 CRS/1000 days of PN. Bilirubin > 30 µmole/l was observed in 16% of patients still dependent on PN after 5.30 ± 3.70 years. No statistical differences on growth were found between the groups, proving that sufficient nutritional intake was provided to achieve optimal growth. The puberty occurred in 8 girls at 12.1 ± 1.0 years and 8 boys at 13.8 ± 0.7 years.

Conclusion: SBS has a very good outcome despite long term PN. HPN is a safe and efficient therapeutic option for long term management of SBS pediatric patients. Such data might be very helpful in addressing criteria for GLP-2 (teduglutide).
The complex relationship between obesity and somatotropic axis

Rosa Lapolla¹, Irene Rutigliano², Sara Gorgoglione³, Michele Conoscitore³, Maria Pastore², Mario D'altilia², Michele Sacco²

¹Paediatrics, University of Foggia, Foggia, Italy
²Paediatrics, Ircss "Casa Sollievo Della Sofferenza", San Giovanni Rotondo, Italy
³University of Foggia, Pediatrics, Foggia, Italy

Objectives and study: The adipose tissue has effect on growth hormone secretion but the metabolic correlates of circulating insulin-like growth factor-1 (IGF1) and IGF1-binding-protein-3 (IGFBP-3) are still unclear. Several studies have suggested that IGF1 modulates adipocyte and there is increasing evidence that IGF1 and IGFBP-3 could be related to metabolic syndrome (MS) in adults. Aim of the study: To investigate the relation between IGF1, IGFBP-3 with adiposity and its metabolic consequences.

Methods: 63 children (43 obese mean age 10.7±2.9 yrs and 20 lean control, age 10.3±3.2 yrs). Collected data included: anthropometry, lipid profile, C-reactive Protein (CRP), insulinaemia, HOMA-IR, oral glucose tolerance test, IGF1, IGFBP-3 (z-score were calculated). Visceral adiposity was assessed with waist-to-height ratio (WtHR). MS was defined according to Cook Criteria.

Results: IGFBP-3 (p=0.029), insulin (p=0.026) levels and HOMA-IR (p=0.04) were higher in obese children than control. In obese group, IGF-I SDS levels were negatively correlated with WtHR (r=-0.358, p=0.021) and CRP (r=-0.337, p=0.036) even after adjustment for pubertal stage. IGFBP-3 SDS concentrations were positively correlated with number of MS features presented (r=0.304, p=0.019). Particularly, mean IGF1-SDS was lower in subjects with impaired glucose tolerance (-2.15±0.55 vs -0.78±0.79, p=0.026) and IGFBP-3 SDS levels were higher among children with hypertriglyceridemia (0.66±0.51 mg/dl vs 0.30±0.29, p=0.007)

Conclusion: A negative association between IGF-1 and visceral adiposity was found in our analysis. Findings link lower circulating IGF1 to greater metabolic risk. Studies are needed to elucidate the role of IGF-1 in regulating adipose tissue development and glucose homeostasis. This could be a new key in defining metabolic dysfunction.
Elevated essential amino acid levels in very preterm infants receiving total parenteral nutrition

Laura Burgess¹, Brian Flanagan², Mark Turner³, Colin Morgan¹

¹Liverpool Women's Hospital, Neonatology, Liverpool, United Kingdom
²University of Liverpool, Women's and Children's Health, Liverpool, United Kingdom
³Department of Women’s and Children's Health, University of Liverpool, Liverpool, United Kingdom

Objectives and study: We have previously shown that there is overprovision of essential amino acids (EAA) in current neonatal parenteral nutrition (PN) formulations, with many EAA levels in the second week of life being above the normal range.¹ Our unit delivers standardised, concentrated, added macronutrient PN by a regimen of incrementally increasing protein, fat and energy intake over the first 7 days of life and routinely measures plasma amino acid (AA) levels on day 10 of life when the infants are fully established on PN. Aim: To assess day 3 levels of AAs prior to maximal protein intake and compare with day 10 levels.

Methods: Infants born <29 weeks’ gestation were eligible for PN. Plasma AA levels were measured on day 3 and day 10 of life using ion exchange chromatography. Daily nutritional intake data (both parenteral and enteral) was collected for the first 10 days of life.

Results: 12 babies had AA levels assessed at both time points. They had a mean gestation of 26±4 weeks and mean birth weight of 832g. The mean protein intake over the 72 hours before the plasma AA level was 2.30g/kg/day for the day 3 sample and 3.76g/kg/day for the day 10 sample. The results for the EAA are shown in Table 1. Many of the day 3 EAA levels were higher than the day 10 levels, despite lower protein intakes. The babies with the highest EAA levels were those with the highest absolute protein intakes, i.e. the largest babies in the cohort.

Table: Mean (sd) plasma EAA levels (µmol/l)

<table>
<thead>
<tr>
<th>EAA</th>
<th>Phenylalanine</th>
<th>Valine</th>
<th>Leucine</th>
<th>Isoleucine</th>
<th>Lysine</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref range</td>
<td>25-80</td>
<td>65-290</td>
<td>44-169</td>
<td>20-91</td>
<td>70-266</td>
</tr>
<tr>
<td>Day 3</td>
<td>95(20)</td>
<td>194(33)</td>
<td>150(24)</td>
<td>53(16)</td>
<td>234(77)</td>
</tr>
<tr>
<td>Day 10</td>
<td>72(19)</td>
<td>147(49)</td>
<td>114(44)</td>
<td>47(17)</td>
<td>275(219)</td>
</tr>
<tr>
<td>p</td>
<td>0.004</td>
<td>0.006</td>
<td>0.009</td>
<td>0.175</td>
<td>0.275</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>EAA</th>
<th>Methionine</th>
<th>Threonine</th>
<th>Histidine</th>
<th>Tryptophan</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ref range</td>
<td>11-49</td>
<td>39-175</td>
<td>43-111</td>
<td>10-19</td>
</tr>
<tr>
<td>Day 3</td>
<td>31(10)</td>
<td>268(91)</td>
<td>103(19)</td>
<td>29(8)</td>
</tr>
<tr>
<td>Day 10</td>
<td>29(12)</td>
<td>432(164)</td>
<td>87(30)</td>
<td>21(8)</td>
</tr>
<tr>
<td>p</td>
<td>0.331</td>
<td>0.003</td>
<td>0.078</td>
<td>0.011</td>
</tr>
</tbody>
</table>

Conclusion: Even a PN regimen with incremental increase in protein results in high day 3 levels of some EAAAs, with some being paradoxically higher than on day 10 when the protein intake is greater. Day 10 profiles may underestimate the degree of plasma AA derangement even in incremental increasing PN regimens.

The influence of macro-nutrients and energy by the processing of bank milk

Fang-Yuan Chang1, Li-Jung Fang1

1Taipei City Hospital, Pediatric, Taipei, Taiwan

Objectives and study: The pasteurization is a mandatory step in order to inactivate pathogenic microorganisms of bank milk. For storage, freezing and thawing are necessary. The concentration of macronutrients and energy of bank milk could be influenced by these procedures which are routinely used in human milk bank. The aim of this study is to analyze the effect of bank milk processing (pasteurization, freezing/thawing) on the macronutrients (fat, protein, carbohydrate) concentration and energy content.

Methods: The samples of donor milk were collected and studied before/after pasteurization and after frozen for 3 months. Total 100 samples of bank milk were tested using an Infrared analyzer. The measurements of fat, protein, carbohydrate, and energy were statistical analyzed by SPSS.

Results: There was a prominent reduction of fat mean concentration following pasteurization and frozen (20.5% and 6.5% respectively). The processing did not cause significant changes in protein content, but there were significant increase after pasteurization and decrease after frozen in carbohydrate (p<0.05). Overall (postpasteurization and frozen storage), a 9.6% decrease was observed for energy content.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Before pasteurization</th>
<th>After pasteurization</th>
<th>After frozen 3 months</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mean±Sd</td>
<td>Median</td>
<td>mean±Sd</td>
</tr>
<tr>
<td>fat</td>
<td>3.08±1.23</td>
<td>2.80</td>
<td>2.45±0.75</td>
</tr>
<tr>
<td>protein</td>
<td>1.02±0.27</td>
<td>1.00</td>
<td>1.05±0.29</td>
</tr>
<tr>
<td>carbohydrate</td>
<td>6.80±1.09</td>
<td>7.10</td>
<td>7.40±0.83</td>
</tr>
<tr>
<td>energy</td>
<td>60.12±12.01</td>
<td>57.00</td>
<td>56.89±8.42</td>
</tr>
</tbody>
</table>

Conclusion: Data published during the past few decades indicate that human milk has particular benefits for infants being treated in neonatal intensive care units, and these benefits are seen with bank human milk. But the processing of bank milk (including Holder pasteurization and storage) decreased fat and energy content of human milk significantly, this could be not enough to meet the specific needs of preterm infants.
The role of FTO rs9939609 A/T gene polymorphisms on the newborn-mother binomas, correlated with anthropometrical and clinical parameters

Marginean Cristina Oana¹, Claudiu Marginean², Lorena Elena Melit², Marius Vicea Calomfirescu³, George Rolea⁴, Claudia Banescu², Maria Oana Marginean⁵

¹University of Medicine and Pharmacy Tirgu Mures, Pediatrics, Tirgu Mures, Romania
²University of Medicine and Pharmacy Tirgu Mures, Tirgu Mures, Romania
³CMI Bucuresti, Bucuresti, Romania
⁴Spitalul Sighisoara, Sighisoara, Romania

Objectives and study: Birth weight is very important, representing a predictor not only for the perinatal health, but also for the development, growth and the afterwards adult period. It is influenced by maternal (mother’s weight, gestational weight gain), obstetrical and gynecological, genetic, environmental, but also socio-economic factors. Excessive GWG leads to increased birth weight and obesity risk, further on in life.

The aim of the study was to investigate the role of FTO rs9939609 gene polymorphisms on the newborn-mother binomas, correlated with anthropometrical and clinical parameters. The groups were evaluated regarding demographic, anthropometric (BMI- body mass index, MUAC – medium upper arm circumference, TST – tricipital skin thickness, weight), clinical, paraclinical and genetic parameters.

Methods: We performed a prospective study on 165 mother-newborn binoma in a tertiary Pediatrics & Obstetrics Gynecology Hospital from Romania, assessing the genetic, anthropometric parameters and laboratory parameters.

Results: We noticed that BMI and MUAC were lower in mothers with AT or AA genotype for FTO rs9939609 (p=0.02 and p = 0.031), while lower BMI values (p = 0.045) were observed in newborns carrying TT genotype and lower MUAC (0.032) value in newborns carrying AA+AT genotype, whose mothers has the same genotype (AT+AA). We did not find any interaction effect between newborn and mother FTO rs9939609 polymorphism and anthropometrical parameters (p=0.124 for MUAC and 0.098 for TST) and also nor with paraclinical parameters (p = 0.067 for GOT, p=0.87 for GPT, p = 0.651 for cholesterol).

Conclusion: We observed that A allele of FTO rs9939609 polymorphism in mothers is correlated with lower value of BMI and MUAC in newborns. So, we can say that mothers’ FTO rs9939609 gene polymorphisms is correlated with newborns’ BMI and birth weight.
Individualized versus standard maternal milk fortification. Effect on plasma IGF-I and ghrelin of preterm infants

Elisavet Parlapani¹, Charalampos Agakidis², Thomais Karagiozoglou-Lampoudi¹, Dimitrios Fletouris³, Kosmas Sarafidis², Vasiliki Tzimouli⁴, Vasiliki Drosou-Agakidou⁴, Elisavet Diamanti²

¹Technological Education Institute of Thessaloniki, Nutrition/Dietetics Dept, Thessaloniki, Greece
²Aristotle University of Thessaloniki, 1st Dept of Neonatology & Nicu, Faculty of Medicine, Thessaloniki, Greece
³Aristotle University of Thessaloniki, Laboratory of Milk Hygiene and Technology, Faculty of Veterinary Medicine, Thessaloniki, Greece
⁴Aristotle University of Thessaloniki, 1st Dept of Pediatrics, Faculty of Medicine, Thessaloniki, Greece

Objectives and study: Several studies reported that early protein and energy intake affect IGF-1 and ghrelin levels which may have long term metabolic effects on the preterm infants (PIs). The aim of this study was to test the hypothesis that different fortification regimens, resulting in different protein intake, may have different effects on postnatal IGF-1 and ghrelin plasma levels of PIs possibly predisposing to long-term consequences.

Methods: This is a randomized controlled study of exclusively maternal milk fed PIs (GA 24-32 weeks, BW<1500g). By the time oral feeding reached 100ml/ kg/day (T1), eligible neonates were randomly allocated: into 2 groups for multinutrient human milk fortifier (HMF) implementation: a) the individualized fortification group (IFG) and b) the standard fortification group (SFG). IFG was based on maternal milk analysis and targeted the recommended daily protein intake. SFG group received 1g protein/100ml of milk. Different fortification lasted until infants reached the 2000 g (intervention period). BIA phase angle (PhA), plasma IGF-1 and ghrelin were assessed at the end of intervention period (T2) and at 40 postconceptional weeks (T3). Nutrition intake and anthropometric parameters were measured during the whole study period.

Results: The IFG and SFG (19 and 21 PIs, respectively) were comparable regarding the perinatal and neonatal characteristics. Mean daily protein, carbohydrate, and protein/energy intake were lower in the IFG group. Mean daily/weekly changes of all anthropometric measurements and the BIA PhA at T2 and T3 did not differ significantly between the two groups. The IFG had lower IGF-1 and higher ghrelin at T2 than the SFG. Moreover, infants receiving protein higher than the recommended intake (2/19 and 19/21 of IFG and SFG, respectively) had higher IGF-1 at T2 and lower ghrelin at T2 and T3, compared to those receiving the recommended protein intake. The IGF-I at T2 was positively correlated with protein intake and protein/energy ratio, changes in growth parameters z-scores, and BIA PhA at T2 and T3. Ghrelin at T2 was negatively correlated with energy intake and changes in growth parameters as well as BMI z-score change during intervention. After adjustment for confounders, the protein intake and intervention group were significant independent predictors of IGF-I at T2 whereas the intervention group was significant independent predictor of ghrelin at T2. IGF-I at T2 was positively correlated with PhA at T2 and T3, and IGF-I at T3 was positively correlated with PhA at T3, before and after adjustment for possible confounders.

Conclusion: We conclude that different fortification regimens are associated with different levels of IGF-1 and ghrelin. These results suggest that in PIs different fortification regimens and protein intake have a measurable effect on nutrition and growth homeostasis which cannot always be detected by conventional anthropometry, but can be assessed through the relevant hormone profile. The significant independent association between IGF-I and PhA indicates that IGF-I can be a useful predictor of nutritional status of PIs.
The lipid metabolism in infants fed formula supplemented with bovine milk fat and bovine milk fat globule membranes

Olga Lukoyanova1, Tatiana Borovik1, Tatyana Bushueva1, Tatiana Stepanova2, Natalia Zvonkova3, Oleg Melnichuk4, Elena Kopyltsova4

1Scientific Centre of Children's Health, Healthy and Sick Child Nutrition Department, Moscow, Russian Federation
2Scientific Centre of Children’s Health, Nutrition Department, Moscow, Russian Federation
3Scientific Center for Children’s Health, Healthy and Sick Child Department, Moscow, Russian Federation
4Scientific Centre of Children’s Health, Moscow, Russian Federation

Objectives and study: It is well known the early nutrition has short- and long-term outcomes to the health of infants. The fat component of the most infant formulas consists of mixtures of vegetable oils. Formula-fed infants have lower intakes of several biologically active components present in human milk. Some of these are the milk fat globule membranes (MFGM). The aim of the present study was to examine the effects of feeding term infants an experimental formula (“Semper Baby Nutradefense 1”, Hero Rus) supplemented with bovine milk fat (cream) and milk fat globule membranes. Our hypothesis was that infants fed experimental formula (EF), compared to infants fed standard formula (SF) would have lipid metabolism more similar to a breast-fed reference (BFR) group.

Methods: In observational study 60 exclusively formula-fed, healthy, term infants were divided into 2 groups to receive EF or SF from <2 months of age. A BFR group consisted of 30 breast-fed infants. The EF was supplemented with cream and a bovine MFGM concentrate. The level of total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides (TG) were measured in every infant. The measurements were made at baseline and after 2 months.

Results: After 2 months of intervention the mean total cholesterol concentration was significantly higher in the BFR group compared to the SF group and did not differ from EF group. The mean HDL and TG concentration did not differ significantly between the three groups. Despite the increase the level of cholesterol (p=0.022) and LDL (p=0.004) in EF group during the intervention these indicators have not exceeded the reference values and were comparable to those of breastfed infants. The mean LDL concentration was significantly higher in the BFR group compared to the SF group but at the same time this indicator did not differ significantly between the EF and BFR groups at the end of the investigation.

Table: Lipid metabolism’s indicators after 2 months of intervention

<table>
<thead>
<tr>
<th>Indicators, mmol/L</th>
<th>The values of indicators, Me (25;75)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EF n= 25</td>
<td>SF n=27</td>
</tr>
<tr>
<td>Cholesterol</td>
<td>3.84 (3.35; 4.63)</td>
<td>3.78 (3.24; 3.98)</td>
</tr>
<tr>
<td>HDL</td>
<td>1.16 (0.97; 1.49)</td>
<td>1.15 (1.04; 1.31)</td>
</tr>
<tr>
<td>LDL</td>
<td>2.61 (2.03; 3.24)</td>
<td>2.23 (1.93; 2.48)</td>
</tr>
<tr>
<td>TG</td>
<td>2.17 (1.19; 2.77)</td>
<td>2.28 (1.69; 3.05)</td>
</tr>
</tbody>
</table>

* p1 – difference between BFR and SF
  p2 – difference between BFR and EF
Conclusion: Our study showed the mean cholesterol and LDL concentration in infants fed formula supplemented with cream and a bovine MFGM concentrate were comparable to those of breastfed infants. This intervention can narrow the gap in serum cholesterol concentrations between formula-fed and breast-fed infants and may contribute to improved short- and long-term health outcomes for formula-fed infants.

Disclosure of interest: Lukoyanova O - Conflict with Hero Rus company.
Borovik T. - Conflict with Hero Rus company.
Bushueva T - Conflict with Hero Rus company.
Stepanova T - Conflict with Hero Rus company.
Zvonkova N - Conflict with Hero Rus company.
Melnichuk O - Conflict with Hero Rus company.
Kopyltsova E - Conflict with Hero Rus company.
Infant dietary intake of iron, copper, and zinc from human milk over the first year of lactation: a GEHM study of three global cohorts

Michael Gray¹, Sarah Maria¹, Shay Phillips¹, Robert McMahon², Christina Valentine¹, Ardythe Morrow³

¹Mead Johnson Nutrition, Pediatric Nutrition Institute, Evansville, United States
²Seven Hills Strategies, Cincinnati, United States
³Cincinnati Children’s Hospital Medical Center, The Perinatal Institute’s Center of Interdisciplinary Research in Human Milk and Lactation, Cincinnati, United States

Objectives and study: Trace minerals in human milk, including iron, copper, and zinc, are critical to infant growth and development. However, differences in stage of lactation or maternal genetics could introduce variability into the elemental composition of human milk and impact infant intake. We characterized human milk iron, copper, and zinc composition over the course of lactation in three distinct populations and utilized these results to calculate estimated human milk intake. The estimated human milk intake was then compared to current recommended dietary allowances (RDA) or adequate intakes (AI) for infants.

Methods: Human milk was collected from mother-infant pairs participating in the Global Exploration of Human Milk (GEHM) in Shanghai, China, Mexico City, Mexico, and Cincinnati, United States. A total of 435 milk samples from 90 mothers at 2, 4, 13, 26 and 52 weeks were analyzed by inductively coupled plasma-mass spectrometry. Trace mineral concentrations were converted to daily intake using estimated values of daily milk consumption per lactation week from stable isotope studies in 12 countries (da Costa et al., 2010).

Results: Human milk exhibited decreasing trace mineral concentrations over lactation that were similar between geographic sites. From 2 to 52 weeks lactation, mean copper intake via human milk dropped from 0.31 to 0.13 mg/day, equating to 156% and 57% of AI. Mean intakes for iron at 2 and 52 weeks were 0.26 and 0.16 mg/day (95% AI and 1.5% RDA, respectively). Zinc had a mean intake of 2.1 mg/day (105% AI) at 2 weeks lactation, but declined across lactation to 0.43 mg/day (14% AI) at 52 weeks. Estimated trace mineral intakes fell below the recommended dietary reference intakes at different stages of lactation with copper declining to 77% of AI at 26 weeks and zinc dropping to 88% of AI at 4 weeks. Iron intake was 95% of AI at 2 weeks but never surpassed the dietary reference intake throughout the first year of lactation.

Conclusion: The data generated in this study suggests the need to examine specific food sources and the timing of complementary food introduction to meet copper, iron, and zinc requirements of human milk-fed infants.

NUTRITION: Neonatal and infant nutrition

N-eP-018

Sialic acid in human milk from three geographically diverse populations through the first year of lactation

Beau Labhart¹, Kelsey Williams¹, Michael Gray¹, Sarah Maria¹, Shay Phillips¹, Ardythe Morrow²

¹Mead Johnson Nutrition, Pediatric Nutrition Institute, Evansville, United States
²Cincinnati Children's Hospital Medical Center, The Perinatal Institute's Center of Interdisciplinary Research in Human Milk and Lactation, Cincinnati, United States

Objectives and study: It has been hypothesized in literature that dietary sialic acid (SA) is a conditionally essential nutrient that contributes to SA accretion in the brain and therefore plays a role in neural development, learning, cognition, and memory. In support of the Global Exploration of Human Milk (GEHM), this study provides a longitudinal assessment of total SA concentrations in human milk across the first year of lactation from mothers in three globally diverse cohorts.

Methods: For this investigation, a total of seventy-five human milk samples were collected from mother-infant pairs in each of three global populations (Mexico City, Mexico, Shanghai, China, and Cincinnati, United States) at 2, 4, 13, 26, and 52 weeks lactation. Since some components of breast milk are known to vary throughout the day, all samples for the GEHM study were collected with a rigorously controlled protocol in the morning by emptying an entire breast via electric pump and then stored frozen until analysis. Total SA (Neu5Ac) concentration of the samples was determined by HPI-C-PAD: the samples were digested with neuraminidase and filtered before being analyzed. The feasibility of this SA determination in the human milk matrix was verified with accuracy and precision assays prior the start of this study.

Results: Each geographically diverse cohort had similar longitudinal trends across lactation though displayed small differences in concentration. The average SA concentration in human milk decreased rapidly from 2 to 13 weeks of lactation and then slowly continued to decline to 52 weeks (1002 ± 295 μg/mL in Mexico, 1211 ± 411 μg/mL in China, and 946 ± 314 μg/mL in the United States).

Conclusion: The foundation of knowledge into sialic acid levels in human milk is strengthened by integrating samples from different geographical populations across multiple points of lactation that were collected using standardized techniques. Utilization of this sample set and similar methodology is planned for the quantification of sialyllactose, a key contributor of SA in human milk, and may offer a better understanding of the relationship between these two carbohydrates.

Target parenteral protein attainment in parenterally fed preterm infants following the implementation of the Concentrated Macronutrients in Parenteral Standardised Solutions (CoMPaSS) programme

Frances Callaghan¹, Colin Morgan²

¹Arlooe Park Hospital, Neonatology, Liverpool, United Kingdom
²Liverpool Women’s Hospital, Neonatology, Liverpool, United Kingdom

Objectives and study: Conventional individualized parenteral nutrition (iPN) regimens fail to achieve higher dose parenteral protein (4g/kg/d) intakes in preterm infants <30 weeks (1). We have previously shown that parenteral protein intake is improved by using a Standardised, Concentrated Added Macronutrients PN (SCAMP) regimen (2) in an RCT setting. Using these research data, a regional translational programme: Concentrated Macronutrients in Parenteral Standardised Solutions (CoMPaSS) was completed. Target nutrient attainment is a method to allow comparison between differing PN protocols. Aim: to audit target parenteral protein attainment following CoMPaSS implementation and compare to that achieved with previous high dose parenteral protein protocols (SCAMP and iPN).

Methods: Detailed nutitional intake data (day 1-15) were collected prospectively from a continuous cohort of 30 surviving patients born after August 2014 at less than 30 weeks gestation and weighing less than 1.5kg who received the CoMPaSS regimen was undertaken using the electronic patient data management system. Actual parenteral protein intake and target parenteral protein intake (based on individual application of protocol) were calculated (g/kg/d) for each infant for each day of full PN. Target attainment (%) was calculated for time periods of 5 days and day 1-15.

Results: PN protein intake (for information) and target parenteral protein attainment (statistical comparison using Kruskal-Wallis one way analysis of variance) are summarized below (Table 1)

Table 1: Mean (sd) protein intake (g/kg) and median (IQR) target protein attainment (%)

<table>
<thead>
<tr>
<th>iPN group (n)</th>
<th>Birthwt</th>
<th>D1-15 (60)</th>
<th>D1-5 (60)</th>
<th>D6-10 (45)</th>
<th>D11-15 (28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein intake</td>
<td>911 (224)</td>
<td>1.61 (0.70)</td>
<td>0.79 (0.26)</td>
<td>2.74 (0.44)</td>
<td>3.46 (0.51)</td>
</tr>
<tr>
<td>Target attainment</td>
<td>75 (66-85)</td>
<td>68 (56-77)</td>
<td>80 (67-87)</td>
<td>86 (83-92)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>SCAMP group (n)</th>
<th>Birthwt</th>
<th>D1-15 (68)</th>
<th>D1-5 (68)</th>
<th>D6-10 (62)</th>
<th>D11-15 (48)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein intake</td>
<td>900 (158)</td>
<td>2.90 (0.36)</td>
<td>2.29 (0.36)</td>
<td>3.64 (0.34)</td>
<td>3.56 (0.44)</td>
</tr>
<tr>
<td>Target attainment</td>
<td>94 (87-97)</td>
<td>91 (84-96)</td>
<td>98 (95-100)</td>
<td>98 (95-99)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>CoMPaSS group (n)</th>
<th>Birthwt</th>
<th>D1-15 (30)</th>
<th>D1-5 (30)</th>
<th>D6-10 (29)</th>
<th>D11-15 (16)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein intake</td>
<td>912 (280)</td>
<td>2.77 (0.27)</td>
<td>2.39 (0.24)</td>
<td>3.04 (0.37)</td>
<td>3.20 (0.51)</td>
</tr>
<tr>
<td>Target attainment</td>
<td>87 [83-90]</td>
<td>87 [82-93]</td>
<td>85 [76-94]</td>
<td>89 [82-96]</td>
<td></td>
</tr>
</tbody>
</table>

ANOVA NS a,b a a,b b

a: CoMPaSS versus iPN p<0.05; b: CoMPaSS versus SCAMP p<0.05

Conclusion: Improvements in nutrition target attainment using standardised concentrated PN regimens can be translated across different neonatal services. Training packages are essential to ensure protocol compliance maximises nutritional intake.

References
The relationship between serum triacylglycerol eicosanoic acid and hippocampal myo-inositol is mediated by hippocampal phosphatidylcholine stearic acid in the young pig

Austin Mudd¹, Rosaline Waworuntu², Brian Berg², Sharon Donovan³, Ryan Dilger⁴

¹University of Illinois, Piglet Nutrition & Cognition Laboratory, Urbana, United States
²Mead Johnson Pediatric Nutrition Institute, Evansville, United States
³University of Illinois, Food Science & Human Nutrition, Urbana, United States
⁴University of Illinois, Animal Sciences, Urbana, United States

Objectives and study: Fatty acids play a pivotal role in the development of the neonate. In paediatric nutrition, it is necessary to identify lipid fractions and specific fatty acids (FA) that are critical for neonatal development. Throughout early life, brain growth is highly dynamic and requires particular FA to ensure a proper developmental trajectory. Previous research has focused on the relationship between serum and brain FA. Provided the recent advances in neuroimaging techniques, the relationship between neurodevelopmental markers and FA found in serum and brain has yet to be explored. A better understanding of these relationships may allow researchers to identify novel mechanisms of brain development. Therefore, the objective of this exploratory study was to elucidate the relationship between serum FA, brain FA, and magnetic resonance imaging (MRI) measures of neurodevelopment in neonatal piglets.

Methods: Beginning at 2 d and continuing until 30 d of age, 24 vaginally-derived male piglets were provided custom milk replacer formulated to meet piglet nutrient requirements. At 30 d of age, piglets underwent magnetic resonance spectroscopy (MRS) procedures to quantify metabolite concentrations in the hippocampus. Following MRS, the right hippocampus and serum were harvested from pigs at 31 d of age for lipidomic profiling. Linear regressions were used to assess the relationship between serum FA and hippocampal MRS metabolites, as well as between serum FA and hippocampal FA. Subsequently, a mediation model was used for serum FA that significantly related to both hippocampal FA and hippocampal MRS metabolites. A bootstrapping method drawing 5,000 samples with replacement from the dataset was implemented to estimate a sampling distribution (95% confidence interval) for the indirect and direct mediation effects.

Results: The mediation analysis revealed that hippocampal phosphatidylcholine stearic acid (PC-18:0) fully mediated the relationship between serum triacylglycerol eicosanoic acid (TG-20:0) and hippocampal myo-inositol (MI) concentrations. First, increased serum TG-20:0 levels were related to increased levels of hippocampal PC-18:0 (P = 0.002). Second, increased serum TG-20:0 levels were related to decreased concentrations of hippocampal MI (P = 0.016). The indirect mediation path (i.e., effect of serum TG-20:0 levels on hippocampal MI concentration through hippocampal PC-18:0 levels) was also significant (P < 0.05; 95% CI: -2.15 - -0.18). The direct mediation pathway (i.e., effect of serum TG-20:0 on hippocampal MI concentration, accounting for hippocampal PC-18:0) was not significant (P > 0.05; 95% CI: -1.84 – 0.69). Thus, hippocampal PC-18:0 levels fully mediated the relationship between serum TG-20:0 and hippocampal MI.

Conclusion: Studies have shown that brain phospholipid levels rise and MI concentrations decline throughout infancy. This study is the first to link these two observations, and offers a possible relationship by which a specific serum fatty acid may be involved. Future work should focus on testing direct relationships between serum TG-20:0 and hippocampal PC-18:0.

Disclosure of interest: This project was funded by Mead Johnson Nutrition.
The metabolic fate of 2′-fucosyllactose depends on its route of administration

Enrique Vazquez1, Clemens Kunz2, Silvia Rudloff3, maria RAMIREZ1, Ricardo Rueda1, Rachael Buck4

1Abbott Nutrition, Strategic R&d, Granada, Spain
2Justus Liebig-University, Institute of Nutritional Science, Giessen, Germany
3University Giessen, Institute of Nutritional Science, Giessen, Germany
4Abbott Nutrition, Strategic R&d, Columbus, United States

Objectives and study: Breast milk is unique in its diversity, quantity and complexity of human milk oligosaccharides (HMOs) with 2′-fucosyllactose (2′-FL) typically the most abundant. HMOs may account for many benefits provided by human milk. In addition to functioning as prebiotics, HMOs impact gut development, immune function and cognition. Recently, 2′-FL was shown to modulate cognition by triggering the gut-brain axis in rodents. Indeed, HMOs were detected in plasma and urine of human milk-fed infants, thus providing support that these compounds might provide additional systemic benefits. However, it remains to be clarified how the dietary administration of 2′-FL is transformed into improved biological functions and whether it is 2′-FL itself or rather its fermentation products that affect those functions. The aim of this study is to determine whether the route of administration of 2′-FL affects its accumulation in target organs or tissues.

Methods: NMRI mice housed in metabolic cages were given 13C-2′-FL through two different administration routes: intravascular (i.v.) or intragastrical (i.g.). Systemically-challenged mice received three equal doses (2.5 mg each) of 13C-2′-FL through the femoral vein. The other mice received a single oral dose of 13C-2′-FL (1 g/kg bw). Following perfusion, tissues, organs, blood, urine and feces were collected for 13C-enrichment determination. 13C-enrichment was determined by Elemental Analysis Stable Isotope Ratio Mass Spectrometry (EA-IRMS).

Results: In animals receiving i.v. administration of 13C-2FL, no retention was observed. No 13C-enrichment was detected in any tissues, but a strong 13C signal appeared in urine. Interestingly, after oral dosing of 13C-2′-FL, 13C-enrichment was detected in all organs, biological fluids and excretions showing a parallel time course in plasma and organs. 13C-enrichment started to increase between 1 and 2 hours after dosage. Maximum 13C-enrichment of plasma and organs was observed when the bolus had reached the lowest part of the intestine.

Conclusion: Systemic administration of 13C-2′-FL did not lead to 13C-enrichment in any peripheral tissue. However, when 13C-2′-FL was administered orally, 13C-enrichment was detected in virtually all tissues/organisms. The late rise in 13C-enrichment when the bolus had already reached the colon and its microbiota suggests that 13C-enrichment may derive from metabolic products rather than from intact 2′-FL.

Disclosure of interest: Enrique vazquez, Maria ramirez, Ricardo Rueda and Rachael Buck are Abbott Nutrition employees
NUTRITION: Neonatal and infant nutrition

N-eP-022

No effect of the probiotic bacterium Lactobacillus reuteri on feeding intolerance in extremely low birth weight infants

Erik Wejryd¹, Giovanna Marchini², Veronica Frimmel², Baldvin Jonsson², Thomas Abrahamsson¹

¹Linköping University, Department of Clinical and Experimental Medicine, Division of Paediatrics, Linköping, Sweden
²Astrid Lindgren's Hospital for Children, Karolinska University Hospital and Institute, Department of Neonatology, Stockholm, Sweden

Objectives and study: While probiotics seem to reduce feeding intolerance, sepsis and necrotizing enterocolitis (NEC) in premature infants with a birth weight above 1000 g, the effect on infants with extremely low birth weight (ELBW; <1000 g) is still questioned. The aim of the study was therefore to evaluate the effect of oral supplementation of Lactobacillus reuteri DSM 17938 on feeding tolerance, growth rate and severe morbidity among ELBW infants.

Methods: This was a randomized, double-blind, placebo-controlled multi-centre trial with 136 infants born before gestational week 28+0 with a birth weight less than 1000 g conducted in Sweden. A daily supplementation of L. reuteri (1.25 x 10⁸ bacteria/day) or placebo was started within 72 hours and continued until gestational week 36+0. Due to 100% coverage of donor milk banks in Sweden, all infants were fed exclusively with breast milk until gestational week 32-33. Primary outcome was time to reach full enteral feeding. Secondary outcomes were growth rate, culture-proven sepsis, NEC (Bell’s stage II – III) and mortality. Growth was calculated comparing the z-score for weight, length and head circumference at birth with the measurements at 14 and 28 days, and at 36 gestational weeks. The results were analysed with an intention to treat approach.

Results: Background factors were similar in the two interventions groups. Mean birth weight was 733 g in the L. reuteri group (n=70) and 740 g in the placebo group (n=66). Mean gestational age was 25.5 weeks in both groups. There were no differences in feeding intolerance between the L. reuteri and the placebo group. The median time to full enteral feeding was 15 days in both intervention groups and the number of days with feeding interruptions 6 in both groups. The growth rate was similar in the two intervention groups, except for head circumference, which was higher in the L. reuteri than the placebo group from birth to 28 days of life. The z-score decreased in both groups, but less in the L. reuteri group compared to the placebo group, -1.2 SD vs. -1.7 SD (p=0.001). No statistically significant differences in severe complications were observed. The incidence of NEC was 10% and 12%, culture-proven sepsis 37% and 39%, and mortality 7% and 8% in the L. reuteri and placebo group, respectively.

Conclusion: In this study with ELBW infants, oral supplementation of L. reuteri had no effect on feeding intolerance or severe morbidity. There was a faster growth rate of the head from birth to day 28 of life in the L. reuteri supplemented infants. The relevance of this finding will be evaluated in a future follow up trial focusing on neurological development.

Disclosure of interest: Erik Wejryd, no conflicts
Giovanna Marchini, no conflicts
Veronica Frimmel, no conflicts
Baldvin Jonsson, no conflicts
Thomas Abrahamsson has received funding for the study, and honoraria for lectures from Biogaia AB.
Chicken liver compared to fortified rice cereal as a first complementary food for breastfed infants: effectivity on zinc intake and status

Klara Yuliarti\textsuperscript{1}, Ester Honoris\textsuperscript{2}, Damayanti Sjarif\textsuperscript{2}

\textsuperscript{1}Dr. Cipto Mangunkusumo Hospital / Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia
\textsuperscript{2}Dr. Cipto Mangunkusumo Hospital / Faculty of Medicine Universitas Indonesia, Pediatrics, Jakarta, Indonesia

Objectives and study: High prevalence of zinc deficiency and growth faltering were observed during the complementary feeding period due to low quality complementary food and high prevalence of infection. Common complementary food given to Indonesian infants were plants sources which contain low zinc and high phytate, thus put Indonesian babies into high risk of zinc deficiency. Chicken liver is a good source of zinc, protein, and iron, also serves as an affordable local food for Indonesian people. This study aimed to evaluate the acceptability and effectivity of chicken-liver-based complementary food compared to fortified rice cereal on zinc intake and status.

Methods: Randomized clinical trial comparing three types of complementary food: (1) chicken-liver-based in puree form, (2) fortified rice cereal containing milk, and (3) fortified rice cereal without milk given to predominantly breastfed infant starting at age around 6 months old. This study took place in four primary health care in Jakarta. The daily chicken liver or cereal was delivered to the primary health care and given for 30 days. Anthropometric measurements and plasma zinc investigation were performed before and after intervention. Amount of consumed food and breastfeeding frequency were recorded daily. The increment of pre-intervention and post-intervention plasma zinc was used to assess the effectivity on zinc status.

Results: Ninety babies were enrolled, 7 subjects refused to continue study and 17 blood samples were hemolyzed thus 66 subjects were analyzed. Mean (±SD) daily zinc intake from complementary food for infants in the chicken liver group was 3.4±1.0 mg, whereas that of the cereal with milk was 4.1±0.9 mg and cereal without milk was 3.4±0.7 mg. All groups met the estimated average requirement of zinc of 3 mg/day. Tolerance and acceptance were comparable for the three groups. The zinc increment (\(\mu g/dL\)) for chicken liver, rice cereal with milk, and rice cereal without milk group were 16.4±17.9; 4.4±1.1; and -4.1±15.0, respectively (p=0.01, Anova). Bonferroni tests to analyze effect size between two groups showed mean difference of zinc increment (\(\mu g/dL\)) were 12.0 (95% CI 0.6;23.4) for chicken liver vs rice cereal containing milk, 20.5 (95% CI 9.6;31.5) for chicken liver vs rice cereal without milk group and 8.5 (95% CI -2.3; 19.3) for rice cereal containing milk vs without milk. In the beginning of study there were five stunted infants (length for age z-score <-2 SD): one in chicken liver group, one in single grain group, and three in single grain group. Four out of 5 stunted babies achieved normal length for age z-score at the end of study.

Conclusion: The three groups showed no difference in acceptability and were able to met daily requirement of zinc. Chicken liver demonstrated better effectivity on plasma zinc compared to fortified rice cereal. The difference in effectivity between chicken liver and fortified rice cereal are likely attributable to poor bioavailability of zinc due to its high phytate. We did not measure the phytate content, but the phytate:zinc molar ration in cereal was estimated to be 7:1 to 20:1, which are the range where negative interaction occurs. Therefore, a further study regarding the influence of phytate:zinc molar ration to zinc bioavailability in cereal-based complementary food is needed. It is preferable to develop population-specific dietary guidelines for complementary feeding based on the food composition of locally available foods.
Setting a benchmark for quality standards: the incidence of central venous catheter infections in children on home parenteral nutrition

Amar Wahid¹, Rachel Cichosz¹, Elaine Sexton², Louise Spencer², Sue Protheroe¹

¹Birmingham Children's Hospital, Paediatric Gastroenterology, Birmingham, United Kingdom
²Birmingham Children's Hospital, Nutritional Care, Birmingham, United Kingdom

Objectives and study: The British Society of Paediatric Gastroenterology, Hepatology and Nutrition (BSPGHAN) Quality Standards working group and the British Intestinal Failure Alliance (BIFA) have this year proposed standards for patients on home parenteral nutrition (HPN). They advise regular audit of patient outcomes, including rates of inpatient catheter related sepsis below 3/1000 catheter days and outpatient rates below 1/1000 catheter days in adults. The expected incidence in children is not yet known. This study reviews the incidence of central venous catheter (CVC) related infections and venous thromboembolisms (VTE) in patients under the care of Birmingham Children's Hospital (BCH) over the past 16 years, and suggests potential interventions to improve outcomes for patients on HPN.

Methods: Data were collected retrospectively using medical notes, microbiology and results, and HPN patient database kept by the nutrition team at BCH from January 2000 to December 2015. The number of CVC infections were collected in 2 yearly intervals and used to calculate the rate of infection per 1000 catheter days using the formula: (Number of catheter-related bloodstream infections/Number of central line days) X 1000. Catheter related sepsis was defined as a febrile episode diagnosed clinically as CVC infection by the admitting consultant and treated with a complete course of intravenous antibiotics, with or without growth on blood culture. As a secondary measure, we looked at the rate of CVC related VTE diagnosed clinically or detected on screening ultrasound of central veins.

Results: CVC related sepsis has declined remarkably over the time period, from 10 infections/1000 catheter days in 2000/01 to 0.8 infections/1000 catheter days in 2014/15. The only episode of VTE occurred in 2001 and there have been nil since.

Conclusion: Rates of infection have reduced as a result of better education for patients and families and the use of agents such as chlorhexidine wash, although Taurolock is not routinely used. BCH have a dedicated nutrition nursing team who reinforce practical measures to keep line sites clean, such as proactively screening for skin colonization and eradication with topical treatments. Line site infections are swabbed and treated. The team has a preference for prompt treatment of suspected infection in the emergency department and removal of lines if the infection does not respond to antibiotics within 24-36 hours. The low levels of VTE are likely due to this practice, as well as improvements in clinical technique at insertion, particularly since a dedicated venous access team was set up, who use ultrasound guiding insertion techniques.
Milk oligosaccharides affect colonic metabolome and stressor-induced immunomodulation in mice

Maciej Chichlowski¹, Robert Jaggers², Amy Mackos², Brian Berg¹, Michael Bailey³

¹Mead Johnson Pediatric Nutrition Institute, Evansville, IN, United States
²The Research Institute at Nationwide Children's Hospital, Center for Microbial Pathogenesis, Columbus, OH, United States
³The Ohio State University College of Medicine, Department of Pediatrics, Columbus, OH, United States

Objectives and study: There are extensive bidirectional interactions between the gut microbiota and the central nervous system (CNS). Dietary interventions that impact the microbiota, such as prebiotics and milk oligosaccharides, have been shown to reduce risk of many deleterious effects of stressor exposure. However, the mechanisms through which the microbiota influence the host are not well understood. We tested whether exposure to a social stressor, called social disruption (SDR), results in metabolomic changes in the colon, and whether prebiotics (blend of galactooligosaccharides (GOS) and polydextrose (PDX)) and/or milk oligosaccharide sialyllactose (Lacprodan SAL-10®, SL) support a normal metabolome in the presence of stress.

Methods: Male mice (postnatal day (P) 48-64) were placed on one of the experimental diets for 14d: a) SL [2.2g/kg], b) GOS+PDX [15g/kg each] + SL [2.2g/kg] or c) Control [cellulose as fiber source]. Mice were then randomly assigned to either the non-stressed control group or to the Social Disruption Stressor (SDR Stressor) condition. SDR stressor entails repeated social defeat for 2 hrs per day on 6 consecutive days. Metabolites in the colonic contents were then assessed using LC/MS, while serum cytokine levels were assessed by ELISA.

Results: Mice fed a control diet and exposed to the stressor showed significant differences in 116 out of 529 detected metabolites, compared to control diet non-stressed mice. This was partly due to significant reductions in dipeptides and amino acids, as well as significant increases in nucleotides and sphingolipids. Interestingly, stress-exposed mice fed diets enriched with prebiotics (either a combination of GOS, PDX, and SL or SL alone) showed similar changes in dipeptides, nucleotides, and sphingolipids, but also showed increases in polyunsaturated fatty acids and endocannabinoids, as compared with the non-stress groups. Polyunsaturated fatty acids and endocannabinoids can have anti-inflammatory effects, thus we determined whether the experimental diets would attenuate stressor-induced increases in inflammatory cytokines. Serum IL-6 and IL-1β were significantly increased in stressor-exposed mice, but this effect tended to be attenuated in mice fed both treatment diets (diet x stress condition interactions, p-values = 0.081 and 0.056, respectively).

Conclusion: This study demonstrates that dietary prebiotics and milk oligosaccharides can impact the colonic metabolome to potentially attenuate stressor-induced immunomodulation.
Dietary beta-cyclodextrin significantly improves hypercholesterolemia in mice independent of intestinal microbiota

Rima Mistry¹, Henkjan Verkade¹, Uwe Tietge¹

¹Dept of Paediatrics, University of Groningen, University Medical Center Groningen, Paediatrics, Groningen, Netherlands

Objectives and study: In recent years non-digestible oligosaccharides have received increasing interest for their perceived health benefits. β-cyclodextrin (βCD) is a cyclic oligosaccharide with proposed cholesterol metabolism modulating properties. Cholesterol is also a major risk factor associated with cardiovascular disease (CVD) which represents the highest cause of mortality worldwide. Currently drug treatment with statins is the mainstay of therapy to prevent heart attacks and stroke. However, the vast use of statins has only decreased the incidence of CVD events by maximally 30%. Therefore, additional therapeutic strategies are warranted. Dietary intervention with non-digestible oligosaccharides appears hereby particularly attractive, since the relatively easy applicability via nutrition and few side effects, which is expected to increase adherence to the treatment.

The aim of the present study was to characterize the impact of dietary βCD on sterol metabolism and reverse cholesterol transport (RCT), a process involving mobilization of cholesterol from macrophage foam cells for excretion via the feces in conventional as well as germ-free mice. Germ-free mice were included to establish whether fermentation products of βCD by the intestinal microbiota contribute to the biological effects of this non-digestible oligosaccharides.

Methods: C57BL/6 conventional and germ-free mice were fed control or βCD supplemented (10%) diet for a period of 14 days followed by bile cannulation and RCT experiment.

Results: βCD-feeding in conventional C57BL/6 wild-type mice decreased plasma cholesterol levels (-40%, p<0.05) and increased fecal neutral sterol excretion significantly (3-fold, p<0.01). Fecal bile acid excretion, hepatic cholesterol levels and biliary cholesterol secretion were unaltered. Changes in cholesterol metabolism translated into increased macrophage-to-feces RCT in βCD-administered mice (1.5-fold, p<0.05). In germ-free mice βCD similarly lowered plasma cholesterol (-40%, p<0.05). However, in germ-free mice βCD diet increased fecal neutral sterol excretion (7.5-fold, p<0.01), bile acid excretion (2-fold, p<0.05) and RCT (2.5-fold, p<0.01) more profoundly than in conventional mice.

Conclusion: Dietary administration of the oligosaccharide βCD lowers plasma cholesterol levels and increases fecal cholesterol excretion in mice. The hypcholesterolemic effect is independent of the presence of intestinal microbiota and thus of bacterial metabolism. The metabolic effects of dietary βCD are expected to translate into cardiovascular health benefits.
Post-prandial kinetics of metabolites following consumption of follow-up formula

Amber Milan¹, Alison Hodgkinson², Elizabeth Carpenter³, Colin Prosser³, David Cameron-Smith¹

¹University of Auckland, Liggins Institute, Auckland, New Zealand
²Agresearch, Hamilton, New Zealand
³Dairy Goat Co-Operative Ltd, Hamilton, New Zealand

Objectives and study: Few human studies have addressed the postprandial metabolic response following consumption of nutritional formula made from different sources of proteins. This trial was a targeted metabolomics study comparing plasma metabolite profiles after consumption of commercially available follow-up formulas containing intact proteins from goat or cow milk or partially-hydrolysed cow whey protein.

Methods: The trial was a double blinded, randomised, cross-over feeding design, conducted in Auckland, New Zealand (Australia and New Zealand Clinical Trials Registry ACTRN12615000147583) with 15 males and 15 females aged 18-28 years. Subjects received formula made from goat milk (GF), cow milk (CF) or partially-hydrolysed cow whey protein (HF) in a randomised order, with a wash-out period between treatments. After an overnight fast preceded by a standardised dinner meal, subjects consumed 500-1000 ml of formula (providing protein at 0.23 g/kg body weight), followed by 1.5 g paracetamol to measure gastric emptying. Venous blood samples were collected at fasting and at regular intervals over 5 hours.

Results: There was no difference between formulas in maximal plasma concentration of paracetamol, but there were differences in rate of appearance. Recovery at 30 min was approximately 30% lower following HF compared to other formulas (p<0.05 HF vs. CF or GF) while CF was 17% lower compared to GF (p<0.01).

Insulin concentrations were lower after GF ingestion compared to CF at 15 min, and at 45 to 120 min (p<0.05), but not at peak concentrations (30 min). Similarly, insulin concentrations after GF were lower compared with HF from peak (30 min) to 120 min (p<0.05). Insulin concentrations after HF were higher compared with CF between 60 and 120 min (p<0.05). This resulted in a significantly higher Area Under the Curve (AUC) for insulin with HF (8088 ± 7516 µmol.hr/ml, p<0.001) compared to other formulas. AUC for GF was significantly lower compared with CF (3796 ± 2790 µmol.hr/ml and 5202 ± 4243 µmol.hr/ml, respectively, p<0.05).

Total amino acid (TAA) concentrations in plasma peaked at 60 min for all formulas. TAA concentrations remained above fasting levels until 240 min after consumption of GF or CF, never falling below fasting levels. After HF ingestion, TAA concentrations rapidly declined, falling to concentrations below fasting by 240 min. A similar pattern of response was observed for branched chain and essential amino acids.

Plasma and chylomicron triglyceride (TG) concentrations were significantly increased above fasting levels after ingestion of HF (p<0.05), peaking at 60 min and rapidly decreasing by 180 min. In contrast, chylomicron TG concentrations after the cow and goat formulas peaked at 180 min, while plasma TG did not increase above fasting levels at any time.

Conclusion: There were substantial differences in the postprandial appearance and clearance of hormones and metabolites between formulas of partially-hydrolysed and intact milk proteins. In contrast, differences between formulas with intact proteins from cow or goat milk were more subtle and the metabolic impact does not markedly differ. The rapid macronutrient clearance observed after the partially hydrolysed formula warrants further exploration into the possible metabolic consequences.

Dietary prebiotics early in life alter exploratory behavior, recognition memory, and brain serotonin in the neonatal piglet

Rosaline Waworuntu1, Stephen Fleming2, Supida Monaikul3, Alexander Patsavas3, Brian Berg1, Ryan Dilger3

1Mead Johnson Pediatric Nutrition Institute, Evansville, United States
2University of Illinois, Neuroscience Program, Urbana, United States
3University of Illinois, Department of Animal Sciences, Urbana, United States

Objectives and study: A prebiotic blend of polydextrose and galactooligoasaccaride (PDX-GOS) represents a mixture of long- and short-chain oligosaccharides. Emerging evidence in rodent models suggests dietary prebiotics are capable of modulating the gut microbiota and animal behavior. A previous study showed this prebiotic blend had the potential to improve memory and social behaviors while reducing anxiety-like behaviors in normally developing rodents. The present research set out to describe the effects of feeding PDX-GOS early in life on cognition, exploratory behaviors and brain neurochemistry using a piglet model.

Methods: Piglets were provided customized milk replacer containing 2 g/L each of PDX and GOS (TEST) or 0 g/L (CONT) from postnatal day (PND) 2-33. Beginning at PND 25, piglets were tested on the novel object recognition (NOR), novel location recognition, and tonic immobility tasks to measure recognition memory and response to restraint stress. At study conclusion, piglets were euthanized, and intestine and brain tissues were collected.

Results: No effects of diet were observed for lengths or weights of intestinal tissues ($P > 0.119$). Concentrations of volatile fatty acids (acetate, propionate, butyrate) were decreased in the ascending colon of pigs in the TEST group ($P < 0.012$), but unchanged in the cecum ($P > 0.383$). Piglets consuming the TEST diet were able to demonstrate NOR after a 48 h delay ($P < 0.001$), but piglets consuming the CONT diet could not ($P = 0.184$). Additionally, piglets consuming the TEST diet visited both the novel and sample objects more frequently (all $P < 0.05$), spent less time per visit exploring the sample object ($P = 0.028$), and exhibited greater total movement during the sample phase ($P < 0.001$) than those on the CONT diet. Neither group was able to complete the novel location recognition task after a delay of 24 h (all $P > 0.320$), and there were no effects of diet observed for outcomes in the tonic immobility task (all $P > 0.537$). Concentrations of serotonin were lower ($P = 0.016$) in the hippocampus of pigs fed the TEST diet and tended to be lower ($P = 0.055$) in the striatum of those same pigs.

Conclusion: These findings suggest that early-life consumption of PDX-GOS results in prebiotic effects in the ascending colon, subtly alters concentrations of catecholamines in the brain and supports recognition memory. We believe this is the first account of non-digestible prebiotic fibers displaying simultaneous effects in the gut and brain of neonatal piglets. Such findings are likely the result of interactions within the gut-microbiome-brain axis, signifying dietary intervention as a possible mechanism to impact both gut and brain development and function in early life.

Disclosure of interest: Rosaline Waworuntu and Brian Berg are employees of Mead Johnson Nutrition.
Stephen Felming, Supida Monaikul, Alexander Patsavas, and Ryan Dilger: no conflict of interest.
Dietary milk fat globule membrane and prebiotics modulate visceral pain and cognitive responses to maternal separation stress

Rosaline Waworuntu1, Karen-Anne McVey Neufeld2, Siobhain O'Mahony2, Matteo Pusceddu2, Brian Berg1, Ted Dinan2, John F. Cryan2

1Mead Johnson Pediatric Nutrition Institute, Evansville, United States  
2Apc Microbiome Institute, Cork, Ireland

Objectives and study: Stressful episodes during critical windows of development can have long lasting consequences on the stability of physiological, cognitive and behavioral systems. Maternal separation (MS) stress of rat pups is a robust model of early life stress that induces long-term alterations to behavior and brain neurochemistry. Nutritional interventions targeting the microbiota-gut-brain axis may be able to modulate stress-induced dysfunction of physiological processes and brain development. In this study the effects of milk fat globule membrane (Lacprodan MFGM-10®, 15 g/kg) and a polydextrose / galactooligosaccharide (7 g/kg each) prebiotic blend were evaluated on early life stress induced alterations.

Methods: The maternal separation protocol was conducted as described in O'Mahony et al., 2009. Rats were separated from their mothers for 3 h/day from postnatal day (PND) 2 to 12. Starting at weaning (PND 21), both non-separated (NS) and maternally separated (MS) offspring were randomized into separate experimental groups and were provided with or without supplementation of MFGM, prebiotic blend or a combination of both. Morris water maze and visceral sensitivity were assessed on PND 61 and 79, respectively.

Results: MS rats demonstrated visceral hypersensitivity to colorectal distension reflected by a lower pain threshold and a higher number of pain behaviours when compared to NS rats. This increase in sensitivity in MS rats was ameliorated by MFGM (p=0.01) and also the combination of MFGM and the prebiotic blend (p=0.045). Furthermore, MS rats showed significant impairments in spatial and reference memory in the Morris water maze. Cognitive performance in this test was improved by the prebiotic blend (p=0.007) and MFGM alone (p=0.019) as well as the combination of both (p<0.0001). Interestingly, the combination of MFGM and prebiotic reversed the impact of early life stress on the mineralocorticoid receptor (MR) expression in the hippocampus, which is associated with negative feedback of the hypothalamic pituitary adrenal (HPA) axis.

Conclusion: Feeding MFGM and prebiotics to rats ameliorated the visceral pain sensitivity and cognitive impairment caused by maternal separation. The changes to MR expression indicate that regulation of the negative feedback of the HPA axis may be partially involved. Further studies are needed to confirm this as well as elaborate on the specific mechanism of actions related to gut and brain neurochemistry. Supported by Science Foundation Ireland and Mead Johnson Nutrition.

Cow’s milk and rice fermented with L. paracasei CBA L74 modulate gut microbiota in children

Roberto Berni Canani1, Rita Nocerino2, Lorella Paparo2, Rosita Aitoro2, Carmen Di Scala2, Margherita Di Costanzo2, Mario Laiola3, Carmen De Caro4, Antonio Calignano4, Francesca De Filippis3, Danilo Ercolini3

1University of Naples “Federico II”, Translational Medical Science-Elfid-CEPTION Advanced Biotechnologies, Naples, Italy
2University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
3University of Naples “Federico II”, Agricultural Sciences, Division of Microbiology, Portici (Naples), Italy
4University of Naples “Federico II”, Department of Pharmacy, Naples, Italy

Objectives and study: Cow’s milk and rice fermented with Lactobacillus paracasei CBA L74 prevent infectious diseases in young schooled children. The mechanisms of this effect is still not completely defined. We speculated that these dietary strategies could shape gut microbiota composition.

Methods: Stool samples (3 gr) were collected from healthy children (aged 12-48 months) before (t0) and after 3 months (t3) of dietary treatment with cow’s milk (FM, group A) or rice (FR, group B) fermented with L. paracasei CBA L74, or placebo (PL, group C). Changes in gut microbiota composition was investigated by 16S rRNA gene amplicon sequencing (V3-V4 region) and innate (α- and β-defensins and cathelicidin LL-37) and acquired immunity biomarkers (secretory IgA) by ELISA.

Results: 30 children (19 males, 63.3%) with a mean (SD) age of 34.3 (9.7) months were randomly assigned to each group (n=10/group). A significant increase of all biomarkers of innate and acquired immunity was observed only in groups A and B but not in group C. Both the treatments (in particular, the rice matrix) led to an increase in Lactobacillus, while PL showed higher levels of Bacteroides after 3 months. Different microbial signatures were detected according to the specific fermented matrix consumed: Oscillospira and Faecalibacterium abundance increased with fermented milk (FM) treatment, while Blautia and Coprococcus were boosted by fermented rice (FR). These genera were also positively associated to the increase in α-defensin, particularly evident in FM treated children. Sub-genus diversity of Blautia, Roseburia and Faecalibacterium was also evaluated. Individual Blautia, Roseburia and Faecalibacterium oligotypes were associated to FM or FR treatments and revealed the presence of sub-genus specific links with the immunity biomarkers. Finally, PICRUSt predicted metagenomes showed an increase in key genes involved in butyrate production pathway (acetate coA/acetoacetate coA-transferase – K01034, K01035; butyrate kinase – K00929) following FM treatment.

Conclusion: Dietary supplementation with cow’s milk or rice fermented with L. paracasei CBA L74 modulates innate and acquired immunity biomarker and these effects are associated with specific signatures in gut microbiota.
Evaluation of \textit{L. rhamnosus} GG heat-stability during formula preparation according to FAO/WHO recommendation

Rosita Aitoro\textsuperscript{1}, Lorella Paparo\textsuperscript{1}, Antonio Amoroso\textsuperscript{1}, Carmen Di Scala\textsuperscript{1}, Margherita Di Costanzo\textsuperscript{1}, Linda Cosenza\textsuperscript{1}, Viviana Granata\textsuperscript{1}, Rita Nocerino\textsuperscript{1}, Roberto Berni Canani\textsuperscript{2}

\textsuperscript{1}University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
\textsuperscript{2}University of Naples “Federico II”, Translational Medical Science-Elfid-Ceinge Advanced Biotechnologies, Naples, Italy

\textbf{Objectives and study:} It has been demonstrated that dietary intervention with extensively hydrolyzed casein formula (EHCF) supplemented with the probiotic \textit{L. rhamnosus}GG (LGG) accelerates tolerance acquisition in infants with cow milk allergy (CMA). Concerns have been raised on LGG stability because FAO/WHO recommend powdered infant formula (PIF) reconstitution with water that is no less than 70°C. We aimed to evaluate if LGG, contained in EHCF could survive during the formula preparation procedure indicated by FAO/WHO.

\textbf{Methods:} We boiled drinking water for 10 min. Water was left at room temperature until a temperature of 70°C was achieved, then EHCF containing LGG powder (Nutramigen LGG, Evansville IN, US) was dissolved in the bottle. Bottle was immediately cooled to feeding temperature by holding the bottom under cold running tap. EHCF supplemented with LGG dissolved in water at room temperature served as control. Samples were diluted 1:1000 in distilled water and 100 µl of each samples was spread on the MRS agar plates. The plates were incubated under anaerobic conditions for 72 h at 37°C.

\textbf{Results:} Manufacturer’s specification indicates a LGG concentration from $2.5 \times 10^7$ to $5 \times 10^8$ CFU/gr with a guaranteed level of $1.46 \times 10^7$ CFU/100 ml (approximately $1 \times 10^6$ CFU/gr). After EHCF containing LGG preparation according to FAO/WHO recommendation the total LGG counts was $2.7 \times 10^7$ that exceeded the guaranteed level of CFU/100 ml.

\textbf{Conclusion:} Reconstitution of EHCF+LGG according to FAO/WHO recommendation for PIF preparation allows an adequate degree of the probiotic survival. Our result suggest that this dietary approach could be efficiently adopted also in Countries where FAO/WHO recommendation are mandatory.
Comparative evaluation of the immunomodulatory effects of an amino acid-based formula, an extensively hydrolysed casein formula supplemented with L.rhamnosus GG or its mediators, in a murine model of cow’s milk allergy

Rosita Aitoro¹, Lorella Paparo¹, Antonio Amoroso¹, Giovanna Trinchese², Rosaria Meli³, Antonio Calignano⁴, Margherita Di Costanzo¹, Rita Nocerino¹, Claudio Pirozzi³, Gabriele Gross⁴, Tim T. Lambers⁵, Eric A.F. Van Tol⁵, Roberto Berni Canani³

¹University of Naples "Federico II", Department of Translational Medical Science, Naples, Italy
²University of Naples "Federico II", Department of Biology, Naples, Italy
³University of Naples "Federico II", Department of Pharmacy, Naples, Italy
⁴Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands
⁵University of Naples “federico II”, Translational Medical Science-Elfid-Ceinge Advanced Biotechnologies, Naples, Italy

Objectives and study: Dietary intervention with extensively hydrolyzed casein formula (EHCF) supplemented with the probiotic L.rhamnosus GG (LGG) accelerates tolerance acquisition in children with cow’s milk allergy (CMA). We aimed to investigate the immunomodulatory mechanisms underlying the clinical benefit of EHCF plus LGG, and compare this with a EHCF formula supplemented with LGG-derived soluble mediators (LEGb), as well as an amino acid-based formula in a mouse model of CMA.

Methods: Three-weeks old female C3H/HeJ mice were sensitized with oral administration of 20 mg of cow’s milk proteins (CMP) using cholera toxin (CT) as adjuvant on days 0, 7, 14, 21, 28. Starting from two weeks prior to sensitization, mice were given four different experimental diets: solid cow milk protein-free diet; amino acid-based formula (AAF); EHCF+LGG; heat-treated EHCF+LGG; and EHCF+LEGb (a standardized preparation of soluble mediators produced from desalted, sterile-filtered and lyophilized late exponential growth phase of LGG culture supernatant). All study formulas were prepared daily by dissolving the powder in distilled water as indicated by the manufacturer, and provided to the mice in sterile bottles. For the heat treatment, drinking water was boiled for 10 min and left at room temperature until a temperature of 70°C was achieved, before dissolving the EHCF plus LGG powder in the bottle. One week after the last sensitization, mice were challenged with 50 mg CMP intragastrically, and the anaphylaxis score was monitored. Rectal temperature was recorded before and every 5 min for 1 h after challenge. Blood samples were collected by submandibular bleeding methods to detect serum MCPT-1 levels. The following day blood, feces, and tissue samples were harvested. Spleens were aseptically excised, processed and splenocytes plated at 2×10⁵ cells per well with media alone, 1 µg/mL antiCD3, or 200 µg/mL of CMP incubated at 37°C for 72 h. After 72 h, plates were frozen at −20°C. Th2 (IL-4, IL-5, IL-13) and Th1 (IL-10, IFN-γ) cytokines concentrations in splenocytes culture supernatants were measured by ELISA. CMP-specific serum IgE were measured by ELISA.

Results: Sensitized and AAF fed mice showed significantly higher anaphylactic symptom scores, body temperature decrease, serum levels of MCPT-1 and CMP-specific IgE and Th2 cytokines production compared with control animals. All of these effects were significantly inhibited in animals fed EHCF+LGG. In addition, EHCF+LGG significantly stimulated IL-10 and IFN-γ production by splenocytes. EHCF+LGG heat-treatment did not impact all these effects. EHCF+LEGb exerted similar effects when compared with EHCF+LGG, but with superior protective actions on mechanisms of allergy (e.g. MCPT-1, IL-13).

Conclusion: This study revealed that EHCF containing LGG, but not AAF, exerts significant preventive effects against CMA. The effect seems heat-stable. Moreover, EHCF supplemented with LGG-derived soluble mediator demonstrated superior immunoregulatory effects. Hence, EHCF supplemented with LGG-derived soluble mediators could be considered a new effective strategy for the management of cow’s milk allergy.
Homemade vs commercial infant food. A nutritional comparison on dietary fibre

Maria Jose Bernal¹, Juan Francisco Haro Vicente¹, Gaspar Ros², Sergio Roman³, Luis Manuel Sanchez-Siles⁴

¹Hero Group, R+D Department, Murcia, Spain
²University of Murcia, Food Science and Nutrition Department, Murcia, Spain
³University of Murcia, Marketing Department, Murcia, Spain
⁴Hero Group, R+D Department, Lenzburg, Switzerland

Objectives and study: The health benefits of fruit and vegetable consumption, from childhood onwards, are well-recognized. Fruits and vegetables are an important source of dietary fibre (DF). An adequate intake of DF has preventive effects for developing the non-communicable diseases in adults, the DF adequate intake is straightforward; but in childhood, DF intake recommendations are only established above 12 months of age, 19 g/day (1.4 g/100 kcal) (IOM 2005) and 2 g/MJ by EFSA 2010 (0.8 g/100 kcal). However, in infants between 6 to 12 months of age, DF recommendations remain undefined. Still, Agostoni et al. (1995) suggested a gradual increase of DF intake of 5 g/day during the second 6 months of life by introducing increasing amounts of fruits and vegetables. Taking into account that complementary feeding is started at 4 to 6 months of age and fruits and vegetables are introduced by either homemade or commercial infant food, we aimed to compare the DF content in homemade meals and fruit purees in comparison to commercial infant foods (CIFs).

Methods: In this observational study, 30 Spanish mothers completed a 3-day food record of their infants aged 7-18 months (11 ± 3.5 months). Frozen samples of their homemade meals and fruit purées were collected in October 2014. Total DF was analysed following the methods described by Prosky et al (1988) and AOAC 991.43 (1998). Spanish CIFs from the four main manufacturers were included to compare them with the homemade samples. DF content was obtained from information shown in the food labels and available on the manufactures' websites. Statistical analyses were performed using SPSS data software (v. 18). Independent t-test was carried out to compare the DF content in homemade vs. CIFs.

Results: A total of 119 homemade analysed samples (47 meat, 28 fish, 9 only veggies, and 35 fruit puree) and 202 Spanish CIFs (84 meat, 19 fish, 10 only veggies and 89 fruit puree) were compared for DF content (Table 1). The DF content of homemade infant meals and fruit purée were significantly higher than DF content in CIFs (Table 1).

Table: DF content (g/100 g) in homemade meals and fruit purées and CIFs. Data expressed in Mean ± SD.

<table>
<thead>
<tr>
<th>Type of Product</th>
<th>Homemade</th>
<th>Commercial infant food</th>
<th>p values</th>
</tr>
</thead>
<tbody>
<tr>
<td>Meals</td>
<td>2.6 ± 0.6</td>
<td>0.8 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Fruit purees</td>
<td>2.0 ± 0.3</td>
<td>1.3 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Total</td>
<td>2.4 ± 0.6</td>
<td>1.1 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

Conclusion: Our study showed that infants fed with homemade meals and fruit purees are likely to have a higher intake of DF as compared to infants fed with CIFs. Interestingly, both type and percentage of vegetables and fruit used in recipes were similar in homemade and commercial foods; therefore, the differences observed could be due to several reasons, such us the use of fruit concentrate instead of purees in some products, as well as the use of technological processes where the DF is partially removed. Also, it is important to take into account that even though we used many homemade samples, they came from 30 mothers, which may limit their generability. We believe that
there is an opportunity for infant food manufactures to mimic as closely as possible the naturally DF content of homemade recipes and therefore increase the DF content in the overall diet of infants.

AOAC Official Method 991.43.
IOM (2005). Institute of Medicine (US), Food and Nutrition Board. NAP

Disclosure of interest: M.J. Bernal, J.F. Haro, L.M. Sanchez-Siles: Conflict with Hero Group
Preventive effect of human milk against food allergy: new insights into butyrate activities

Roberto Berni Canani¹, Rosita Aitoro², Lorella Paparo², Antonio Amoroso², Giovanna Trinchese³, Rosaria Meli⁴, Antonio Calignano⁴, Carmen De Caro⁴, Annalisa Passariello², Mariangela Montella⁵, Francesco Messina⁵, Rita Nocerino⁶, Cathryn Nagler⁶

¹University of Naples “Federico II”, Translational Medical Science-Elfid-Geinge Advanced Biotechnologies, Naples, Italy
²University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
³University of Naples “Federico II”, Department of Biology, Naples, Italy
⁴University of Naples “Federico II”, Department of Pharmacy, Naples, Italy
⁵Villa Betania Hospital, Operative Unit of Neonatology and Neonatal Intensive Therapy, Naples, Italy
⁶University of Chicago, Department of Pathology, Illinois, United States

Objectives and study: The mechanisms of the preventive effect of breast milk (BM) against food allergy (FA) are still largely undefined. The short chain fatty acid butyrate has a pivotal role in immune tolerance. We aimed to see whether BM butyrate concentrations are able to exert immune and non-immune tolerogenic effects in human enterocytes, peripheral blood mononuclear cells (PBMCs) from children affected by FA, and in FA animal model.

Methods: Mature BM butyrate concentrations from 98 healthy women (aged 21-42 yrs) were assessed by gas-chromatography. Dose-dependent effects of butyrate in human enterocytes (Caco-2 cells) on immune (beta-defensin-3, HBD-3) and non-immune (mucus production; mucin 2, MUC2; tight-junction proteins, zonulin and occludin) were analyzed. PBMCs from 6 children with challenge-proven FA (2 cow milk allergy, 2 peanut allergy, 2 egg allergy; age range 1-5 yrs) were stimulated with β-lactoglobulin (BLG;100µg/ml), peanut extract (PE;200µg/ml) or ovalbumin (OVA;200µg/ml) in the presence or absence of butyrate. Expression and DNA methylation rate of IL4, IL5, IL-10, IFN-γ and Treg-specific-demethylated region (TSDR) Forkhead box Protein 3 (FoxP3) were assessed. Four-weeks-old female C3H/HeJ mice were used in FA animal model. Two weeks before first sensitization, oral gavage with 30 mg/kg/d of butyrate was started and continued during the whole study. Mice were sensitized orally on day 0, 7, 14, 21, 28 with 20 mg of BLG or 1 mg of OVA or 12 mg of PE mixed with 10 µg cholera toxin (CT) as adjuvant. Control mice receive CT only. On day 35 mice were challenged by gavage with BLG (50mg) or OVA (5mg) or PE (36mg). Anaphylaxis score and rectal temperature were assessed for 1 h after challenge and blood samples were collected to measure MCPT-1 and sIgE. After 24h, mice were sacrificed, colon, ileum and spleen were collected.

Results: Mean butyrate concentration in BM was 0.75 mM (SD±0.15). Butyrate stimulates HBD-3, mucus production and MUC2, zonulin and occludin expression with maximal effective doses between 0.75 and 1 mM in human enterocytes. PBMCs stimulation with BLG, PE, OVA resulted in a significant increase in IL-4 and IL-5 production. A significant inhibition of IL-4 and IL-5 production was observed with 0.75 mM butyrate. Butyrate stimulated, in a dose-dependent manner (maximal effective dose 0.75 mM), IL-10 and IFN-γ production through a demethylation of respective genes and TSDR FoxP3 demethylation. Pre-treatment with butyrate significantly reduced anaphylactoid score, body temperature decrease, serum MCPT-1 and sIgE levels. Butyrate stimulated mucus and IL-10 and IFN-γ production and inhibited IL-4, IL-5 and IL-13 production.

Conclusion: Our data support the role of butyrate as effective human milk component able to prevent food allergy through a wide range of immune and non-immune tolerogenic mechanisms.
Impact of docosapentaenoic acid n-3 (DPA) supplementation on n-3 fatty acid composition of tissues in rats

Gaetan Drouin¹, Daniel Catheline¹, Charlotte Baudry², Pascale le Ruyet², Frédérique Pédrono¹, Philippe Legrand¹

¹Inra / Agrocampus Ouest, Biochemistry and Human Nutrition, Rennes, France
²Lactalis R&d, Nutrition, Retiers, France

Objectives and study: The role of Polyunsaturated Fatty Acids (PUFA) n-3 on lipid metabolism is well known. However, most research focuses on docosahexaenoic acid (DHA, C22:6 n-3) and eicosapentaenoic acid (EPA, C20:5 n-3). Few studies concern docosapentaenoic acid n-3 (DPA n-3, C22:5 n-3), which is not commercially available in sufficient amount for in vivo studies. This fatty acid is an intermediate between EPA and DHA in the n-3 PUFA conversion pathway from α-linolenic acid (ALA, C18:3 n-3). It could be of interest both for DPA ability to be converted to EPA or DHA, mostly in the liver; and for its potential specific physiological effects. To our knowledge, no studies have been able to observe globally the specific enrichment of this fatty acid in the tissues when it was supplemented in vivo.

The objective of this study is therefore to examine the effect of DPA supplementation at a physiological dose on the PUFA composition of the main tissues in rats in order to guide future studies towards the search for physiological effects.

Methods: DPA was purified by preparative liquid chromatography. Two groups of Sprague Dawley male rats (n= 8 / group) were fed for 3 weeks from weaning with a 10% weight lipid diet supplemented or not with 0.5% DPA of total fatty acids (TFA) and containing ALA (2.3% of TFA, ratio n-6/n-3= 5). The TFA composition of 20 tissues was investigated by gas chromatography coupled to a mass spectrometer. The two groups were compared by Student's t-test (p< 0.05).

Results: When supplemented, the proportion of DPA is significantly increased in the heart (x2.1), lung (x1.8), spleen (x1.6), bone marrow (x1.5) and kidney (X1.3). Its proportion tends to increase in the red blood cells (x1.4) and the pancreas (x1.2) but remains stable in the liver, plasma, brain and retina that are known to be impacted with diets supplemented with EPA or with DHA.

DHA status was significantly increased in the spleen (x1.2), lung (x1.2) and tends to increase in the bone marrow (x1.6). DPA supplementation would therefore increase the conversion to DHA.

The proportions of EPA were significantly increased in the liver (x2.0), plasma (x2.0), spleen (x1.5), lung (x1.3) and bone marrow (x1.1). This would confirm direct or indirect retroconversion through DHA from DPA to EPA.

Concerning the n-6 series PUFAs in competition with the enzymes of the n-3 conversion pathway, the proportions of DPA n-6 (C22:5 n-6) and arachidonic acid (C20:4 n- 6) decreased in some tissues specifically (red blood cells, heart, kidney, spleen, lung).

Conclusion: DPA supplementation at 0.5% of TFA results in enrichment of n-3 PUFA and depletion of n-6 PUFAs targeted in some tissues. This suggests a potential and specific action of this fatty acid. Future studies are now scheduled to determine the potential physiological effects of DPA in these organs as compared to DHA and EPA.

Disclosure of interest: This work was supported by the Lactalis group.

Pascale le Ruyet and Charlotte Baudry are employees of Lactalis Research and Development (Nutrition Research Department).
Expression of miRNAs related to obesity and diabetes in human milk

Yaffa Elbaum Shiff¹, Regina Golan-Gerstl², Shimon Reif²

¹The School of Nutritional Sciences, The Hebrew University, Jerusalem, Israel
²Hadassah Medical Center, Department of Pediatrics, Jerusalem, Israel

Objectives and study: Several different epidemiological studies have demonstrated that breastfeeding can reduce the rate of obesity and diabetes. We, as well as others, have demonstrated that human milk contains exosomes, which have the ability to transfer miRNA intracellular by fusion. Moreover, we found that also the fat layer in milk is rich in miRNA.

We hypothesized that human milk contains beneficial miRNAs that can be involved in the preventive effect of milk in childhood diseases such as obesity and diabetes.

Methods: Milk miRNAs were isolated from the exosomes in the skim milk and from the fat globules in the lipid layer of human milk. Next sequencing generation (NGS) and Real Time PCR was performed to study the profile expression of miRNAs in milk.

Results: We have determined the profile expression of miRNA in milk from 15 mothers of term and preterm babies at different periods of lactation. The main miRNAs that we found in the skim and fat fraction of human milk were miRNA-148a-3p (mir-148a), miRNA-320-3p (mir-320), miRNA 375 and miRNA 146a. miRNA 148a (related to adipocyte differentiation) was the most dominant miRNA and its expression was conserved between preterm and term mother milks. In contrast mir-375 and mir-320 (both related to insulin resistance and fat metabolism) were more expressed in colostrum of term babies compared to preterm infants in whey as well in fat fraction (p<0.01). At 1 and 3 month age this trend was observed without statistical difference.

Conclusion: We found different expression of beneficial miRNAs in human milk that can regulate target genes related to obesity and diabetes. Those miRNA may account for the observed protective effect of human milk against obesity and diabetes. Our results have experimental basis in attempt to add beneficial miRNAs carried by exosomes and fat globules from milk to infant formula.
Metabolic syndrome in obese children

Agim Gjikopulli¹, Laurant Kollcaku¹, Paskal Cullufi¹

¹University Hospital Centre “mother Teresa”, Pediatric Department, Tirana, Albania

Objectives and study: To evaluate obese children for the presence of Metabolic Syndrome (MetS).

Methods: Subjects enrolled in our study had been referred to our clinic for obesity from January 2010 to September 2016. They presented a BMI exceeded the 85-th percentile for age and sex. We recorded the anthropometric data and performed: fasting and 2-h after loading blood glucose and insulin (standard OGTT); fasting blood lipid profile; hormonal profile and arterial blood pressure. MetS was defined using modified criteria of the National Cholesterol Education Program Adult Treatment Panel (NCEP ATP III). MetS was defined if 3 or more of the 5 criteria were met.

Results: There were 69 obese children; 49(71%) boys and 20(29%) girls. Mean chronologic age was 9.47±3.73 years, (range 2.59÷15.9). 62(90%) were pre-puberty and 7(10%) were in different stages of puberty. MetS was identified in 25(36.23%) patients; 18(72%) boys and 7 (28%) girls. Mean chronicologic age of the subgroup with MetS was 9.49±4.12 years. With 4 criteria were 9 children; 5 boys and 4 girls, mean chronicologic age was 10.61±4.07 years. With 3 criteria were 16 children; 13 boys and 3 girls, mean chronicologic age was 8.85 ± 4.15 years. Homa-IR index was the major determinant of MetS in our obese children, followed by low levels of HDL-cholesterol, high level of triglycerides and high arterial pressure. There were significant changes between two subgroups with and without MetS for mean values as below (table 1).

Table:

<table>
<thead>
<tr>
<th></th>
<th>without MetS</th>
<th>with MetS</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMiz-score</td>
<td>4.21 ± 2.63</td>
<td>5.68 ± 2.71</td>
<td>*</td>
</tr>
<tr>
<td>Fasting glucose (mg/dL)</td>
<td>72.9 ± 9.03</td>
<td>81.8 ± 8.51</td>
<td>*</td>
</tr>
<tr>
<td>2-h post loading glucose (mg/dL)</td>
<td>96.3 ± 17.7</td>
<td>104 ± 13.37</td>
<td>*</td>
</tr>
<tr>
<td>Fasting insulinaemia (µUI/ml)</td>
<td>23.9 ± 14.64</td>
<td>30.5 ± 11.28</td>
<td>*</td>
</tr>
<tr>
<td>2-h post loading insulinaemia (µUI/ml)</td>
<td>63.6 ± 5.9</td>
<td>109.8 ± 7.7</td>
<td>*</td>
</tr>
<tr>
<td>Homa-IR index</td>
<td>4.6 ± 2.6</td>
<td>6.14 ± 2.6</td>
<td>*</td>
</tr>
<tr>
<td>HDL-cholesterol (mg/dL)</td>
<td>49.4 ± 16.5</td>
<td>32.6 ± 6.7</td>
<td></td>
</tr>
<tr>
<td>Triglyceridet (mg/dL)</td>
<td>85.6 ± 34.2</td>
<td>136 ± 60.4</td>
<td>**</td>
</tr>
<tr>
<td>Max.arterial pressure (mmHg)</td>
<td>115 ± 9.92</td>
<td>130.5 ± 13.6</td>
<td>**</td>
</tr>
<tr>
<td>Min.arterial pressure (mmHg)</td>
<td>69.8 ± 8.94</td>
<td>72.9 ± 8.89</td>
<td></td>
</tr>
</tbody>
</table>

* p-value < 0.05, ** p-value < 0.0001

Conclusion: MetS coexist with obesity in obese children in 36.23%. Fasting and 2h-post load insulin or HOMA-IR index are strictly associated with MetS. The degree of the obesity appears to influence on the prevalence of IR and both of them are the common risk for developing MetS. We recommend screening for all obese children of any age to detect those who require more intense interventions.
Characterization and biological functions of milk-derived miRNAs

Regina Golan-Gerstl¹, Shimon Reif¹, Yaffa Elbaum Shiff²

¹Hadassah Medical Center, Department of Pediatrics, Jerusalem, Israel
²The School of Nutritional Sciences, The Hebrew University, Jerusalem, Israel

Objectives and study: Breastfeeding is associated with reduced risk of infection, immune mediated disorders, obesity and even cancer. Infants who are breastfed enjoy significant health benefits in comparison to those fed with infant formulas. However, the mechanisms governing the beneficial effects of breastfeeding remain unclear. Breast milk contains a variety of microRNAs (miRNAs) in the skim and in the fat layer that can be transferred to the infant, and appear to play important roles in modulating postnatal development.

Methods: This study applied Next Generation Sequencing (NGS) and quantitative real time PCR (qRT-PCR) analysis to determine the miRNA expression profile of the skim and fat fraction of human, goat, and bovine milk as well as infant formulas. Normal and tumor cells were incubated with exosomes and fat globules derived from milk and the profile expression of miRNA was analyzed by real time PCR.

Results: Human and mammalian milk were found to contain beneficial miRNA in the exosomes but also in the fat layer such as mir-148a, mir-320, mir-375, mir-146b and mir-99a. These miRNAs are highly conserved in human, cow and goat milk. Further, miRNAs present in milk exosomes and in the fat milk fraction can enter normal and tumor cells and affect their biological functions. Following incubation of milk derived human miRNA with normal (CRL1831) and cancer (Lim 1215) cells, the expression of miRNA-148a was upregulated and the expression of the DNA methyltransferase1 (DNMT1) target gene of miRNA-148a was down regulated in these cells.

Conclusion: We found expression of beneficial miRNA in milk that can regulate target genes with potential molecular and physiological functions, which might account for the observed immunity-based benefits those breast-fed infants. Our results will give the experimental basis in attempt to add beneficial miRNA from milk to infant formulas.
A novel methodological approach to optimally adjust pancreatic enzyme replacement therapy in cystic fibrosis

Joaquim Calvo Lerma1, Irene Peinado2, Ana Belén Heredia Gutiérrez3, Carmen Ribes Koninckx4, Ana María Andrés Grau3

1Instituto de Investigación Sanitaria La Fe, Valencia, Spain
2Universitat Politècnica de València, Valencia, Spain
3Universitat Politècnica de València, Instituto de Ingeniería de Alimentos Para el Desarrollo, Valencia, Spain
4La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

Objectives and study: dietary lipids' hydrolysis is a challenge for patients with Cystic Fibrosis, due to a lack of digestive enzymes. Patients have to take in every meal a pancreatic enzyme supplement to enable for digestion. However, an evidence-based and successful method to adjust the dose is inexistent, being fat contents of meals the reference. As a part of MyCyFAPP project (www.mycyfapp.eu), the present study was conducted with the aim of proposing a scientific-valid method/procedure to adjust the optimal dose of enzymatic supplements.

Methods: In this study, an in vitro digestion model was used to estimate the optimal dose of PERT for maximum lipids digestibility in a selection of 8 foods: chocolate milk, breakfast cereal, bread toast with butter, ham and cheese sandwich, chocolate biscuit, high-fat yogurt, green salad with olive oil and pizza. Foods were selected in order to conform a usual hyper-caloric diet of 5 meals. The simulation was conducted at oral pH7 (5 minutes) gastric pH3 (2h) with a pepsin solution, intestinal pH6 (2h) and bile concentration 1mM. Simulated digestive fluids (salivary, gastric and intestinal) were prepared according to the harmonized international protocol proposed by Infogest (Minekus et al. 2014). A range of doses of the enzymatic supplement was tested: 1000, 2000, 3000 and 4000 Lipase Units / g of dietary fat (LU/g) for each food.

Results: lipolysis extensions after 2h of intestinal phase in the 8 foods were used for modeling of the results in terms of lipolysis extension (%) vs. dose of enzymes (LU/g fat). This parameter quantifies the fatty acids released from the triglyceride, thus expresses the percentage of lipids digestion. Results were then fitted into predictive equations to estimate the optimal doses of enzymes. We found that different doses were needed to achieve 90% of lipolysis regardless the content of lipids: for example, yoghurt (10% fat) required 550 LU/g while salad (9.5% fat) and chocolate milk (3.6% fat) required 1000 LU/g. Additionally, results evidenced two patterns among the tested foods. A group of foods (salad, yoghurt, chocolate milk and breakfast cereal) reached 100% of lipolysis with a linear increase (with a sharp slope) of the extension as the dose incremented: even at the lowest LU/g fat, high extensions of lipolysis were obtained. The other group (pizza, sandwich, toast and chocolate biscuit) described an inflexion point in the lipolysis extension from which the slope became less sharp and thus the increase of the LU/g fat led to a very low increase of the extension.

Conclusion: we have established a first approach towards a novel method for PERT dose estimation, which evidences that besides the lipids content, other inherent-to-food properties (type of fat and food matrix) should be considered in order to determine the most appropriate / accurate dose of enzymes. We conclude that in vitro digestions are a promising methodology, that further explored, can set the basis to a more efficient adjustment of PERT in the near future.
Relationship of the adipokines leptin and adiponectin with children’s metabolism: metabolomics reveals an entanglement with fatty acid oxidation and gluconeogenesis

Franca Kirchberg, Stephanie Brandt, Wolfgang Koenig, Dietrich Rothenbacher, Hermann Brenner, Berthold Koletzko, Martin Wabitsch, Christian Hellmuth

1Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
2University Medical Center Ulm, Department of Pediatrics and Adolescent Medicine, Division of Pediatric Endocrinology and Diabetes, Ulm, Germany
3Department of Internal Medicine II - Cardiology, University of Ulm Medical Center, Ulm, Germany, Centre for Cardiovascular Research, Partner Site Munich Heart Alliance, Munich, Germany, Ulm, Germany
4Universität Ulm, Institute of Epidemiology and Medical Biometry, Ulm, Germany
5Deutsches Krebsforschungszentrum, Division of Clinical Epidemiology and Aging Research, Heidelberg, Germany
6Universitätsklinik für Kinder- und Jugendmedizin Ulm, Department of Pediatrics and Adolescent Medicine, Division of Pediatric Endocrinology and Diabetes, Ulm, Germany

Objectives and study: Leptin and adiponectin are important players in the regulation of energy homeostasis, but their regulatory role might be impaired in disease states such as adiposity. The points of action of the adipokines have been characterized quite well, however no study investigated the overall effect of the adipokines on the metabolism at the molecular level in vivo. Population-based cohorts offer the possibility to examine these effects in the presence of no or only few pathogenic conditions. We investigated the joint associations of the adipocytes leptin and adiponectin, and of insulin to the metabolic profile which reflects anabolic and catabolic pathways and hint towards their degree of activation in a cohort of 8 years old children.

Methods: We measured plasma metabolite concentrations of 196 metabolites in 400 healthy, fasted 8 years old German children, which were part of the Ulm Birth Cohort Study (UBCS). We furthermore quantified the concentrations of leptin, adiponectin, and insulin. Using multiple linear mixed models, we evaluated the associations between hormones and metabolites. To adjust for multiple testing, we used Bonferroni correction.

Results: Mean values (± SD) of leptin, adiponectin, and insulin were 5.2 ± 5.76 µg/l, 12.5 ± 3.68 µg/ml, and 2.9 ± 1.52 mU/l, respectively. Leptin was exponentially related to the BMI. Leptin was furthermore strongly associated to the amino acids alanine and aspartate (Bonferroni corrected P [PBF ] = 5.7×10-8 and 1.7×10-6, respectively), and negatively associated to the sum of the non-esterified acids (NEFA) and the sum of the long-chain acylcarnitine species C12 – C18 (PBF = 0.009 and 0.0001, respectively). We found similar results for insulin, although the associations were less strong than for leptin. Adiponectin was not related to BMI or any metabolite.

Conclusion: The absence of any association to adiponectin suggests that adiponectin only modulates the metabolic responses in children with already manifested obesity. However, high alanine concentrations and the lower concentrations of NEFA in children with high fasting leptin concentrations might arise from an increased gluconeogenesis and from the dis inhibiting effect of leptin on the carnitine palmitoyltransferase-1 (CPT-1), respectively. As insulin has the same trend towards these associations, both hormones seem to be related to processes that provide the body with energy in the fasting state.
Breast milk cholesterol concentration in mice is resistant to genetic and dietary hypercholesterolaemia

Mirjam Lohuis¹, Lidiya Dimova¹, Uwe Tietge¹, Henkjan Verkade¹

¹Dept of Paediatrics, University of Groningen, University Medical Center Groningen, Paediatrics, Groningen, Netherlands

Objectives and study: Breast milk, in many species, contains high cholesterol concentrations, which impact long-term cholesterol homeostasis in the offspring. The regulation of milk cholesterol concentration is, however, largely unknown. We studied in mice to what extent milk cholesterol concentrations are influenced by genetic and dietary manipulations of plasma cholesterol levels.

Methods: We used a dietary intervention and genetic approaches to increase plasma cholesterol concentrations (LDL-receptor knock-out, ABCG8 transporter knock-out). The LDL-receptor mediates disposal of cholesterol-rich lipoproteins from the systemic circulation, while ABCG8 facilitates excretion of cholesterol from the body. We sampled blood, milk and organs at day 14 of lactation from C57BL/6J (WT), ABCG8-KO, and LDLR-KO dams on either control or high cholesterol (HCh; 0.5%, 3 weeks) diets. Milk was obtained after ~3h separation from their pups.

Results: HCh-feeding induced hypercholesterolemia in each of the mouse models used (+48 to +150% plasma cholesterol; each p<0.05). Similarly, liver and mammary gland cholesterol levels increased in these dams (+305 to +1396%, and +20 to +57%, respectively; each p<0.05). Interestingly, these substantially increased plasma, liver and mammary gland cholesterol levels did not affect milk cholesterol concentration in either the WT or genetic knockout models. HCh-feeding decreased de novo cholesterol synthesis in liver and mammary gland, but this did not affect milk cholesterol concentration (-85 to -117%; each p<0.05).

Conclusion: Our results demonstrate that milk cholesterol concentration in mice is stable under profoundly increased plasma cholesterol levels. We speculate that the robustness of milk cholesterol concentration points to an important function of early cholesterol supply for the offspring.
Vitamin B12 deficiency exacerbates loss of epithelial barrier function in vitro and in vivo models of colitis

Eberhard Lurz1, Pekka Maattanen2, Richard Wu2, Kathene Johnson-Henry2, Philipp M Sherman2

1The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada
2Hospital for Sick Children, Research Institute, Cell Biology Program, Toronto, Canada

Objectives and study: Inflammatory bowel disease (IBD) refers to a spectrum of autoimmune diseases which result in chronic intestinal inflammation. Although the etiology is not completely known, IBD is likely the result of complex interactions between host genetics, gut microbes and environmental factors such as diet. Vitamin B12 is a critical water-soluble vitamin produced primarily by bacteria. Deficiency in vitamin B12 generates hyper-homocysteinemia – one of the critical features identified in gut tissues of IBD patients. However, the exact role of vitamin B12 deficiency in IBD is undefined.

Hypothesis: Vitamin B12 impacts gut epithelial barrier integrity.

Aims: The objectives of this study were to: 1) determine if vitamin B12 alters barrier function in an established in vitro model and 2) assess the effects of a vitamin B12 deficient diet in vivo using two complementary murine models of colitis.

Methods: Caco2-Bbe epithelial cells were seeded onto 6-mm Transwells until transepithelial electrical resistance (TER) reached > 800 Ω/cm², indicative of a polarized cell monolayer. Monolayers were then incubated with either 1000 mcg cobalamin or vehicle placed into the basolateral compartment. After 18 h, apical challenge with entero-hemorrhagic Escherichia coli (EHEC) O157:H7 (~10⁸ CFU) was performed. Alterations in barrier function were analyzed by measuring TER.

For in vivo studies, C57BL/6 female mice at three weeks of age were allowed free access to diets containing: 1) sufficient vitamin B12 (16 ppb), 2) deficient vitamin B12 (0 ppb) or 3) supplemented vitamin B12 (126 ppb) for 28 days. Blood vitamin B12 levels were measured at 28 d by chemiluminescent microparticle immunoassay. Mice were then challenged once orogastrically with C. rodentium (10⁶ CFU) or with dextran sodium sulfate (DSS 2%) in drinking water for 5 d. At 10 d post infection and 7 days after initial DSS administration, animals were sacrificed and biosamples were collected. High-performance liquid chromatography was used to determine homocysteine levels.

Results: Vitamin B12 enhanced epithelial barrier function in vitro: TER of EHEC-challenged monolayers was higher when epithelia had been incubated with vitamin B12 supplemented medium, compared to controls (n=7; p=0.04). In-vivo, dietary vitamin B12 deficiency led to significantly lower vitamin B12 blood levels mean 1,363 pg/ml (SEM 197) vs 2,2337 pg/ml (SEM 1432) in the regular and 3,6321 pg/ml (SEM 599) in the supplemented group (p=0.001). Homocysteine levels did not differ between the 3 study groups. Colon length was shorter in vitamin B12 deficient mice infected with C. rodentium (n=15/group, p=0.001) and animals administered DSS (n=20/group, p=0.005; one-way ANOVA). Fluorescein isothiocyanate-conjugated dextran flux, used as a marker of intestinal epithelial macromolecular uptake, was increased in vitamin B12 deficient mice compared to supplemented (n=5, p=0.045) in the DSS model. The ratio of Firmicutes/Bacteroides was lower in the vitamin B12 supplemented diet group (0.3) compared with the sufficient (0.7) and vitamin B12 deficient diet (0.7) fed mice (n=3/group).

Conclusion: Vitamin B12 impacts epithelial barrier function in both in vitro and in vivo models of intestinal injury. Restriction in dietary B12 accentuated chemically-induced colitis, potentially mediated via effects on the composition and function of the gut microbiome rather than via homocysteine.
Bioactive lipids in Infant formulas enriched with milk fat and milk fat globule membrane

Esther Matencio¹, Fernando Romero¹, Bertine Philipsen², Catharina Tennefors³, Stefan Bodenstab⁴, Luis Manuel Sanchez-Siles⁴

¹Hero Group, R+d Department, Murcia, Spain
²Hero Benelux, R+d Department, Breda, Netherlands
³Semper Ab, R+d Department, Stockholm, Sweden
⁴Hero Group, R+d Department, Lenzburg, Switzerland

Objectives and study: Currently the Milk Fat Globule Membrane (MFGM) and concretely its lipids, have gained interest in relation to its nutritional composition and functional properties. MFGM is perfectly structured and it contains bioactive polar lipids such as cholesterol, sphingomyelin, gangliosides. In fact, diverse beneficial health effects have been attributed to MFGM bioactive lipids such as antimicrobial and antiviral effects. This could explain the possible beneficial effects found in Infant Formulas (IFs) supplemented with MFGM since it seems to have health promoting effects in neurodevelopment and defense against infections (Hernell et al. 2016). Regarding the MFGM composition, more studies about the characterization of its components are needed with the aim to understand the role of bioactive lipids and proteins found in the MFGM structure. We aimed to quantify the bioactive lipids in IFs enriched in Milk Fat (MF) and MFGM and to compare them with IFs without these two ingredients.

Methods: Four IFs enriched with milk fat and MFGM marketed in Czech Republic, Netherlands, Spain and Sweden were compared to the most sold IFs without MF and MFGM in each country. Bioactive lipids (Gangliosides, cholesterol, β-palmitate, sphingomyelin) were analyzed. Gangliosides GM3 and GD3 were identified and quantified by HPLC-MS/MS (method described by Sorensen with modifications); sphingomyelin analyzed by 31P-NMR (method described by García et al. with modifications); cholesterol analyzed by GC-FID-MS (Al-Hasani et al. 1993) and β-palmitate analyzed by GC-FID (method described by Lopez et al. with modifications). Duplicate analyses were performed on each sample (double sample preparation and double detection).

Results: Infant formulas enriched in MFGM and MF, showed significantly higher amounts of cholesterol, gangliosides, sphingomyelin and SN-2 palmitate than infant formulas without them (Table 1).

Table 1: Mean values (sd) of bioactive lipids in infant formulas with and without milkfat and MFGM.

<table>
<thead>
<tr>
<th>Bioactive lipids mean (SD)</th>
<th>IFs with MF and MFGM (N=4)</th>
<th>IFs without MF and MFGM (N=4)</th>
<th>p - value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gangliosides (GD3+GM3) (mg/100 ml)</td>
<td>1.64 (0.36)</td>
<td>1.11 (0.159)</td>
<td>0.002</td>
</tr>
<tr>
<td>Cholesterol (mg/100ml)</td>
<td>6.49 (1.05)</td>
<td>2.46 (0.49)</td>
<td>0.001</td>
</tr>
<tr>
<td>Sphingomyelin (mg/100ml)</td>
<td>13.94 (0.67)</td>
<td>5.75 (2.14)</td>
<td>0.001</td>
</tr>
<tr>
<td>SN2 Palmitate (%)</td>
<td>23.12 (2.75)</td>
<td>10.12 (2.90)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion: Our results showed that the addition of milkfat and MFGM increase the quantity of bioactive lipids in infant formulas. The quantification of these bioactive compounds could help to understand the beneficial health effects of MFGM enriched IFs. Research related to MFGM components and its beneficial effects have been focused on protein components and it seems that
bioactive lipids may also play an important role. More studies are needed to characterize and quantify MFGM and milkfat bioactive compounds.


**Disclosure of interest:** E. Matencio, F. Romero, B. Philipsen, C. Tennefors, S. Bodenstab, L.M. Sanchez-Siles: Conflict with Hero Group
Effects of dietary sialyllactose on growth and intestinal development in the neonatal piglet

Maciej Chichlowski¹, Marcia Monaco², Mei Wang², Xiao Pan¹, Qian Li¹, James Richards¹, Brian Berg¹, Ryan Dilger³, Sharon Donovan²

¹Mead Johnson Pediatric Nutrition Institute, Evansville, IN, United States
²University of Illinois, Food Science & Human Nutrition, Urbana, United States
³University of Illinois, Animal Sciences, Urbana, United States

Objectives and study: Oligosaccharides are the third most abundant component in human milk and modulate neonate microbiota, gut and immune development. We investigated potential dose-dependent effects of sialyllactose (Lacprodan SAL-10⁸, SL) on growth and gut development of neonatal piglets.

Methods: Beginning at 2 d of age, 38 vaginally-derived male piglets (mean body weight (BW) 1.64 ± 0.04 kg) were randomized to diets formulated to contain: control (CONT) [0 mg SL/L milk replacer], low (LOW) [130 mg SL/L], moderate (MOD) [380 mg SL/L], and high (HIGH) [760 mg SL/L]. Diets contained 4 g/L of a 1:1 mixture of polydextrose and galactooligosaccharides. Diets were prepared at 20% (wt/vol) and piglets received 285 mL and 325 mL per kg BW on d2-5 and 5-33, respectively. On d32 or 33, piglets were euthanized and samples were collected. Outcomes were analyzed using a one-way ANOVA; significance was set at p ≤ 0.05 and trends at 0.05 < p < 0.10.

Results: Dietary SL was well tolerated regardless of dose and growth patterns were similar among the groups. Weight gain between d2 and 33 did not differ among the groups and the average gain was 4.23 ± 0.29 kg (CONT: 4.19 kg ± 0.42; LOW: 4.08 kg ± 0.64; MOD: 4.43 kg ± 0.69; HIGH: 4.22 kg ± 0.68). Similarly, intestinal length and weight, villus and crypt morphology in the small and large intestine and the number of acidic sulfated mucin-secreting goblet cells did not differ among the groups. Short-chain and branched-chain fatty acid profiles in colonic contents were similar between all four groups. No differences in complete blood counts were observed and serum clinical chemistry values were similar (minerals, electrolytes, protein, enzymes, kidney function, liver function and acid:base balance and prothrombin time), except for activated partial thromboplastin time (aPTT) and glutathione dehydrogenase (GLDH). APTT (seconds) in HIGH (12.6 ± 0.5) was lower (p<0.02) than CONT (14.1 ± 0.2), LOW (13.8 ± 0.4) and MOD (13.6 ± 0.2). GLDH (U/L) in CONT (0.9 ± 0.1) was lower (p<0.02) than LOW (1.3 ± 0.1) and MOD (1.5 ± 0.2) and tended (p<0.09) to be lower than HIGH (1.2 ± 0.08). Due to the low magnitude of differences and lack of a clear dose response, the differences in aPTT were not clinically significant. In addition to a lack of dose-response in our study, normal values for other liver enzymes suggest that slightly higher GLDH values are also unlikely of clinical significance.

Conclusion: In conclusion, dietary SL at up to 760 mg/L was well tolerated and supported similar growth and intestinal development as the CONT formula in neonatal piglets.
Mirnome analysis highlights a specific cow's milk allergy-related epigenic signature

Lorella Paparo¹, Valeria D'Ar genio², Valentina del Monaco², Fatima Domenica Elisa De Palma², Rita Nocerino¹, Francesca D' Alessio², Feliciano Visconte², Valentina Discepolo³, Franco Salvatore⁴, Luigi Del Vecchio², Roberto Berni Canani⁶

¹University of Naples "Federico II", Department of Translational Medical Science, Naples, Italy
²University of Naples "Federico II", Ceinge-Biotecnologie Avanzate.C.Ar.L. and Department of Molecular Medicine and Medical Biotechnologies, Naples, Italy
³University Federico II, Department of Translational Medical Sciences, Section of Paediatrics, Naples, Italy
⁴Ceinge-Biotecnologie Avanzate S.C.A r.L. and Department of Molecular Medicine and Medical Biotechnologies, University of Naples Federico II, Naples , Italy
⁵University of Naples “Federico II”, Translational Medical Science-Elfid-Ceinge Advanced Biotechnologies, Naples, Italy

Objectives and study: Epigenetic mechanisms involving DNA methylation of the promoter region of Th1 and Th2 cytokine genes affect the course of cow's milk allergy (CMA). Preliminary evidence has implicated also the miRNome in the pathogenesis of allergy. To address this issue, we comparatively analyzed the miRNA profiles from peripheral blood mononuclear cells (PBMCs) of children affected by IgE-mediated CMA and in healthy children using a next-generation sequencing (NGS)-based approach.

Methods: PBMCs were isolated from peripheral whole blood samples using the Ficoll-Paque method. Total RNA was isolated from PBMCs samples using the Trizol Reagent kit. Small RNA library preparation was performed using the TruSeq Small RNA Sample Prep kit, according to the manufacturer’s indications. Eleven libraries were pooled in equimolar amounts. Sequencing 120 reactions were carried out using the Illumina MiSeq instrument.

Results: Among the miRNAs differently expressed between CMA children and healthy controls, 5 were up-regulated and 20 were down-regulated. Notably, mir193a-5p expression differed significantly between CMA patients at diagnosis and healthy controls. This miRNA could influence the expression of genes involved in interleukin-4 production. The expression of mir193a-5p did not differ between children who outgrew CMA and healthy controls.

Conclusion: Mir193a-5p is involved in the Th2 response in children affected by CMA. This miRNA could be an useful marker for CMA diagnosis and monitoring.
**Objectives and study:** We showed that extensively hydrolyzed casein formula containing the probiotic *L. rhamnosus* GG (EHCF+LGG) stimulates tolerance acquisition in children with cow milk allergy (CMA). We aimed to investigate tolerogenic immune and non-immune mechanisms elicited by LGG-derived CpG immunostimulatory DNA sequence (ODN ID35) and by the three most abundant β-casein-derived peptides contained in the formula.

**Methods:** Immune mechanisms were investigated in PBMCs from children with challenge-proven IgE-mediated CMA (all Caucasian; mean age 2.4, range 1-5 yrs) stimulated with beta-lactoglobulin (β-LG; 100µg/ml) in the presence or absence of ODN ID35 (1µM) for 24 h. Production and DNA methylation rate of IL4, IL5, IL-10 and IFN-γ were assessed by ELISA and HRM Real Time PCR, respectively. Non-immune mechanisms were investigated in human enterocytes (Caco-2) stimulated with ODN ID35 (1µM) and with β-casein-derived peptides (β-CN) 60-69, β-CN 110-113, β-CN 193-209 (500µg/ml). Cell growth was assessed by colorimetric assay (MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide); mucus production was analyzed by histochemistry after culture. Mucin 2 (MUC2) and tight junction proteins (zonulin and occludin) were analyzed by Real Time PCR using enterocytes RNA.

**Results:** PBMCs stimulation with ODN ID35 resulted in a significant decrease in IL-4 and IL-5 production and in an increase of DNA methylation rate of the two cytokines. Instead, the stimulation with ODN ID35 increased IL-10 and IFN-γ production but was unable to modulate DNA methylation rate of these cytokines. ODN ID35 stimulated mucus production and MUC2 expression in human enterocytes. The three β-casein-derived peptides regulated cell growth and MUC2; β-CN 193-209 alone was able to regulate zonulin and occludin expression.

**Conclusion:** Through a direct interaction with human cells, LGG DNA and β-casein-derived peptides regulates immune and non-immune mechanisms involved in tolerance acquisition.
Impact of Lactobacillus Fermentum CECT5716 on juvenile growth upon undernutrition

Pierre Poinsot¹, François LEULIER², Marie Caroline Michalski³, Melanie Mitchell², Valerie Sauvinet⁴, Armelle Penhoat⁵, Noel Peretti⁶

¹Hospices Civils de Lyon, Hépatologie, Gastro-Entérologie et Nutrition Pédiatrique, Lyon, France
²Institut Genomique Fonctionnelle de Lyon, Lyon, France
³Carmen Laboratory, Lyon, France
⁴Centre de Recherche En Nutrition Humaine Rhône-Alpes, Lyon, France
⁵Carmen Laboratory, Lyon, France
⁶Hcl Inserm, Université Claude Bernard Lyon 1, Faculté de Médecine Lyon-Est, Inserm U1060, Carmen Laboratory, Lyon, France

Objectives and study: 31 millions of children younger than 5 years old die every year of undernutrition. It represents a high cost for public health system and became a priority health politic axis in many countries. Specifically in paediatrics, under-nutrition has a real impact on children growth. After an early loss of weight, a decrease of the systemic growth rate leads to poor height for age in these children. Since a few years, the gut microbiota appears to be essential to maintain juvenile growth. Moreover, several strains of Lactobacillus plantarum have shown the capacity to resume this promoting-growth effect in mono-associated germ free drosophila. The Lactobacillus fermentum CECT5716 (Lf⁵⁷) is a strain isolated from mother’s breath milk. The aim of this work is to study whether Lf⁵⁷ could promote juvenile growth in a drosophila model and to know if this promoting-growth effect could be associated with an increased absorption of lipids on a Caco2/TC7 cells models.

Methods: Germ free (GF) drosophila yellow white larvae were incubated with Lf⁵⁷ in undernutrition conditions. After 7 days, the larvae size was measured and compared to GF and to two control strains known to have a promoting growth effect (Lactobacillus plantarum WJL and Lactobacillus plantarum Nizo21). The promoting effect of an infant formula supplemented with Lf⁵⁷ was assessed to. After 21 days, the pupae’s emergence was assessed to qualify the impact of Lf⁵⁷ on maturation time. Then Caco2/TC7 cells were incubated with Lf⁵⁷ and challenged with mixed bile salt micelles during 24 hours on trans-well to study its impact on baso-lateral lipid secretion.

Results: GF larvae were statistically shorter (2.5 mm; 1.4-4) than mono-associated larvae with Lf⁵⁷ (3.7 mm; 2.2-5.4; p < 0.0001). When Lf⁵⁷ was added to the infant formula (10⁸ CFU), this growth-promoting effect was conserved. This effect was qualified of intermediate compared to the control strains Lactobacillus plantarum WJL and Nizo21. The maturation time of GF larvae was statistically longer and was delayed by 1.6 days compared to the Lf⁵⁷ mono-associations (p=0.01). Moreover, Lf⁵⁷ statistically increases the uptake of acid oleic when Lf⁵⁷ was incubated in the optimal load with an up-regulation of MTTP and SRB1 gene transcription.

Conclusion: Lf⁵⁷ was qualified as an intermediate growth-promoting strain upon under nutrition in drosophila model. This effect was conserved when Lf⁵⁷ was added to an infant formula in appropriate concentration. Finally, the Lf⁵⁷ seems to have an impact on lipid absorption by Caco2/TC7 cells but which need to be precised.

Disclosure of interest: The research and Pierre POINSOT were funded by LACTALIS France for this work.
NUTRITION: Basic science

N-P-018

Advanced glycation end products in formula

Colin Prosser1, Elizabeth Carpenter1, Alison Hodgkinson2

1Dairy Goat Co-Operative Ltd, Hamilton, New Zealand
2Agresearch, Hamilton, New Zealand

Objectives and study: Advanced Glycation End-products (AGEs) are being investigated for potential risk of children developing diabetes (Mehta and Deeth, 2016, Comprehensive Reviews in Food Science and Food Safety, 15, 206-218) and food allergy (Smith, Masilamani, Li, Sampson 2016, Journal of Allergy and Clinical Immunology doi: 10.1016/j.jaci.2016.05.040). Nε-carboxymethyllysine (CML) is an example of an AGE formed between the amino acid lysine and lactose during heating of milk. Studies have shown that infants can absorb CML from infant formula (Sebekova et al 2008, Ann. N.Y. Acad. Sci. 1126: 177). Formation of CML reduces bioavailability of lysine and provides a means of monitoring the production of AGEs during manufacture of different milk formulae. As lysine residues are higher in whey compared to casein, it is anticipated that formula with added whey or hydrolysates of whey will have more CML than formula without whey adjustment.

Methods: The powdered formulas were sourced from within New Zealand. The formulas were made from cow or goat milk, both with or without whey adjustment. Formulas made with hydrolysates of cow milk derived whey proteins were also tested. Formulations made with intact cow milk or hydrolysates of whey were sourced from four different manufacturers, whereas formulations from goat milk were from one manufacturer. CML in all samples were measured using a commercial CML ELISA kit sourced from Echelon Biosciences (AGE:CML Competitive ELISA II, Cat# K3900s; Salt Lake City, Utah, USA) and used according to their instructions. Formulas were made up to 10% (w/v) for testing. CML levels were expressed per mg of total protein. Values were log-transformed for statistical analysis.

Results: CML concentrations ranged from 3 to 971 ng/mg protein in all formulas tested. Formulas made with goat milk were consistently lower than formulas made with cow milk. In general, CML was elevated in formula made with added whey proteins, irrespective of whether this was from goat or cow milk. CML in formulas made with hydrolysates of whey was also elevated compared to formula made with intact proteins.

Table: CML concentrations (ng CML/mg protein) in various types of formula

<table>
<thead>
<tr>
<th>Protein source</th>
<th>Casein:whey ratio</th>
<th>n</th>
<th>CML Mean (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow</td>
<td>40:60</td>
<td>15</td>
<td>146 (56,236)</td>
</tr>
<tr>
<td>Cow</td>
<td>80:20</td>
<td>11</td>
<td>46 (21,73)</td>
</tr>
<tr>
<td>Goat</td>
<td>40:60</td>
<td>8</td>
<td>17 (12,22)</td>
</tr>
<tr>
<td>Goat</td>
<td>80:20</td>
<td>33</td>
<td>9 (4,11)</td>
</tr>
<tr>
<td>Cow whey hydrolysate</td>
<td>NA</td>
<td>4</td>
<td>192 (49,732)</td>
</tr>
</tbody>
</table>

Conclusion: This study shows that there is a very large variation in CML concentrations across different formula types. Formulas containing added whey proteins resulted in higher concentrations of CML, irrespective of whether the whey was from goat or cow milk. This result is consistent with higher lysine residues in whey compared to casein. While the biological significance of the long-term intake by infants of AGEs is being debated, it would seem prudent to explore options for reducing AGEs in the production of formula for infants and young children.

Protein and fat content in commercial infant meals in Spain, Sweden and the UK

Juan Francisco Haro Vicente1, Maria Jose Bernal1, Sergio Roman2, Stefan Bodenstab3, Luis Manuel Sanchez-Siles3

1Hero Group, R+D Department, Murcia, Spain
2University of Murcia, Marketing Department, Murcia, Spain
3Hero Group, R+D Department, Lenzburg, Switzerland

Objectives and study: Several observational studies in infants (especially in non-breast-fed infants) and young children in Europe have shown some nutritional imbalances due to certain dietary habits and infant feeding practices. Among those imbalances, an excessive intake of protein (Hornell et al., 2013; Alles et al., 2014; Damianidi et al., 2016) and an insufficient fat intake have been reported (Fantino 2008; Goldbohm et al., 2016; Yuan et al., 2016). There is some evidence revealing that a high protein intake during the complementary feeding period is associated with an increased risk of later obesity. According to several scientific bodies, the contribution of fat to energy intake during the complementary food period should be between 35 and 40% (FAO 2010; EFSA 2010). Together with breastmilk and/or formula milk, infant meat/fish meals (whether commercial and/or homemade) are important sources of protein and fat during the complementary feeding period. This study aimed to compare the protein and fat contents of commercial infant meals (CIM) marketed in three different EU countries: UK, Spain and Sweden.

Methods: In this cross-sectional study, CIM targeted to infants under 18 months produced by the main infant food manufacturers in the UK, Spain and Sweden were analyzed. Nutritional data was collected from information shown in food labels and available on the manufactures’ websites. All CIM included in the study were based on meat or fish. Vegetarian meals were excluded. The analysed CIM represented more than 85% of the commercial infant food market in each country. All data was collected between August and October 2016. Protein was evaluated in g/100 Kcal and fat was evaluated in % contribution to the energy. Statistical analyses were performed using SPSS data software (v.18).

Results: A total of 320 CIM were analyzed in 3 countries (Table 1). Protein content in CIM marketed in Spain and UK were significantly higher than CIM marketed in Sweden (p<0.05). The fat content in CIM was significantly different among all countries (p<0.05).

Table: Protein and fat content in CIM in 3 countries. Data are expressed as mean (sd).

<table>
<thead>
<tr>
<th>Country</th>
<th>Nº products</th>
<th>Protein (g/100 Kcal)</th>
<th>% Energy from fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>130</td>
<td>4.67a (0.98)</td>
<td>28.50a (6.64)</td>
</tr>
<tr>
<td>Spain</td>
<td>103</td>
<td>4.65b (0.68)</td>
<td>30.76b (4.04)</td>
</tr>
<tr>
<td>Sweden</td>
<td>87</td>
<td>4.06c (0.57)</td>
<td>33.62c (3.44)</td>
</tr>
<tr>
<td>All</td>
<td>320</td>
<td>4.5 (0.83)</td>
<td>30.62 (5.53)</td>
</tr>
</tbody>
</table>

a,b,c values with different letter were significantly different at p<0.05

Conclusion: Our results suggest that infants being fed with CIM are exposed to different proportions of protein and fat depending on the country. In particular, CIM marketed in Sweden were lower in protein and higher in fat than the CIM marketed in the UK and Spain. Still, all analyzed CIM’s compositions were fully compliant with current EU legislation in force. The results of this study are useful to understand the different nutritional environments to which infants are exposed, depending on the countries they live in. These results could be used by the industry R+D departments and even
nutritional policy makers to improve the nutritional profile of CIM and therefore to improve the nutritional status of European infants.

Hornell et al. (2013), Food Nutr Res 57, 1–42.
Alles et al. (2014), Ann Nutr Metab 64, 284–293.
Fantino et al. (2008), Arch Pediatr 15, 446–455.
Goldbohm et al. (2016), Nutrients 8(7), 428.
EFSA (2010), EFSA Journal 8, 1461-1566.
FAO (2010), Fats and fatty acids in human nutrition.

Disclosure of interest: M.J. Bernal, J.F. Haro, S. Bodenstab, L.M. Sanchez-Siles: Conflict with Hero Group
Obesity associated sex differences in the metabolome of pre- and post-pubertal children

Sebastian Rauschert1, Marie Standl2, Olaf Uhl1, Elisabeth Thiering3, Irina Lehmann4, Berthold Koletzko1, Joachim Heinrich2, Christian Hellmuth1

1Dr. von Hauner Children's Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
2Institute of Epidemiology I, Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany
4Ufz - Helmholtz Centre for Environmental Research Leipzig, Department of Environmental Immunology, Leipzig, Germany

Objectives and study: According to the developmental origins of health and diseases hypothesis, metabolic alterations early in life might influence the development of diseases, such as obesity and diabetes, later in life. In addition, it has been described, that the sex differences in the development and severity of obesity and diabetes as risk factors for cardiovascular diseases are well described. Despite this fact, analysis of sex differences are highly underrepresented in metabolomics studies in children and adults. The aim of this study was to evaluate if there are differences in the disease related metabolome between male and female pre- and post-pubertal healthy German children and adolescents, participating in the 10 and 15 years follow ups of the GINIplus and LISApplus studies.

Methods: Metabolomics analysis on serum samples from the 10 and 15 year follow up of the GINIplus and the LISApplus studies has been conducted by using a liquid chromatography coupled to tandem mass-spectrometry approach to measure and quantify amino acids, acylcarnitines (acyl-carn), phospholipids (sphingomyelin (SM) and phosphatidylcholine (PC)), non-esterified fatty acids (NEFA) and citric acid cycle intermediates.

To analyse potential sex differences in the metabolome of the 10 and 15 years old participants, we applied multiple linear regression models (n= 897) with the child’s sex as predictor and single metabolite concentration as the outcome for both time points. Afterwards, we analysed the metabolites that differed between the two follow ups with regards to pubertal stage by principal components analysis and regression models. The significance level was set to a Bonferroni corrected p-value < 0.05.

Results: At the 10 year follow-up, acyl-Carn C14:1, Citric acid, Gly, NEFA C14:0, NEFA C14:1, NEFA C16:0, NEFA C16:1, NEFA C17:1, NEFA C18:1, Orn, Ser, SmA C32:2, SmA C34:2, SmA C35:2 and SmA C36:2 have been significantly different between males (lower concentrations) and females (higher concentrations). In the 15 year olds 48 metabolites differed significantly, including 6 amino acids, 2 acyl-carnitines, 3 LPCs, 6 non-esterified fatty acids, 4 PCaa, 11 PCae and 17 sphingomyelins - all significantly associated phospholipids mainly consisting of monounsaturated fatty acids. 42 metabolites were associated with sex at age 15 years, but not at 10 years. Of those, 27 metabolites increased with pubertal stage and 15 decreased. PCae C40:3 and SmA C31:1 have been significantly associated with higher pubertal stage after Bonferroni correction, although principal components analysis didn’t show components to discriminate between the different pubertal stages.

Conclusion: Sex differences in the metabolites that have previously been associated with obesity and insulin resistance already exist at an early pubertal stage at 10 years of age and are more prominent with advanced pubertal stage. This means, sex should be considered in mechanistic studies not only after, but also in the early stages of puberty. The metabolites we found in both time points of this analysis have been associated with obesity in adults in previous studies. Therefore, puberty seems to be a very sensitive window for changes in the metabolome that might already set the direction of the development of cardiovascular diseases.
Parents' concerns about infant weight and complementary feeding practices. An empirical nationwide study in Spain

Sergio Roman\textsuperscript{1}, Maria Jose Bernal\textsuperscript{2}, Juan Francisco Haro Vicente\textsuperscript{2}, Luis Manuel Sanchez-Siles\textsuperscript{3}

\textsuperscript{1}University of Murcia, Marketing Department, Murcia, Spain
\textsuperscript{2}Hero Group, R+D Department, Murcia, Spain
\textsuperscript{3}Hero Group, R+D Department, Lenzburg, Switzerland

Objectives and study: Parents' concerns about the child's risk of being overweight have received a lot of attention from scholars. Results from these studies reveal that parents' use of controlling and restrictive feeding practices is a consequence of parents’ concern about their child becoming overweight. This stream of research has been mostly conducted on samples of parents of children older than 2 years. The objective of this study is to analyze the influence of parents’ concerns of their infants’ (aged 6 to 18 months) weight on the introduction of complementary foods. Feeding practices at this stage of life are essential for the development of healthy eating habits in the long-term (Schwartz et al., 2011).

Methods: A research firm collected the data from their online national panel and randomly selected a final sample of 634 Spanish parents, responsible for feeding their infants (aged 6 to 18 months). A 2-item scale (e.g., “I am concerned about my child becoming overweight”; Cronbach’s $\alpha = 0.70$) adapted from Birch et al. (2001), was used to measure concern about weight. Items were measured on a 5-point Likert scale from 1 (lowest) to 5 (highest). In addition, parents were asked to indicate whether or not they were feeding their child with several complementary foods (Table 1). One-way analysis of variance (ANOVA) was used to analyze data with SPSS (v.18).

Results: The final sample for this study consisted of 634 parents ($\text{Mean}=34.7\pm4.1$; 77.9% female) of infants aged 6 to 18 months ($\text{Mean}=12.05\pm3.4$, 48.4% female). Parents concern in the overall sample was $2.95\pm1.12$. Results from the ANOVA (Table 1) revealed that concern about infant weight was significantly lower when infants were fed with complementary foods (in all cases).

Table: Mean differences in concern about weight (sd) associated with type of complementary food given to children (n=634)

<table>
<thead>
<tr>
<th>Type of complementary food</th>
<th>Child does not eat this food</th>
<th>Child eats this food</th>
<th>F-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant cereals</td>
<td>3.22 (0.94)</td>
<td>2.92 (1.13)</td>
<td>3.82*</td>
</tr>
<tr>
<td>Fruits</td>
<td>3.48 (0.89)</td>
<td>2.88 (1.13)</td>
<td>18.14**</td>
</tr>
<tr>
<td>Vegetables</td>
<td>3.40 (0.96)</td>
<td>2.86 (1.13)</td>
<td>18.75**</td>
</tr>
<tr>
<td>Yogurt</td>
<td>3.22 (1.07)</td>
<td>2.84 (1.12)</td>
<td>13.91**</td>
</tr>
<tr>
<td>Meat</td>
<td>3.42 (0.98)</td>
<td>2.80 (1.12)</td>
<td>35.05**</td>
</tr>
<tr>
<td>Cheese</td>
<td>3.06 (1.08)</td>
<td>2.77 (1.15)</td>
<td>10.48**</td>
</tr>
<tr>
<td>Fish</td>
<td>3.30 (1.00)</td>
<td>2.81 (1.14)</td>
<td>21.79**</td>
</tr>
<tr>
<td>Eggs</td>
<td>3.42 (1.01)</td>
<td>2.75 (1.16)</td>
<td>23.95**</td>
</tr>
<tr>
<td>Pulses</td>
<td>3.25 (1.04)</td>
<td>2.79 (1.18)</td>
<td>11.50**</td>
</tr>
</tbody>
</table>

Notes: 1 Analysis with fish only for children > 8 months (n=568); 2 Analysis with eggs and pulses only for children > 12 months (n=351); *(p<0.05); **(p<0.01).

Conclusion: Our results show that exposure of new (complementary) foods to infants is associated with parents’ concerns about their infant weight. In particular, increased dietary variety was significantly related to lower levels of concern. Exposure to new foods at early stages in life is critical in
the development of infants’ eating behavior, and does not necessarily lead to infants overweight. In fact, the restriction of complementary foods can provoke overall dietary nutrient inadequacy and suboptimal childhood growth and development (Siega-Riz et al., 2010). Health professionals could advice parents, who are concerned about their infant weight, about the many benefits of offering infants nutritionally adequate and varied complementary foods.

Schwartz et al. (2011), Appetite 57, 796–807
Siega-Riz et al. (2010), J Am Diet Assoc 110, S38-S51.

Disclosure of interest: M.J. Bernal, J.F. Haro, L.M. Sanchez-Siles: Conflict with Hero Group
Factors associated with parental pressure to eat among Spanish infants

Sergio Roman1, Juan Francisco Haro Vicente2, Maria Jose Bernal2, Luis Manuel Sanchez-Siles3

1University of Murcia, Marketing Department, Murcia, Spain
2Hero Group, R+d Department, Murcia, Spain
3Hero Group, R+d Department, Lenzburg, Switzerland

Objectives and study: Pressure to eat, a parental controlling feeding practice aimed at encouraging a child to eat more can impede the development of adequate self-control of eating in the child and provoke severe disordered eating symptoms (Ellis et al., 2016). Research on parental pressure to eat: has paid special attention to the consequences of this practice (neglecting its antecedents), and has mostly been conducted with parents of preschool and school-age children. Accordingly, the objective of this study is to explore if infant and parent variables (e.g., gender, age, parent’s concern about weight, etc.) as well as type of food given to children (homemade) have an influence on parents “pushing” their infants to increase their intake of foods. Feeding practices at this stage of life are crucial in determining children health, development and growth.

Methods: A research firm collected the data from their online national panel and randomly selected a final sample of 715 Spanish parents, responsible for feeding their infants (aged 0 to 18 months). Pressure to eat was measured with a 3-item scale (e.g., “I have to be especially careful to make sure my child eats enough”; Cronbach’s α = .63) from Birch et al. (2001). A 2-item scale (e.g., “I am concerned about my child becoming underweight”; Cronbach’s α = .73) from Baughcum et al. (2001), was used to measure concern about underweight. Two-tailed Pearson correlations and one-way analysis of variance (ANOVA) were used analysis data with SPSS (v.18). Demographic questions for both the infant and the parent were also included in the survey, as well as the type of food given to infants. Infant weight for age percentile was calculated using the WHO guidelines.

Results: The final sample consisted of 715 parents (Mage=34.5±4.2; 77.6% female) of infants aged 0 to 18 months (Mage=11.10±4.2, 48.3% female). Parental pressure to eat was moderately high in the overall sample (3.46±0.81). It was positively correlated to parents’ concern about infant underweight (r=0.49, p<0.01) and negatively to infant weight percentile (r=-0.10, p<0.01). Significant differences in pressure to eat based on ANOVA are shown in Table 1.

<table>
<thead>
<tr>
<th>Male infants</th>
<th>Female infants</th>
<th>6.66**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infant is also fed with homemade food</td>
<td>Infant is not fed with homemade food</td>
<td>7.16**</td>
</tr>
<tr>
<td>3.44 (.81)</td>
<td>3.77 (.80)</td>
<td></td>
</tr>
<tr>
<td>Male parent</td>
<td>Female parent</td>
<td>3.95*</td>
</tr>
<tr>
<td>3.58 (.70)</td>
<td>3.43 (.84)</td>
<td></td>
</tr>
<tr>
<td>Younger parent (&lt;30 years)</td>
<td>Older parent (30≥ years)</td>
<td>4.02*</td>
</tr>
<tr>
<td>3.60 (.74)</td>
<td>3.44 (.82)</td>
<td></td>
</tr>
<tr>
<td>Parent working full-time</td>
<td>Parent working part-time</td>
<td>8.37**</td>
</tr>
<tr>
<td>3.50 (.78)</td>
<td>3.27 (.76)</td>
<td></td>
</tr>
</tbody>
</table>

F-value * Analysis in this case with children > 6 months (n=634). *p<0.05; **p<0.01.

Conclusion: Our results are consistent to previous studies with older populations of children in that concern about underweight and weight percentile were significantly related to pressure to eat. Interestingly, our study adds to the literature by identifying other infant and parent relevant antecedents. In particular, higher levels of pressure to eat were found among female infants, male.
parents, and those who are younger parents and work full-time. Also, pressure to eat was lower when the infant was also fed with homemade food. A better understanding of the factors that lead to parental pressure to eat can help health professionals define more effective strategies when working with families.

Ellis et al. (2016), Appetite 97, 58-63.

**Disclosure of interest:** M.J. Bernal, J.F. Haro, L.M. Sanchez-Siles: Conflict with Hero Group
NUTRITION: Basic science

N-P-023

Naturally occurring sugar content in commercial infant fruit-based products in 4 countries. A nutritional benchmarking study

Luis Manuel Sanchez-Siles¹, Maria Jose Bernal², Sergio Roman³, Juan Francisco Haro Vicente², Stefan Bodenstab¹

¹Hero Group, R+D Department, Lenzburg, Switzerland
²Hero Group, R+D Department, Murcia, Spain
³University of Murcia, Marketing Department, Murcia, Spain

Objectives and study: Extant research shows food preferences formed in infancy shape later food preferences. Today’s infants are exposed to a much sweeter environment than any previous generation, which may ultimately lead to obesity and associated diseases. The preferences for sweetness in specific foods can be influenced by prior exposure to those foods early in life. During the first 2 years of life, commercial infant foods are widespread used in developed countries. As fresh fruits, commercial infant fruit-based products (CIFBP) are an important source of naturally occurring sugars, since most of the energy is coming from sugar. The objectives of this study were (1) to compare the naturally occurring sugar content of CIFBP marketed in United Kingdom, the United States, Spain and Sweden and (2) to compare them with naturally sugar content in fresh fruit.

Methods: In this cross-sectional study, CIFBP targeted to infants under 1 year and from the main infant food manufacturers in the UK, Spain, Sweden and US were analyzed. Nutritional data was collected from the information declared in the food labels and available on the manufactures’ websites. All products included were spoonable fruit purees with a minimum content in fruit of 95%. Fruit juices & fruit drinks and were excluded. The CIFBP included in the analyses represented more than 85% of the commercial infant food market in each country. For the total sugar content estimation in fresh fruit, we calculated the mean of the 15 most frequently used fruits and we collected the nutritional data from USDA database. All data were collected between August and October 2016. Sugar content was evaluated in g/100 g. Statistical analyses were performed using SPSS data software (v. 18.0). One-way ANOVA was carried out to test whether the four countries differed in their sugar content of the CIFBP selected.

Results: A total of 390 CIFBP were analyzed in 4 countries (Table 1). The naturally occurring sugar of the CIFBP marketed in Spain and US was significantly higher than in the other countries (p<0.05). The estimation of the mean naturally occurring sugar content in fresh fruit was 10.39 (2.94). CIFP marketed in US and Spain were significantly higher (21 % and 20 % respectively) than the mean content in fresh fruit (p<0.05).

<table>
<thead>
<tr>
<th>Country</th>
<th>Nº products</th>
<th>Sugar (g/100 g)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spain</td>
<td>59</td>
<td>12.45ᵃ (1.94)</td>
</tr>
<tr>
<td>Sweden</td>
<td>65</td>
<td>10.54ᵇ (2.17)</td>
</tr>
<tr>
<td>UK</td>
<td>79</td>
<td>11.03ᵇ (2.65)</td>
</tr>
<tr>
<td>USA</td>
<td>102</td>
<td>12.54ᵇ (2.79)</td>
</tr>
<tr>
<td>All</td>
<td>305</td>
<td>11.71 (2.62)</td>
</tr>
</tbody>
</table>

ᵃᵇ Values with different letter were significantly different at p<0.05

Table: Naturally occurring sugar in CIFBP in 4 countries. Data are expressed as mean (sd).
**Conclusion:** Our findings show that infants (under one year) have a higher probability to be exposed to a “sweeter environment” in Spain and USA, as compared to UK and Sweden, where CIFBP have a similar sugar content to the mean content in fresh fruits. These differences could be related to different use for sweeter fruits (e.g., banana or grape juice) vs. less sweet fruits (e.g., apple and red fruits). Sweetness exposure is linked to sweeter food preferences later in life. Thus, there is challenge and an opportunity for infant food manufactures to make the naturally occurring sugar content of their CIFBP more similar to the mean content in fresh fruit. The use of different, less sweet, fruit types would not only improve the range of flavors offered to consumers (infants and their parents), but also would have important positive public health implications.

**Disclosure of interest:** M.J. Bernal, J.F. Haro, S. Bodenstab, L.M. Sanchez-Siles: Conflict with Hero Group
NUTRITION: Basic science

N-P-024

NLRP3 inflammasome activation contributes to liver injury in a mouse model of parenteral nutrition

Jiang Wu1, Wei Cai2

1Xin Hua Hospital, Department of Clinical Nutrition, Shanghai, China
2Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Pediatric Surgery, Shanghai, China

Objectives and study: The pathogenesis of parenteral nutrition associated liver diseases (PNALD) remains unclear. Previous studies indicated a pathogenic role of the NACHT, LRR and PYD domains-containing protein 3 (NLRP3) inflammasome in mediating inflammatory responses after activation by a wide spectrum of pathogenic or danger signals. This study aimed to investigate the roles of NLRP3 and the underlining mechanisms in a PNALD mice model.

Methods: Thirty-two C57BL/6 mice (4-6 weeks old) were divided into 4 groups and administered intravenous 0.9% normal saline (control), parenteral nutrition (PN), intravenous 0.9% normal saline plus NLRP3 shRNA-transfected (control + shNLRP3), and PN plus NLRP3 shRNA-transfected (PN + shNLRP3) for 7 days. At the end of the experiment, blood biochemistry analysis and histologic examination of the liver were performed; inflammatory marker tumor necrosis factor-a (TNF-a), interleukin-1β (IL-1β) and IL-18 levels of serum and liver tissues; protein and mRNA expressions in the NLRP3-caspase-1 pathway were measured in liver tissues.

Results: PN mice showed impaired liver function and significant pathologic liver injury with elevated levels of serum endotoxin and intestinal permeability. These results were attenuated by transfection of Nlrp3 shRNA. Compared with control group, PN upregulated NLRP3, ASC and caspase-1 mRNA and protein expressions in both isolated Kupffer cells and liver tissues with elevated IL-1β and IL-18 levels. NLRP3 inhibition by shNLRP3 significantly reduced liver injury with down-regulation of both the mRNA and protein expressions within the related pathway in PN animals.

Conclusion: Our study found that NLRP3 inflammasome activation induced inflammation and liver injury in animals on parenteral nutrition, which helps to further elucidate the molecular mechanisms of PNALD and identify key molecular targets for future prevention and therapy.
Postprandial response of non-esterified fatty acids to meal challenge

Olaf Uhl¹, Hans Demmelmair¹, Berthold Koletzko¹, Christian Hellmuth¹

¹Dr. von Hauner Children's Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany

Objectives and study: In type-II-diabetes mellitus patients, non-esterified fatty acids (NEFA) are enhanced and are under suspicion as the underlying mechanism in lipid-induced insulin resistance. NEFA are released from subcutaneous adipose tissue in the fasting state to provide energy for muscle cells and liver metabolism, but in early childhood life there are no long term fasting periods. Thus lipid and energy metabolism in the postprandial state is important. We examined NEFA levels and their dynamics after a dietary challenge to assess individual post-prandial NEFA species time courses.

Methods: Nine healthy adults (3 males, 6 females) with a mean age of 33.4 years and a mean BMI of 22.4 kg/m² received a standardized breakfast comprised of a muffin, a chicken sandwich with mayonnaise and a glass of orange juice after overnight fasting. The meal contained 893 kcal with about 43% of the calories from carbohydrate, ~45% from fat and ~11% contributed by protein. The fat was composed of high amount of linoleic acid (59%). A basal blood sample and hourly postprandial blood samples were obtained until 7 hours after the meal. The NEFA concentrations were analyzed with liquid chromatography coupled to triple quadrupole mass spectrometry. Phospholipid and triacylglycerol fatty acid concentrations were determined by gas chromatography after separation of lipid fractions by thin-layer chromatography. Results were expressed relative to baseline and as area under the curve (AUC). Differences in AUC were tested by one-sample Wilcoxon-test. Significance was accepted at p<0.05.

Results: Triacylglycerol fatty acids peaked 2h after the breakfast and subsequently declined to the lowest values 7 hours after the meal. Fatty acids of phospholipids did not show any changes during the postprandial period. The AUC of 13 out of 44 determined NEFA species decreased significantly after ingestion of the meal, while 5 species increased (p<0.05). The lowest concentrations of the decreasing NEFA species were found between 1 and 2 hours postprandial, the baseline value of the median was reached at 6 hours postprandial and the highest levels were detected after 7 hours. The five increasing species were NEFA 18:2, NEFA 22:0, NEFA 24:0, NEFA 26:0 and NEFA 26:2 with AUC values of 6.8, 26.6, 18.4, 8.4 and 1.06 respectively. Furthermore, individual response curves could be seen between subjects and a negative association between the 2 hour relative differences to baseline and the total baseline NEFA was calculated (R=0.867).

Conclusion: With this trial, we could show that a postprandial time period of 6 hours is necessary to reach fasting state in respect to NEFA levels. After 7 hours, the values were higher than after overnight fasting, which could reflect a higher energy demand during the day due to physical activity. The increase of NEFA 18:2 could be explained by spill over effects of digested lipids, since the breakfast meal had high content of linoleic acid. However, the massive increase of NEFA 22:0, NEFA 24:0 and NEFA 26:0 could not be explained, but could be highly relevant, since their concentration was increased by factor of 7.0, 5.7 and 2.8, respectively and long-chained saturated fatty acids are potential metabolites to induce insulin resistance in paediatric population.
P38 MAPK pharmalogical inhibitor SB203580 alleviates total parenteral nutrition-induced loss of intestinal barrier function but promotes hepatocyte lipoapoptosis

Wei Cai

1Xinhua Hospital, School of Medicine, Shanghai Jiaotong University, Pediatric Surgery, Shanghai, China

Objectives and study: Our previous studies have provided evidence that p38 mitogen-activated protein kinase (MAPK) is involved in total parenteral nutrition (TPN)-associated complications, but its exact effects and mechanisms have not been fully understood. This study aimed to evaluate the roles of p38 MAPK inhibitor SB203580 in the TPN-induced loss of intestinal barrier function and liver disease.

Methods: A rodent model of TPN was used to analyze the roles of SB203580 in TPN-associated complications. Intestinal barrier function was evaluated by transepithelial electrical resistance (TER) and paracellular permeability in Caco-2 cells. The palmitic acid (PA) was used to induce hepatic lipoapoptosis in vitro. The lipoapoptosis was detected using Caspase-3/7 and lipid staining.

Results: In the present study, we showed that SB203580 treatment significantly suppressed TPN-mediated intestinal permeability in rats. SB203580 treatment significantly inhibited IL-1β-induced an increase in tight junction permeability of Caco-2 cells via repressing the p38/ATF-2 signaling. Unexpectedly, SB203580 treatment enhanced hepatic lipoapoptosis in the model of TPN. Palmitic acid (PA)-induced hepatic lipoapoptosis in human liver cells was significantly augmented by the SB203580 treatment.

Conclusion: We demonstrate that the p38 MAPK inhibitor SB203508 ameliorates intestinal barrier function but promotes hepatic lipoapoptosis in model of TPN.
Effects of early different feeding patterns on NRG4 expression in adipose tissue

Fan Yang¹, Yanyan Dai², Xiaonan Li¹

¹Department of Children Healthcare, Nanjing Children’s Hospital Affiliated to Nanjing Medical University, Nanjing, China
²Nanjing Medical University, Nanjing, China

Objectives and study: Early life nutrition plays an important part in regulating the metabolism in adulthood. Neuregulin 4 (NRG4), mainly expressed in adipose tissue, is involved in lipogenesis in hepatocytes. The present study aimed to evaluate the effects of postnatal different feeding patterns on NRG4 mRNA expression in various parts of adipose tissue and the relation with fatty liver occurrence.

Methods: Male Sprague-Dawley rat pup litters were adjusted to litter sizes of three (small litters, SL) or ten (normal litters, NL) on postnatal day 3. At postnatal week 3 (W3), the NLs were given standard chow or high fat diet, while the SLs were given standard chow, fish oil diet enriched with polyunsaturated fatty acids (SL-FO) or high fat diet (SL-HF) until postnatal week 13 (W13). Liver ultrasonography was performed in all rats of 13 weeks. In vitro, HepG2 cells were induced by oleate (OA) and then stimulated by recombinant NRG4 protein for 48h. The mRNA expression in white adipose tissue (WAT), Brown adipose tissue (BAT) and HepG2 cells was determined by real-time qPCR.

Results: 1. The weight gain of SLs was significantly more than those of NLs at W3 (P<0.05) and lasted to W13 (P<0.05), but there was no significant difference between NL and SL-FO group at W13(P>0.05). The body weight of SL-HF group was significantly higher than that of other groups(P<0.05). 2. At 13W, liver ultrasonography showed normal liver in NLs and mild fatty liver in SL group, and SLs with fish oil diet was similar to NLs. However, high-fat diet led to both NLs and SLs with fatty liver presence, and the latter was much more obvious and severe. 3. The expression of NRG4 mRNA in BAT was significantly higher than in WAT in all groups. Moreover, the expression of NRG4 mRNA in BAT was significantly lower in SL-HF group(P<0.05), but significantly increased in SL-FO group(P<0.01). The postweaning high fat diet did not affect the NRG4 mRNA expression in BAT of NLs and SLs. Changes of NRG4 mRNA expression in WAT were similar to those in BAT in different treatment groups. 4. In vitro, SREBP-1c and ACC mRNA expressions were up-regulated and intracellular lipid accumulation increased in HepG2 by OA induced, while they were reversed after treatment with recombinant NRG4 protein(P<0.05).

Conclusion: Overnutrition during the immediate postnatal period in rats leads to permanent effect on NRG4 expression in BAT and WAT and increases risk of fatty liver. Postweaning dietary intervention with fish oil could upregulate NRG4 expression and improve clinical outcomes, NRG4 regulates hepatic lipid synthesis by ErbB4 and SREBP-1c.
Outreach parental nutrition program: experience of a tertiary care hospital in Saudi Arabia

Badr Al Saleem¹, Nurah Al Banyan², Abdulrahman Al Hussaini¹, Ali Asery¹, sameh awwad², Amna Ahmed¹, khurram lone³, Suzan Al Obaid³, Sarah Alqahtani³, Elizaeth Mthombeni⁴

¹King Fahad Medical City, Pediatric Gastroenterology, Hepatology & Nutrition, Riyadh, Saudi Arabia
²King Fahad Medical City, Pharmacy, Riyadh, Saudi Arabia
³King Fahad Medical City, Clinical Dietitian, Riyadh, Saudi Arabia
⁴King Fahad Medical City, Nursing, Riyadh, Saudi Arabia

Objectives and study: Parenteral nutrition (PN) is a lifesaving therapy for patients with intestinal failure. However, it's a complex prescription therapy and associated with numerous complications, all of which increase morbidity and mortality. Long hospital stay and cost are a major challenges faced in our institution. Therefore, outreach parenteral nutrition (OPN) program involved multidisciplinary team was initiated to send the patients home over all Saudi Arabia. Currently this is the only program in Saudi Arabia.

Objectives: To report on current OPN program practice, and related obstacles. Also, to evaluate the impact of OPN program on hospital stay, cost and outcome, in tertiary care hospital in Saudi Arabia.

Methods: Retrospective chart review of patients with intestinal failure over a 13-year period was performed. Outcomes of patients followed up by outreach parenteral nutrition program (2008-2016) were compared to a historical data (2004-2007). Demographic, length of therapy, diagnosis, rehospitalization, catheter related infection, hospital stay and cost were compared.

Results: Twenty-five patients with intestinal failure were enrolled in the OPN program while the historical date was formed by 15 patients. Female were 65%. The mean (± SD) age was 5±4 years. The primary indication for OPN was Congenital tufting enteropathy 44%. The average hospital stay decreased from 870 days to 130 days. The cost per patient, per year for patients on OPN has decreased from about 400 thousands dollars to about 121 thousands dollars. Patients followed up by OPN program has less rate of catheter related infection, 0.4-0.6 per 1000 catheter day compare to 8.1 per 1000 day.

Conclusion: Team approach to manage nutrition support resulted in improvement in many aspects of patient care. Discharging patient who fit criteria of OPN significantly can reduce cost and rate of infections. Such program should be enhanced and implanted in other areas of Saudi Arabia.
Intravenous ferric carboxymaltose was effective and safe as treatment of iron deficiency in children < 2 years of age with intestinal failure

Ilektra Athiana1, Kajsa Waldenvik1, Mattias Paulsson1, Helene Engstrand Lilja2, Anna Lundberg3, Yigael Finkel1, Niklas Nyström1

1Uppsala University Children’s Hospital, Gastroenterology and Nutrition, Uppsala, Sweden
2Uppsala University Children’s Hospital, Paediatric Surgery, Uppsala, Sweden
3Uppsala University Hospital, Clinical Pharmacology, Uppsala, Sweden

Objectives and study: Children with intestinal failure (IF) are dependent on parenteral nutrition (PN) for normal growth and development. In our practice individualized PN contain iron-free pediatric trace element mixtures due to the high risk of compatibility problems when iron is added to multinutrient PN admixtures. Therefore, children with IF who are treated with iron-free PN are at risk for developing iron deficiency (ID). Furthermore, oral or enteral iron supplementation (IS) is generally avoided in children with IF because of the reduced absorptive capacity and increased risk for gastrointestinal side effects. Intravenous IS with ferric carboxymaltose (FCM) is a safe and effective treatment of ID in older children and adults, however there are no published reports on the effectiveness and safety of intravenous FCM treatment of ID in children < 2 years of age.

Methods: All 14 children with IF and ID who had been treated with intravenous FCM before 2 years of age at our tertiary center for pediatric IF, were retrospectively investigated. Ganzoni’s equation was used for calculating the FCM dose. Total Iron Deficit = Weight (kg) x (Target Hb – Actual Hb) (g/l) x 2.4 + Iron stores (mg). Serum levels of Hemoglobin (Hb), Mean Corpuscular Volume (MCV) and ferritin were measured before and 1-3 months after FCM treatment.

Results: All children received one or two doses of FCM administered as intravenous infusion. All children responded to FCM treatment with complete or partial normalization of biochemical markers for ID. No major or minor adverse events were reported.

Conclusion: In this retrospective study intravenous ferric carboxymaltose treatment for iron deficiency was effective and safe in children < 2 years of age with intestinal failure.
Body composition analysis of a group of Mexican children with ectodermic dysplasia using anthropometric parameters and bioelectrical impedance

Roxy Ayala, Ericka Montijo, Carola Duran, Alejandro Loredo, Flora Zarate, Roberto Cervantes, Jaime Ramirez

1Instituto Nacional de Pediatría, Gastroenterology and Nutrition, Mexico, Mexico
2Instituto Nacional de Pediatría, Pediatric Gastroenterology and Nutrition, Mexico, Mexico

Objectives and study: To describe the body composition of a group of Mexican children with ectodermic dysplasia using anthropometric parameters and bioelectrical impedance using the InBody 230® body composition analyzer. Compare results with anthropometric normal values for age, and to assess body composition with the machine’s reference values to better understand the nutritional status of these children.

Methods: A total of 24 children with clinical and genetic diagnosis of ectodermic dysplasia (20 boys, 4 girls), aged 4 to 18 years were assessed. Weight and height were measured using SECA 874 flat scale and a SECA 213 portable stadiometer respectively. Body composition parameters (total body water, lean body mass, fat body percentage) were measured with a body composition analyzer (InBody 230®). Anthropometric results were compared to age specific values and used to establish clinical nutritional status. Body composition results were compared to the Analyzer’s normal reference values.

Results: Of the total of patients studied, 83.3% (n=20) were male, aged 4-18 years old (mean 11.5). The range of measured Body Mass Index (BMI) was 11.5kg/m² to 26.1 kg/m² (mean 17.15kg/m²). The nutritional assessment, based on BMI/age relationship, was reported in a 54.17% (n=13) as normal, 16.67% (n=4) as underweight, 12.5% (n=3) as moderate malnutrition, 8.33% (n=2) as severe malnutrition, 4.17% (n=1) as overweight and 4.17% (n=1) as obesity.

The chart below shows the Body Composition values (total body water, total lean mass and body fat percentage) measured in the total of patients.

<table>
<thead>
<tr>
<th></th>
<th>AVERAGE</th>
<th>MEDIAN</th>
<th>MIN</th>
<th>MAX</th>
<th>INBODY Ref Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TOTAL BODY WATER</td>
<td>21.06Lt</td>
<td>19.95Lt</td>
<td>8.3Lt</td>
<td>36.5Lt</td>
<td>Low (n=18)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td></td>
<td>25% (n=6)</td>
<td>High</td>
<td>0% (n=0)</td>
</tr>
<tr>
<td>TOTAL LEAN MASS</td>
<td>15.3kg</td>
<td>14.1kg</td>
<td>4.6kg</td>
<td>28.1kg</td>
<td>Low (n=16)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td></td>
<td>21% (n=5)</td>
<td>High</td>
<td>13% (n=3)</td>
</tr>
<tr>
<td>BODY FAT PERCENTAGE</td>
<td>21.57%</td>
<td>20.05%</td>
<td>3%</td>
<td>46.60%</td>
<td>Low (n=2)</td>
</tr>
<tr>
<td></td>
<td>Normal</td>
<td></td>
<td>54% (n=13)</td>
<td>High</td>
<td>38% (n=9)</td>
</tr>
</tbody>
</table>

Conclusion: The data obtained from our results showed that anthropometric evaluation of children with ectodermic dysplasia is often not a good indicator of the child’s lean body mass and total water content. Most of the patients evaluated were classified with a normal BMI or underweight. However, when using body composition analysis, we observed most have low total lean mass and body water, showing the need of both tools in order to make accurate assessments and therapeutic nutritional interventions.
Body composition analysis has become more important in recent years as a tool to evaluate nutritional status. In children with specific pathological states, such as children with ectodermal dysplasia, this evaluation can allow us to develop techniques to better nourish patients in the future.
Blended diet for enteral feeding - identifying current practice in a paediatric community setting and developing a clinical tool to improve patient care

Charlie Bigwood

1Chailey Clinical Services, Nutrition and Dietetics, Lewes, United Kingdom

Objectives and study: A growing number of parents and carers in the UK have adopted blended diet (BD) via feeding tube due to perceived health benefits. Current guidance advises against the use of BD. However due to its increasing parental use, it is essential to develop guidelines to facilitate safer practice, support informed choices and work in partnership with parents who want to give their children BD. The setting was a specialist residential school for children with complex neurodisability which has onsite clinical services. The objectives of the study were to:

1. Identify the prevalence of BD usage
2. Explore parents’ views of perceived benefits
3. Develop a risk assessment and care planning tool for administering BD in a community setting

Methods: Case notes of all patients on the dietetic caseload were reviewed and informal interviews were conducted during clinic sessions with parents, carers and key stakeholders to find out:

- How many families have already adopted BD?
- What are the families giving?
- How are families providing BD?
- Why have families started using BD?
- What are the associated risks for BD?

Risks were also identified by reviewing current literature. Discussions with multidisciplinary team members facilitated the development of the clinical tool.

Results: Use of BD among families:

Of a total of 54 patients receiving enteral nutrition, 15 (28%) were receiving BD. Eleven received BD in conjunction with commercial formula, ranging from BD providing the majority of nutritional requirements to supplementary fluids such as fruit tea or probiotic drinks. Four exclusively used BD. Various methods of administration were used but all used bolus feeding. BD consistency varied from single cream to thick custard.

Reasons parents gave for using BD:

- Give more ‘naturally made’ feed
- Normalizing meal times
- Feeling more able to nurture their child
- Regaining control
- Ability to provide bespoke nutrition and cater for specific requirements
- Supporting their child to develop food preparation skills
- Management of symptoms such as reflux, vomiting, diarrhoea, poor weight gain and oral food aversion

Risks of using BD:

- Tube occlusion
- Higher risk of microbial contamination
- Compromised nutritional intake due to unknown concentration of puree
- Poor volume tolerance
- Initial weight loss

A risk assessment and care planning tool was developed as a result of this work.

Conclusion: A significant proportion of children were receiving BD and parents reported a range of perceived physical and psychological benefits. There was a lack of clear guidance and support available to families and carers. In order to resolve this, a clinical tool was developed. This ensured each patient had a detailed individualised plan to enable nursing and non-clinical staff to safely deliver BD in this community setting.
A handheld laser device to measure standing height and supine length in children

Charlotte Blank¹, Nawal Djedou², Yigael Finkel¹

¹Sachs Children’s and Youth Hospital, Gastroenterology and Nutrition, Stockholm, Sweden
²Sachs Children’s and Youth Hospital, Stockholm, Sweden

Objectives and study: There may be several barriers to measuring a child confined to a bed, including lack of equipment to measure supine length and medical and nursing factors. Height and supine length measurements are important for nutrition screening and calculating drug dosage according to body surface. We validated the utility of a small handheld laser device (LD) to measure standing height and supine length in 62 children; 2-6 years (n=20), 7-12 years (n=22) and 13-18 years (n=20). The children and their caregivers were asked to participate in the study at the time they arrived for elective or emergency visits or admittance to a ward.

Methods: The Bosch GLM 30 laser measuring device was initially designed for construction work. It operates by pressing one measure button and should be placed on a level, flat surface. According to the manufacturer, it has a measurement deviation of +/- 2 mm. To create a stable surface for the laser meter we used a perpendicular console that was placed at right angles to the wall and bed. Supine height (length) by LD: The children/adolescents were instructed to lie in the supine position on a bed and to lightly press the top of their head to the bed’s headboard and flex their feet to vertical position. They were then asked to straighten and face upwards. The angle console was placed against one foot sole and the children/adolescents were asked to roll over to the side without the sole of the foot being in contact with the angle console. The measurement was displayed on the LD by pressing twice on the measure button.

Results: Mean standing height by the LD differed by -0.01 -0.3 cm from the stadiometer height measurements (maximum difference was 1.4 cm). The difference was significant only in adolescents. The measurement of supine height (length) with the LD resulted in a significant greater mean height in all three age-groups (table 2). The maximum differences in measuring supine length between the LD and stadiometer were 2.6-3.7 cm.

Table:

Table 1 Differences in the standing heights between the stadiometer and LD.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>n</th>
<th>mean</th>
<th>SD</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6</td>
<td>20</td>
<td>-0.01</td>
<td>.46</td>
<td>-.80</td>
<td>1.20</td>
</tr>
<tr>
<td>7-12</td>
<td>22</td>
<td>-0.18</td>
<td>.73</td>
<td>-1.70</td>
<td>1.40</td>
</tr>
<tr>
<td>13-18</td>
<td>20</td>
<td>-0.33</td>
<td>.45</td>
<td>-1.20</td>
<td>.40</td>
</tr>
</tbody>
</table>

Table 2 Differences in the supine heights between the stadiometer and LD.

<table>
<thead>
<tr>
<th>Age (yrs)</th>
<th>n</th>
<th>mean</th>
<th>SD</th>
<th>min</th>
<th>max</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-6</td>
<td>20</td>
<td>-1.27</td>
<td>1.1</td>
<td>-3.50</td>
<td>.40</td>
</tr>
<tr>
<td>7-12</td>
<td>22</td>
<td>-0.95</td>
<td>1.21</td>
<td>-3.70</td>
<td>1.40</td>
</tr>
<tr>
<td>13-18</td>
<td>20</td>
<td>-1.21</td>
<td>.90</td>
<td>-2.60</td>
<td>1.00</td>
</tr>
</tbody>
</table>

Conclusion: The LD is simple to use and its feasibility may simplify measuring children on wards where stadiometers are not always available, and for supine height in bedridden children. Although significant differences were noted for supine length, these do not considerably influence BMI or bodysurface calculations.
MDT led jejunal feeding. Nurse and dietetic led pathways in the development of an MDT complex enteral feeding service

Michelle Brooks¹, Hazel Duncan², Fiona Cameron³, James Andrews⁴, Diana Flynn¹, Gregor Walker⁴, Vikki Garrick¹, Andrew Barclay¹

¹Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Glasgow, United Kingdom
²Royal Hospital for Children, Department of Nutrition and Dietetics, Glasgow, United Kingdom
³Yorkhill Children's Hospital, Glasgow, United Kingdom
⁴Royal Hospital for Children, Department of Paediatric Surgery, Glasgow, United Kingdom

Objectives and study: Pathways for the management of jejunally fed patients are often variable between medical and surgical sub-specialities due to the small numbers of specialist staff appropriately experienced to make management decisions, resulting in delays in treatment for patients who require care unexpectedly or out of hours. We describe the development of our nurse and dietetic led pathways which have improved our service by standardising care and creating a trouble-shooting guide for jejunally fed patients within our regional service.

Methods: A comparison of the service structure and pathways prior to, and after, appointment of a clinical nurse specialist into the complex enteral feeding service (August 2013), and the development of a multi-disciplinary complex enteral feeding clinic.

Results: Pre August 2013, patients for jejunal feeding or fundoplication were seen in isolation by either paediatric gastroenterology or paediatric surgical services from a variable referral pattern. Patients were seen in OPD a median of >2 occasions, with investigations coordinated in-between assessments, the decision for jejunal feeding was made in isolation by single clinician and feeding regimen, selected device (jejunal extension, GJ button), insertion method (endoscopic, radiological) feed escalation, length of stay and follow up all varied amongst clinicians. Responsibilities for unplanned tube troubleshooting were not clear. Key documents and nurse/MDT developed pathways are presented in table.
### Table:

<table>
<thead>
<tr>
<th>Document Description</th>
<th>Resulting systemic change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nurse-led clinic proforma (2014)</td>
<td>Nurse led history gives greater relevant clinical detail, complex investigations and medical manipulations all performed prior to single MDT clinic visit where decision on jejunal feeding made</td>
</tr>
<tr>
<td>Pre-clinic patient evaluation, Rx, investigation pathway</td>
<td></td>
</tr>
<tr>
<td>Jejunal tube placement flow chart (2014)</td>
<td>Standardisation of tube use, ability to make tube replacement decision in absence of primary clinician, improved ability to optimise stock use and nurse referral to radiology</td>
</tr>
<tr>
<td>Agreed pathway for decision on tube type and method placement of tubes</td>
<td></td>
</tr>
<tr>
<td>Jejunal pump feeding competency (2015)</td>
<td>Standardises training and assessment of jejunal competency of families prior to discharge</td>
</tr>
<tr>
<td>Jejunal feeding training pack</td>
<td></td>
</tr>
<tr>
<td>Jejunal tube trouble-shooter (2016)</td>
<td>Increased jejunal tube awareness and competence in non-specialist staff, patient specific information on clear referral pathway onto specialist staff</td>
</tr>
<tr>
<td>Actions for non specialist staff for blocked/displaced tubes and contacts</td>
<td></td>
</tr>
<tr>
<td>Jejunal tube de-escalation plan (2016)</td>
<td>Patient specific information with reference to short term tolerance of gastric clear fluids or feeds and urgency of tube replacement reduces unnecessary use of out of hours specialist services and allows patient discharge prior to jejunal tube replacement</td>
</tr>
<tr>
<td>Patient specific pathway for unplanned blockage or displacement</td>
<td></td>
</tr>
<tr>
<td>Jejunal starter feed pack (2016)</td>
<td>Complete feed escalation for new jejunal tubes reduces specialist input prior to discharge</td>
</tr>
<tr>
<td>Dietetic feed plan for new jejunal feeder</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** We present our nurse and dietetic led pathways which have developed, streamlined and standardised care, with greater clarity and ease of access to out of hours care. To our knowledge, this is the only complete package of such MDT pathways to be presented.
Long term outcome of intestinal rehabilitation in children over a period of 15 years - a single centre experience

Sarah Brown, Natalie Davies, Nicky Heather, Caroline Cole, Enda Smyth, RM Beattie, Akshay Batra

1University Hospitals Southampton NHS Trust, Paediatric Gastroenterolgy, Southampton, United Kingdom
2University Hospital Southampton NHS Trust, Paediatric Diетetics, Southampton, United Kingdom
3University Hospital Southampton NHS Trust, Paediatric Pharmacy, Southampton, United Kingdom
4Southampton Children’s Hospital, Paediatric Gastroenterology, Southampton, United Kingdom

Objectives and study: Home Parenteral Nutrition (HPN) is the primary treatment for patients with irreversible intestinal failure (IF). Outcomes for these patients have improved over recent years, attributed to provision of care via a multidisciplinary nutritional support team.

Aim: To describe the efficacy and safety outcome measures of Intestinal Rehabilitation (IR) in children over a period of 15 years.

Methods: Efficacy of IR was measured using the following parameters - growth and nutritional status, proportion of total enteral calories, dependence on enteral tube feeding (ETF), duration between initiation of PN and discharge home. Parameters used to measure safety of HPN included mortality, prevalence of intestinal failure associated liver disease (IFALD) and catheter related blood stream infections (CRBSI); and number of inpatient days because of complications of PN. Data was collected from patient notes and hospital records.

Results: 31 patients (17 females) received HPN between 2001 and 2016. 3 of these patients were administered PN as part of palliative care package therefore not included. 17 (60%) patients had short bowel syndrome (SBS), 2 of these had ultra-short bowel syndrome (bowel length <10cms. 6(21%) had chronic intestinal pseudo-obstruction (CIPO). 5 (18%) enteropathy (4 congenital, 1 immunodeficiency).

12 patients remain on HPN (2016) and 10 achieved enteral autonomy. 2 patients died because of complications of PN (1 on waiting list for liver and small bowel transplant) and 1 died post transplant. Among those on PN 3 patients were receiving less than 50% calories via PN, 7 were on 50-80% and 2 were on >80% PN calories. Growth and nutritional intake was assessed for patients being followed up at the time of the study (n=22). WFH (z-score for weight for height) was within 2 SD for all patients and HFA (z-score for height for age) was within 2 SD for all except 2 patients where it was -2.16 and -4.49. In only a third (8/22) of the patients enteral tube feeding was needed to support their nutrition and 20 patients ate a varied diet.

The median length of stay from initiation of PN to discharge home was 152 days (Interquartile range IQR 128). Median number of days of readmission into hospital because of complications of PN was 14 days (IQR 31). The commonest reason for readmission was CRBSI followed by blocked catheter.

Measures of safety of PN were compared between 2 defined periods, first 10 years (before establishment of NST) and subsequent 5 year
Table: Measures of safety of PN compared between 2 defined periods, first 10 years (before establishment of NST) and subsequent 5 years.

<table>
<thead>
<tr>
<th></th>
<th>2001-2011 (n= 13)</th>
<th>2011-2016 (n=15)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PN days</td>
<td>10,213</td>
<td>18,446</td>
</tr>
<tr>
<td>Mortality</td>
<td>2 (15%)</td>
<td>1 (7%)</td>
</tr>
<tr>
<td>IFALD</td>
<td>2 (15%)</td>
<td>2 (13%)</td>
</tr>
<tr>
<td>CRBSI/1000PN days</td>
<td>4</td>
<td>1.92</td>
</tr>
</tbody>
</table>

Conclusion: The number of patients being managed on HPN has increased with a reduction in morbidity and mortality. Most children achieved good linear growth and none of them were classified as obese. 20/22 current patients ate a varied diet and only a third of the patients needed support by enteral tube feeding.
Multicentre comparison of nutrient and food group intake among pediatric patients with cystic fibrosis in Europe

Joaquim Calvo Lerma1, Jessie Hulst2, Ine Claes3, Inês Asseiceira4, Mar Ruperto5, Carla Colombo6, Sandra Woodcock7, Mieke Boon8, Tiago Martins9, Maria Garriga5, Anna Bulfamante6, Sylvia Walet7, Celeste Barreto4, Christiane De Boeck9, Carmen Ribes Koninckx10

1Instituto de Investigación Sanitaria La Fe, Valencia, Spain
2Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
3University Hospitals Leuven, Leuven, Belgium
4Associação Per a la Investigación e Desenvolvemento Facultade de Medicina, Lisbon, Portugal
5Hospital Universitario Ramón Y Cajal, Madrid, Spain
6Cystic Fibrosis Center, Milano, Italy, Milan, Italy
7Erasmus MC - Sophia Children's Hospital, Rotterdam, Netherlands
8Universitair Ziekenhuis, Leuven, Belgium
9University Hospitals Leuven, CF Center, Leuven, Belgium
10La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

Objectives and study: Nutritional intervention in Cystic Fibrosis (CF) is based on recommendations of energy and nutrients intake. Its success relies also on individual food choices, and in clinical practice it is often difficult to make food items recommendations to achieve the nutrients goals. Responding to this need, MyCyFAPP Project aims at developing nutrition educational tools for patients’ self-management by means of a mobile APP. In the present study we aim to obtain information about the contribution of different food groups to overall macronutrient intake and to identify possible differences among centres participating in the project.

Methods: A cross-sectional study in 207 European CF patients (53% male, 91% pancreatic insufficient) aged 2-17 years old (mean age 8.3±1.2) followed-up at the CF centres of Leuven, Lisbon, Madrid, Milan, Rotterdam and Valencia. All participants completed a 4-day food record. Data were transferred to a calculation system, fed by country-specific nutritional composition databases. Nutritional information for all items included energy, protein, carbohydrates (CH), sugar, and fat (monounsaturated, polyunsaturated (PUFA) and saturated fatty acids (SFA)). Each food item was assigned to a food group according to common consensus classification criteria, e.g. milk & dairy, meat, etc. Results were expressed as mean % each food group contributed to the total macronutrient intake.

Results: 828 dietary records were obtained in which 4,554 meals were reported. Overall, the mean daily percentage of calories from fat, protein and carbohydrate were 34%, 14% and 51% respectively.

Milk & dairy followed by meat and processed products were the three food groups contributing the most to total fat intake in all centres. The highest contribution of a food group was found in Milan where milk & dairy represented 28.2% of the fat intake, followed by processed products in Rotterdam (26.3%) and Leuven (23.5%). In the Spanish and Portuguese centres, meat provided the highest contribution to fat intake (21.9-25.4%). These fat sources lead to a high SFA intake (>50% of the total fat). Oils had a major contribution in Milan, Valencia and Madrid (20-25%), and butters were more important sources of fat in the other centres (6.9-11.1%). Lipids from nuts, egg or fish had a negligible representation in all the centres, PUFA representing <25% of the total fat intake.

Meat products were the main source of protein in all the centres (25.1-38.0%) followed by milk (23.1-27.3%), and starchy products (14.0-27.3%). The 4th source was represented by processed products in Rotterdam, Leuven and Milan, and by fish in the others.
Starchy products contributed the most to CH intake in all the centres (36.5-46.8%), and the 2nd source was represented by processed products in the Northern centres, while milk & dairy contributed equally in the other centres. Fruit, vegetables and legumes contributed for <10%, 5%, and <1% respectively in all centres. Concerning sugar, in the southern centres the 1st source was milk (16.1–19.1%) and the 2nd were the processed products (8.1–14.0%), while an opposite trend was observed in the Northern centres.

**Conclusion:** The contribution of different food groups to overall macronutrient intake shows large variation between European CF centres. These findings may form the basis for more targeted dietary intervention and education, addressing specific imbalances related to regional particularities.
NUTRITION: Clinical nutrition

Use of specific infant formulas for minor digestive discomforts by Spanish paediatricians

Alicia Santamaria-Orleans\(^1\), Raquel de la Iglesia-Arnæz\(^1\), Alejandro Canals-Baeza\(^2\)

\(^1\)Laboratorios Ordesa S.L., Scientific Communication, Barcelona, Spain
\(^2\)Cs Alicante-Sta Faz., Pediatrics, Alicante, Spain

Objectives and study: Minor digestive discomforts are quite common during first months of life due to infant digestive immaturity. Several specific infant formulas destined for improving these situations can be found in Spanish market with nutritional modifications regarding to normal ones. The aim of the present study was to analyze clinical practice and recommendations regarding the use of infant formulas destined to minor digestive discomforts given by Spanish paediatricians and in particular, about 3 range of formulas within this category: [Blemil plus AR] (anti-regurgitation formula), [Blemil plus AC] (anti-colic formula) and [Blemil plus 1 and 2 AE] (anti-constipation formulas). Additionally, information about patients profile to whom the formulas were recommended as well as data about efficacy and satisfaction level were compiled.

Methods: Clinical practice questionnaires were facilitated to 198 paediatricians both in public and private centers, providing retrospective data on 742 infants to whom the studied formulas were recommended. Statistical analysis of the results was performed with the IBM SPSS Statistics 22.0 program, and Chi-square, Mann-Whitney and Kruskal-Wallis tests were applied.

Results: Paediatricians estimated that in infants younger than 6 months around 21% present infant colic, 14% constipation and 14% regurgitations. Colic and regurgitations decrease in infants between 6 and 12 months (5,7% and 6,6 respectively) and constipation remain similar (12,6%). 100% used specific formulas for minor discomforts and 45% recommended them when symptoms last for more than one week. 57% of paediatricians recommended infant massages in case of colic and 85% digestive infant teas. Between, specific infant teas and formulas for infant colic, 35% gave priority to infant formulas, 7% to infant teas, and 58% combined both kind of products. In regurgitation, positional therapy is less recommended by younger health professionals (p=0,015). Main characteristics for evaluating a formula were previous experience with products (8,9/10), tolerability (8,7/10) and clinical trials (8,6/10). For younger professionals the more important characteristic was a fast efficacy (p=0,091) and they also gave more relevance to parents suggestions (5.6 vs 3.6/10, p= 0,011). Of the 742 studied infants, 32% had infant colic, 31% constipation and 28% regurgitation, and the rest a combination of them. Average number of days to perceive an improvement in symptoms was different depending on the symptoms and the formula used (p=0,003), 5,9±5,3 days for regurgitations, 6,7±4,5 days for colic and 7,9±6,6 days for constipation. Average time of consumption of the specific products presented no differences between formulas, 3±4,1 months for [Blemil plus AC], 3,3±3,0 months for [Blemil plus AR] and 4,0±2,0 for [Blemil plus 1 and 2 AE]. In 94% of cases overall improvement was ranked as high, with differences between [Blemil plus AC] (90,6%), and [Blemil plus AR] (95,8%) and [Blemil plus 1 and 2 AE] (96,7%).

Conclusions:

- 100% of consulted Spanish paediatricians recommended formulas for minor digestive discomfort.
- Some factors of clinical practice and recommendations were influenced by paediatrician age.
- With specific formulas, average improvement of digestive symptoms took place during the first week.
- Satisfaction level with studied products was high (<90%) in all cases.

Disclosure of interest: Raquel de la Iglesia, Conflict with Laboratorios Ordesa S.L.
Alicia Santamaria, Conflict with Laboratorios Ordesa S.L.
N-P-039

Provision of Corstop at Bristol Royal Hospital for Children

Lisa Cooke¹, Alice Gibson²

¹Bristol Royal Hospital for Children, Nutrition and Dietetics, Bristol, United Kingdom
²Plymouth University, Dietetics, Plymouth, United Kingdom

Objectives and study: In February 2016, Bristol Royal Hospital for Children (BRHC) implemented the use of the Corstop© device in children who had been fitted with a gastrostomy or button, in the event of tube displacement. In the incidence of simple tube displacement, the stoma can close within a relatively short time period (90 to 120 minutes), which may necessitate an additional invasive intervention to form a new stoma. The Corstop© is designed to maintain the stoma patency until a trained person can insert a new feeding tube (in the community or hospital), thus avoiding a visit to the emergency department and an unnecessary procedure. A guideline was written and placed on the hospital document management system along with a parent/carer information leaflet and various sizes of Corstop© devices were ordered in.

Methods: Between February and June 2016 an audit was completed looking at all patients who had had a gastrostomy or button fitted and whether the guidelines were followed and the parent information given. A list of patients was provided from the community home enteral feeding team including all relevant discharges between this period. The dietetic and medical notes were checked to find the following information:

1. Did the child discharge with a Corstop©
2. Was the Corstop© given an appropriate size for the gastrostomy device insitu?
3. Was the patient/carer Corstop© training completed prior to discharge?
4. Was the patient information sheet for home given to the family prior to discharge?

All audit questions were based on the standards of care where the percentage required was 100.

Results: 33% of patients were given a Corstop© device on discharge. None were given the correct size. 17% of parents and carers had training provided. None were given the patient information leaflet. The provision of Corstop© is poorly documented within the medical and dietetic notes. The completion of patient training is low and the correct size of the device is not given. The responsibility of who gives out the device is unclear and there was no obvious place to record that the device, size and information for carers given within the notes.

Conclusion: Dissemination of the guideline with a clear pathway is required to ensure that all patients leaving the hospital with a gastrostomy or button have; training on how to use the Corstop© device, are given supporting written information and the correct sized device. A hospital wide action plan to include; the development of an electronic information form attached to the patients detailing the Corstop© standards and will be put into place through the enteral feeding strategy group to take these actions forward. A reaudit will be performed in early 2017.
Micronutrients in children receiving Home Parenteral Nutrition - a single centre experience

Sian Copley1, David Derry1, Karen Hartley1, Karen Thomson1, Joanne Pena1, Ruth Stanley1, Elizabeth Renji1, Susan Bunn1, Julian Thomas1, Maureen Lawson1

1Great North Children's Hospital, Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom

Objectives and study: Parenteral nutrition (PN) is a well-established mode of nutrition for neonates, infants and children. In addition to providing calories it provides micronutrients required for the prevention of disease and for normal physiological functioning.

Aim: We retrospectively reviewed the micronutrients in 14 children receiving bespoke home PN from our unit.

Methods: Serial results of Zinc Copper Selenium Manganese Vitamin A,E,B12 and Folate were retrospectively reviewed over a 2 year period. Children were divided into two groups - 7 children requiring 100% of their estimated energy requirements (EER) as PN (Group 1);7 children requiring an average of 70% of EER as PN (Group 2). All children requiring home PN for at least 2 years were included in the study. Children were excluded from the study if intestinal failure requiring PN was primarily due to an inflammatory cause or were noted to have abnormal liver function tests at the time of sampling.

Results:

Group 1
Vitamin A and E levels were noted to be higher than the upper limit of the reference range in children receiving greater than 85% of the recommended dose of fat soluble vitamins.
Vitamin B12 was uniformly raised above the normal reference range and vitamin D levels were uniformly low.
Three children were noted to have high manganese levels at a period when they were noted to have recurrent central line sepsis, with manganese normalising on resolution of the central line sepsis.
Two children were noted to have low copper levels associated with normal zinc levels. In one child low copper levels despite supplementation to 150% of estimated requirements resulted in neutropenia, which resolved on changing the amino acid source from Vaminolact to Aminoven.

Group 2
EER from PN ranged 19% to 85%.
Vitamin B12 and folate were within the normal reference range in children receiving 50% or less of their EER as PN.
Vitamin D levels were uniformly low and required supplementation.
Vitamin A and E levels were within the reference ranges for age in children receiving less than 70% of requirement in PN.
One child was noted to have a persistently raised manganese level despite removing manganese from his PN; this was thought to be due to manganese in his enteral nutrition providing 1.5mg/day.

Conclusion: Aside from one child presenting with neutropenia all children remained well and asymptomatic.
Vitamin D was uniformly low in both groups and required additional supplementation.
Changes in Manganese levels noted require further investigation.
Uniformly high vitamin E levels in children may be attributed to the presence of Vitamin E in SMOF used as the lipid source in this group of patients.
Current recommended dosing of micronutrients in children receiving parenteral nutrition does not ensure optimal blood levels.
Frequent and meticulous monitoring of micronutrients in children receiving parenteral nutrition is essential to prevent side effects from over or under dosing.
Growth and nutrient intakes of children with food allergies

Enza D’Auria¹, Elvira Verduci², Carlotta Lassandro², Giuseppe Banderali², Silvia Dalmazzone³, Gian Vincenzo Zuccotti⁴

¹Vittore Buzzi Children’s Hospital. University of Milan, Paediatric Department, Milan, Italy
²San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
³San Paolo Hospital, Department of Health Sciences-University of Milan, Pediatrics, Milan, Italy
⁴V. Buzzi Children’s Hospital University of Milan, Paediatric Department, Milan, Italy

Objectives and study: Growth impairment has been reported in children with food allergy (FA). However controversial data exist about dietary intakes in these children.

The aim of the present study was to assess the food intakes and anthropometry of children with food allergies (FA) on elimination diets compared to children with no FA (controls).

Methods: Fifty-six children with FA (mean age [SD] 5.6[4.1] years) were age and sex matched with 56 children with no FA. Anthropometry was assessed using measurements of weight, height, body mass index (BMI) and Z scores for weight-for-age, height-for-age and BMI, respectively. Nutrient intakes assessment was based on a 3-day diet record. Children were categorized into five classes according to age (0-1 years, 1-3 years, 4-7 years, 7-10 years, >10 years, respectively).

Results: Children with FA had height for age z-score and BMI z-score lower than controls (p= 0.032 and p= 0.009, respectively). Children allergic to two foods or more exhibited lower height for age z-score than children with allergy to one food without reaching statistical significance (-0.067 vs -0.060; p= 0.058). Children with cow’s milk allergy and children with nuts’ allergy both were shorter than controls (p= 0.037 and p= 0.047, respectively).

Energy and protein intakes were lower in children with FA aged 1-3 years than controls (p= 0.023 and p= 0.015 respectively), while carbohydrate intake was higher in FA children aged 1-3 years (p = 0.049), 4-7 years (0.011) and 7-10 years (p= 0.028) than controls.

Calcium and iron intake were lower in children with FA, especially in children aged 4-7 years (ρ = 0.03 and ρ= 0.04, respectively). Children aged 4-7 years showed major impairments in macro and micronutrient intakes (lipids ρ=0.034, calcium ρ=0.031, iron ρ=0.046, potassium ρ=0.041) being the group with the highest number of children with cows’ milk allergy.

Conclusion: Lower nutrient intakes may explain the growth impairment of children with FA, even if the effect of the disease itself can not be excluded. Nutritional evaluation is essential for the follow-up of children with FA.
The impact of banana on stool composition

Thierry De Vreker¹, Koen Huysentruyt², B Danau³, Yvan Vandenplas⁴

¹Universitair Kinderziekenhuis Brussel, Kindergastro-Enterologie, Brussels, Belgium
²Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
³Erasmus Hoge School, Brussels, Belgium
⁴Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives and study:

The incidence of constipation is 1-30 % in toddlers and children. Although banana is considered to increase stool consistency, and therefore aggravate constipation, not any study has been undertaken till now on the impact of banana on stool consistency. The aim was to evaluate the effect of banana consumption on stool consistency in 1 - 2.5 year old toddlers.

Methods:

23 parents of the hospital day care center signed the informed consent. During a one-week run-in period (normal intake), the staff of the day-care center made photos of each stool. During the two weeks intervention period, the dietary intake was the same plus one extra banana per day. Again, the staff took a picture from each defecation. All photos were made anonymous. Nine health care providers (pediatric gastro nurses, dieticians and doctors) scored each photo according to volume and consistency, unaware of the photo was from the run-in or intervention period.

Results: No parent spontaneously complained about increased stool consistency during the consumption of banana.

Table: Evaluation of stool volume and consistency during the study:

<table>
<thead>
<tr>
<th>Volume</th>
<th>Week 1</th>
<th>Week 2</th>
<th>Week 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>&gt; 50 % diaper</td>
<td>46 %</td>
<td>27 %</td>
<td>19 %</td>
</tr>
<tr>
<td>25-50 % diaper</td>
<td>43 %</td>
<td>40 %</td>
<td>67 %</td>
</tr>
<tr>
<td>&lt; 25 % diaper</td>
<td>11 %</td>
<td>33 %</td>
<td>14 %</td>
</tr>
<tr>
<td>Consistency</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard</td>
<td>11 %</td>
<td>20 %</td>
<td>0 %</td>
</tr>
<tr>
<td>Formed</td>
<td>30 %</td>
<td>53 %</td>
<td>81 %</td>
</tr>
<tr>
<td>Soft</td>
<td>53 %</td>
<td>27 %</td>
<td>11 %</td>
</tr>
<tr>
<td>Watery</td>
<td>6 %</td>
<td>8 %</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: In contrast to parental belief, daily consumption of a banana does not induce hard stools, and even seems to soften the stools.
Consumption of energy drinks in Belgian secondary schools

Thierry De Vreker¹, Koen Huysentruyt², B Spruyt³, Yvan Vandenplas⁴

¹Universitair Kinderziekenhuis Brussel, Kindergastro-Enterologie, Brussels, Belgium
²Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
³Erasmus Hoge School, Brussels, Belgium
⁴Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives and study: Energy drinks (ED) contain guarana, taurine and a high amount of carbohydrates and caffeine. Children and adolescents are populations at risk for adverse effects. The aim was to evaluate the consumption of ED in a population of Belgian 11-19 year-old school children and inquire for the motives for ED consumption.

Methods: An anonymous questionnaire was sent to 1260 children and adolescents. Descriptive analyses were performed using R, $\chi^2$-testing was done to determine differences in proportions.

Results: The mean (SD) age of the 1252 respondents (47.5% male) was 10.5 (1.7) years; 729 attended general (ASO), 225 technical (TSO), 190 vocational/art (BSO) and 97 special secondary education (BuSO). ED were consumed by 58.2% of the population, with 189 (15.2%) consuming ED’s at a regular or daily basis. The proportion of children that consumed ED differed according to the type of school (lowest in ASO, 49.7% and highest in BSO, 75.8%; $p<0.001$), presence/awareness of rules forbidding ED at school ($p=0.002$) and sex (higher in boys (65.4%) vs girls (51.8%), $p<0.001$). Only 29.5% of the respondents were aware of a formal prohibition of ED at their school. The mean (SD) age of consumers was higher ($p<0.001$) than that of non-consumers (15.3 (1.7) vs 14.7 (1.6) years). ED’s were acquired at home in 15.7% of the total population. The most common reasons among consumers for ED consumption were good taste (554, 76.4%), stay awake/have more energy (263, 36.3%) and better concentration (65, 9.0%). Reasons among non-consumers not to consume ED were no need for ED (370, 71.2%), unhealthy (230, 44.2%) and sportive personality (102, 19.6%).

Conclusion: More than half of the teenagers consume ED, with 15% consuming ED’s at a regular or daily basis. Motives for drinking ED are the taste, optimizing concentration and stay awake at school, while motives for not drinking ED are the unhealthy aspect, not feeling the need and being sportive. Information campaigns, with an active role for schools, are needed to inform teenagers for the potential adverse effects of ED’s.
Feed choice when patients are jejunally fed

Hazel Duncan¹, Michelle Brooks², James Andrews³, Diana Flynn², Fiona Cameron⁴, Gregor Walker³, Elaine Buchanan¹, Andrew Barclay²

¹Royal Hospital for Children, Nutrition & Dietetics, Glasgow, United Kingdom
²Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology and Nutrition, Glasgow, United Kingdom
³Royal Hospital for Children, Department of Paediatric Surgery, Glasgow, United Kingdom
⁴Yorkhill Children's Hospital, Glasgow, United Kingdom

Objectives and study: There is limited current evidence regarding optimal feed choice when initiating jejunal feeding in paediatrics. Concerns include concentration, osmolality and the protein base of feeds which may affect tolerance. Most recent evidence suggests peptide based feed is best tolerated however current practice varies. The aim of this study is to review feed type and enteral tolerance when initiating jejunal feeding in our centre.

Methods: Patients who commenced jejunal feeding between April 2015 and November 2016 were identified from a prospectively recorded database. The choice of feed commenced, any changes made and clinical outcomes were retrospectively reviewed from electronic records.

Results: 18 patients (12 male, median age 2.9yrs, range 0.4-15.8yrs) were identified. Prior to jejunal feeding 13/18 had a gastrostomy in situ the remaining 5/18 had nasogastric tube. Jejunal feeding was employed for foregut dysmotility associated with neurological impairment in 10 patients, isolated foregut dysmotility in 6 patients and in 2 patients with significant cardiac anomalies where gastrooesophageal reflux (GORD) was a concern. 15/18 had PEGJ for jejunal feeding with the remaining 3/18 having NJT. 12/18 (66%) were already established on a whole protein feed prior to jejunal feeding. Of this group, 5/12 (42%) were established on 1kcal/ml feed and the remaining 7/12 (68%) on 1.5kcal/ml feed. 5/18 were established on peptide based feed and 1/18 on elemental feed whilst being fed gastrically. Once jejunal feeding was established 8/18 (44%) of patients tolerated a whole protein feed, 62% (5/8) of these tolerated a 1kcal/ml feed, but tolerance of 1.5kcal/ml feed reduced to 38% (3/8). 3/18 required a feed change to peptide based feed due to tolerance issues which included pain and loose stools. 1/18 remained on an elemental feed. The patient group most likely to require a change to peptide feeds were those with isolated foregut dysmotility concerns (table).

Table: Peptide feeds per patient sub group

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Numbers</th>
<th>% Requiring Peptide Feeds</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Before jejunal tube</td>
</tr>
<tr>
<td>Complex neurodevelopment</td>
<td>10</td>
<td>30%</td>
</tr>
<tr>
<td>Isolated GI dysmotility</td>
<td>6</td>
<td>17%</td>
</tr>
<tr>
<td>Cardiac with GORD</td>
<td>2</td>
<td>50%</td>
</tr>
<tr>
<td>All Patients</td>
<td>18</td>
<td>28%</td>
</tr>
</tbody>
</table>

Conclusion: The majority of patients in our study tolerated their established feeding formula following initiation of jejunal feeding. Patients with GI motility concerns were the group most likely to require a change to peptide feeds. Following this audit the clinical practice within the unit is to recommence patients on their pre-existing feed when starting jejunal feeding. We would consider a change to peptide based feed only if there were clinical concerns regarding tolerance.
Changes in body composition following hematopoietic stem cell transplantation in children who develop acute graft-versus-host disease

Yi Feng¹, Li Hong¹, Liya Pan¹, Liyuan Shen¹, Panpan Chang¹

¹Shanghai Children's Medical Center, Clinical Nutrition, Shanghai, China

Objectives and study: This study investigated changes in anthropometric parameters and body composition following hematopoietic stem cell transplantation (HSCT) in children who developed acute graft-versus-host disease (aGVHD).

Methods: Children receiving HSCT were recruited from Shanghai Children's Medical Center between January 2012 and December 2012, and anthropometric parameters and body composition were measured. Children were divided into the aGVHD group and non-aGVHD group. Body mass index Z-scores (BMI-Z), arm muscle area index (AMAI), fat mass index (FMI), and fat-free mass index (FFMI) were compared between the two groups on the day of transplantation and 30, 60, and 100 days after transplantation. The influences of total body irradiation, use of glucocorticoid, mucositis, and infection on anthropometric parameters and body composition were further evaluated after HSCT.

Results: In the aGVHD group, the absolute rate of change in BMI-Z after HSCT increased significantly compared to that on the day of transplantation, and the absolute rate of change in BMI-Z at 30 days after HSCT was significantly different from that in the non-aGVHD group (–23.8% vs. 55.9%, respectively, *P* = 0.008). In the aGVHD group, AMAI decreased continuously from the day of transplantation to 100 days after HSCT and FFMI in the aGVHD group was lower than that of the non-aGVHD group, but there were no significant differences between the aGVHD group and the non-aGVHD group. At 60 and 100 days after HSCT, FFMI in the aGVHD group was significantly lower than that of the non-aGVHD group (H60: 12.5 ± 1.1 kg/m² vs 13.7 ± 1.6 kg/m², respectively, *P* = 0.014; H100: 13.0 ± 1.1 kg/m² vs. 13.9 ± 1.2 kg/m², respectively, *P* = 0.032). Analysis with a generalized estimating equation showed that the change in body composition in the aGVHD group was affected mainly by the use of glucocorticoid and mucositis.

Conclusion: In aGVHD children, the body composition changes in the acute phase of HSCT and is characterized by reductions in lean body mass and increases in adipose tissues. The use of glucocorticoid and mucositis are two important factors that affect body composition after HSCT.
**Principal gastrointestinal manifestations in overweight and obesity patients in a gastroenterology, hepatology and nutrition paediatric center**

Wilson Daza¹, Silvana Dadan¹, Michelle Huguera¹, Emilia Prieto¹

¹Gastronutriped, Bogota, Colombia

**Objectives and study:** This study sought to assess the motives for consultation and the gastrointestinal manifestations referred by patients and relatives of overweight and obesity patients attending GASTRONUTRIPED between January 2009 and June 2015.

**Methods:** Descriptive retrospective study, conducted in a gastroenterology, hepatology, and paediatric nutrition center in Bogotá, GASTRONUTRIPED. Clinical charts and the database of all patients who attended consultation from 2009 to 2015, selecting patients with overweight and obesity diagnosis. Weight and height were taken by the paediatric gastroenterologist and the nutritional state was interpreted by the nutritionist, based on data yielded by the Anthro and Anthro Plus software for children <5 and >5 years of age, respectively. Descriptive analysis of the data was performed with Epi Info® software v. 7.1.3.

**Results:** In total, 222 participants were included, aged between 1 and 223 months, with a mean of 71 (RIQ 19-124); 53.1% corresponded to females, 60.3% were the first child. With respect to the reason for consultation, only 23.4% consulted due to overweight/obesity, the rest consulted for other motives, like abdominal pain (18.5%) and constipation (12.2%). As pathological antecedents, 17.6% referred gastroesophageal reflux. The principal gastrointestinal diagnosis was constipation in 59.9%.

**Conclusion:** Gastrointestinal diseases may be among the motives that induce relatives of overweight-obesity children to consult with the specialist more than due to their overweight-obesity condition. During pediatric controls, patients and/or relatives must be warned of their nutritional state, inquiring about eating habits, assessing risk factors for overweight and obesity, and providing general recommendations on healthy eating habits and life styles, as prevention measures against some gastrointestinal diseases that can be associated to obesity.
Peripherally inserted central catheters (PICCs) in home parenteral nutrition

Marta German¹, Carmen Gallego², José Manuel Moreno³

¹‡12 de Octubre* Hospital, Infant Nutrition Unit, Madrid, Spain
²‡12 de Octubre* Hospital, Pediatric Radiology Unit, Madrid, Spain
³‡12 de Octubre* Hospital, Infant Nutrition Unit. Comité DE Nutrición Aep, Madrid, Spain

Objectives and study: Home parenteral nutrition (HPN) has become a common therapy, with tunneled central venous catheters (CVCs) being preferred for its administration. In the last few years some cases about the use of peripherally inserted central catheters (PICCs) in adult patients on HPN have been published. Nevertheless, in the pediatric population there is little experience with long-term, daily use of these catheters. The objective of the present study is to describe the experience of a third level hospital with the long-term use of PICCs in children with HPN over the last 6 years.

Methods: Over a six-year period (2010-2016), we found 10 patients with HPN delivered by a PICC. The following data was collected by reviewing their medical records: sex, age, diagnosis, PN indication, total number of PICCs placed per patient, department responsible for its placement, location of PICCs, size, model and number of lumens, number of days each PICC was in place, reason for removal, and PICC-related complications (occlusion/thrombus, infection, breakage). Data was analyzed using SPSS (version 20; SPSS Inc, Chicago, IL) and reported as medians with range for continuous variables and with frequency and percentages for categorical data. The rates of catheter-related complications were recorded as the number per 1000 catheter days.

Results: Over the study period 10 patients received HPN through a PICC. The PN indications in these patients were: 4 short bowel syndrome, 2 severe chronic diarrhea, 2 motility disorder, 1 malnutrition secondary to immunodeficiency and 1 pancreatic fistula. 7 (70%) were males. The median age at the time of the initial PICC insertion was 2.95 years (0.16-15 years). 19 episodes were collected, with a median duration of 80 days (10-717 days); accounting for a total of 2201 catheter days. The most common reason for choosing a PICC as a catheter was the previous repeated loss of tunneled CVCs in 5 patients, followed by need for PN for a short period (3 patients) and preference by the interventional radiologist (2 patients). In 84.3% of the cases, the PICC was placed by the interventional radiologist and in 2 cases (12.5%) by the anaesthetist. The most common location was the basilic vein, in 15 episodes (78.95%), followed by the femoral vein, in 4 (21.1%). All of the implanted PICCs were composed of polyurethane, being [Cook Medical, Bloomington, IN] and [Bard Medical, Covington, GA] the most commonly used models. All PICCs were either 3-F or 4-F; single or double-lumen. The median number of PICCs placed per patient was 2 (1-4 PICCs). The reasons for PICC removal were infection (36.8%), the catheter was no longer required (31.6%), occlusion/thrombosis (10.5%) and mechanical complications (10.5%). In one case there was accidental exit and currently 1 PICC is still being used. The overall incidence of catheter-related infection was 3.2/1000 catheter days, with a catheter-related bloodstream infection (CRBSI) rate of 1.4/1000 catheter days and an exit-site/tunnel infection rate of 1.8/1000 days. In three episodes treatment with taurolidine line lock was performed as prophylaxis. The overall incidence of occlusion was 0.9/1000 catheter days and 4 PICCs broke during the study period.

Conclusion: PICCs offer a valid alternative for HPN in pediatric patients, being specially indicated for patients with previous problems related to permanent venous access or need for PN for a short period.
Is undernutrition of hospitalized children correctly screened and managed?

Marie JAMIN¹, Dominique Guimber², Ley Delphine³, Stephanie Coopman², Dominique Turck³, Frédéric Gottrand², Laurent Michaud², Nathalie Wizla⁴

¹Clinic, Lille, France
²Jeanne de Flandre Children's Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases, Lille, France
³Chru, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Reference Center for Congenital and Malformative Esophageal Diseases., Lille, France
⁴Clinic Jeanne de Flandre, Lille, France

Objectives and study: Although prevalence of undernutrition remains high about 10% of the hospitalized children, there is currently few data about its recognition and treatment. The objective of this study was to assess screening and management of undernutrition in a tertiary university children hospital.

Methods: This is an observational, retrospective and monocentric study of 460 hospitalized children at the pediatric cardiology and surgery departments, between January and February 2015. Anthropometric data were recorded to define undernutrition (BMI<-2SD). In children presenting with malnutrition, medical files were reviewed to check if undernutrition was diagnosed (including final coding in the hospital data system), if intervention was started (nutrition changes or supplement, enteral and/or parenteral nutrition, call for the nutritional team) as well as billing of the hospitalization to the medical care system.

Results: In 42% of children height was not measured, so that diagnosis of undernutrition could be missed. In the 266 in whom weight and height were both available (mean age 6.3±5.5 years; length of stay 4.2±4.6 days) 33 children (12.4%; 11% in surgery, 17% in cardiology departments) were undernourished (mean age 5.5±5.4 years, therefore younger than the total population; mean BMI 13.8±1.2 kg/m²). Diagnosis of malnutrition and nutritional intervention were performed in only 8 children (24%), while 76% remained undiagnosed.

When looking at coding in the medical information system, missing diagnosis of undernutrition accounts for a negative balance of 29 141 euros.

Conclusion: Improving undernutrition screening and treatment is urgently needed, through awareness and training of medical and health allied professionals. This would result in a reduction in morbidity, cost and length of hospital stay.
Stability assessment of neonatal total nutrition admixture with various amino acid concentration

Li Hong¹, Yingfen Gu², Yi Feng¹

¹Shanghai Children's Medical Center, Clinic Nutrition, Shanghai, China
²Shanghai Children's Medical Center, Shanghai, China

Objectives and study: For the high-risk of genetic metabolic disease in NICU population, Pediatric Compound Amino Acid Injection was limited to use in the parenteral nutrition (PN) support for the newborns with amino acid metabolism disorder. However, a certain concentration of amino acid was thought to be necessary to ensure the compatibility of Total Nutrition Admixture (TNA) solutions. The purpose of this study was to explore the influence of various concentrations of amino acid on the stability of neonatal TNA solutions.

Methods: Five formulations were designed with 5 different amino acid concentrations containing the same components, including lipid emulsion. The final amino acid concentrations of admixtures were 0%, 1%, 2%, 3% and 3.5%, respectively. The appearance, pH and osmolality were observed after preparation (0 h) and at 12, 24, 48 and 72 h after preparation. The average size and the size distribution of the lipid globules were also evaluated by laser nanometer particle size analyzer.

Results: There was no observable alteration in color, phase separation, precipitate and flocculation in any admixture at any of the observation time points. The mean pH value for all groups were between (5.49 ± 0.01) to (6.19 ± 0.01) within 72 h. The mean osmolality for all groups were between (774 ± 3) to (1 106 ± 13) mOsm / kg. The mean diameter of lipid globules for all groups were between (280.6 ± 0.7) to (332.2 ± 2.0) nm. The mean PDI for all groups were between (0.200 ± 0.011) to (0.245 ± 0.012). The enrichment of amino acid concentration was linked to lower pH (P < 0.05), higher osmolality (P < 0.05) and larger average lipid globules size (P < 0.05). However, there was no distinct linear dependence between amino acid concentration and PDI value (P > 0.05).

Conclusion: After 72 h of storage at room temperature, the appearance, pH, osmolality and the average lipid globules diameter of the PN solutions are within the safe range when the amino acid is not contained or the concentrations are no more than 3.5%.
OBJECTIVES AND STUDY: Effective treatments for core symptoms of autism spectrum disorders (ASD) are lacking. We systematically updated evidence on the effectiveness of a gluten-free and casein-free (GFCF) diet as a treatment for ASD in children.

METHODS: The Cochrane Library, MEDLINE, and EMBASE databases were searched up until August 2016, for randomized controlled trials (RCTs); additional references were obtained from reviewed articles.

RESULTS: Six RCTs (214 participants) were included. With few exceptions, there were no statistically significant differences in autism spectrum disorder core symptoms between groups, as measured by standardized scales. One trial found that compared with the control group, in the GFCF diet group there were significant improvements in the scores for the ‘communication’ subdomain of the Autism Diagnostic Observation Schedule and for the ‘social interaction’ subdomain of the Gilliam Autism Rating Scale. Another trial found significant differences between groups in the post-intervention scores for the ‘autistic traits’, ‘communication’, and ‘social contact’ subdomains of a standardized Danish scheme. The remaining differences, if present, referred to parent-based assessment tools or other developmental/ASD-related features. No adverse events associated with a GFCF diet were reported.

CONCLUSION: Overall, there is little evidence that a GFCF diet is beneficial for the symptoms of ASD in children.

DISCLOSURE OF INTEREST: AH and AP are the recipients of a grant from the Fundacja Nutricia (Nutricia Foundation) under Grant RG8/2013 to carry out the study on ASD and a gluten-free diet. Other authors declare no conflict of interest.
Assessment of energy metabolism and nutritional supply in children with mechanical ventilation

Jian Ji, Suyun Qian

1Beijing Children’s Hospital, Capital Medical University, Pediatric Intensive Care Unit, Beijing, China

Objectives and study: To determine the resting energy expenditure on mechanical ventilation in pediatric intensive care unit (PICU) by indirect calorimetry, and analyze the distribution of metabolic states. The nutrition supply was assessed according to the resting energy expenditure.

Methods: An observational study was held in PICU of Beijing Children’s Hospital from November 2013 to April 2014. Critically ill children with mechanical ventilation were enrolled. The inclusion criteria included the following: (1) pediatric critical illness score < 90, or meeting the United States PICU admission criteria; (2) age > 29 days, < 18 years old; (3) time of mechanical ventilation > 24 hours; (4) volume of mechanical ventilation > 60 ml. Resting energy expenditure was determined by US Med Graphic Company CCM / D energy metabolism test system. Predictive resting energy expenditure was calculated for each subject with age-appropriate equation (Schofield-HTWT). According to the actual energy intake records and required energy intake (10% higher than the measured value) to define the nutritional status. The selected subjects were grouped according to gender, age, disease and nutritional status, and compared the metabolic status and nutritional supply of different groups.

Results: Sixty-eight children were enrolled in this study, 46 were boys and 22 were girls, including 25 cases of pneumonia with respiratory failure, 23 cases of central nervous system diseases complicated with respiratory failure, 20 cases of postoperative tracheal intubation. The ratio of boys and girls was 2:1. The results showed 36 patients in a low metabolic state, accounting for 53%; 23 patients in a high metabolic state, accounting for 34% and 9 patients (13%) in the metabolism of the normal state. For boys, 12 cases (26%) were in the high metabolism and 26 cases (57%) were in the low metabolism and 8 cases (17%) were in the normal metabolism. For girls, 11 cases (50%) were classified into high metabolism, 10 cases (45%) into low metabolism and 1 case (5%) was classified into normal metabolism. There was no significant difference in the distribution of metabolic status among different gender ($\chi^2=4.176$, $P=0.095$). In terms of ages, 15 cases (63%) were mainly in high metabolism in the patients at age < 3 years. 19 and 11 patients in 3~9 and 10~18 years age group respectively are mostly in low metabolism. As to the diseases, pneumonia complicated with respiratory failure and central nervous system diseases complicated with respiratory failure with mechanical ventilation respectively 15 cases (60%) and 12 cases (52%) were in low metabolism mainly; 11 cases of postoperative tracheal intubation were in high metabolism states, accounting for 55%. The distribution of metabolic status in different age and clinical diagnosis had significant difference. 31 patients had normal nutrients supply, accounting for 46%; 37 patients had inappropriate nutrition supply, accounting for 54%, including insufficient supplies of nutrients were 22 cases, accounting for 32%; excessive supplies of nutrients were 15 cases (22%). There were no statistically significant differences among the different types of diseases.

Conclusion: There are differences in the metabolic state of the mechanical ventilation in critically ill patients, mainly in low metabolic state. The age and types of diseases can affect the metabolic status of patients. Empirical nutritional support is not applicable to patients.
Quality Improvement Initiative: Growth and intake outcomes of infants following Kasai portoenterostomy

Beth Haliburton\(^1\), Inez Martincevic\(^1\), Binita M. Kamath\(^2\), Vicky Lee Ng\(^2\), Simon Ling\(^3\), Marialena Mouzaki\(^3\)

\(^1\)The Hospital for Sick Children, Clinical Nutrition, Toronto, Canada
\(^2\)The Hospital for Sick Children, Division of Paediatric Gastroenterology, Hepatology and Nutrition, Toronto, Canada
\(^3\)The Hospital for Sick Children, Division of Gastroenterology, Hepatology and Nutrition, Toronto, Canada

Objectives and study: The nutritional management of infants with biliary atresia (BA) following Kasai portoenterostomy (KPE) is not protocolized. The aim of this quality improvement initiative was to review the nutritional management and outcomes of BA infants following KPE at the Hospital for Sick Children in an effort to develop institutional nutritional care guidelines.

Methods: Single center, retrospective chart review of patients with confirmed BA and KPE performed at our institution between January 2010 and December 2015. Exclusion criteria: other concurrent liver disease. Data were collected from different time points: time of KPE (C0), three subsequent clinic visits post-operatively (C1, C2, C3) and at 1 year of age (C12). Data for patients listed for transplantation were collected until time of listing. Data collection included anthropometric measurements, feed type and caloric intake. Intake was expressed as the ratio of caloric intake from formula, excluding breastfeeding, to dietary reference intakes (DRI) for energy (http://www.nap.edu). Statistical analyses were performed using Stata MP v13.0.

Results: 30 patients underwent KPE (40% male); 50% were listed for transplantation by 7.2±2.7 months of age. Median age at KPE was 69 (22-105) days. Age at C1, C2, and C3 was 87±19; 113±29; 149±35 days, respectively. At C0, 87% of patients were taking feeds at standard calorie concentration (0.68 kcal/ml), 13% of patients were receiving feeds fortified to 0.8 kcal/ml and mean caloric intake was 94% of DRI. At C1, 17% were fortified and intake was 155% of DRI. By C2, 57% were fortified (37% at 0.8 kcal/ml, 17% at 0.9 kcal/ml and 7% at 1.0 kcal/ml) and intake was 132% DRI. By C12, 81% of DRI was met by formula/ breast milk and all patients were eating solids. At all clinic visits, feed types varied and included any combination of breastfeeding, expressed breast milk, supplemental formula, and/or exclusive formula. Formula type included standard infant formula and/or medium chain triglyceride-rich formula (Pregestimil A+®). Weight and length z-scores improved significantly from C1 to C12 (-0.9 to +0.4, p<0.01; -0.02 to +0.72, p=0.04). The differences in weight, length and caloric intake at C1, C2 and C3 between those who were and were not listed for transplant by 24 months of age was not significant and is shown in Table1.
### Table: Demographic, anthropometric and intake summary

<table>
<thead>
<tr>
<th></th>
<th>Not listed by 24 months of age, n=15</th>
<th>Listed by 24 months of age, n=15</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>C1</strong></td>
<td>Weight z-score</td>
<td>Length z-score</td>
</tr>
<tr>
<td></td>
<td>-0.87±1.09</td>
<td>-0.21±1.34</td>
</tr>
<tr>
<td></td>
<td>Kcal intake/DRI</td>
<td>1.52±0.44</td>
</tr>
<tr>
<td></td>
<td>-1.20±1.15</td>
<td>-0.65±1.78</td>
</tr>
<tr>
<td></td>
<td>1.56±0.90</td>
<td></td>
</tr>
<tr>
<td><strong>C2</strong></td>
<td>Weight z-score</td>
<td>Length z-score</td>
</tr>
<tr>
<td></td>
<td>-0.92±0.94</td>
<td>0.10±1.26</td>
</tr>
<tr>
<td></td>
<td>Kcal intake/DRI</td>
<td>1.31±0.61</td>
</tr>
<tr>
<td></td>
<td>-1.34±1.25</td>
<td>-0.67±1.43</td>
</tr>
<tr>
<td></td>
<td>1.32±0.49</td>
<td></td>
</tr>
<tr>
<td><strong>C3</strong></td>
<td>Weight z-score</td>
<td>Length z-score</td>
</tr>
<tr>
<td></td>
<td>-0.50±0.98</td>
<td>0.32±1.24</td>
</tr>
<tr>
<td></td>
<td>Kcal intake/DRI</td>
<td>1.34±0.64</td>
</tr>
<tr>
<td></td>
<td>-1.23±1.19</td>
<td>-0.28±1.46</td>
</tr>
<tr>
<td></td>
<td>1.27±0.37</td>
<td></td>
</tr>
</tbody>
</table>

Values are expressed as means ±SD. P value for all comparisons is > 0.05
Kcal: calories, DRI: dietary reference intake

**Conclusion:** For BA infants nutritional intake and anthropometrics did not differ between those listed and those not listed for liver transplantation during the first six months of life. Aggressive nutritional monitoring and the provision of up to 50% more calories than estimated improved growth parameters. Feed type post KPE and throughout follow-up was not standardized. The development of nutritional care guidelines in this population may help to optimize nutritional status pre-listing for liver transplantation.
Conicity index as a tool for estimate body fat mass in children and adolescents

MERCEDES JUSTE¹, Ernesto Cortes², Rosmari Vázquez³, Francisco Carratala⁴, Ana Naso⁵

¹San Joan University Hospital, Pediatrics, San Joan, Spain
²Miguel Hernandez University, Pediatrics, Alicante, Spain
³Elche University Hospital, Pediatrics, Elche, Spain
⁴Hospital Clinico San Juan, Pediatrics, Alicante, Spain
⁵Hospital Clinico Universitario San Juan, Pediatrics, Alicante, Spain

Objectives and study: Our principal aim was to know if the named Conicity Index (CI) shows a good correlation with the value of Body Mas Index (BMI) and with fat mass percentage measured by Radiological Absortiometry Double Foton (DEXA), and if it could be an easy tool to estimate fat mass in children and adolescents as it has been described in obese adults.

Methods: 431 children and adolescents were included in the study. All of them were attended in the Nutrition and Metabolism Unit at the San Joan University Hospital (Alicante. Spain). They were between 4-18 years of age (media 11,4 SD 2,8 years). Of them, 202 were female (46,9%). Patients were distributed in groups according their nutritional status using Z Score of BMI (Weight (Kg) / Height (cm)²). Height, weight and waist circumference was measured in all the patients in order to calculate BMI and CI and they had a study of fat mass percentage by DEXA. The calculation of CI is:

I.C. = Perímetro de la cintura (m) / (1.109 x peso (Kg)¹/²) / Talla (m)

Results: The distribution of nutritional status was as follow: normal in 27(6,3%), 66 (15,3%) were overweight, 145 (33,6%) were obese and 193 (44,8%) very obese. There was not differences in the distribution of Z score of BMI related to gender (Pearson’s Chi Squared = 5.221; p=0.156). In the total sample it was proved a good relationship between % Total Fat Mass measured by DEXA and BMI both in male as in the female group. (Figure 1)

CI showed a good relationship with BMI in the patients included. This happened in the males group (r² = 0,850) as in the females (r² = 0,929), as it is showed in the figure 2
Table:

<table>
<thead>
<tr>
<th>% Total Fat DXA vs</th>
<th>Male (n=219)</th>
<th>Female (n=202)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI</td>
<td>0.556</td>
<td>0.604</td>
</tr>
<tr>
<td>Z-score BMI</td>
<td>0.419</td>
<td>0.404</td>
</tr>
<tr>
<td>Conicity Index</td>
<td>0.274</td>
<td>0.409</td>
</tr>
</tbody>
</table>

**Conclusion:** Conicity index is a good tool to estimate BMI but not so useful to estimate Fat Mass in children and adolescents with different nutritional status.
Identification of risk factors for impaired nutritional status in paediatric patients with neurological disorders

Vasiliki Katseni¹, Euthymia Varigiam², Maria Kyriazi², Triantafyllia Doulopoulou¹, Joanna Elisabeth Katamoutou¹, Thomais Karagiozoglou-Lampoudi¹, Dimitrios Zafeiriou²

¹Alexander Technological Educational Institute of Thessaloniki, Laboratory of Clinical Nutrition, "Christos Mantzoros" Department of Nutrition - Dietetics, Thessaloniki, Greece
²Aristotle University of Thessaloniki, 1st Department of Pediatrics, Thessaloniki, Greece

Objectives and study: To identify the risk factors contributing to impaired nutritional status in children with neurological disorders (ND), utilizing WHO growth standards, and to evaluate their impact on the growth of children with ND.

Methods: In 90 paediatric patients (mean age 77 ± 46.82 months, 4.5% with gastrostomy tube), anthropometry, calorimetry and food intake records were assessed. Z-scores were calculated using WHO Anthro software. Intake (I) to requirements [both calculated (R) as well as measured by indirect calorimetry (C)] ratio were calculated. Patients were classified according to their ICD¹⁰ diagnose and Gross Motor Function score (GMFCS). Dysphagia Severity Scale (DSS), Manual Ability (MACS), and Feeding Ability (FA), drooling severity (SSS), meal duration and gastrointestinal complications (GIC) were also assessed.

Results: Based on weight for age z-score (WAz), 28 patients (31.1%) were undernourished and 16.9% according to triceps skin fold thickness for age z-score (TSFz). No association was found between WAz and GMFCS, whereas DDS (r=-.423) MACS (r=-.329), and SSS (r=-.307), GIC (r=.339), and FA (r=.361) displayed a significant correlation to WAz (p < 0.05). GMFCS was associated with TSFz (r=-.239), GIC (r=.272) as well as FA (r=-.505), (p < 0.05). No association was found between both WAz and TSFz to either I/R ratio or to I/C ratio. A multiple regression was run to predict WAz from DSS, SSS, MACS, FA, and GIC. These variables statistically significantly predicted WAz, F (5, 78) = 5.253, p < .0005, R² = .252. From the variables entered only DDS added statistically significantly to the prediction, p < .05.

Keywords: Neurological disorders, nutritional status, DSS, MACS, gastrointestinal complications, children

Conclusion: Patients with ND were undernourished in a substantial proportion. Nutrition intake as assessed by food records was not found to be associated to the nutritional status questioning the validity of records in this setting. When making decisions about ND patients' nutrition support choices, apart from anthropometry, FA, DSS, SSS and MACS evaluation, as well as the presence of GI complications have to be considered.
Early and rapid changes in body composition occur during the first month of cancer treatment in children

Juyoung Kim¹, Hyoung Soo Choi¹, Hye Ran Yang²

¹Seoul National University Bundang Hospital, Pediatrics, Seongnam-Si, Korea, Rep. of South
²Seoul National University College of Medicine, Pediatrics, Seoul, Korea, Rep. of South

Objectives and study: Cancer treatment may seriously affect body composition in growing children, and the changes in body composition may be related to physical growth, disease course and outcomes in pediatric cancer patients.

The aim of this study was to evaluate short-term and long-term changes of body compositions in pediatric cancer patients during the first year of cancer treatment.

Methods: This prospective study recruited 30 pediatric cancer patients (mean age 10.9 ± 3.8 yrs; 21 boys, 9 girls; 19 hematologic malignancies, 11 solid tumors) and 30 healthy controls. Anthropometric measurements and body composition analysis using whole body dual energy X-ray absorptiometry was performed at baseline and 1 month, 6 months, and 12 months during the first year of cancer treatment in each pediatric cancer patient.

Results: Among children with hematologic malignancies, those with solid tumors, and healthy controls, there were no significant differences in age, sex, weight, height, body mass index, abdominal circumferences, body fats, and most lean body masses at baseline. During one year follow-up of cancer treatment, total lean body mass significantly decreased during the first month and between 6 and 12 months (P = 0.008 & P = 0.000) although total mass did not change significantly. In contrast, total fat mass and total body fat percentage increased significantly (P = 0.000 & P=0.002) during the first month, but there were no significant changes from 1 month through 12 months. Changes in fat percentages during the first month of cancer therapy were significant both in the extremities and in the trunk (P = 0.000 & P = 0.000). Generalized estimation equation analysis of trends for changes in body fat percentages in each pediatric cancer group revealed that there were significant upward trends during the first year of cancer treatment in children with hematologic malignancies, but not in those with solid tumors.

Conclusion: Cancer treatment significantly causes the changes in body composition during the first year, especially during the first month after initiating treatment, resulting in a significant increase in body fat and a decrease in lean body mass, particularly in children with hematologic malignancies. Therefore, individualized strategies for changes in body composition based on underlying cancer are needed during early period of cancer treatment in children.
Prevalence and effects of paediatric home tube feeding in the Netherlands

Hilde Krom¹, Suzanne van Zundert², Marie-Anne Otten³, Liesbeth v.d. Sluijs Veer⁴, Marc Benninga¹, Angelika Kindermann¹

¹Academic Medical Center/Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Academic Medical Center/Emma Children’s Hospital, Department of Dietetics, Amsterdam, Netherlands
³Academic Medical Center/Emma Children’s Hospital, Department of Rehabilitation, Amsterdam, Netherlands
⁴Academic Medical Center/Emma Children’s Hospital, Psychosocial Department, Amsterdam, Netherlands

Objectives and study: Tube feeding ensures growth in children who are unable to eat or drink by themselves, but may also have negative effects on health (side-effects, complications, a difficult transition to oral feeding) and psychosocial functioning (parental distress, impaired interaction between parents and child). It is a financial burden as well. We aimed to assess the prevalence and possible side-effects of home tube feeding in Dutch children since there are no data available in the Netherlands so far.

Methods: The prevalence of paediatric home tube feeding was calculated using data of both the Medicines and Devices Information Project of the National Health Care Institute¹ and the Statistics Netherlands² (2010-2014). A cross-sectional parental online questionnaire was used to obtain data regarding demographics, history, tube feeding and side-effects. Dutch children (<18 years old) with tube feeding ≥2 weeks were included.

Results: During 2010-2014 the prevalence of home tube feeding varied between 83 and 92 : 100,000/year. In 2014, n=2853 children received tube feeding (51.5% male)¹. The prevalence of home tube feeding decreased with increasing age (from 234 : 100,000 in the 1 year olds to 50 : 100,000 in the age category 10-17 years).

A total of 279 children (53% male) were included in our survey; age category 0 (8.6%), 1 (15.8%), 2 (14.7%), 3 (11.8%), 4 (10.4%), 5-9 (22.2%), and 10-17 (16.5%) years of age. 60% (n=168) had a gastrostomy tube and 33% (n=93) a nasogastric tube. 31% (n=68) were tube fed since birth and 88% (n=244) had ≥1 medical diagnosis (most common were congenital abnormalities (42%), perinatal problems (38%), neurologic disorders (16%)). Parents of 74% reported ≥1 side-effects: vomiting (37%), lack of appetite (29%), and gagging (29%). Neither gagging nor vomiting were associated with type of tube (p=0.092 and p=0.191 respectively) or diet (p=0.435 and p=0.627 respectively). The nasogastric tube was replaced by home care (81%), hospital (35%) or parents (22%), and resulted in negative experiences in 94% of the patients.

Conclusion: The prevalence of paediatric home tube feeding in the Netherlands is 83-92 : 100,000/year. Parents do report frequent side-effects and negative experiences of tube replacement or the tube itself. These results may lead to a more careful monitoring of tube feeding, but more prospective research is necessary.

¹GIP / National Health Care Institute the Netherlands, April 2016
²http://statline.cbs.nl/Statweb/ Access May 2016
International survey among experts on defining and measuring paediatric disease-related malnutrition

Jessie Hulst\textsuperscript{1}, Koen Huysentruyt\textsuperscript{2}, Feifei Bian\textsuperscript{3}, Philip Arthur\textsuperscript{3}, Bashar Alhashash\textsuperscript{4}, Titia Vanderstelt\textsuperscript{5}, Raanan Shamir\textsuperscript{6}, Melinda White\textsuperscript{7}, Rafael Galera Martinez\textsuperscript{8}, Ana Moráis\textsuperscript{9}, Aydan Kansu\textsuperscript{10}, Konstantinos Gerasimidis\textsuperscript{11}

\textsuperscript{1}Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
\textsuperscript{2}Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Department of Pediatric Gastroenterology, Brussels, Belgium
\textsuperscript{3}Royal Hospital for Sick Children, University of Glasgow, Human Nutrition, School of Medicine, College of Medicine, Veterinary and Life Sciences, Glasgow, United Kingdom
\textsuperscript{4}Royal Hospital for Sick Children, University of Glasgow, Glasgow, United Kingdom
\textsuperscript{5}Royal Hospital for Sick Children, University of Glasgow, Human Nutrition, School of Medicine, College of Medicine, Veterinary and Life Sciences., Glasgow, United Kingdom
\textsuperscript{6}Schneider Children's Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach-Tikva, Israel
\textsuperscript{7}Lady Cilento Children's Hospital, Department of Dietetics and Food Services, Brisbane, Australia
\textsuperscript{8}Hospital Torrecárdenas, Servicio de Pediatrría, Almeria, Spain
\textsuperscript{9}“LA Paz” University Hospital, Pediatric Nutrition AND Metabolic Diseases, Madrid, Spain
\textsuperscript{10}Ankara University School of Medicine, Paediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
\textsuperscript{11}University of Glasgow, Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, Glasgow Royal Infirmary, Glasgow, United Kingdom

Objectives and study: A consensus on which criteria to use for defining and measuring disease-related malnutrition (DRM) in children has not yet been reached. This survey aimed to 1) inquire which indicators are found to be important by clinical nutrition experts to define malnutrition and malnutrition risk; 2) explore differences across countries and professions.

Methods: A web-based questionnaire survey was sent out to paediatric gastroenterologists (MD) and dieticians (RD) in seven countries (the Netherlands, Belgium, UK, Australia, Israel, Spain and Turkey). The survey was distributed via the local professional associations in participating countries.

Results: In total, 693 experts (Australia: n=89; Belgium: n=34; Israel: n=126; the Netherlands: n=73; Spain: n=139; Turkey: n=79; UK: n=153) responded; 45.5\% were MD and 54.5\% RD with a different distribution of professions across countries (p<0.001). No Belgian RD's were included. MD's and RD's had respectively a median of 15 (10;25) and 9 (3;14) years' experience in paediatrics. The majority worked in a tertiary (50.6\%) and/or district general hospital (33.3\%), with differences noted across countries. Suboptimal intake was ranked the most important cause (1\textsuperscript{st} out of 4 possibilities) of malnutrition by 44.9\% of the respondents, but also the least important by 16.8\%; inflammatory response was considered the least important cause by 42.7\% and the most important by 13.4\%. Significant differences existed across countries and profession (p<0.01). Table 1 shows how often experts rate certain findings as highly important or as not/slightly important in relation to the definition and criteria of DRM.
Table: Experts’ rating of issues related to definition and criteria of disease related malnutrition in children (n=693).

<table>
<thead>
<tr>
<th></th>
<th>highly important (%)</th>
<th>not/slightly important (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthropometric indicators of DRM</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>on-going weight loss*#</td>
<td>80</td>
<td>0</td>
</tr>
<tr>
<td>low BMI (47% highly important)*</td>
<td>47</td>
<td>3</td>
</tr>
<tr>
<td>low fat and low lean mass*</td>
<td>43</td>
<td>5</td>
</tr>
<tr>
<td>low fat with normal lean mass*</td>
<td>5</td>
<td>31</td>
</tr>
<tr>
<td>short stature*</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td><strong>Indicators of nutritional risk</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>increased energy/nutrient losses*#</td>
<td>73</td>
<td>1</td>
</tr>
<tr>
<td>low energy/macronutrient intake*#</td>
<td>69</td>
<td>1</td>
</tr>
<tr>
<td>history of high nutritional risk condition*#</td>
<td>67</td>
<td>0</td>
</tr>
<tr>
<td>low micronutrient intake*#</td>
<td>40</td>
<td>3</td>
</tr>
<tr>
<td>abnormal blood markers*</td>
<td>50</td>
<td>1</td>
</tr>
<tr>
<td>prematurity*</td>
<td>33</td>
<td>6</td>
</tr>
<tr>
<td>on-going systemic inflammation*</td>
<td>25</td>
<td>6</td>
</tr>
</tbody>
</table>

*significant difference across countries; #significant difference across professions

**Conclusion:** Suboptimal intake was considered the most important cause of malnutrition for half out of the 700 international field experts. On-going weight loss, increased energy/nutrient losses, low energy/macronutrient intake and abnormal blood parameters were estimated as highly important indicators of malnutrition/malnutrition risk by half or more of the respondents. Across-country differences were noted for nearly all questions, suggesting difficulties in reaching international consensus.
Central-line associated bloodstream infections in children on parenteral nutrition: a retrospective study

Fabrizia Chiatto¹, Andrea Lo Vecchio¹, Alessia Morlando¹, Alfredo Guarino¹, Maria Immacolata Spagnuolo¹

¹University of Naples Federico II, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy

Objectives and study: Central-line associated bloodstream infections (CLABSI) are a common complication in the management of children on parenteral nutrition (PN), due to the long CL dwell time, the infusion of nutrients and the underlying disease and the home management of CL. The aim of our study was to evaluate the incidence of fever episodes and CLABSI in a paediatric population on long-term PN and to analyse major determinants of infection.

Methods: We carried out a 1-year retrospective study between January and December 2015. All children with CL admitted to the Reference Centre for Paediatrics Artificial Nutrition of the University “Federico II” of Naples were monitored. Fever episodes were defined by the presence of body temperature of 38°C in at least two determinations within 1 hour. CLABSI rates were calculated according to the Center for Diseases Control and prevention definitions and normalized for 1000 CL days.

Results: Nineteen children on PN were included in the study: 9 with short bowel (47%), 2 with intestinal pseudo-obstruction disorders (10%), 6 with systemic diseases requiring artificial nutrition (31%) and 2 with neurological disease (10%). Out of them 11 (58%) reported at least one episode of fever, with a cumulative fever incidence rate of 36.7/1000 at-risk patients days. Twelve episodes of CLABSI were eventually recorded in 9 children with mean CLABSI rate of 17.6/1000 CL days [95 % confidence interval (CI) 0-86.9]. Staphylococcus aureus was the most commonly isolated pathogen (41%); other pathogens isolated were Coagulase Negative Staphylococcus (33%), Streptococcus (8%), Klebsiella (8%) and Pseudomonas Aeruginosa (8%). In six children (31%) CL was removed during infection episode.

Fever management required a mean hospital stay of 15.3 days/episode. However, most children had a good response to antibiotic treatment with a mean duration of fever of 3.8 days after admission. Although children with motility disorders underwent more episodes of CLABSI, no significant correlation between underlying disease and risk of CLABSI was observed.

Conclusion: Infections are a major cause of morbidity in children on PN. Additional studies are needed to investigate major risk factors for CLABSI and to determine effective interventions that may reduce PN-associated CLABSI.
Prognostic significance of energy and protein adequacy provided by enteral nutrition in children with sepsis in pediatric intensive care unit

Chen Lu

1Beijing Children's Hospital/Pediatric Intensive Care Unit, Beijing, China

Objectives and study: Nutritional support is one of the most important aspect in intensive care unit. If there was no obvious contraindication, enteral nutrition was preferred. In this artical, we observe the energy and protein intake provided by enteral nutrition in patients with sepsis in pediatric intensive care unit, and to analyze the Correlation between the adequacy of enteral nutrition and Disease prognosis.

Methods: We conducted a prospective observational study of consecutive children with sepsis in PICU of Beijing Children's Hospital form Nov. 2012 to Apr. 2013. The energy and protein intake by EN were daily recorded and the adequacy was calculated according to 64 kcal/kg/d and 1.5g/kg/d respectively. The prognosis variables were compared between children with adequate EN and inadequate EN.

Results: Totally 62 children were included. The adequacy of energy by EN was 0.84 ± 0.38kcal/kg/d, while the adequacy of protein was 0.94 ± 0.46g/kg. Children reached adequate energy and protein intake by EN during observational periods were 25 (40.32%) and 29 (46.8%)cases respectively. Children with inadequate energy intake by EN were older (P=0.02), with lower pediatric critical illness score(77.12±10.21 vs 82.88±7.03, P=0.02) and longer invasive mechanical ventilation duration (P=0.03). Children with inadequate protein intake by EN had higher weight (P=0.00), higher percent of children with severe sepsis (42.4% vs17.2%, P=0.03) and more dysfunctional organs (P =0.01). Children with inadequate energy (16.2% vs 4.0%) and protein (15.2% vs 6.9%) intake by EN also had higher mortality at 28th hospital day.

Conclusion: Majority of children with sepsis or severe sepsis in PICU suffered from inadequate energy and protein intake by EN, especially in older and higher weight patients. Inadequate energy intake by EN may associate with duration of invasive mechanical ventilation, may take higher hospital fees, while inadequate protein intake by EN may be associated with increased risk of organ dysfunction. Inadequate energy or protein intake by EN may increase mortality of children with sepsis or severe sepsis in PICU.
OBEMAT2.0 methods: a clustered randomized controlled trial for the treatment of childhood obesity through a motivational approach

Veronica Luque¹, Albert Feliu², Raquel Monné³, Joaquin Escribano¹, Desirée Gutiérrez¹, Núria Guillen⁷, Judit Muñoz⁷, Mireia Alcázar¹, Mercè Núñez¹, Natalia Ferre¹, Josep Basora⁴, Gemma Flores-Mateo², Pablo Hsu⁴, Clara Alegret⁴, Marta Zaragoza-Jordana¹, Mariona Gispert-Llauradó¹, Carme Rubio-Torrents¹, Nuria Sanz⁵, Susana Gil⁷, Ana Alejos⁷, Ana Rea⁷, Félix Aguado⁶, Eva Muí³, Miriam Domingo⁹, Ricardo Closa-Monasterolo¹⁰

¹Universitat Rovira I Virgili, Iispv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
²Hospital Universitari Sant Joan de Reus, Reus, Spain
³Institut Català de la Salut, Centre D’atenció Pediàtrica Rambla Nova, Tarragona, Spain
⁴Institut Universitari D’investigació En Atenció Primària Jordi Gol (Idiap Jordi Gol), Reus, Spain
⁵Institut Català de la Salut, Centre D’atenció Primària Les Borges del Camp, Les Borges del Camp, Spain
⁶Institut Català de la Salut, Centre D’atenció Primària Sant Pere, Reus, Spain
⁷Hospital Lleuger de Cambrils, Cambrils, Spain
⁸Centre D’atenció Primària Marià Fortuny, Reus, Spain
⁹Institut Català de la Salut, Centre D’atenció Primària de Salou, Salou, Spain
¹⁰Hospital Universitari de Tarragona Joan XXIII, Servei de Pediatria, Tarragona, Spain

Objectives and study: Childhood obesity treatment is challenging and not always successful. Evidences suggest that motivational/behavioural interventions in young adults improved the efficacy of the obesity treatment to lose weight and improving serum biochemical parameters by means of increasing desire to control weight. In children aged 2 to 8, a motivational interview and dietary counselling leaded to a significant reduction in body mass index (BMI).

In a prospective observational study on obese adolescents, a structured motivational therapy in a reference hospital facility was highly effective at clinical and metabolic levels. This study aims: to assess the efficacy of a structured motivational therapy, coordinated between hospitals and primary care centres (PCC) on families with an 8-13 years old obese child, to lose weight and to reduce the cardiovascular risk. Secondary aim is to validate techniques to assess body composition in obese children and adolescents.

Methods: Clustered randomized clinical trial, in which the intervention to be tested is a multicomponent motivational and educational plan; this will be compared to a control group consisting on the regular recommendations performed at PCC (n=334, 167 per group). In both cases the treatment will last 12 months and will consists of 11 treatment visits at PCC, plus an initial and final assessment visits at the reference hospitals. At the assessment visits, before and after the treatment takes place, anthropometry, bioimpedance, deuterium oxide dilution (D₂O) in a subsample of 75 children, air displacement plethysmography (Bod-Pod) and Dual X-Ray Absorptiometry (DXA) will be performed. The intervention will consist of: 11 structured visits with a specific topic to be treated in each, which will lead to specific objectives for weight, diet and physical activity, as well as signed compromises and home activities promotion; children will be given a wearable wrist band to monitor their steps; and 3 group workshops will be performed for education on 1. Promotion of physical activity, 2. Food products labelling and appropriate portion control, 3. Healthy cooking techniques and recipes. Main outcomes measures are: Changes in BMI z-score between the first visit and 12 months. As well as changes in waist circumference and body composition (fat mass index and lean mass index through DXA, Bod-Pod, D₂O and 4-components model). In parallel, a blood, urine and faeces samples collection is being performed before and after the intervention.

Results: Sixty-four therapists from 10 PCC were recruited and attended to a 2h training course on the project; half of them received additional 12h on motivational therapy and the structure of the intervention; the intervention therapists have been provided with the material for children education at each visit. In 5 months 122 (48 control) obese children have been recruited, assessed at hospitals and have started the treatment at PCC, 117 of them accepted to participate in the sample collection for further analyses. There are not registered withdrawals yet.
**Conclusion:** The motivational program has been implemented successfully in the PCC. The therapists performing the motivational intervention are recruiting faster and so more motivated to participate in the study. This clinical trial study may be able to show the efficacy of the treatment results from 2019 onwards.
Bioimpedance analysis for optimization of a program of body weight correction in children who are obese or overweight

Svetlana Makarova¹, Tamara Chumbadze¹, Dmitry Yasakov¹

¹Federal State Autonomous Institution “Scientific Center of Children's Health” of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Objectives and study: Based on the evidence of 2004, 5.5–11.8% of children in the Russian Federation are overweight and about 5.5% are obese. The purpose of the study: to evaluate the effectiveness of the application of bioimpedance analysis of body composition to optimize recommendations for diet correction, water intake schedule and physical activity in children who are overweight or obese.

Methods: 74 children aged 6–18 years who were overweight or obese have been examined; 45 girls (62.5%) and 29 boys (37.5%). The component body composition was studied using bioimpedance analysis with the definition of the following parameters: body mass index (BMI), fat mass (FM) (as a percentage and in kg), lean body mass (LBM), active cell mass (ACM), specific (normalized for body surface area) basal metabolism, total body, phase angle. The assessment of actual nutrition was made using a questionnaire (3 days), and a computer program for calculating the chemical composition of the diet.

Results: 16 children (21.6%) were overweight, 31 children (41.8%) had 1st degree obesity and 27 children (36.4%) had 2nd degree obesity (p<0.05). According to the bioimpedance analysis, all children examined had an excess of fat mass, and water retention in the body was revealed in 44 girls (59.5%) and 30 boys (40.5%). Active cell mass was more often reduced in children with 1st–2nd degree obesity, (in 46 children out of 58 (79.31%), as compared to children who were overweight, (10 children out of 16 (62.5%)). This indicated a lack of the protein component of food in both children who were overweight, and children who presented different degrees of obesity. A decrease in phase angle was noted in all subjects, with reduced ACM, increased FM (both kg and percentage) and reduced specific basal metabolism, reflecting a state of hypodynamia in the children examined. After diet therapy, with food and water intake schedule observed, appetite-stimulating products eliminated and fasting days used, as well as additional measures such as an increase in physical activity, a change in eating behavior and the keeping of a food diary, component body composition was repeatedly estimated over a period of 1 to 1.5 months. In 51 children (68.9%), body composition measurements showed positive signs: a decrease in BMI, a decrease in FM (both in kg and in percentage), and an increase in ACM, specific basal metabolism and phase angle. In 18 of the children (24.3%) who did not keep to a diet, the bioimpedance analysis indices remained unchanged.

Conclusion: The application of bioimpedance analysis of dynamics within the program of body weight correction provides an opportunity to evaluate the effectiveness of diet therapy, water intake schedule and physical activity in children who are overweight or obese.
Clinical complexities and dietetic outcomes of paediatric patients receiving a high energy, peptide-based tube feed for 4 weeks

Katy Sorensen1, Amanda Judd2, Sarah Trace3, Jennifer Livingstone4, Lindsay Rosie4, Heather Grant4, Carolyn Patchell5, Karen Poulton5, Samantha Armstrong5, Chris Smith6, Katie Clark6, Susan Meredith7, Emma Stone8, Gary Hubbard1, Rebecca Stratton7

1Nutricia, Medical Affairs, Trowbridge, United Kingdom
2Bristol Home Management Service, Nutrition and Dietetics, Bristol, United Kingdom
3Bristol Royal Hospital for Children, Nutrition and Dietetics, Bristol, United Kingdom
4Royal Hospital for Sick Children, Nutrition and Dietetics, Edinburgh, United Kingdom
5Birmingham Children's Hospital, Nutrition and Dietetics, Birmingham, United Kingdom
6Royal Alexandra Children's Hospital, Nutrition and Dietetics, Brighton, United Kingdom
7Birmingham Community Nutrition, Nutrition and Dietetics, Birmingham, United Kingdom
8West Suffolk Hospital, Nutrition and Dietetics, Bury St Edmunds, United Kingdom

Objectives and study: Nutrient malabsorption can result from disease or its treatment, contributing to faltering growth in paediatric tube-fed patients. Peptide-based tube feeds (PTF) containing hydrolysed protein (peptides, measured in kilodaltons (kDa)) and medium chain triglycerides (MCT) can be used to manage faltering growth in paediatric patients with malabsorption and feeds with a higher proportion of smaller peptides may improve nutrient absorption. This study aimed to explore the complex medical conditions and dietetic outcomes of paediatric patients receiving a high energy PTF (HEPTF) with 91% of peptides <1.5kDa and 52% MCT.

Methods: 16 patients (mean age 6yr 5mo (1yr 2mo – 14yr 11mo), mean weight z-score -1.373±2.15) were recruited from UK hospitals (n=6, 38%), outpatient clinics (n=5, 31%) and community services (n=5, 31%) onto this prospective, longitudinal study. Patients received a HEPTF (1.5kcal/ml, 91% of peptides <1.5kDa, 100% whey protein, 52% MCT: Nutrini Peptisorb Energy, Nutricia) for 28 days. All patients had complex clinical conditions with multiple diagnoses, primarily gastrointestinal (GI) (n=6, 38% i.e. intestinal failure, enteropathy, fistula, atresia), cancer (n=4, 25% i.e. leukaemia, brain tumour, histiocytic sarcoma, aplastic anaemia), central nervous system (n=3, 19% i.e. cerebral palsy, epileptic encephalopathy, microcephaly), chronic lung disease (n=1, 6%), heart failure (n=1, 6%) and intracranial haemorrhage (n=1, 6%). All patients had impaired absorption or tolerance with GI symptoms such as diarrhoea, constipation, abdominal pain and vomiting, either secondary to their medical condition or its treatment. Primary dietetic goals for 4wks on the HEPTF were growth (50%), growth and tolerance (31%) and tolerance (19%).

Prescriptions of the HEPTF were 330-880ml/d as a sole source of nutrition (n=6 (38%), mean age 4yr 10mo) or 270-1000ml/d in addition to oral intake (n=10 (63%), mean age 7yr). Medical and dietetic histories and dietetic goals were recorded at baseline. GI tolerance, feed compliance (% consumed vs prescribed), energy and protein intake, weight, height and achievement of dietetic goals were recorded during the study.

Results: At baseline, 12 patients (75%) were already receiving a PTF (1kcal/ml n=7, 44%; 1.5kcal/ml n=5, 31%) and 4 (25%) were receiving a polymeric tube feed (1kcal/ml n=1, 6%; 1.5kcal/ml n=3, 19%), via nasogastric or gastrostomy tube. Only 4 patients (25%) tolerated their baseline feed without issue, and no patients receiving polymeric feeds at baseline tolerated these well.

Whilst receiving the HEPTF, decreases in diarrhoea, abdominal pain, constipation, bloating and burping were reported (NS). Compliance was high (mean 99%). Mean energy and protein intakes were maintained (+111kcal/d (p=0.15); +0.5g/d protein (p=0.89)). Weight significantly increased (+0.33kg, p=0.03), with increases in weight z-score (+0.034, p=0.63), height (+0.72cm, p=0.07) and height z-score (+0.771, p=0.43) after 28 days. 80% of patients achieved their primary dietetic goal.
Conclusion: This group of paediatric patients requiring PTF with complex clinical conditions achieved good tolerance, high feed compliance and significant weight gain with the HEPTF. As energy increases were nominal, it is possible that the significant weight gain was due to improved absorption aided by the high proportion of small peptides in the HEPTF (91% <1.5kDa), but further explorative research is needed.

Disclosure of interest: Katy Sorensen, Conflict with: Nutricia Ltd; Amanda Judd: None declared; Sarah Trace: None declared; Karen O’Connor: None declared; Jennifer Livingstone, Conflict with: Has received speaker fees from Nutricia/Danone; Lindsay Rosie: None declared; Carolyn Patchell: None declared; Karen Poulton: None declared; Chloe Millington: None declared; Samantha Armstrong: None declared; Chris Smith, Conflict with: Has received speaker fees from Nutricia/Danone; Katie Clark: None declared; Susan Meredith: None declared; Emma Stone: None declared; Gary Hubbard, Conflict with: Nutricia Ltd; Rebecca Stratton, Conflict with: Nutricia Ltd
NUTRITION: Clinical nutrition

N-P-064

Analysis of nutritional screening tools applied to hospitalized pediatric patients: narrative review

Martha Patricia Marquez Aguirre¹, Paul Ríos ², Daffne Danae Baldwin Monroy¹

¹National Institute of Pediatric, Intensive Care Unite, Mexico City, Mexico
²Institute National of Peadiatric, Obesity Clinic and Intensive Critical Care, Mexico City, Mexico

Objectives and study: Review published scientific evidence regarding nutritional screening tools in hospitalized paediatric patients to evaluate their future application in patients at the National Paediatric Institute as part of their integral nutritional evaluation.

Methods: A search was performed in the Pubmed, Medline, Cochrane Central, Scopus, LILACS, Google Academic. The availability of texts has been search for full texts in publications from January 2006 to July 2016. The descriptors used in accordance with the Descriptors in Health Sciences (DeCS) and Medical Subject Headings (MeSH) list were nutritional status, screening, hospitalized children, malnutrition, nutritional risk.

Results: The authors identified 8 tools that met the criteria for nutritional risk detection in hospitalized paediatric patients: NRS, PNRS, STAMP, SGNA, SME, STRONG-kids, SCAN and SGA. After applying the selection criteria, 558 articles were identified, at the end of the selection process 80 articles were quantified and analyzed in full, of which 26 were included by the meeting of the pre-established criteria in the selection criteria and were therefore included in the review. Separating patients with surgical related conditions from patients with non surgical conditions we found that 80% of the screening strategies were applied to patients with medical conditions not associated with surgery.

Table:

Table. Description of Paediatrics tools

<table>
<thead>
<tr>
<th>Tools</th>
<th>Year</th>
<th>Study group</th>
<th>Age</th>
<th>n</th>
</tr>
</thead>
<tbody>
<tr>
<td>NRS</td>
<td>1995</td>
<td>Medical*</td>
<td>&lt;2 years****</td>
<td>26</td>
</tr>
<tr>
<td>PNRS</td>
<td>2000</td>
<td>Medical &amp; surgical</td>
<td>&gt;1 month-18 years</td>
<td>296</td>
</tr>
<tr>
<td>SGNA</td>
<td>2007</td>
<td>Surgical</td>
<td>&gt;1 month-18 years</td>
<td>175</td>
</tr>
<tr>
<td>STAMP</td>
<td>2008</td>
<td>Medical &amp; surgical</td>
<td>2-17 years</td>
<td>110</td>
</tr>
<tr>
<td>PYMS</td>
<td>2010</td>
<td>Medical &amp; surgical</td>
<td>1-16 years</td>
<td>247</td>
</tr>
<tr>
<td>STRONG-kids</td>
<td>2010</td>
<td>Medical &amp; surgical**</td>
<td>&gt;1 month-18 years</td>
<td>423</td>
</tr>
<tr>
<td>SGA</td>
<td>2012</td>
<td>Medical</td>
<td>2-12 years</td>
<td>140</td>
</tr>
<tr>
<td>SCAN</td>
<td>2016</td>
<td>Oncological</td>
<td>5-18 years</td>
<td>90</td>
</tr>
</tbody>
</table>

NRS = Nutrition Risk Score; PNRS = Pediatric Nutritional Risk Score; STAMP = Screening Tool for the Assessment of Malnutrition in Paediatrics; SGNA = Subjective Global Nutritional Assessment; PYMS = Paediatric Yorkhill Malnutrition Score; STRONG-kids = Screening Tool for Risk Of Impaired Nutritional Status and Growth; SCAN= Pediatric oncology nutrition screening tool; SGA=Subjective Global Assessment

*Medical= medical pathology not related to surgical procedure
**Excluded renal, cardiology, orthopedic and critical pathology
***>2% weigh loss
**** the study included patients up to 17 years of age
**Conclusion:** The narrative review we found 8 useful and replicable tools for the detection of nutritional risk in hospitalized paediatric patients. These tools have been applicable in the referred group that includes a high degree of sensitivity and specificity in the detection of nutritional risk. Nutrition screening tools designed to Paediatric patient can be used for the recommendation of clinical practice guidelines in relation to a nutritional assessment at hospital admission.
**NUTRITION: Clinical nutrition**

N-P-065

**Renal function in children on long-term home parenteral nutrition**

Assylzhan Messova¹, Robert Dziubak², Anna Hughes³, Jutta Koeglmeier³

¹Great Ormond Street Hospital, Paediatric Gastroenterology, London, United Kingdom
²Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, Neurogastroenterology and Motility Division, London, United Kingdom
³Great Ormond Street Hospital for Children, Paediatric Gastroenterology, Division of Nutrition, Intestinal Failure and Rehabilitation, London, United Kingdom

**Objectives and study:** Home parenteral nutrition (HPN) has dramatically improved quality of life and long term outcome of children with prolonged or irreversible intestinal failure (IF). Data obtained from adults suggests a decline in renal function (RF) on long term PN over time but little is known in paediatric IF patients. The aim of this study was to look at RF in children on HPN.

**Methods:** Children who received HPN for a minimum of three years were identified from the IF clinic of a large tertiary referral centre. Estimated glomular filtration rate (eGFR) was calculated using the Schwartz formula at discharge on HPN, after 6 months, 1, 2, and 3 years. Decreased RF was classified as mild when eGFR was 89 to 60 mL/min/1.73 m², moderate when eGFR was 59 to 30 mL/min/1.73 m², and severe when eGFR was <30 mL/min/1.73 m².

**Results:** Twenty five patients (40% male) fulfilled the inclusion criteria. The median age at start of PN was 30 months. The indications for HPN were due to an underlying motility disorder in 56% (14/25), enteropathy in 24% (6/25) and short bowel syndrome in 20% (5/25). At the start of HPN 80 % (20/25) had a normal eGFR. Five children (20%) had an abnormal eGFR. In the group of patients with normal eGFR at the start of HPN 30 % (6/20) had at least one episode of decreased GFR in the following three years, however there was no significant decline in eGFR at the end of the 3 year study period. Only one child had a constant decrease in eGFR, Of the five children who had an eGFR below the normal range at the start of HPN again only one child had a constant decline of eGFR over the duration of the study. Overall there was no statistically significant deterioration of eGFR in the study population (p = 0.7898). In those patients with an abnormal GFR no statistical correlation could be found with underlying IF etiology (p =1) prematurity (0.7144), total versus partial HPN (p = 1), pre existing kidney disease (p = 0.749) and steroid medication (p = 0.749). However, the number of children in each category was small.

**Conclusion:** In our cohort of children on long term HPN no significant decline of eGFR could be demonstrated.
The effect of whey protein hydrolisate and Eicosapentaenoic acid (EPA) supplementation on prealbumin level and muscle mass in children with acute leukemia

Maria Mexitalia¹, Novrianti Hawarini¹, Bambang Sudarmanto¹

¹Faculty of Medicine Diponegoro University/Dr. Kariadi Hospital, Pediatrics, Semarang, Indonesia

Objectives and study: Acute leukemia is a type of cancer most commonly found in children. Giving a high whey protein hydrolisate in cancer patients can reduce the loss of weight and body mass. Whey, a protein complex derived from milk, is being touted as a functional food with a number of health benefits due to its immune-enhancing effect. Eicosapentaenoic acid (EPA), which is an n-3 polyunsaturated fatty acids, also has beneficial for cancer patients in light of inflammatory response associated with metabolic changes, reduce the loss of muscle protein in cancer cachexia and reducing tumor growth. Prealbumin levels are low in patients with malignancy. Giving diet with high whey protein hydrolisate (WPH) and Eicosapentaenoic acid (EPA) can reduce the loss of weight and body mass. The purpose of the study was to determine the effect of supplementation WPH and EPA on prealbumin levels and muscle mass in children with acute leukemia.

Methods: Randomized control trial pre and post design was conducted in 2015 to patients with acute lymphocytic leukemia and acute myeloblastic leukemia in Dr. Kariadi Hospital Semarang Indonesia. Subjects were taken by consecutive sampling, and were divided by random allocation into treatment group (n=14) that received whey protein hydrolisate and EPA and control group (n=14) that received standard milk for 4 weeks. Anthropometry including weight and height, and mid upper arm circumference (MUAC) were measured by Tanita, and triceps skinfold (TSF) was measured by Holtain caliper. Besides we also measured the food intake by 3 days food recall. Statistical analysis was done by wilcoxon test (paired data) and mann-whitney test (unpaired data).

Results: The mean age of the subjects was 10.2 years. After supplementation the prealbumin level increased on both groups, i.e. on treatment group from 152(68.3) mg/dL to 182(103.4) mg/dL (p=0.003); and control group from 131(52.2) mg/dL to 158 (54.5) mg/dL (p< 0.001). The increasing of prealbumin on intervention group was significantly higher than control group (p=0.001). Meanwhile the increased of MUAC and TSF on intervention group were not significant difference with the control group.

Conclusion: Supplementation of whey protein hydrolisate and EPA for 4 weeks increased prealbumin level in children with acute leukemia.
Risk factors of eating disorders in adolescents with type 1 diabetes

Cristina Maria Mihai¹, Tatiana Chisnoiu¹

¹Clinical County Emergency Hospital of Constanta, Pediatric Department for Diabetes, Nutrition, and Metabolic Disorders, Constanta, Romania

Objectives and study: People with type 1 diabetes, especially adolescents may develop eating disorders. Treatment with insulin cause weight gain and so adolescents with type 1 diabetes to prevent weight gain a compensatory behavior, namely intentional insulin omission. The aim of this study is to highlight risk factors for developing eating disorders.

Methods: This study consisted in evaluation of 155 patients between 10 and 18 years with type 1 diabetes, during December 2015- November 2016. All patients were evaluated based on several parameters, including a questionnaire designed to collect information directly from them, that contains questions for parents (age, studies, type organization of the family, chronic disease, eating behavior, background environment) and for children ( age, sex, eating behaviour, did you calculate your meals, how many episode of hypoglycemia/hiperglicemia have in the last month, how comfortable are you about your physical appearance, do you ever take less insulin than you should?

Results: According to these study eating disorders in adolescents with type 1 diabetes are present in 45 patients, with a higher incidence in girls (90%). Low self-esteem and trend to depression was met in 65% of adolescence girls. The prevalence of intentional insulin omission has been shown to increase with age from 27% among girls aged 10-12 years, 73% among girls aged 13-18 years. The average value of glycated haemoglobin was 10.5%, that show a poor glycemic control. Recurrent episodes of diabetic ketoacidosis was met in 22 case of children that need hospitalized. The strict dietary regimen that is a component of type 1 diabetes management is associated with recurrent hypoglycemic episodes. The study has revealed that in 21 cases the children experienced hypoglycemia, 10 of them need hospitalized. Poor communication and less trust in the relationships of girls with their parents were present in 32 patients. The prevalence of families in which a parent have anorexia or bulimia nervosa was 8%. Frequently missed medical appointments and refusal to be weighed is characteristic for all 45 patients.

Conclusion: Diagnosis of eating disorders in adolescents with type 1 diabetes may be difficult. We highlighted that the most important risk factors to develop eating disorders are poor glycemic control, recurrent diabetic ketoacidosis and the relationship of children with their family, especially with mothers. Early diagnosis is essential, because the coexisting of eating disorders and diabetes increased appearance of short or long-term complications. A multidisciplinary treatment includes insulin pump therapy, compliance with food restriction, and psychological or psychiatric examination.
Children referred to a hospital obesity clinic: descriptive study of a Spanish sample

Héctor Ruiz¹, Ana Moráis¹, Ana Bergua¹, Belén Delgado¹, Irene Merinero¹, Rosa A Lama¹

¹“La Paz” University Hospital, Pediatric Nutrition and Metabolic Diseases, Madrid, Spain

Objectives and study: To determine the clinical characteristics of patients referred to a hospital obesity clinic since 2008.

Methods: Cross-sectional retrospective study. Medical records were reviewed, collecting information about demographic data, body composition analysis, and biochemical and other additional examinations performed at the first visit. Anthropometry (Seca™ scale and Holtain™ stadiometer) is expressed as z-score (mean±SD). Fat (FBM) and lean body mass (LBM) were estimated by bioelectrical impedance analysis (BIA) using RJL Systems™ device and expressed as percentages of specific age and sex normal values (mean±SD). Biochemistry data included iron status and lipid and carbohydrate metabolism profile. Other data recorded included blood pressure, echocardiography, and abdominal ultrasound. A p value <0.05 was considered significant.

Results: 75 patients (48% male) reviewed; mean age 12±3.5 years. Patients were mostly referred to the clinic from the Endocrinology Department (92%), after having been referred there from Primary Care. Anthropometry: mean z-weight 3.99±2.02. Mean z-height 0.58±1.27. Mean z-BMI 4.28±2.02. Morbid obesity (z-BMI≥120% of 95th percentile or absolute BMI≥35) was found in 53 patients (70.67%), whose mean age was 12±3.24 years. Mean waist / height ratio was 0.69±0.08. BIA: mean FBM was 350.48±180.76% of normal values (range 1002.10%-99.74%) and mean LBM was 117.14±22.58% (range 74.26%-182.69%). Self-perception of body image was positive in 34.25% (average z-BMI in this group 3.84±1.44), neutral in 31.50% (average z-BMI 3.78±1.45) and negative in 34.25% (average z-BMI 5.19 ± 2.64) [p>0.05].

Biochemistry: iron deficiency was found in 17.02% of those analysed (n=47). Lipid profile: mean total cholesterol 164.29±29.75 mg/dL, mean HDL 44.68±12.02 mg/dL, mean LDL 99.78±23.99 mg/dL, mean triglycerides 103.98±60.93 mg/dL. Abnormal carbohydrate metabolism was observed in 34.28% of patients. No relationship between the severity of obesity and laboratory abnormalities was found. Abdominal ultrasound was performed in 39 patients with signs of hepatic steatosis in 38.46%. No significant differences in triglycerides levels were observed between patients with and without steatosis. No relationship was found between the severity of obesity and excess of FBM and the presence of ultrasonographic changes.

Conclusion: No age differences between morbid and non-morbid obese children were observed, which may indicate that morbid patients have faster progress or an earlier start. In most patients, overweight corresponded to an isolated increase in FBM with adequate LBM, which is of concern when establishing therapeutic goals. Obesity seemed to have negative influence on self-perception of body image only in those with highest BMI.
Quality-of-life of children receiving long-term home parenteral nutrition

Léa Tran¹, Gill Lazonby², Anne-Dominique Pham³, Donna Ellis², Jenny Goldthorpe², Natalia Iglesias⁵, Julie Steele⁵, Veena Zamvar², John William Lambert Puntis⁴, Rakesh Vora²

¹Chu de Caen, Pediatrie Generale, Caen, France
²Leeds General Infirmary, Paediatric Gastroenterology, Leeds, United Kingdom
³Chu de Caen, Statistics and Clinical Research, Caen, France
⁴Leeds, United Kingdom

Objectives and study: Home Parenteral Nutrition (HPN) has dramatically enhanced the daily lives of patients with prolonged intestinal failure, allowing them to move from the hospital to their homes. Children and their parents have to manage complex nutritional issues but also other difficulties such as family dysfunction or lack of clinical support. The HPN-Quality of life (HPN-QOL) tool, for assessing the QOL of adult patients receiving HPN, has been rigorously developed using standard guidelines and measuring various dimensions of QOL (1). Our aim was to explore how HPN influences QOL of paediatric patients: to understand aspects which specifically impacted QOL and to identify patient/family perspective by measurement of QOL in order to improve future clinical decision making.

Methods: The questionnaire (HPN-QOL Version 1) (1) was modified to suit a paediatric HPN population. Questionnaires were anonymized and handed out in HPN clinics or posted to the paediatric HPN cohort. Data on demographics, aetiology of intestinal failure and duration of HPN was collected from HPN database. QOL grading of functional scales (general health, physical and emotional function), HPN specific items (logistical support from the HPN team), Symptoms scales and overall QOL Numerical Rating Scales (scale of 1 to 5) were collected from parent completed questionnaires. Data were collated on Microsoft Excel sheet and analysed. Mann-Whitney test and corrected percentages were used for statistical comparisons between patients with and patients without stoma.

Results: Fourteen out of seventeen families returned the completed questionnaires. Aetiology was Short bowel syndrome (n=10), motility disorders (n=6) and Microvillous inclusion disease (n=1). The median duration of HPN was 32 months. QOL was significantly impaired by increased dependency in these children with items of daily living such as eating, dressing, washing, mobility (n=6), but was not affected in the domains of school attendance (n=8), general fatigue (n=10) and body image (n=11). Patients without stoma (n=6) and their parents developed coping strategies, allowing an improved physical functioning (47%) and less worries (63%), although patients with stoma (n=8) felt less fatigue (63%). There were no significant differences in QOL when patients with and without bowel stoma were compared. Patients (n=13) felt well supported by the hospital Nutrition team in managing logistics related to HPN.

Conclusion: QOL in HPN patients is not significantly affected by the medical aspects of care. This probably reflects support and training offered by the nutritional team at home and at school. This study highlights the need for further integration of medical and social care in complex patients as QOL was impaired in activities of daily care and social functioning. Future routine use of these questionnaires in HPN clinics will help us to involve young children and families to identify areas where they may need further support.

High-dose vitamin A and DHA as a therapeutic option in retinitis pimentosa: experience in three pediatric patients

Ana Moráis¹, José Miguel Martínez de Zabarte¹, Belén Delgado¹, Ana Bergua¹, Susana Noval²

¹"La Paz" University Hospital, Pediatric Nutrition and Metabolic Diseases, Madrid, Spain
²"La Paz" University Hospital, Ophthalmology, Madrid, Spain

Objectives and study: Retinitis pigmentosa (RP) is a group of rare, genetic disorders that involve a breakdown and loss of retinal cells, leading to progressive visual loss. Poor processing of vitamin A metabolites in the retina seems to be implicated in the development of degenerative changes of the RP spectrum. Recently, combined therapy with high-dose vitamin A and docosahexanoic acid (DHA) has shown promising results in adult RP patients, although clinical data in children are lacking. Experience in 3 pediatric patients is provided.

Methods: Subject inclusion criteria: Patients <18 years old with RP; absence of malabsorptive disorders; absence of any condition that contraindicated therapy with high-dose vitamin A (eg pregnancy); normal liver and renal function; normal levels of serum retinol binding protein (RBP); parental informed consent and mature minors consent form. Prescription: oral retinyl acetate (15,000 IU/day) and DHA (300 mg/day + 400 g of oily fish weekly). Clinical control and laboratory tests were performed at 1, 3, 6, 9, 12 months during the first year and semi-annually thereafter. Abdominal ultrasound every 6 months. Ophthalmic controls every 3 months.

Results: Patients age and follow-up are indicated in the table.

All patients stopped the progression of RP after initiation of treatment. Liver function and ultrasound, and serum levels of vitamin A and vitamin A/RBP ratio remain normal in all of them. None have shown signs or symptoms of possible side effects related to vitamin A therapy.

Table:

<table>
<thead>
<tr>
<th>Gender</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at RP diagnosis</td>
<td>7 y</td>
<td>11 y</td>
<td>12 y</td>
</tr>
<tr>
<td>Age at therapy onset</td>
<td>13 y</td>
<td>11 y</td>
<td>14 y</td>
</tr>
<tr>
<td>Current follow-up</td>
<td>24 months*</td>
<td>33 months</td>
<td>6 months</td>
</tr>
</tbody>
</table>

*After the first 18 months she disrupted treatment during 6 months and then resumed until the present moment (24 months of follow-up since the restart).

Conclusion: Treatment with high-dose vitamin A and DHA appears to be a safe short-term option in adolescents <18 years old with RP. Its real effectiveness on clinical course remains to be established with longer follow-up.
Incidence of renal impairment, nephrocalcinosis and kidney stones in children with intestinal failure on long-term parenteral nutrition

Judith Pichler¹, Tom Watson², Kieran McHugh², Jutta Koeglmeier³, Susan Hill³

¹University Clinics Vienna, Department of Paediatric Nephrology and Gastroenterology, Vienna, Austria
²Great Ormond Street Hospital NHS, Department of Paediatric Radiology, London, United Kingdom
³Great Ormond Street Hospital for Children, Paediatric Gastroenterology, Division of Nutrition, Intestinal Failure and Rehabilitation, London, United Kingdom

Objectives and study: The aetiology of nephropathy in children with intestinal failure (IF) treated with long-term parenteral nutrition (PN) is multifactorial and includes fluid and electrolyte disturbances, nephrocalcinosis/nephrolithiasis and chronic renal failure (CRF). Risks include infections, presence of urologic and nephrologic diseases and hypovolemic state with chronic dehydration. Our aim was to review incidence of nephropathy such as renal function, nephrocalcinosis/nephrolithiasis in children on long-term PN treatment.

Methods: Renal and urinary tract imaging and relevant clinical details were reviewed in 55 children (28, 5% male) with IF treated with PN at home. Underlying diagnoses were short bowel syndrome (SBS) in 20 (28%), small intestinal enteropathy in 34 (48%) and motility disorder in 17 (24%). CRF was defined as glomerular filtration rate (GFR) <60mL/1.73 m2/min. To investigate urinary biomarkers of glomerular and tubular damage calcium, protein and N-acetyl-β-D-glucosaminidase (NAG) were used and creatinine-ratio (CR) were calculated. Data was collected on IF related factors and nutritional intake.

Results: CRF was observed in 4 (7%) children with a median GFR of 56.5 (range: 24-65). The prevalence of proteinuria and calciuria was 5.1% and 3.2%. An apparent renal tubulo-interstitial injury with high NAG was found in 12.2%. Eleven patients (7%) had increased echogenicity or nephrocalcinosis on ultrasound. Two of these children had a nephrolithiasis at the age of 4.5 and 6.3y. Both had concomitant nephrocalcinosis in the scan, one had a pathologic calciuria and the other cholelithiasis. There were no differences in high GFR or occurrence of nephrolithiasis and the underlying diagnosis leading to IF, but patients with SBS were at risk for nephrocalcinosis (p=0.008). High serum creatinine was associated significantly with increased echogenity (p=0.005) and nephrocalcinosis (p=0.036). There was no association between renal injury and PN exposure, volume and calories intake or calcium administration.

Conclusion: Renal abnormalities were common in children with severe IF on PN. Most common pathologies were increased echogenicity/nephrocalcinosis that can lead to nephrolithiasis. Regular abdominal scans and check for renal function are of great importance for the management.
Discolouration of the PN filter in children receiving home parenteral nutrition (PN)

Sharon Probert¹, David Derry¹, Karen Hartley¹, Joanne Pena¹, Ruth Stanley¹, Karen Thomson¹, Anirban Mukhopadhyay¹, Susan Bunn¹, Maureen Lawson¹

¹Great North Children's Hospital, Department of Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom

Objectives and study: Parenteral nutrition (PN) provides lifesaving nutrition for children with intestinal failure. In our unit children requiring long term PN are entered into a home PN programme. The parents of 3 children well established on home PN for over 2 years reported the recent discolouration of the 1.2 µm filter used for the administration of the aqueous solution. All three children are dependent on 100% of their estimated energy requirement as PN delivered via a 2 bag system with a SMOF as the lipid solution and a cysteine containing amino acid aqueous solution. Initial measurements of micronutrients aside from vitamin E were all within the reference range for age. However serial repeat investigations revealed falling serum copper levels with haematological changes associated with copper deficiency noted in one patient.

Aim: To investigate the cause of low serum copper levels in 3 children receiving their total estimated energy and nutrient requirements as parenteral nutrition

Methods: 3 children with low serum copper levels and reported discolouration of the filter used for aqueous solution following the administration of cysteine containing home PN solution were identified. Analysis of the aqueous PN solution was performed for zinc pre and post filter. A separate analysis for copper was performed on each child’s bespoke aqueous PN solution using 3 different filters currently used by children receiving home PN in our unit. The process was then repeated using a non-cysteine containing PN solution

Results: In the cysteine containing solutions there was an obvious discolouration to the filters and a reduction in the post filtration copper content. The amount of reduction differed for each solution by 45%, 51% and 60%. The zinc content remained stable. Repeating the process with a non-cysteine amino acid source showed no discolouration in the filter or reduction in copper levels

Conclusion: All three patients were converted to a non-cysteine PN solution with no alteration in copper or zinc prescription. Biochemical and haematological resolution was noted in all cases.

Copper deficiency, has been reported but is rare in patients receiving PN supplemented with adequate amounts of copper.

Brown discoloration of filters associated with a possible incompatibility between a cysteine-containing paediatric amino acid solution and copper sulphate in PN has been reported.

Investigation as to the chemical nature of the precipitant in the filters is ongoing
NUTRITION: Clinical nutrition

N-P-073

Growth of intestinal bacteria in enteral feeding

Vojtech Rada¹, Monia Stemberkova¹, Sarka Musilova¹, Jiri Nevoral²

¹Czech University of Life Sciences, Department of Microbiology, Nutrition and Dietetics, Prague, Czech Republic
²University Hospital Motol, 2nd Medical School, Charles University, Pediatrics, Prague, Czech Republic

Objectives and study: The aim of this study was to test the growth of intestinal bacteria in enteral feeding. The hypothesis was that enteral nutrition containing prebiotics will support the growth of probiotics bacteria while potentially harmful microorganisms (clostridia) will be suppressed. Intestinal microbiota has significant effects on the anatomical, physiological and immunological development of the host. It is microbiological barrier against pathogens and potentially pathogens. Probiotics are live microorganisms, they have beneficial effect on the host. Probiotics microorganisms are bacteria of genera Bifidobacterium, Lactobacillus, Escherichia, Enterococcus, Streptococcus and yeast Saccharomyces boulardii. Prebiotics are food supplements or food that contain indigestible components. These substances support the growth of beneficial bacteria in the colon. Oligosaccharides are presented in human milk or plants (for example chicory or Jerusalem artichoke). Enteral feeding (EF) is nutrition administered to patients who are unable to receive normal food. EF are also used in the treatment of Crohn’s disease, it is gastrointestinal defect which affect small intestine or colon.

Methods: Practical determination of bacterial growth was carried out using microtitre plate. To the microtiter plate was pipetted 90 µl of enteral feeding and 10 µl of bacteria (approx. 10⁷ CFU). The microtiter plate was cultivated at 37 °C for 24 hours anaerobically. After 24 hours were inuculated to the Petri dishes containing agar Wilkins-Chalgren. In the microtiter plate was measured pH and lactate concentration. Petri dishes was cultivated anaerobically in anaerobic jar at 37 °C for 48 hours. After 48 hours were counted number of colonies and the results were statistically analyzed. Wilkins-Chalgren broth with soya peptone was used as a control medium. Seven strains of Bifidobacteria and 7 strains of Clostridia in the 7 enteral feedings were tested.

Results: The strains of animal (Bifidobacterium animalis ssp. lactis 1 and 2) had the lowest growth in Fresubinu Chocolate (4.15 log CFU/g) and the highest growth in Nutridrink Compact (6.26 log CFU/g). The strains of bifidobacteria of human origin (Bifidobacterium bifidum and longum) had the lowest growth in Nutridrink Compact (6.02 log CFU/g) and the highest growth in Fresubin chocolate (7.91 log CFU/g). The strains of human Clostridia had the lowest growth in Nutridrink Compact (7.87 log CFU/g) and the highest growth in Nutridrink Vanilla (8.26 log CFU/g).

Conclusion: The strains of animal origin (Bifidobacterium animalis ssp. lactis 1 a 2) had worse growth than the strains of human origin (Bifidobacterium bifidum and B. longum).
Vitamin D status in children with type 1 diabetes mellitus

Irene Rutigliano¹, Maria Pastore¹, Mario D’altilia¹, Antonio Marseglia¹, Mariantonietta Borrelli², Michela Casolino², Francesca Consiglio², Angelica Di Rodi², Michele Sacco¹

¹Paediatrics, Irccs "Casa Sollievo Della Sofferenza", San Giovanni Rotondo, Italy
²Paediatrics, University of Foggia, Foggia, Italy

Objectives and study: There is an ongoing interest on vitamin D (vitD) status and its relationship with several pathologic condition in pediatric population. In particular, children affected by type 1 Diabetes Mellitus (DM1) are at higher risk of vitD deficiency, but its role on metabolic control and glycemic homeostasis is unclear. Aim of the study: to investigate vitD status in children affected by DM1 and its relation with glycemic control.

Methods: Serum 25-hydroxyvitamin D (25OHD) concentration was assessed; Vitamin D status was defined as follows: deficiency with serum 25OHD < 10 ng/ml, insufficiency among 10-29.9 ng/ml, sufficiency with serum 25OHD among 30-100 ng/ml. Collected data included age, gender and laboratory findings, in particular glycated haemoglobin (Hb A1c).

Results: The study population consisted of 38 children and adolescents affected by DM1 (mean age 11.2±4.22 yrs, range 3.4-18 yrs), 21 males, mean DM1 duration 4.1±4.7 yrs 0.21-15.83 yrs. Vitamin D levels were in normal range (sufficiency) in only 7 children (18.4%), while 81.6% (31 subjects) of our population presented abnormal levels of vitD: in particular, 39.5% had vitD deficiency and 42.1% vitD insufficiency. Children with vitD deficiency and insufficiency had higher mean levels of HbA1c (68.6±11.5 mmol/mol and 66.3±17.9 mmol/mol, respectively) than children with vitD sufficiency (58.29±15 mmol/mol), this difference was not statistically significant (p=0.34), but this trend showed a statistically relevance at Jonckheere- Terpstra test (p=0.049).

Conclusion: VitD insufficiency is largely present in children with DM1 and it could be a relation between glycemic control and vitD status. Our study is a pivot study, but further evaluations are needed to establish the possible role of vitamin in optimizing metabolic control, to define supplementation guidelines in DM1 children.
Decreased malnutrition rates in paediatric inpatients following introduction of national obligatory screening

Anemone van den Berg¹, Aeltsje Brinksma², Joanne Olieman³, Koen Joosten⁴, Jessie Hulst⁵

¹Juliana Children's Hospital/Haga Teaching Hospital, Paediatric Gastroenterology, The Hague, Netherlands
²University Medical Center Groningen, Groningen, Netherlands
³Erasmus MC - Sophia Children's Hospital, Dietetics, Rotterdam, Netherlands
⁴Erasmus MC - Sophia Children's Hospital, Paediatric Intensive Care, Rotterdam, Netherlands
⁵Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands

Objectives and study: Disease related malnutrition in children is associated with prolonged hospital stay and more complications. From 2008, Dutch hospitals have been required to screen for and treat acute malnutrition in paediatric patients on admission as part of a national quality indicator. The requirements stipulate that all hospitals report the number of children actually screened on admission and the energy and protein intake on day 4 of admission in those children deemed malnourished on admission. The aim of this study was to assess if the introduction of this malnutrition quality initiative altered 1) the number of children screened for malnutrition on admission and 2) the treatment of malnutrition.

Methods: centrally reported data of all Dutch hospitals with a paediatric in-patient ward regarding screening for malnutrition (measurement of weight and height), and its treatment (energy and protein intake on day 4) from 2008-2015 were analysed. Acute malnutrition was defined as a weight for age <-2 SDS in patients <1 year of age and as weight for height <-2 SDS in patients aged 1-18 years. For children >1 year of age nutritional intake data on day 4 were compared to set energy requirements calculated using the Schofield formula +30% and protein requirement of 1.2-1.5 g/kg/day. Exclusion criteria were single day admissions and infants <28 days of age.

Results: from 2008 onwards the number of children screened for malnutrition on admission rose from 22% to 75%. The number of children suffering from acute malnutrition dropped from 9.4% to 6.5%, as did the absolute number of children with acute malnutrition. From 2008, the number of children with an adequate energy and protein intake on day 4 of admission has remained more or less the same (Table).

Conclusion: Over the last 7 years, since hospitals have been required to report on screening for malnutrition on admission and its treatment, screening numbers have increased significantly and prevalence rates of malnutrition in paediatric patients have dropped. The number of children with adequate energy and protein intake on day 4 of admission has remained the same. The increased awareness of malnutrition among admitted paediatric patients may have led to this decrease in rate of acute malnutrition.
Table. Acute disease-related malnutrition in children admitted to Dutch hospitals: 2008-2015. *

<table>
<thead>
<tr>
<th></th>
<th>2008a</th>
<th>2009a</th>
<th>2010a</th>
<th>2011a</th>
<th>2012a</th>
<th>2013a</th>
<th>2014a</th>
<th>2015a</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Screening</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Institutions (n)a</td>
<td>34a</td>
<td>63a</td>
<td>79a</td>
<td>87a</td>
<td>88a</td>
<td>90a</td>
<td>91a</td>
<td>90a</td>
</tr>
<tr>
<td>Admissions (n)a</td>
<td>47.595a</td>
<td>69.282a</td>
<td>94.289a</td>
<td>103.114a</td>
<td>92.897a</td>
<td>86.410a</td>
<td>87.048a</td>
<td>86.656a</td>
</tr>
<tr>
<td>Screening (n)a</td>
<td>10.539a</td>
<td>30.567a</td>
<td>46.054a</td>
<td>53.985a</td>
<td>58.946a</td>
<td>61.591a</td>
<td>65.973a</td>
<td>65.720a</td>
</tr>
<tr>
<td>Acute malnutrition (n)a</td>
<td>993a</td>
<td>3280a</td>
<td>4422a</td>
<td>4723a</td>
<td>5010a</td>
<td>4981a</td>
<td>4551a</td>
<td>4277a</td>
</tr>
<tr>
<td>Screening (weighted %)ab</td>
<td>22.1a</td>
<td>44.1a</td>
<td>48.8a</td>
<td>52.4a</td>
<td>63.5a</td>
<td>71.0a</td>
<td>75.8a</td>
<td>75.8a</td>
</tr>
<tr>
<td>Acute malnutrition (weighted %)ab</td>
<td>9.4a</td>
<td>10.7a</td>
<td>9.6a</td>
<td>8.7a</td>
<td>8.5a</td>
<td>8.1a</td>
<td>6.9a</td>
<td>6.3a</td>
</tr>
<tr>
<td><strong>Treatment</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Adequate protein intake (weighted %)ab</td>
<td>56.7a</td>
<td>75.6a</td>
<td>69.7a</td>
<td>72.8a</td>
<td>55.6a</td>
<td>75.5a</td>
<td>63.1a</td>
<td>66.7a</td>
</tr>
<tr>
<td>Adequate energy intake (weighted %)ab</td>
<td>56.7a</td>
<td>76.0a</td>
<td>65.8a</td>
<td>67.1a</td>
<td>57.9a</td>
<td>72.8a</td>
<td>60.3a</td>
<td>62.9a</td>
</tr>
</tbody>
</table>

1 (children screened: (n)/admissions: (n))^100.
2 (children screened: (n)/malnourished children: (n))^100.
3 (adequate protein or energy intake: (n)/malnourished children at admission day: 4: (n))^100.
Long term outcome 6-12 months after treatment with hospital parenteral nutrition (PN) for >27 days in a specialist children’s hospital

Vinod Sharma¹, Abhishek Singh¹, Jutta Koeglmeier², Mark Cowles¹, Susan Hill²

¹Great Ormond Street Hospital, Paediatric Gastroenterology, London, United Kingdom
²Great Ormond Street Hospital for Children, Paediatric Gastroenterology, Division of Nutrition, Intestinal Failure and Rehabilitation, London, United Kingdom

Objectives and study: Parenteral nutrition (PN) is essential supportive treatment for severe intestinal failure (IF). However long–term PN carries the risk of developing life threatening liver disease. Our aim was to review all hospitalised children on PN for more than 27 days to determine incidence, aetiology, intestinal failure-associated liver disease (IFALD) and outcome 6-12 months later.

Methods: All inpatients requiring PN for more than 27 days were included in this study. Data was collected from patients’ notes and electronic data record of hospital on a pre-set required format. We reviewed and analysed data from June to November 2015.

Results: A total of 61 patients including 11(18%) neonates were reviewed (M: F; 28:33). There were 9 pre-term neonates including 2 extreme (< 27 Weeks) preterm babies. Mean age was 4.8 years. Mean duration of PN was 72 days. Primary digestive disorder (PDD) was noted in 31 (51%) children with 11(18%) children having enteropathy and 2(3%) dysmotility. 17(28%) children had surgical diagnoses: necrotising enterocolitis (NEC) in 11(18%) gastrochisis in 2(3%), Hirsch sprung disease in 2(3%) and atresia in 2(3%) children. Thirty (49%) children had Primary non-digestive disorder: oncology 20(36%) cardiology 4(6%), Immunology 2(3%) and other 4(6%). Thirteen (21%) children developed Intestinal failure-associated liver disease (IFALD). One child progressed to stage 2 and another to stage 3 IFALD. 11(85%) children with IFALD were <one-year-old. Only 4 (6%) patients were noted to have sepsis. 42 (69%) children were noted to have hypoalbuminemia (<34g/L) and 15 (25%) severe hypoalbuminemia (<25g/L) before PN was started. After four weeks of parenteral nutrition treatment hypoalbuminemia (<34g/L) was noted in 32 (52%) children and severe hypoalbuminemia (<25g/L) in 4(6%) children. IFALD was associated with younger age, p=0.0005, prematurity, p= 0.003, surgical diagnosis, p=0.002 and hypoalbuminemia before starting on PN, p=0.039. IFALD was not associated with sepsis. All patients were followed-up between 6 months and 12 months of starting on PN. On follow-up, 5(8%) children were reported to have died, all with Primary non-digestive disorder (PNDD). The cause of death in these children were complications related to primary diagnosis but not PN related problems. Of 56 surviving children, enteral autonomy was established in 48(86%) children. Eight (14%) children were on long term home PN, all with Primary Digestive Disorder (PDD). None of the child in both groups was noted to have stage 2 or 3 IFALD. In the group of home PN children, one child was noted to have IFALD 1. There was 15% rise in mean albumin in home PN group patients. No death was reported related to PN complications.

Conclusion: Although Parenteral nutrition is associated with life threatening complications it can now be considered relatively safe lifesaving supportive treatment for severely unwell children with intestinal failure associated with a wide range of underlying diseases in a specialist hospital setting. Mortality is related to the underlying disease as opposed to the PN itself.
Implementing STRONGkids screening tool for nutrition risk- from planning to pilot

Johanna Sjomar1, Jenny Stålhammar2, Niklas Nyström3, Yigael Finkel4

1Uppsala Children’s University Hospital, Paediatric Nutrition Department, Uppsala, Sweden
2Uppsala Children’s University Hospital, Paediatric Nutrition Unit, Uppsala, Sweden
3Uppsala University Children’s Hospital, Gastroenterology and Nutrition, Uppsala, Sweden
4Sachs Children’s AND Youth Hospital, Gastroenterology and Nutrition, Stockholm, Sweden

Objectives and study: There are several reports of disease-related undernutrition in hospitalized children, showing a prevalence of underweight from 4-9%. Standard hospital admittance routine include measuring height and weight which can be used for nutritional status. However, assessment of nutritional risk (defined as the risk for nutritional intervention or nutritional deterioration) requires use of a screening tool. There are a number of screening tools for nutrition risk of hospitalized children. The STRONGkids tool is validated from one month to 18 years. The screening tool consists of 4 questions: 1. Is there an underlying illness with risk for malnutrition or expected major surgery? 2. Is the patient in a poor nutritional status judged with subjective clinical assessment? 3. Is one/several of the following items present - Excessive diarrhea > per day and /or vomiting ( > 3 times/day) -Reduced food intake during the last few weeks -Pre-existing nutritional intervention -Inability to consume adequate nutritional intake because of pain? 4. Is there weight loss or no weight increase (infants<1 year) during the last weeks-months? The patients are scored to either low, medium or high risk of malnutrition.

The objectives with the study is to report the steps from planning to implementation of STRONGkids in the standard hospital care at Uppsala Children’s University Hospital.

Methods: Selection of screening tool: STRONGkids was selected because it is validated for use in children from one month of age. Translation: STRONGkids in English was cross-translated to Swedish by validated method by external expertise. Incorporation into existing electronic patient record: computerized data regarding number of patients admitted, diagnoses, planned surgical interventions, ages, proportion of patients scored, the scoring results, rescoring results after each week of hospital stay. Delegation to the nursing staff to perform and record scorings. Training: obligatory training sessions for the staff was organized. Surveys during the first implementation phase; feasibility and scoring results.

Results: During the test period 70 children were admitted to a mixed neurological and orthopaedic ward and but only 32 were screened. Nrs: < 1 yr 6; 1 < 5 yrs 7; 5-18 years 19. Risk for malnutrition: low 22 (68.8%), moderate: 5 (15.6%) high 5 (15.6%). Only 30% of the nurses completed the feasibility survey. The reported experience from the nurses was that the scoring tool was easy to use and that the extra workload was negligible.

Conclusion: The results shows that a nutrition screening tool is important to identify the patients at nutritional risk. Implementation of a screening tool requires time for planning, training and monitoring.
Malnutrition: a serious concern of pediatric hospitalized patients in India

Lekha Sreedharan¹, Dhanasekhar Kesavelu², Bhuvaneshwari Shankar³

¹Apollo Children's Hospitals, Clinical Nutrition, Chennai, India
²Apollo Children's Hospitals, Gastroenterology, Chennai, India
³Apollo Main Hospital, Clinical Nutrition, Chennai, India

Objectives and study: Malnutrition is consistently associated with adverse clinical outcomes, including increased morbidity, mortality, and length of hospital stay as well as reduced quality of life. It is essential to identify malnourished children and also children at increased risk of malnutrition in order to devise a comprehensive nutrition care program. To evaluate the frequent occurrence of malnutrition among hospitalized children's in to a tertiary care centre in India and to relate nutritional status with adequate intake of nutrients prior hospitalization.

Methods: Throughout the year in 2015, a sample population of 999 pediatric patients (575 male; 424 female) aged 0 months to 17 years were included. Baseline demographics and anthropometric data were analyzed with reference to age using weight for height, height for age and Body Mass Index for age percentile using World Health Organization (WHO) and Multi Centric Growth Reference Study chart. The type, severity, and prevalence rate of malnutrition were defined based on WHO criteria. The diet history and food frequency was recorded for 3 days and the mean energy and protein intake adequacy were evaluated. According to the nutritional status and diet intake, the data was assessed descriptively and comparatively by t-test to determine the mean differences.

Results: On classification based on nutritional status, 382 (38.2%) children's were found to be well nourished and 617 (61.8%) children's were malnourished. Among the malnourished, 28.6% children's draw closer to wasting (weight-for-height ≤ -2 SD), 11% of them come under both wasting and stunting and minimal (1.9%) children's were stunt ((height-for-age ≤ -2 SD) in their growth whilst among the over nourished group, 9.8% children's were overweight and 10.4% children's were obese. Malnutrition severity was not related to the diagnosis. However, cardiac patients were associated with a higher prevalence of malnutrition. Severe malnutrition (30%) was common in 0-6 months and obesity was more in 10-12 years age group. The diet intake showed 50.5% of children have consumed lesser than their calorie requirement, 26.02% children's consumed excess calories and 23.48% children's met their requirement. In terms of protein intake, 60.4% children have met their requirement, while 39.9% children's consumed less than their requirement. There are statistically significant differences among malnourished and normal patients in relation to BMI (p < 0.001), energy adequacy (p < 0.001) and protein intake (p < 0.05).

Conclusion: It is extremely important to identify at risk population to prevent its devastating effects on the patients and the possible impact on healthcare system. This study shows malnutrition rates remain high in children's and this could be attributed to the unhealthy dietary practices. Therefore meticulous attention needs to be provided for comprehensive nutrition.
Home parenteral nutrition for very low birth weight infants is safe

Kajsa Waldenvik\textsuperscript{1}, Yigael Finkel\textsuperscript{2}, Helene Engstrand Lilja\textsuperscript{3}, Niklas Nyström\textsuperscript{1}

\textsuperscript{1}Uppsala University Children’s Hospital, Gastroenterology and Nutrition, Uppsala, Sweden
\textsuperscript{2}Sachs Children’s AND Youth Hospital, Gastroenterology and Nutrition, Stockholm, Sweden
\textsuperscript{3}Uppsala University Children’s Hospital, Paediatric Surgery, Uppsala, Sweden

Objectives and study: Guidelines for HPN (home parenteral nutrition) in children with IF (intestinal failure) rarely advice on age and/or weight limits for hospital discharge to HPN for premature infants who are at higher risk for infectious, metabolic and technical complications associated with long-term PN. HPN for children in Sweden fully depends on the successful management by the caretakers. There are no home service companies and there are no hospital based home visit services. The objectives of this study was to review growth and infectious complications during the first three months after discharge in VLBW (very low birth weight) infants on HPN.

Methods: A retrospective study of medical records of all VLBW infants discharged with HPN from our tertiary care hospital during 2012-2016. All children had single lumen tunneled central venous catheters. PN (containing Omegaven\textregistered 0, 5-1 g/kg BW) and all additives was compounded in the hospital pharmacy on individual prescriptions. TauroLock\textregistered was started when cyclic PN was commenced. HPN training in the hospital took part during 2-3 weeks.

Results: Seven post-surgical VLBW infants (4 boys) and (3 girls) with a median gestational age of 25 weeks (25-31), median BW of 0,8 kg (0,73-1,44), diagnoses of necrotizing enterocolitis (4), volvolus, gastroschisis and perforated small bowel were discharged to HPN at a median postconceptional age of 48,5 weeks (37-63) with a median weight of 4,6 kg (2,43-5,1) and a median standard deviation (SD) weight of -0,9 (-3- 0).

After three months on HPN none of the children had experienced metabolic, infectious or thrombotic events. Their median SD BW had increased to -0,1 (-2,1-0,8).

Conclusion: Discharge of VLBW infants to home with HPN cared for by well-trained caretakers, appears to be a safe practice.
NUTRITION: Clinical nutrition

N-P-080

The role of fish oil supplementation on preventing weight loss and the changes level of AMPK during chemotherapy in children with acute lymphoblastic; Leukemia

Nur Aisiyah Widjaja¹, Siti Azizah¹, Roedi Irawan¹, IDG Ugrasena¹

¹Airlangga University/Dr.Soetomo Hospital, Child Health Department, Surabaya, Indonesia

Objectives and study: Malnutrition and weight loss are common among cancer patients and are due to a variety of mechanisms involving the tumour, the host response to the tumour, and anticancer therapies. It is a major cause of morbidity and mortality. Symptoms may occur at all stages of the cancer during treatment. Acute Lymphoblastic Leukemia (ALL) is the most common hematological malignancy and the main cause of cancer-related deaths in children. Eventhough, mechanisms of cancer-associated malnutrition are complex. Studies have shown that an increased elevated acute-phase protein response and high level of pro-inflammatory cytokines have been subsequently shown to be associated with the development of cancer-associated malnutrition. The AMP-activated protein kinase (AMPK) is a central regulator of cellular metabolism and energy homeostasis. Supplementation of fish oil that contain omega-3 PUFA can activate AMPK to induce growth inhibition and apoptosis cancer cell. This is probably because the enrichment with polyunsaturated fatty acids makes leukemia cells more susceptible to lipid peroxidation and more sensitive to drug therapy. Studies suggest that supplementation with of omega-3 (fish oil) fatty acids suppresses the acute phase protein response, which attenuate cancer-induced weight loss and may be promising in treating cancer-associated malnutrition.

Methods: A randomized control trial study was undertaken in 1 – 10 years children admitted to Pediatric haematology ward Soetomo hospital from April 2015-February 2016. Thirty-two eligible subjects were equally randomized into the two groups: the trial group (TG) and control group (CG). The trial group had consume capsule of fish oil per day during chemotherapy (induction and consolidation phase) The levels of AMPK were measured before study and during induction phase and consolidation phase. Body weight was measure before and after consuming fish oil capsule during chemotherapy. Data was analyzed by t - test.

Results: Out of 32 children , 56,2 % were male. The TG group showed increment in body weight (1,10 kg vs -0,25 kg) compared with CG group at 12 weeks (p 0.013 ) although not statistical significant. There was a significant increase in AMPK level of TG after induction and consolidation phase chemotherapy(1,91 ng/ml vs -1,70 ng/ml ) and (4.74 ng/ml vs -0.80 ng/ml) respectively (p<0.005 ) compared with CG group.

Table: AMPK level between TG and CG during chemotherapy phase

<table>
<thead>
<tr>
<th>AMPK level (ng/ml)</th>
<th>Trial Group Mean (SD)</th>
<th>Control Group Mean (SD)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before Induction Phase</td>
<td>6.46 (3.51)</td>
<td>10.52 (6.58)</td>
<td>0.064*</td>
</tr>
<tr>
<td>After Induction phase</td>
<td>8.79 (4.93)</td>
<td>8.55 (6.27)</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>1.91 (1.96)</td>
<td>-1.70 (3.38)</td>
<td>0.002*</td>
</tr>
<tr>
<td>Before Consolidation phase</td>
<td>6.46 (3.51)</td>
<td>10.52 (6.68)</td>
<td>0.064*</td>
</tr>
<tr>
<td>After Consolidation phase</td>
<td>11.20 (3.96)</td>
<td>8.80 (6.93)</td>
<td></td>
</tr>
<tr>
<td>Difference</td>
<td>4.74 (3.75)</td>
<td>-0.80 (2.67)</td>
<td>&lt; 0.0001*</td>
</tr>
</tbody>
</table>
"T test

**Conclusion:** Supplementation of fish oil has a positive effect on AMPK level during chemotherapy and body weight increment among children with acute lymphoblastic leukemia.
Pancreatic exocrine insufficiency in malnourished children: new insights on the possible cause of the never-ending problem of childhood malnutrition

Ariani Dewi Widodo, Saptawati Bardosono, Ina Susianti Timan, Widdy Winarta, Dwi Prasetyo, Agus Firmansyah

1Harapan Kita Women and Children Hospital, Gastrohepatology Division, Department of Pediatrics, Jakarta, Indonesia
2Faculty of Medicine University of Indonesia, Department of Clinical Nutrition, Jakarta, Indonesia
3Faculty of Medicine Universitas Indonesia, Department of Clinical Pathology, Jakarta, Indonesia
4Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia
5Faculty of Medicine Padjajaran University, Bandung, Indonesia
6Gastrohepatology Division, Department of Child Health, Faculty of Medicine, Universitas Indonesia - Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Objectives and study: Malnutrition (in this context refers to undernutrition) is a global issue and is one of an important target of the Millenium Development Goals (MDGs). The prevalence of childhood malnutrition is still increasing despite efforts to prevent it, for example in Indonesia acute malnutrition increased from 17.9% (2010) to 19.6% (2013) and chronic malnutrition from 35.6% (2010) to 37.2% (2013). Severe malnutrition has 9-fold risk of mortality, while severe stunting due to chronic malnutrition has a 4-fold risk of mortality. Previous studies have found that intestinal vili are destructed in malnutrition, thus decreasing secretin and cholecystokinin secretion which was supposed to stimulate the exocrine pancreas to produce digestive enzymes. As a result, food are not properly digested and nutrition not properly absorbed, making the malnutrition even worse. The aim of this research is to study which of acute or chronic malnutrition relates with pancreatic exocrine insufficiency in children.

Methods: This is a cross sectional study in thirty undernourished children under five years of age taken from pediatric outpatient clinics of five hospitals in Jakarta. WHO 2005 criteria was used as a reference. Acute malnutrition was defined by weight-for-length of less than -2 standard deviations (SD). Chronic malnutrition was defined by length-for-age of less than -2 SD. One-time stool sample was taken to determine pancreatic exocrine function in all children based on fecal elastase-1 (FE-1) test.

Results: Median value of length-for-age was -1.04 (-4.01–1.79) and median value of weight-for-length was -0.89 (-3.1–2.99). Chronic malnutrition was found to be significantly correlated with level of FE-1 (p = 0.014; r = 0.437), while acute malnutrition was not significantly correlated with FE-1 (p = 0.102; r = 0.299).

Conclusion: Chronic malnutrition was found to be significantly correlated with pancreatic exocrine insufficiency, while acute malnutrition is not.
Assessment of nutritional status in patients with primary immunodeficiency

Asuman Karhan¹, Saliha Eren², Ersin Gumus³, Betül Karatmaca³, Aysel Yuce¹, Deniz Çağdaş Ayvaz², Hasan Ozen¹, Inci Nur Saltik Temizel¹, Hulya Demir¹, İlhan Tezcan²

¹Hacettepe University Faculty of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
²Hacettepe University, Faculty of Medicine, Department of Pediatric Immunology, Ankara, Turkey
³Faculty of Medicine, Hacettepe University, Pediatric Gastroenterology, Hepatology, and Nutrition, Ankara, Turkey

Objectives and study: Primary immunodeficiency (PID) patients may have nutritional problems for many reasons; increased catabolism due to recurrent infections, persistent diarrhea and malabsorption, as well as decreased food intake due to the loss of appetite. Nutritional status is one of the most important factor that primarily affects immune defense and nutritional insufficiencies can directly worsen immune defense in PID patients. The aim of this study is to evaluate the nutritional status and the prevalence of malnutrition and nutritional deficiencies among different PID groups.

Methods: PID patients of 0-18 years old who were admitted to the Paediatric Immunology Department between September and December 2015 were evaluated. Anthropometric measurements were calculated for weight for age, height for age, weight for height and body mass index (BMI), as well as Z scores for BMI and weight for age. Patients who had malnutrition were referred to the Paediatric Gastroenterology Department and were also evaluated for daily caloric intake and deficiencies of iron, zinc, folic acid, and vitamins A, B12, D and E. The patients were given nutritional advise.

Results: 59 patients were evaluated; 31 were male and 28 were female (M/F=1.1) and the mean age of the patients was 11.25 ± 4.89 years (2.3 to 18). Twenty-six (44.1%) patients had cellular, 19 humoral and the remaining 14 patients had other immunodeficiencies. Malnutrition was detected in 18 of 59 patients (30%), among them 40% had severe and 40% moderate malnutrition. Their age was 9.75 ± 4.44 years (2.3 to 17.5). The prevalence of malnutrition was markedly high in patients with cellular immunodeficiencies (42.3%) and among SCID (71.4%, n=5/7) and AT (57.1%, n=4/7) patients. Daily caloric intake was low in all of the patients with malnutrition. Serum zinc and B12 levels were normal for all patients with malnutrition, but vitamin A (72.2%) and vitamin D (44.4%) deficiencies were common.

Conclusion: Patients with PID have a high prevalence of malnutrition. Vitamin A and D were the most common deficiencies among patients with malnutrition. These patients must be evaluated carefully regarding nutritional status, daily caloric intake and vitamin supplementation. Early diagnosis and taking measurements will help to decrease morbidity and mortality related with PID. Besides the primary disease, long term follow up nutritional status is also essential for a good quality of life.
The changes of body composition, glucolipid and bone metabolism in obese children and adolescents after weight loss

Xuelin Zhao¹, Qingya Tang¹, Huijuan Ruan¹, Jiang Wu¹, Yang Niu¹

¹Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Clinical Nutrition, Shanghai, China

Objectives and study: To observe the changes of anthropometric parameters and indicators of glucolipid and bone metabolism after weight loss in obese children and adolescents, and explore the effectiveness of weight loss camp and its influences on glucolipid and bone metabolism.

Methods: This study recruited children and adolescents (aged 9 to 17 years) of simple obesity who completed the six-week weight loss camp. Before and after weight-loss, all subjects accepted anthropometric measurements, and collection of fasting blood samples for testing indicators of glucolipid and bone metabolism. Anthropometric parameters included height, weight, waist circumference (WC) and hip circumference (HC), triceps skinfold thickness (TST) and subscapular skinfold thickness (SST), blood pressure, and calcaneus ultrasound bone mineral density (BMD). The indicators of glucolipid metabolism included fasting blood glucose (FBG), fasting insulin (FINS), total cholesterol (TC), triglyceride (TG). The indicators of bone metabolism included 25-hydroxyvitamin D (25-OHD), osteocalcin (OC), parathyroid hormone (PTH), bone specific alkaline phosphatase (BALP), total propeptide of type I procollagen (T-PINP) and β-isomerized form carboxy-terminal telopeptide of type I collagen (β-CTX). All subjects accepted appropriate diet control and regular aerobic exercise training (indoor) under closed-off management.

Results: Finally 53 subjects completed the six-week weight loss camp, including 35 males and 18 females. Their average age was (13.6±1.8) years old. After weight loss, almost all of anthropometric parameters and glucolipid indicators were improved significantly (p<0.001). The average weight decreased by 10.4kg (11.9%), and body mass index decreased by 4.81kg/m² (15.1%). SST reduced by 12.8mm (32.6%), and TST reduced by 6.2mm (20.1%). WC reduced by 11cm (10.9%) and HC reduced by 8.7cm (8.1%). SBP decreased by 6.5mmHg (5.0%) and DBP decreased by 7.8mmHg (10.5%). FBG, FINS and Homeostatic model assessment of insulin resistance (HOMA-IR) decreased by 0.46mmol/L (7.7%), 88.5pmol/L (64.0%) and 3.01 (67.35%), respectively. TC reduced by 1.00mmol/L (20.1%), and TG reduced by 1.12mmol/L (50.4%).

Before weight loss, serum 25-OHD levels of all subjects were lower than 20ng/ml in the status of vitamin D deficiency, and the average level was 13.81ng/ml. After weight loss, serum 25-OHD level elevated to 26.82ng/ml. Only two of them (3.8%) were still in the status of vitamin D deficiency, and 13 of them (24.5%) reached vitamin D sufficiency. Serum PTH and OC elevated by 27.0pg/ml (128%, p<0.001) and 20.87ng/ml (44%, p<0.001) respectively. BALP and T-PINP declined by 256ng/ml (38.8%, p<0.001) and 51.9ng/ml (43.6%, p<0.001). β-CTX elevated by 0.3ng/ml (33%, p<0.05), and BMD also increased significantly (p<0.001).

Conclusion: After weight loss, weight, BMI, skinfold thickness and blood pressure of obese children and adolescents decreased significantly. The indicators of glucolipid metabolism improved comprehensively. Serum 25-OHD level elevated to twice as much as the level before weight loss, and the incidence of vitamin D deficiency decreased significantly. Serum OC and PTH also increased significantly. After weight loss, BMD of obese children and adolescents increased. Nevertheless, the level of bone resorption elevated and the level of bone formation declined.
Does serum proteins status reflect undernutrition in hospitalized children with chronic heart failure?

Natalia Zvonkova¹, Tatiana Borovik², Leila Gandaeva³, Elena Basargina³, Eduard Gemdzhian⁴

¹Scientific Center for Children's Health, Healthy and Sick Child Department, Moscow, Russian Federation
²Scientific Center of Children's Health, Healthy and Sick Child Nutrition Department, Moscow, Russian Federation
³Scientific Center for Children's Health, Cardiology Department, Moscow, Russian Federation
⁴National Research Center for Hematology, Biostatistics, Moscow, Russian Federation

Objectives and study: Prevalence of undernutrition in children with chronic heart failure (HF) is high worldwide¹. Evaluation of nutritional status in children with HF is an important part of clinical examination allowing to determine undernutrition and to start nutritional support. Serum proteins (e.g. albumin, prealbumin) indexes analysis is traditionally used for nutritional status assessment. The aim of the study was to evaluate serum proteins levels in undernourished children with HF.

Methods: In 153 patients (83 girls) from 1 month to 16 years with HF (class II-IV according to Ross) due to various cardiac diseases (congenital heart disease, cardiomyopathies), anthropometric data (height, weight) and serum proteins (total protein, albumin, prealbumin, C-reactive protein, transferrin) concentration analysis were performed during 48 hours after admission to cardiology department of Scientific Centre of Children’s Health from October 2013 to April 2016. Anthropometric analysis was accomplished through the calculation of Z-scores with the support of the WHO Anthroplus, 2009 software. Undernutrition was defined using WHO classification (Z-scores weight/height, body mass index (BMI)/age, height/age ≤ -2.0). Statistical analysis included the multidimensional contingency tables analysis.

Results: Concentrations of serum proteins in children with moderate and severe undernutrition (n=49) and in children with adequate nutritional status (n=84) had no statistically significant differences on admission to the clinic: in 90-100% of children the level of serum proteins (depending on the type of serum protein) was in the normal range, and in 1-10% of children this level was either higher or lower than normal.

Conclusion: In patients with chronic heart failure, associated with moderate to severe undernutrition, serum proteins levels (total protein, albumin, prealbumin, transferrin, C-reactive protein) do not reflect the degree of undernutrition, even in HF class II-IV according to Ross. And so, anthropometric data analysis is the main method in undernutrition identification. Serum proteins status has additional value for nutritional assessment and characterizes protein-synthesizing function of the liver in children with chronic heart failure.

Levels of pro-vitamin A compounds and tocopherol in mother-infant pairs from Midwest USA and correlations with fetal growth

Corrine Hanson¹, Elizabeth Lyden², Jeremy Furtado³, Mariana Schumacher⁴, Matthew Van Ormer⁵, Elizabeth McGinn⁶, Kara Weishaar⁶, Caleb Cave⁶, Rebecca Johnson⁶, Ann Anderson Berry⁷

¹University of Nebraska Medical Center, Medical Nutrition Education, Omaha, United States
²University of Nebraska Medical Center, College of Public Health, Omaha, United States
³Harvard University, Boston, United States
⁴Unmc, Pediatrics/Medical Nutrition, Omaha, United States
⁵University of Nebraska Medical Center, Omaha, United States
⁶Unmc, Pediatrics, Omaha, United States
⁷University of Nebraska Medical Center, Pediatrics, Omaha, United States

Objectives and study: Evaluate correlations between maternal and cord blood levels of pro-vitamin A compounds and vitamin E derivates tocopherol isoforms with newborn growth variables, including percentiles rankings for weight, head circumference and length at birth. Newborns with poor growth have higher risks of neonatal morbidity and mortality. Fetal growth restriction and SGA is a predictors of later impaired neurodevelopment and adult chronic disease. Risk factors for poor fetal growth include primiparity, low pre-pregnancy body mass index (BMI), smoking and preeclampsia. Free radicals and maternal antioxidant defenses may be involved in the fetal growth. Nutritionally derived antioxidants represent potentially modifiable exposures, and it has been hypothesized that higher levels of antioxidants in maternal blood may provide protection from growth restriction.

Methods: Samples of maternal and infant cord blood were collected on 189 mother-infant pairs at delivery. Concentrations of alpha and beta-carotene, beta-cryptoxanthin, lycopene, retinols, lutein and tocopherols were measured using high-performance liquid chromatography. Birth growth variables were plotted on appropriate charts for determination of percentile rankings. Descriptive statistics were calculated and Spearman correlations coefficients were used to look at the association of maternal and cord pro-vitamin A compounds and tocopherol measurements. Independent sample t-tests were used to compare continuous measures between dichotomous groups. P<0.05 was considered statistically significant.

Results: Significant correlations were observed between birth weight and length percentiles and maternal levels of lutein + zeaxanthin (p=0.005 and p=0.010, respectively) and of beta-cryptoxanthin (p=0.041 and p=0.028). Correlations between maternal levels of total-lycopene (and its derivatives trans and cis-lycopene) and percentiles of birth weight and head circumference were statistically significant (p<0.05). Levels of maternal alpha-carotene were significantly correlated with all birth growth variables (p=0.001, p=0.009 and p=0.03 for percentiles of birth weight, head circumference and length, respectively). No statistically significant difference was present between retinol levels and percentile rankings for infant birth weight, head circumference, or length. Maternal levels of alphatocopherol were also statistically associated with all the birth growth percentiles (p=0.024; p=0.032; p=0.039 for weight, head circumference and length, respectively).

Conclusion: Our findings suggest a possible negative influence of low levels of pro-vitamin A compounds, but not retinol levels, and of vitamin E isoforms in newborn growth outcomes. Whether higher levels of these substances would be protective is still unknown. Large studies assessing the association between nutritionally derived antioxidant levels in pregnancy and risk of growth restriction are necessary.
In vitro digestion of infant formula fat blends with varying proportion of goat milk fat

Eva-Lotta Andersson¹, Colin Prosser², Olle Hernell¹

¹Umea University, Clinical Sciences/Pediatrics, Umea, Sweden
²Dairy Goat Co-Operative Ltd, Hamilton, New Zealand

Objectives and study: Fat is the major source of calories in infant formula, providing 40-55% of energy for infant growth. The milk fat is typically discarded and replaced by vegetable oils when manufacturing infant formulas. Recently, the value of milk fat has been re-evaluated (Timby N et al. Am J Clin Nutr 2014;99:860-8). Hence, an alternative method is to use a mixture of % milk fat combined with a selection of vegetable oils to provide the desired fatty acid profile. As most of the membrane proteins and phospholipids are retained in the milk lipid droplet, i.e. the milk fat globule membrane (MFGM) the lipid structure in formula with milk fat is expected to be more similar to the complex lipid structure in human milk. This study was initiated to determine how the relative proportions of milk fat and vegetable oils might influence the lipolysis of fat droplets.

Methods: The fat blends were made by combining selected vegetable oils with the cream fraction of goat milk to yield 11, 28 and 51% milk fat in the final fat blend. The fatty acid (FA) composition in the fat blends was matched by varying the quantity of coconut, high oleic sunflower, safflower, canola and palm oils. Lipolysis was assessed in vitro under experimental conditions resembling the small intestine of newborn infants. Two sources of digestive enzymes were used. One was a mixture of purified human Gastric Lipase (GL), Bile Salt- Stimulated Lipase (BSSL) and pancreatic lipase related protein-2 (PLRP2). The other used gastric (GJ) and jejunal juices (JJ) from ~3-mo-old prematurely born infants. The samples were initially mixed with 20µl GJ or 5µg purified GL, 2 mM bile salt mixture (resembling the composition in duodenal juice of a preterm infant) (taurocholic acid, taurochenodeoxycholic acid, glycocholic acid and glycochenodeoxycholic acid) and 0.1µg colipase in a total volume of 1.5 ml, pH 6.0 and incubated at 37°C. After 30 min the pH was raised to 7.4 with NaOH, then 2µg BSSL and PLRP2, or 10 or 50µl JJ were added and incubated for another 120 min. After the incubation the lipids were extracted and separated by TLC. The amount of lipid in each spot was expressed as a proportion of total lipids.

Results: There was limited lipolysis, assessed as the ratio of free fatty acid to triglyceride, using GL or GJ alone to mimic the gastric phase of digestion. Lipolysis was enhanced in the presence of JJ or with the combination of BSSL and PLRP2 to mimic the intestinal phase of digestion. In all situations, the fat blend containing 51% goat milk fat showed the greatest release of free fatty acid compared to lower proportions of milk fat.

Table: Ratio of free fatty acids to triglyceride after in vitro digestion of fat blends containing different amounts of goat milk fat. Data are presented from in vitro incubations with GL and then varying amounts of JJ, or GJ with BSSL, PLRP2.

<table>
<thead>
<tr>
<th>% milk fat</th>
<th>10µl JJ</th>
<th>50µl JJ</th>
<th>BSSL + PLRP2</th>
</tr>
</thead>
<tbody>
<tr>
<td>11%</td>
<td>0.77</td>
<td>2.27</td>
<td>0.34</td>
</tr>
<tr>
<td>28%</td>
<td>1.05</td>
<td>1.99</td>
<td>0.37</td>
</tr>
<tr>
<td>51%</td>
<td>1.86</td>
<td>3.48</td>
<td>14.7</td>
</tr>
</tbody>
</table>

Conclusion: Inclusion of goat milk fat in the fat blend for infant formula has no detrimental effect on lipolysis under in vitro conditions mimicking infant digestion. These in vitro data are consistent with a previous clinical trial confirming that growth of infants fed formula with goat milk fat was comparable to that of breastfed infants (Zhou SJ et al. Brit J Nutr 2014;111:1641-51). The added advantage with
inclusion of milk fat is that the formula will contain potential functional components contained within the MFGM.

**Disclosure of interest:** E-L Andersson: None declared, C Prosser conflict with: funded by Dairy Goat Co-operative Ltd, O Hernell conflict with: consultant to Dairy Goat Co-operative Ltd
CoMiSS usage in practice - our first experience

Kateřina Bajerova¹, Milan Bajer¹

¹University Hospital Brno, Pediatric Clinic, Brno, Czech Republic

Objectives and study: CoMiSS-questionnaire is a simple tool that should be useful for detecting infants with potential risk of cow’s milk allergy (CMA). Scoring the gravity of atopic dermatitis, colic behavior, type of stools, regurgitation and respiratory symptoms may help to recognize risky patients by reaching or crossing the level of 12 points.

Methods: We used CoMiS-questionnaire to detect individuals with risk of CMA. We obtained 527 completed questionnaires from 121 infants (63 males, 58 females) aged 6 weeks to 1 year. No of completed questionnaires by 1 infant (parent) were 2-7. Questionnaires were completed by parent during regular preventive visitations in pediatrician GP in 6 weeks, 3, 4, 6, 8, 10 and 12 months of infant’s age. None of tested infant had proven CMA before entering the study. The endpoint was to find out whether the recommended level of 12 points is sensitive enough to define candidates for elimination/exposition test resp. patients suffering from CMA.

Results: Scores that we obtained were 0 to 11, none of infants reached 12 points. Nevertheless elimination/exposition test was performed in 21 patients (17.35 %), who presented atopic dermatitis (8 / 6.61%) allergic colitis (7 / 5.78 %), colic behavior (1 / 0.83%), hives (1 child/0.83%), failure to thrive (1 / 0.83%), or combination of symptoms (3 / 2.48%). Those symptoms appeared in infants after having food challenge with cow’s milk, either via breast milk (14/66,67%) or being fed by cow’s milk infant formula (7/33,33%). Out of those 21 patients finished the EET 18, 3 did not undergo the challenge complete and thus the CMA could not be diagnosed according to guidelines. 11 patients (7,44%) were proven to suffer from CMA (positive EET). In these patients the maximum CoMiSS-score was 11 (hives), and minimum was 6 (patients with colitis only). In infants, who did no present symptoms of CMA and did not undergo the EET (100 patients) the CoMiSS-score was 0-8, but only 2 patients of those reached the score of 8 (2%). There were 4 patients out of 11 with CMA, who reached 8 CoMiSS-points. The difference of 8 points appearance in these two groups was statistically important (P<0,05).

Conclusion: In our study were 11 patients (7,44 %) out of 121 proven to suffer from CMA. None of them reached 12 points according to CoMiSS-questionnaire for detecting CMA with non-specific symptoms. Lower CoMiSS-score may be more sensitive to detect patients with CMA risk. Further observation using CoMiSS is needed.
Shorter time to full enteral feedings among infants fed an intact protein (IP) vs an extensively hydrolyzed (EH) formula does not appear to be related to differences in gastric emptying

Maria Elisabetta Baldassarre1, Antonio Di Mauro2, Margherita Fanelli3, Osvaldo Montagna1, Jennifer Wampler4, Timothy Cooper4, Nicola Laforgia5

1 University of Bari-Policlinico Hospital, Neonatology and Neonatal Intensive Care Unit, Department of Biomedical Science and Human Oncology, Bari, Italy
2 University of Bari "Aldo Moro", Neonatology and Neonatal Intensive Care Unit, Department of Biomedical Science and Human Oncology, Bari, Italy
3 University of Bari "Aldo Moro", Department of Interdisciplinary Medicine, Bari, Italy
4 Mead Johnson Nutrition, Department of Medical Affairs, Evansville, United States
5 University of Bari "Aldo Moro", Department of Biomedical Science and Human Oncology, Bari, Italy

Objectives and study: Hydrolyzed cow’s milk protein infant formulas are often used in preterm infant feeding despite little clinical evidence of improvement in feeding advancement or markers of feeding tolerance. An objective of the current study was to evaluate the relationship of days to full feeding with gastric emptying time in preterm infants randomly assigned to receive one of two marketed study formulas for the first 14 feeding days.

Methods: In this double-blind, controlled, parallel-group, prospective study, eligible infants (28-33 weeks' gestational age; birth weight of 700-1750g and AGA) were enrolled within 24 hours of first enteral feeding. All mothers were encouraged to provide their own breast milk; study formula was supplemented as needed per randomization. The primary outcome was days to full enteral feeding (≥140 mL/kg/day). Gastric emptying rate and half-emptying time (T1/2) were assessed by real-time ultrasonography on Study Day 14 using antral measurements from 0 (before bolus) to 90 min (15-min intervals). Populations for analysis included participants who 1) completed the study per protocol and 2) received ≥75% study formula intake.

Results: Of 65 enrolled preterm infants (IP: n=32; EH: n=33), 60 completed the study per protocol (IP: 30; EH: 30); of these, 54 (90%) received some breast milk and 23 received ≥75% study formula intake (IP: 11; EH: 12). Median time to achievement of full feeding was significantly shorter for the IP vs EH group (Day 10 vs 14, P=0.030) for participants receiving ≥75% study formula intake. Achievement of full enteral feeding by Day 14 was similar between groups overall (IP: 24/30, 80%; EH: 19/30, 63%; P=0.121), but higher in the IP group for participants receiving ≥75% study formula intake (IP: 10/11, 90.9%; EH: 6/12, 50% P=0.069). Median gastric emptying at Day 14 was significantly slower for the IP vs EH group overall (T1/2; 59 vs 54 min; P=0.031) and in participants who received ≥75% study formula intake (62 vs 53 min, P=0.018). However, gastric emptying time had no correlation with achievement of full feeding for participants who completed the study per protocol (r²=0.008; P=0.49) (Figure). No group differences were detected in tolerance measures (abdominal distention, regurgitation/emesis, feedings withheld ≥4h, or bloody stools) or in positive cultures for sepsis (IP: 2, EH: 3; evaluations performed in 63.3% of participants). No episodes of NEC were reported.
**Conclusion:** Feeding intact cow milk protein formula vs extensively hydrolyzed casein formula was associated with shorter time to full enteral feeding. However, faster emptying with extensively hydrolyzed formula did not predict feeding success, raising questions around the clinical relevance of this surrogate marker of feeding tolerance.

**Disclosure of interest:** ME Baldassarre: none declared
A Di Mauro: none declared
M Fanelli: none declared
O Montagna: none declared
JL Wampler, conflict with: Mead Johnson Nutrition
T Cooper, conflict with: Mead Johnson Nutrition
N Laforgia: none declared
**Personalized nutrition kit development to determine secretotype of Chinese mother by detecting a specific single nucleotide polymorphism (rs1047781)**

Xiaolei Ze\(^1\), Liang Chen\(^1\), Patrice Malard\(^1\), Ming Liu\(^1\), Yongmei Peng\(^2\)

\(^1\)Biostime Institute of Nutrition and Care, Guangzhou, China  
\(^2\)Shanghai Center for Women and Children's Health, Shanghai, China

**Objectives and study:** It has been a recent trend to link personal genome information with specific nutritional advice in order to improve health status, in other words, ‘personalized nutrition’. Easy, convenient, cost-saving and reliable detection would provide effective tools for people to explore their own genetic information and lead them to a healthier diet and living habit. At the early stage of life, it is widely accepted that the optimal source of nutrition is breast milk, with human milk oligosaccharides (HMOs) thought to play an important role in protection against invading pathogens, the stimulation of immune response of intestinal cells and the nourishing of beneficial commensal bacteria. However, due to the inactive of secretor gene (FUT2), some mothers (non-secretors) have altered HMO composition and quantification, in particular the \(\alpha\)-1,2-fucosylated oligosaccharides. Thus, there is demand for mothers to find an easy and convenient way to gain the information of their milk HMO composition and to make a better feeding plan. In this pilot study, we developed an easy & convenient kit for mothers to collect oral mucosa cells at home, and examined secretor status of Chinese breast feeding mothers using the DNA extracted either from oral cells or from milk. We also measured the HMO (2'-fucosyllactose (2'-FL), representative of 1,2-fucosylated oligosaccharides) concentration, to verify the reliability and feasibility to use the quick and cost-saving gene detection as a tool of personalized nutrition for mothers and their infant.

**Methods:** Oral mucosa cells and breast milk samples of 10 subjects were randomly selected from those of 100 recruited Chinese mothers. DNA was extracted from oral cells or milk. Secretor status and was determined by detecting the genotype of the FUT2 SNP site rs1047781, which was previously reported to be a specific SNP for Asian population. The 2’-FL in milk was separated by high performance anion ion exchange Chromatography and then measured by an electrochemical detector and quantified with external standard method.

**Results:** The oral cell collection kit allows sufficient biological sample collection and delivery at room temperature. The DNA extracted both from oral swabs and milk were of good quality for subsequent gene detection, and the genotype results gained from both type of samples were consistent. 7 of the 10 mothers were secretors with the genotype AA or AT (AA, \(n=3\); AT, \(n=4\)) while the other 3 mothers were non-secretors, with the genotype TT. The concentration of 2’-FL in milk of secretor mothers were: AA, 1.54 ±0.86 g/L (\(n=3\)), AT, 0.56±0.17g/L (\(n=4\)), respectively. The 2’-FL concentration was under detection limit in the milk of non-secretor mothers (\(n=3\)).

**Conclusion:** This pilot study confirmed that the genotype of SNP rs1047781 can be used as an indicator for HMO composition. Our kit provides mother an easy, reliable and feasible tool of personalized gene detection for maternity and infant nutrition.
Association of linear growth velocity and behavior at 18 months of life in healthy children

Ana Nieto Ruiz\(^1\), Florian Herrmann\(^2\), Natalia Sepúlveda Valbuena\(^3\), Maria Teresa Miranda\(^4\), Mireia Morera\(^5\), Cristina Campoy Folgoso\(^6\)

\(^1\)University of Granada, Euristikos Excellence Centre for Paediatric Research; Brain, Mind and Behavior International Centre, Granada, Spain
\(^2\)Euristikos Excellence Centre for Paediatric Research, Department of Pediatrics, School of Medicine, University of Granada, Spain, Granada, Spain
\(^3\)Euristikos Excellence Centre for Paediatric Research, University of Granada, Spain, Nutrition and Biochemistry Department, Faculty of Sciences, Pontificia Universidad Javeriana, Bogota, Colombia, Bogota, Colombia
\(^4\)University of Granada, Department of Biostatistics, Granada, Spain
\(^5\)Ordesa Laboratories S.L., Medical Department, Barcelona, Spain
\(^6\)University of Granada, Centre of Excellence for Paediatric Research Euristikos, Granada, Spain

Objectives and study: Growth velocity during the first years of life it's the result of child health and nutritional status. Has been reported that growth has an impact on neurocognitive and psycho-behavior development. Environmental and nutritional factors such as deficiency or excess, have will determine an adequate neurodevelopment and growth during early life. We aimed to analyse the association of linear growth velocity and infant behavior development at 18 months of life. A total of 170 healthy infants between 0-2 months of age were included in a randomized double-blind study to receive either a standard infant formula (F1: n=85) or a formula containing long chain polyunsaturated fatty acids (LC-PUFAs), milk fat globule membrane components and symbiotics (Nutriexpert® factor) (F2: n=85). As a control group, 50 breastfeed infants (BF) were included.

Methods: The linear growth velocity was evaluated taking into account increments in length from birth to 6 months of life. WHO growth and development standards, adjusted by sex, were used to obtained the 6 month increments; linear growth velocity was categorized as slow (SG: <-1 SD), normal (NG: ≥-1 SD and ≤ + 1 SD) and rapid (RG: > +1 SD). The assessment of behavioral development was performed using the Child Behavior Checklist (CBCL) at 18 months of age. Statistical analysis: Not normal distribution was assumed using Kolmogorov-Smirnov. Depending on growth velocity, CBCL scores were compared between groups by Kruskal-Wallis test and Chi-Square test for categorical variables using SPSS 22.0.

Results: No differences in linear growth velocity were found between the three study groups. At 18 months RG infants (n=7) presented higher scores in anxious/depressed (p=0.019), anxiety (p=0.034), pervasive developmental (p=0.019), oppositional defiant (p=0.010) and sleep problems (p=0.005) than NG infants (n=42). Also, SG infants (n=54) and NG showed lower scores compared to RG in emotionally reactive (p=0.010) and total problems (p=0.042).

Conclusion: Rapid velocity of linear growth during the first 6 months of life is associated with long-term effects determining a higher incidence of children's psycho-behavior problems at 18 months of life.

Disclosure of interest: This project has been funded by Ordesa Laboratories, SL Contract General Foundation of University of Granada, No.3349; Partially funded by EU Project DynaHEALTH (HORIZON 2020-GA No.633595) and SMARTFOODS (CIEN), Ministry of Industry, Spain.
Human milk microbiota profiles according to gestational age

Cristina Alcantara¹, Cecilia Martinez Costa², Maria Carmen Collado¹

¹Iata-Csic, Biotechnology, Valencia, Spain
²Hospital Clínico Universitario, Pediatric Gastroenterology Unit, Valencia, Spain

Objectives and study: Beyond nutritional aspects, human milk is an important source of bacteria and oligosaccharides, which are essential for the neonatal microbiome colonization. Little is known about what factors shape the human milk microbiome. The aim of this work is to examine the milk microbiota composition in preterm deliveries according to different gestational age.

Methods: We characterized the milk microbiome composition and diversity in breast milk samples from preterm and term deliveries (n=19) at three different time points during lactation by specific quantitative PCR and 16S gene sequencing. Total content of protein, fat and lactose were also analysed.

Results: We observed that milk bacterial communities from preterm deliveries were complex, and showed individual-specific profiles. Despite inter-individual variability in bacterial composition, bacteria belonging to Staphylococcus, Streptococcus, and Enterobacteriaceae dominated milk microbiota composition. We found detected the presence of some bacterial genera in the milk of mothers with preterm deliveries related to the oral microbiota, specifically with oral nitrate reducing bacteria such as Veillonella, Rothia and Actinomyces spp. Higher presence of oral bacteria was related to lower gestational age milk samples. We also found associations between specific bacteria and the amount of total protein, fat and lactose.

Conclusion: Our results indicate that gestational age has an impact on the breast milk microbiota composition and, also, in the relationship with other milk components, consequently, may affect the neonatal intestinal colonization and immune system maturation.

The authors declare no conflicts of interest
Adverse reactions to foods introduced in complementary feeding in infants with food allergies

Wilson Daza¹, Silvana Dadan², Emilia Prieto³, Clara Plata⁴

¹Universidad El Bosque-Gastronutriped, Pediatric Gastroenterology, Bogota, Colombia
²Universidad El Bosque-Gastronutriped, Pediatric Nutrition, Bogota, Colombia
³Gastronutriped, Bogota, Colombia
⁴Universidad El Bosque, Pediatric Gastroenterology, Bogota, Colombia

Objectives and study: Food allergy is an entity with increasing incidence worldwide. Infants are the most affected age group and cow's milk protein is the allergen involved in most cases. Current recommendations for the introduction of complementary feeding to infants with a food allergy are the same as for healthy children, except for the introduction of cow's milk products. The data on the frequency and type of adverse reactions that these children present when exposed to new foods is very scarce. The main objective of the study was to describe the adverse reactions of patients with a cow’s milk protein allergy that presented when introduced to new foods.

Methods: We retrospectively reviewed the medical records of all patients diagnosed with food allergy between 2010-2015. We included all patients who started complementary feeding as guided by the clinical nutritionist of our center. The basic demographic information, the type of clinical manifestation of the food allergy, the immunological mechanism involved (IgE, Mixed, Non-IgE), the foods that produced adverse reactions, the type of adverse reaction, and the age at which the adverse reaction presented were recorded in a database.

Results: Of a total of 248 patients with food allergy, 70 met the inclusion criteria. Female gender predominated with 55.7% (n = 39). The most frequent type of allergic manifestation was: Allergic proctocolitis 28% (n = 20), Atopic dermatitis 24.29% (n = 17), allergic enteropathy 24.9% (n = 17) and less frequently others such as esophagitis and eosinophilic gastroenteritis. Within the included group, 29 patients (41.4%) had more than one clinical expression of food allergy. The immunological mechanism related to the diagnosis was: non-IgE in 57% of the patients (n = 40), followed by mixed 41% (n = 29) and only one patient with IgE allergy. Of the 70 patients, 54% (n = 38) presented adverse reactions during the introduction to one or more foods. 21.4% (n = 15) of the children presented a reaction to more than one food. In total, 83 adverse reactions were recorded. The most frequently implicated foods were: chicken 10 (12%), rice 8 (9.6%), mango 7 (8.4%), pumpkin 5 (6.02%), beans 4 (4.8%) and beef 3 (3.6%). The rest of the reactions were to different food groups. Regarding the type of adverse reaction presented, rash was the most frequent manifestation in 32 cases, followed by diarrhea in 14, vomiting in 10 and rectal bleeding in 7. Other manifestations that presented were abdominal distension, anal erythema, colic, and dermatitis.

Conclusion: Per the results obtained in the studied group, it seems that adverse reactions to the exposure of new foods in infants with food allergy are very frequent. Due to the lack of published information, additional studies are needed to corroborate these findings with other groups of allergic children and to compare it with the occurrence of reactions in healthy children. Within our population, chicken, rice and mango were the foods that caused reactions most frequently.
True ileal protein digestibility and digestible indispensable amino acid score of goat and cow milk based infant formulas vs. human milk in a dynamic gastrointestinal model

Annet Maathuis¹, Robert Havenaar¹, Tao He², Susann Bellmann¹

¹Triskelion B.V., Zeist, Netherlands
²Ausnutria Hyproca, Zwolle, Netherlands

Objectives and study: To determine true ileal protein digestibility and digestible indispensable amino acid score (DIAAS) of a goat and a cow milk based infant formula (IF) in comparison with human milk (HM) using a dynamic gastrointestinal (GI) model simulating infant digestive conditions.

Methods: The goat and cow milk based IF had comparable protein contents (whey:casein=60:40). HM was collected 3-5 months postpartum and pooled (n=6). The IFs and HM were investigated in a dynamic in vitro GI model with compartments for the stomach and the small intestine, simulating digestive conditions in infants of 1-6 months of age. For dialysis of digested compounds, a hollow fibre semi-permeable membrane was connected to the intestinal compartment. Amino acids (AA) and small peptides in the dialysate are available for intestinal absorption (measured as bioaccessible nitrogen) and provide insights into protein and AA digestibility. Samples at 15, 30 or 60 min aliquots were collected from the dialysate for nitrogen and AA analysis. Bioaccessible endogenous nitrogen and AA were determined in blank experiments to calculate the true ileal protein digestibility and DIAAS. Simulated digestion was performed for 4 h in duplicate experiments.

Results: The nitrogen intake via the reconstituted goat and cow milk IF and HM were 340±1 mg, 323±1 mg, and 207±1 mg, resp. The endogenous nitrogen from the secretion fluids was 280±1 mg. The true ileal protein digestibility, calculated as exogenous nitrogen in the dialysate as percentage of nitrogen intake is shown in Fig. 1. The amount of bioaccessible nitrogen during digestion of goat milk IF showed a similar time profile to that of HM. The cow milk IF showed a delay in amount of bioaccessible nitrogen in comparison with goat milk IF and HM. In the 1st hour of digestion, the bioaccessible amount of nitrogen was 19.9±3.5% and 23.3±1.3% of nitrogen intake for goat milk IF and HM, resp., while it was 11.2±0.6% for cow milk IF (P > 0.05 vs goat milk IF; P < 0.02 vs HM). However, in the 3rd hour of digestion, the amount of bioaccessible nitrogen was higher (P < 0.02) for cow milk IF (28.9±1.2%) than those for goat milk IF (22.5±1.6%) and HM (20.6±1.0%). After 4 h of digestion the total true ileal protein digestibility (not corrected for non-protein nitrogen) of goat and cow milk IF and HM were 78.3±3.7%, 73.4±2.7% and 77.9±4.1%, resp. (P > 0.05). The 4 h true ileal AA digestibility of the goat milk IF was ≈5% higher for all indispensable AA in comparison to cow milk IF, corresponding with the slightly higher protein digestibility. The analysed AA composition of HM matched with FAO reference data. The DIAAS for goat and cow milk IF and HM as determined for 0-6 m old infants were 80%, 76% and 78% for aromatic AA when corrected for 10%, 7% and 22% non-protein nitrogen in goat and cow milk IF and HM, resp.

Figure 1:
**Conclusion:** The true ileal protein digestibility of the goat and cow milk based IF is comparable to that of HM. In terms of kinetics of protein digestion, the goat milk based IF is more comparable to HM than the cow milk based IF.

Haematochezia caused by eosinophilic proctocolitis in a newborn before any oral feeding: allergic or new transient entity?

Marie-Julie Debuf¹, Tania Claeys², Jean-Philippe Stalens³, Luc Cornette²

¹Université Catholique de Louvain, Brussels, Belgium
²Az Sint-Jan Brugge-Oostende, Brugge, Belgium
³Centre Hospitalier de Wallonie Picarde, Tournai, Belgium

Objectives and study: Haematochezia is a frequent symptom in early infancy. However, it occurs very rarely within the immediate neonatal period, especially before any oral intake. We here report a newborn that presented with an impressive haematochezia immediately after birth. A rectosigmoidoscopy revealed a severe inflammation associated with diffuse eosinophilic infiltration on biopsy. The clinical outcome of the patient was favourable after introduction of an amino acid formula diet. Reintroduction of standard formula milk at the age of 3 months was successful.

Methods: We discuss the possible aetiology of “congenital” eosinophilic inflammation of the distal colon.

Results: Multiple case series show that haematochezia in the very young healthy infant mostly improves spontaneously or does not reoccur after a food challenge test. The term “neonatal transient eosinophilic colitis” is postulated for this clinical entity. A food protein induced allergic proctocolitis (FPIAP) can only be diagnosed after a provocation test, showing recurrence of rectal bleeding, severe eczema or another unambiguous adverse reaction. Because of the congenital presentation of haematochezia, we initially considered our case to be a non-classical potentially severe type of FPIAP, possibly by in utero sensitization. Surprisingly, at the age of three months, a challenge with cow’s milk formula was well tolerated, excluding cow’s milk protein allergy as the cause for this eosinophilic proctocolitis. Hence, either the child reacted to another food protein (egg or soy) through in utero sensitization, or maybe there was no food allergy at all, and we observed a “neonatal transient eosinophilic colitis”. Our case is the first newborn in Europe that fits this diagnosis, presenting with haematochezia before the first feed, with upon investigation blood eosinophilia (up to 32%), as well as eosinophilic infiltrate into the gut tissue. So far, only two similar Japanese cases have been described. These infants improved spontaneously after being exclusively parenterally fed during a few days, and tolerated normal breast milk later on. Lymphoid hyperplasia within the gut as well as eosinophilia are two characteristic findings of haematochezia in early infancy, whether in FPIAP or neonatal transient eosinophilic colitis. Both entities present with early rectal bleeding and both involve eosinophils. We hypothesize that different chemical mediators are released in these entities, based on a different pathophysiological process. Indeed, eosinophils can release several inflammatory mediators. It is unclear at this stage which chemical mediator released by these eosinophils causes either a benign, transient inflammation versus FPIAP.

Conclusion: In summary, if a well-looking newborn infant presents with haematochezia before its first oral feed, FPIAP is a probable cause, but this diagnosis needs to be confirmed by an abnormal oral challenge test once the haematochezia has disappeared. If such challenge cannot demonstrate an allergic origin, like in our case, then the aetiology of this haematochezia is not FPIAP but rather a neonatal transient eosinophilic colitis. We believe that neonatal transient eosinophilic colitis occurs more frequently than previously thought. Further research is needed to clarify the different pathophysiological roles of eosinophils in early haematochezia.
Hypoallergenic formula-fed cow’s milk allergy infants have a trend towards impaired growth and body fat accumulation

Ping Dong1, Jing-jing Feng1, Dong-yong Yan1, Yu-jing Lyu1, Xiu Xu1

1Children’s Hospital of Fudan University, Department of Child Healthcare, Shanghai, China

Objectives and study: To date, the growth of hypoallergic formula (HF)-fed cow’s milk allergy (CMA) children has not been thoroughly assessed, especially in the item of body composition. The aim of present study was to compare anthropometric and body composition measurements of HF-fed CMA infants with matched human milk (HM) and common cow-milk formula (CF) fed health controls at similar age.

Methods: We recruited 35 children diagnosed with CMA who were under four months of age from our hospital between 2014.1- 2015.9, and the choosing of a HF (amino acid-based or extensively hydrolyzed formula) was determined by their doctors. According to the principle of 1:1 matching, we chose 35 healthy children at similar age who were HM or CF fed as two controls, respectively. Dietary intake was collected by using a diet diary which was recorded by the parents 3 days before each visit. We gave the children a routine physical examination till 1 year old and detected the body composition by using PEA POD Infant Body Composition System at 4 and 6 months.

Results: HF-fed CMA infants consumed less formula to satiation than did CF-fed health controls (mean volume intake, 122.5 ± 6.1 ml/kg/d versus 140.3 ± 7.4 ml/kg/d, P =0.035); the mean total daily caloric intake of HF-fed CMA infants was also lower than that of CF-fed health controls (79 ± 5.1 kcal/kg/d versus 97 ± 6.9 kcal /kg/d, P < 0.001) across the study period. HF-fed CMA children had significantly lower z scores for weight-for-age from 9 to 12 months and weight-for-length across ages 6 to 12 months. At months 6, percent body fat of HF-fed CMA children were significantly lower than HM- and CF-fed health controls (26.2% versus 30.3% versus 29.5%, P=0.015); In terms of mean fat mass index (FMI), HF-fed CMA children gained slightly lower while HM-fed healthy gained slightly more FMI at 4 (3.65 kg/m² versus 4.12 kg/m² versus 3.89 kg/m²) and 6 (4.75 kg/m² versus 5.12 kg/m² versus 4.99 kg/m²) months postpartum as compared to their counterparts, but the differences were not statistically significant.

Conclusion: HF-fed CMA children have a trend towards both impaired weight gain and body fat accumulation. A better knowledge of the energy intake and the metabolism of these children are needed.
Evaluation of the individual and combined effects of dietary oligofructose and 2′fucosyllactose on growth and development of neonatal piglets

Marcia Monaco1, Mei Wang1, Anna Dilger2, Jose Manuel Ramos Nieves3, Jonas Hauser3, Jian Yan4, Ryan Dilger2, Sharon Donovan1

1University of Illinois, Food Science & Human Nutrition, Urbana, United States
2University of Illinois, Animal Sciences, Urbana, United States
3Nestle Research Center, Lausanne, Switzerland
4Nestlé Nutrition R&d, King of Prussia, United States

Objectives and study: Human milk oligosaccharides (HMO) are an important component of human milk and associated with infant growth and body composition. The objective of this study was to determine whether the addition of 2′fucosyllactose (2′FL) (an HMO) to an OF-containing formula would affect growth and development of newborn piglets and their glucose and insulin response.

Methods: Beginning at 2 d of age, 36 vaginally-derived male piglets were randomized (n=12 per diet) to receive one of three diets formulated to contain: control (CON) [0 g/L OF + 0 g/L HMO, Purina ProNurse milk replacer], OF [CON + 5 g/L OF], or OF + HMO [CON + 5 g/L OF + 1.0 g/L HMO (2′FL)]. All diets were supplemented with lactose to equalize the added carbohydrate to 8 g/L. Body weights (BW) were measured daily and body circumference and crown-rump length measurements were taken on d 2 and 32 of age. Fasting blood samples were collected on postnatal d 7, 14, 21, 28 and 32 for assessment of serum glucose and insulin concentrations. Proximate analysis was conducted on soft tissue to determine its composition. All outcomes were subjected to a one-way ANOVA to assess the effect of dietary treatment, and statistical significance was defined as p ≤ 0.05..

Results: Randomization assured that all treatment groups had similar BW at the beginning of the study (average BW = 1.83 kg ± 0.04). Overall, no significant differences were observed for body weight gain, absolute or relative organ weights, or soft tissue composition. In addition, fasting serum glucose and insulin concentrations were unaffected by dietary oligosaccharide supplementation.

Conclusion: Together these data indicate that the provision of OF or OF+HMO to a CON diet was well tolerated and supported normal growth pattern and body composition of young pigs, with no change in blood glucose and insulin responses. This project was funded by Nestlé Nutrition Research.

Disclosure of interest: Jose Manuel Ramos Nieves is an employee of Nestle Nutrition Research
Jonas Hauser is an employee of Nestle Nutrition Research
Jian Yan is an employee of Nestle Nutrition Research
Ryan N Dilger has received grant funding and consulted for Nestle Nutrition Research
Sharon M. Donovan has received grant funding and consulted for Nestle Nutrition Research
Too add or not to add probiotics to infant formulae? An updated systematic review with meta-analysis

Maciej Kołodziej¹, Agata Skórka¹, Małgorzata Pieścik-Lech¹, Hania Szajewska²

¹Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
²The Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland

Objectives and study: In 2011, the Committee on Nutrition of the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) concluded that evaluated probiotic-supplemented formulae given to healthy infants do not raise safety concerns; however, there is insufficient data to recommend their routine use. We aimed to update the 2011 evidence on the effects of the administration of probiotic-supplemented infant formulae.

Methods: The MEDLINE, EMBASE, and Cochrane Library databases were searched up to September 2016, with no language restrictions, for randomised controlled trials (RCTs) that evaluated infant formulae supplemented with probiotics compared with unsupplemented formulae. Trials evaluating acidified, partially or fully hydrolysed formulae were excluded.

Results: Twenty-one eligible RCTs were identified, including 5 new RCTs. Supplementation of infant formula with B lactis, either alone or with Str thermophilus, had no effect on growth, number of respiratory illness episodes, antibiotic use, colic and crying, stool frequency, or stool consistency. However, there was a significant reduction in the number of episodes of diarrhoea. Supplementation of infant formula with L acidophilus johnsonii-La1 had no effect on growth, gastrointestinal infections, or respiratory illness episodes. There were no positive effects of supplementation of infant formula with B longum BL999 alone or with L rhamnosus LPR. Supplementation of infant formula with L rhamnosus GG was associated with better growth; it had no effect on colic, crying, or irritability, and it was associated with significantly greater summative indexes of loose stools and a higher defecation frequency. Supplementation of infant formula with L reuteri ATCC 55730 had no effect on growth, colic, crying, irritability, respiratory illness episodes, antibiotic use, stool frequency, or stool consistency; however, it was associated with a reduction in the number of episodes of diarrhoea. Supplementation of infant formula with L salivarius CEC5713 had no effect on growth, colic, crying, or irritability; however, it resulted in a significant reduction in the rate of diarrhoea and in the number of episodes of respiratory infection.

Conclusion: In line with the 2011 ESPGHAN document, the available scientific data suggest that the administration of currently evaluated probiotic-supplemented formulae to healthy infants does not raise safety concerns with regard to growth and adverse effects. Some beneficial clinical effects are possible; however, there is no existing robust evidence to recommend their routine use. The latter conclusion may reflect the small amount of data on a specific probiotic strain(s) and outcomes, rather than a genuine lack of an effect.

Disclosure of interest: Hania Szajewska had academic-associated speaking engagements and/or received research funding from companies manufacturing infant formulas. The authors have no non-financial interests that may be relevant to the submitted work.
Breast feeding initiation time: experience in a Nigerian tertiary health facility

Christopher Eke¹, Anthony Ikehuna², Chika Onwasigiwe³

¹University of Nigeria Teaching Hospital Enugu, Paediatrics, Enugu, Nigeria
²Department of Paediatrics, University of Nigeria Teaching Hospital, Enugu, Nigeria
³Department of Community Medicine, University of Nigeria Teaching Hospital, Enugu, Nigeria

Objectives and study: The ‘Ten Steps to successful breastfeeding under the frame work of baby friendly hospital initiative is aimed at protecting, promoting and supporting breastfeeding which is the special role of maternity services. Its fourth step - Breastfeeding initiation within an hour of delivery has been adjudged the desired following its link with reduced neonatal mortality index. The objectives of the study were to determine the prevalence and associated factors of correct breastfeeding initiation time among newborns delivered in University of Nigeria Teaching Hospital (UNTH), Enugu.

Methods: This was a cross sectional study conducted between January and April, 2016. Study ethical approval was obtained from the Health Research Ethics Committee of UNTH, Enugu. Respondents were consented mother-infant pairs delivered in the facility. Relevant maternal and newborn birth characteristics were obtained using a semi-structured questionnaire. Data was analyzed using SPSS version 20.0. Multivariate logistic regression was applied to determine the maternal and newborn factors that were significantly associated with correct breast feeding initiation time (p<0.05).

Results: A total of 321 mother and new born pairs were studied. Eighty-six (26.8%) of the respondents correctly initiated breast feeding within one hour of delivery. Planned pregnancy, making of decision on infant feeding option before pregnancy, mode of delivery, postnatal medical condition of the new-born, and maternal breastfeeding support from attending healthcare workers intra-partum were significantly associated with an increase in having the correct time of initiation of breast feeding.

Conclusion: Timely initiation of breast feeding in newborns studied was adjudged low. Efforts should be made to complement baby friendly hospital initiative with baby friendly community initiative to improve the rate of correct breast feeding initiation time in our setting.
An infant formula enriched with the human milk strain Lactobacillus fermentum CECT5716 is safe and reduces diarrhea incidences during first year of life

Juristo Fonollá¹, José Antonio Maldonado-Lobón¹, Mercedes Gil-Campo², Jose Maldonado³, Katherine Flores⁴, María Rosario Benavides⁴, Reyes Jaldo⁵, Inmaculada Jiménez del Barco⁶, Antonio David Valero¹, Federico Lara⁷, Mónica Olivares¹

¹Biosearch Life, Granada, Spain
²Hospital Universitario Reina Sofía, Córdoba, Spain
³Hospital Universitario Virgen de Las Nieves, Granada, Spain
⁴Clínica Pediátrica Roquetas, Roquetas del Mar (Almería), Spain
⁵Servicio de Atención Primaria (Sas), Peligros (Granada), Spain
⁶Policlínica Cristo de la Salud, Albolote (Granada), Spain
⁷Lactalis Puleva, Granada, Spain

Objectives and study: It is a randomized double blind controlled study. The aim was to evaluate the effects in infants from 1 to 12 months the daily intake of the probiotic strain Lactobacillus fermentum CECT5716 added in an infant formula.

Methods: 160 infants at the age of 1 month were randomly assigned to either infant formula enriched with L. fermentum CECT5716 (n=83), or to the same formula without the probiotic strain (n=77). The main outcome of the study was the safe of infants. Secondary outcomes were growth, fecal microbiota and incidence of infections. The protocol was approved by the Regional Ethics Committee and the study was carried out according to the Helsinki Declaration.

Results: No adverse effects were observed in any infant. The z-scores of weight, length and head circumference for age were calculated based on the WHO Child Growth Standards. Growth parameters in probiotic group did not differ from the control group and no significant differences were observed between both groups. Infants in probiotic group showed significantly higher counts of Lactobacillus spp. in faeces (p=0.000) along the study. Regarding infections, there was a significant reduction (44%, p=0.058) in the incidence rate of gastrointestinal infections in probiotic group (IR: 0.385±0.077) respect the control group (IR: 0.688±0.106). The number of infants needed to treat (NNT) to reduce one event of diarrhoea is 3.

Conclusion: The consumption of an infant formula enriched with the human milk probiotic strain Lactobacillus fermentum CECT5716 during the first year of life is safe and could be useful in the prevention of gastrointestinal infections in infants.

Disclosure of interest: Juristo Fonollá, José Antonio Maldonado-Lobón, Antonio David Valero, and Mónica Olivares belong to Biosearch Life, producer and marketing company of Lactobacillus fermentum CECT5716. Federico Lara-Villoslada belongs to Lactalis Puleva, manufacturer of the infant formula analysed in the present study.
Bifidobacterium longum subsp. infantis EVC001 remodels the intestinal microbiome and metabolome in breast-fed infants

Steven Frese¹, Andra Hutton¹, Lindsey Contreras², Claire Shaw², Carlito Lebrilla³, Daniela Barile⁴, J Bruce German⁵, David Mills⁴, Jennifer Smilowitz⁶, Mark Underwood⁷

¹Evolve Biosystems, Inc, Davis, United States
²Evolve Biosystems, Davis, United States
³University of California - Davis, Chemistry, Davis, United States
⁴University of California - Davis, Food Science and Technology, Davis, United States
⁵University of California - Davis, Food Science and Nutrition, Davis, United States
⁶University of California - Davis, Food Science and Technology, Davis, United States
⁷University of California - Davis Medical Center, Neonatology, Sacramento, United States

Objectives and study: Human milk has evolved to foster not only the growth of the infant, but also the shape of the infant gut microbiome via complex human milk oligosaccharides. Based on historical observations of a Bifidobacterium dominant gut community in breast-fed infants, and the genetic adaptations specific to Bifidobacterium longum subsp. infantis, we hypothesized that supplementation of this organism to breast-fed infants would remodel the gut microbiome and significantly impact the metabolome.

Methods: Exclusively breastfed infants, delivered vaginally or by cesarean section, were randomized to receive either lactation support and a novel commercial preparation of Bifidobacterium longum subsp. infantis EVC001 (ATCC SD-7035) for their infants or lactation support alone (n=33 per group). Infants consumed the preparation mixed with expressed breast milk for 21 days, and fecal samples were collected through day 60. Bacterial DNA was extracted from samples, and was analyzed by quantitative PCR and 16S rRNA marker gene sequencing.

Results: Invariably, infants that received EVC001 were rapidly and stably colonized at high numbers by a single strain of the organism at 10¹¹ CFU/g feces, while control infants had significantly lower levels of fecal Bifidobacterium. This stable colonization was evident more than 30 days after supplementation ended. Colonization by Bifidobacterium was associated with decreased relative abundances of Enterobacteriaceae, Bacteroidaceae, Clostridiaceae when compared by multivariate linear modeling. We also observed a significant decline in fecal microbiome alpha diversity, but surprisingly, a concomitant increase in community stability. These changes were so profound that differences in the microbiome due to delivery mode (cesarean section and vaginal delivery) were no longer evident in EVC001-supplemented infants. Colonization by EVC001 resulted in significant changes in fecal biochemistry, as determined by mass spectrometry, including a decrease in pH and fecal HMOs and a concomitant increase in lactate and acetate, two key energy signaling molecules. Stool frequency and consistency also improved.

Conclusion: Introduction of a novel preparation of Bifidobacterium rapidly and effectively resulted in a high level of Bifidobacterium longum subsp. infantis colonization in breast-fed infants, regardless of delivery mode, and remained stable through 30 days post-supplementation. Additionally, these dramatic changes in the gut microbiome resulted in concomitant alterations to the gut metabolome, indicating potential physiological benefits to the host.

Disclosure of interest: Frese, Hutton, Contreras, and Shaw are employees of Evolve Biosystems, Inc. Lebrilla, Barile, German, and Mills are consultants of Evolve Biosystems, Inc.
Difference in gut microbiota development in breastfed and formula-fed healthy infants during the first months of life, estimated using the real-time PCR

Svetlana Makarova¹, Margarita Boldyreva², Natalia Sannikova³, Tatiana Borodulina³, Elena Tiunova³, Sergei Nikitin³, Natalia Sokolova⁴, Olga Bokovskaya⁵

¹Federal State Autonomous Institution “Scientific Center of Children's Health” of the Ministry of Health of the Russian Federation, Moscow, Russian Federation
²“dna-Technology” LLC, Moscow, Russian Federation
³Ural State Medical University, Yekaterinburg, Russian Federation
⁴Beryozovsky Central Municipal Hospital, Beryozovsky, Sverdlovsk Region, Russian Federation
⁵Infaprim, Jsc, Moscow, Russian Federation

Objectives and study: to study gut microbiota development in breastfed and formula-fed infants during the first months of life, using the real-time polymerase chain reaction (PCR).

Methods: A sample of 55 healthy infants aged 1-2 months was involved in the study. Infants who entered the study had a gestational age of 38-40 weeks and Apgar scores of 7-9 points. The study excluded infants with infectious diseases and perinatal pathology. Of the 55 infants who entered the study, 23 were exclusively breastfed (BF) and 32 were bottle-fed using basic infant formula (FF). The average age of children at the time of inclusion in the study was 1.6±0.6 months in the BF group and 1.7±0.7 months in the FF group. Real-time PCR was used to evaluate the intestinal bacterial groups: Clostridium leptum group, Clostridium coccoides group, Clostridium difficile group; and the bacteria: Bacteroides spp, Prevotella spp, Porphyromonas spp, Anaerococcus spp, Eubacterium spp, Peptostreptococcus spp, Lactobacillus spp, Staphylococcus spp, Streptococcus spp, Enterococcus spp, Enterobacteriaceae, Bilobacterium spp, Fusobacteriaceae, Helicobacter spp, Campylobacter spp. The quantity of bacteria (Lg10) was calculated by the cycle threshold number.

Results: Clostridium difficile group bacteria were detected only in FF infants (median Lg10=4.1), and were not found in BF infants (p=0.002); on the contrary, BF infants had a greater number (Lg10=3.5) of Staphylococcus spp than FF infants (Lg10=2.6, p=0.001). BF and FF infants did not differ in terms of other groups of bacteria. A month later, the Clostridium difficile group continued to be detected only in FF infants (median Lg10=4.35), and was not found in BF children (p=0.011). It was also found that the BF children had a greater number (Lg10=4.1) of Staphylococcus spp than FF infants (Lg10=3.1, p=0.004). Lactobacillus spp increased during the month in BF infants, unlike with FF infants, and, as a result, BF and FF began to differ in the number of Lactobacillus spp (Lg10=4.8; Lg10=3.0 respectively; p=0.024).

Conclusion: Use of the real-time PCR established the differences in the gut microbiota composition in infants who are breastfed and formula-fed. Statistically significant differences were observed within one month of follow-up, for the following bacteria: Clostridium difficile group, Staphylococcus spp, Lactobacillus spp.
Prevalance of Vit D deficiency among postpartum women and their newborns

Junaid Khan

1Abu Dhabi, United Arab Emirates

Background: Vitamin D deficiency during pregnancy has been linked with number of serious short and long term health problems in offspring, therefore adequate maternal vitamin D levels are pivotal for neonatal calcium hemostasis. The objective of this study is to evaluate vitamin D deficiency among post-partum women and their newborns.

Method: 360 pregnant women were enrolled from Liaquat National Hospital. Serum levels of 25-hydroxyvitamin D3 were assayed in maternal and cord blood samples collected at the time of delivery.

Results: The prevalence of vitamin D deficiency in maternal and cord blood was 69.6% and 58.2% respectively. There was significant correlation between maternal and cord blood serum concentration of Vitamin D3. In mothers who were deficient in Vitamin D3, cord blood Vitamin D3 levels were lower than those from normal mothers. (P=.001). A significant direct correlation was also found between parda/veil observers mothers and levels of Vitamin D3 (P<0.002).
<table>
<thead>
<tr>
<th>Variable</th>
<th>No. of women</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age in years</td>
<td></td>
</tr>
<tr>
<td>&lt;20</td>
<td>7</td>
</tr>
<tr>
<td>21-30</td>
<td>265</td>
</tr>
<tr>
<td>&gt;30</td>
<td>77</td>
</tr>
<tr>
<td>Parity</td>
<td>130</td>
</tr>
<tr>
<td>Primi</td>
<td>169</td>
</tr>
<tr>
<td>1-2</td>
<td>49</td>
</tr>
<tr>
<td>3-4</td>
<td>1</td>
</tr>
<tr>
<td>&gt;4</td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>3</td>
</tr>
<tr>
<td>&lt;18.5</td>
<td>239</td>
</tr>
<tr>
<td>18.5-24.9</td>
<td>107</td>
</tr>
<tr>
<td>25-29.9</td>
<td></td>
</tr>
<tr>
<td>&gt;30</td>
<td>0</td>
</tr>
</tbody>
</table>

**Maternal & Cord Blood Levels of Vitamin D**

<table>
<thead>
<tr>
<th>Maternal Levels</th>
<th>Cord Levels</th>
</tr>
</thead>
<tbody>
<tr>
<td>ng/ml</td>
<td>≤ 30 ng/ml</td>
</tr>
<tr>
<td>≤ 30 (n=243)</td>
<td>115 (63.8%)</td>
</tr>
<tr>
<td>≥ 30 (n=106)</td>
<td>48 (45.3%)</td>
</tr>
</tbody>
</table>
**Conclusion:** Keeping in view the high prevalence of vitamin D deficiency, considerations should be made for Vit.D supplementation in antenatal period to prevent hypovitaminosis in both mother and babies.
Objectives and study: Our study is substantiated by the insufficient data about vitamin D status in very preterm infants (VPI) in Russia, and absence of uniform recommendations for the prevention of its deficit among VPI and VPI with cholestasis syndrome. 

The aim was to estimate vitamin D status in VPI for the first 2 months (m) of life and to compare the data between the two groups of the VPI - with and without cholestasis.

Methods: The 111 infants with gestational age (GA) less than 32 weeks (28.6±1.8, M±Sd) and birth weight (BW) less than 1500 g (1089±295) were included in the study. The boys were 55/49.5%. The 51/46% babies were born from multiple pregnancy. Serum level of 25-hydroxyvitamin D (25OHD) was determined by enzyme-linked immunosorbent assay at 2-10 days, 1 m and 2 m of age. The impact of parity, GA, BW and season on the vitamin D status within the first 10 days of life has been estimated. Comparative analysis of the serum level of 25OHD was performed in VPI with cholestasis (group 1, n=13) and without cholestasis (group 2, n=98). GA between the groups did not differ [median 29.0 weeks (min 25 - max 30) and 29.0 (24-31), respectively]. BW was lower in group 1 [841g (490-1490) vs 1149g (495-1495), p <0.05]. The infants received vitamin D by parenteral nutrition at a dose 160 IU/kg/day. After establishment of full enteral nutrition and reaching the age of 3-4 weeks, vitamin D supplements were commenced that provided a total daily intake of 700-1250 IU of vitamin D.

Results: The serum level of 25OHD in infants from group 1 and group 2 is presented in the Table. Correlation between serum level of 25OHD and GA, BW, season on the vitamin D status within the first 10 days of life has been estimated. Comparative analysis of the serum level of 25OHD was performed in VPI with cholestasis (group 1, n=13) and without cholestasis (group 2, n=98). GA between the groups did not differ [median 29.0 weeks (min 25 - max 30) and 29.0 (24-31), respectively]. BW was lower in group 1 [841g (490-1490) vs 1149g (495-1495), p <0.05]. The infants received vitamin D by parenteral nutrition at a dose 160 IU/kg/day. After establishment of full enteral nutrition and reaching the age of 3-4 weeks, vitamin D supplements were commenced that provided a total daily intake of 700-1250 IU of vitamin D.

Table: Characteristic of the vitamin D status in VPI by groups.

<table>
<thead>
<tr>
<th>Groups</th>
<th>Serum level of 25OHD / Age</th>
<th>3-10 day</th>
<th>1 m</th>
<th>2 m</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>mediana [min-max], ng/ml</td>
<td>9.1 [5.6-25.2]</td>
<td>11.8 * [4.6-27.0]</td>
<td>22.0* [12.7-43.6]</td>
</tr>
<tr>
<td>Group 1</td>
<td>Deficit (&lt;10 ng/ml), %</td>
<td>57</td>
<td>43*</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Insufficiency (10-29.9 ng/ml), %</td>
<td>43</td>
<td>57</td>
<td>70*</td>
</tr>
<tr>
<td></td>
<td>Normal (30-100 ng/ml), %</td>
<td>0</td>
<td>0</td>
<td>30*</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group 2</td>
<td>mediana [min-max], ng/ml</td>
<td>14.3 [2-48.1]</td>
<td>23.6 [3.1-94]</td>
<td>42.1 [13.0-96.8]</td>
</tr>
<tr>
<td></td>
<td>Deficit, %</td>
<td>32</td>
<td>9.5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>Insufficiency, %</td>
<td>61</td>
<td>63.5</td>
<td>28</td>
</tr>
<tr>
<td></td>
<td>Normal, %</td>
<td>7</td>
<td>27</td>
<td>72</td>
</tr>
</tbody>
</table>

*p<0.05 between groups
Conclusion: Low serum level of 25OHD has been found in 93.7% VPI within the first 10 days after birth, including deficit of vitamin D - in 34.5%. By the age of 1 m low serum level of 25OHD is still observed in 73%, by the age of 2 m - in 28% cases. Especially premature babies born in the winter may be exposed to vitamin D deficiency. Cholestasis is a significant factor in promoting vitamin D deficiency in VPI. In light of this, definite recommendations for serum level normalization of 25OHD for VPI and VPI with cholestasis are needed.
Significant loss of macronutrients during passage through feeding tube - an observational study

Hadar Lev¹, Mohammad Azaiza², Laurence Mangel³, Amit Ovental², Ronit Lubetzky⁴, Dror Mandel²

¹“Dana Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Tel Aviv, Israel
²“Dana Dwek” Children’s Hospital, Tel Aviv Medical Center, Neonatology, Tel Aviv, Israel
³Lis Maternity Hospital, Tel Aviv Sourasky Medical Center, Neonatology, Tel Aviv, Israel
⁴“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatrics, Tel Aviv, Israel

Objectives and study: Providing appropriate nutrition for growth and development is a cornerstone in the care of preterm infants. Feeding infants born before week 34 of gestation is based mainly on providing nutrition directly to the gastrointestinal tract through a naso-gastric tube (NGT). Little is known about the impact of formulas passage through NGT on the macronutrient content. The aim of our study was to evaluate changes in macronutrient content of various formulas after transfer through a feeding tube.

Methods: Eleven frequently used formulas were chosen. Included were 2 preterm formulas (#1 and 2), 4 extensively hydrolyzed formulas (#3-6), 2 amino acid based formulas (#7 and 8) and 3 standard cow’s milk based formulas for term infants (#9-11). Ten consecutive measurements were performed for each formula by a single investigator (MA). Simulated tube feeding was performed by using an infusion pump (Alaris™ CareFusion) connected to a feeding tube (Metric/x-ray, 40 cm CH 05, Unomedical) to transfer 30 ml of formula at a speed of 30 ml/h into 10 ml tubes. Human Milk Analyzer, using an infra-red spectroscopy method was used to compare the pre-infusion and post-infusion macronutrients contents of the different formulas.

Results: A total of 220 measurements were performed. One of the amino acid based formulas was excluded from further analysis as the reconstituted liquid was unstable. Variations in at least one macronutrient were observed in 5 out of 10 formulas. In general, we observed a reduction of 0.05±0.09 in fat content after transfer through feeding tube (from 4.48±0.863, (3.1-6.1) g/dL to 4.432±0.855, (2.9-5.9) g/dL, p< 0.00001) which reflects a mean reduction of 1.1 % of the fat content. Fat and energy content were modified in one of the preterm formula (#1). Fat content was altered in two other extensively hydrolyzed formulas (#3 and #5) whereas carbohydrate content was affected in the fourth extensively hydrolyzed formula (#6). Protein and energy content were affected in the second preterm formula (#2) (Table).
Table: Significant changes in macronutrient content after transfer through NGT.

<table>
<thead>
<tr>
<th>Formula</th>
<th>Macronutrient</th>
<th>Content Before transfer*</th>
<th>Content After transfer*</th>
<th>Loss %</th>
<th>p-value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>Fat (g/dL)</td>
<td>5.98 ± 0.09 (5.8-6.1)</td>
<td>5.85 ± 0.08 (5.7-5.9)</td>
<td>2</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td>Energy (kcal/dL)</td>
<td>92.8 ± 0.92 (91-94)</td>
<td>91.4 ± 1.35 (89-93)</td>
<td>1.5</td>
<td>0.007</td>
</tr>
<tr>
<td>#2</td>
<td>Protein (g/dL)</td>
<td>2.7 ± 4.68 (2.7)</td>
<td>2.64 ± 0.05 (2.6-2.7)</td>
<td>2.2</td>
<td>0.005</td>
</tr>
<tr>
<td></td>
<td>Energy (kcal/dL)</td>
<td>89.8 ± 0.42 (89-90)</td>
<td>88.9 ± 0.31 (88-89)</td>
<td>1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>#3</td>
<td>Fat (g/dL)</td>
<td>4.32 ± 0.06 (4.2-4.4)</td>
<td>4.25 ± 0.08 (4.1-4.3)</td>
<td>1.6</td>
<td>0.04</td>
</tr>
<tr>
<td>#5</td>
<td>Fat (g/dL)</td>
<td>5.18 ± 0.04 (5.1-5.2)</td>
<td>5.1 ± 0.06 (5-5.2)</td>
<td>1.5</td>
<td>0.01</td>
</tr>
<tr>
<td>#6</td>
<td>Carbohydrate (g/dL)</td>
<td>6.86 ± 0.15 (6.6-7)</td>
<td>6.64 ± 0.084 (6.5-6.7)</td>
<td>3.35</td>
<td>0.0026</td>
</tr>
</tbody>
</table>

*Mean±SD, (range), **dependent-t-test

Conclusion: Changes in the macronutrient content after tube feeding transfer were observed for some infant formulas including those designed for very low birth weight (VLBW) infants. These alterations might relate to the specific formulation of each formula. Furthermore, the triglyceride fatty acid composition might influence its adherence to feeding tube. The biological significant of our results to the VLBW infant should be further studied.
**Complex lipid composition of breast milk from Chinese and Malay mothers**

Kevin Ma¹, Xihong Liu², Mohamed Hamid Jan³, **Paul McJarrow**⁴, Angela Rowan⁵, Bertram Fong¹

¹Fonterra Research and Development Centre, Food Chemistry, Palmerston North, New Zealand  
²Guangzhou Woman and Children’s Medical Center, Guangzhou Hospital, Department of Clinical Nutrition, Guangzhou, China  
³Universiti Sains Malaysia, School of Heath Sciences, Kelantan, Malaysia  
⁴Fonterra Research and Development Centre, Functional Ingredients, Palmerston North, New Zealand  
⁵Fonterra, Nutrition, Palmerston North, New Zealand

**Objectives and study:** Complex lipids, such as gangliosides and phospholipids, play important roles in intra- and inter-cellular signalling, migration, proliferation, neurological development, and inflammatory and immune responses. These lipids are found in various biological fluids, including the milk fat globule membrane.

Growing evidence shows that complex lipids, such as those from human milk, play an important role in infant development, which has led to studies of human milk composition. Furthermore, it has been suggested that human milk composition may be influenced by diet and population demographics.

The objective of this study was to use a validated high-performance liquid chromatography-mass spectrometry (HPLC-MS) method to determine the ganglioside and phospholipid classes and concentrations in breast milk from a cross section of Chinese and Malay mothers throughout an eight- and 12-month lactation period, respectively.

**Methods:** The Chinese and Malay human breast milk samples were obtained from the Guangzhou Women and Children’s Medical Centre and Hospital Universiti Sains Malaysia, respectively. Twenty Chinese mothers provided samples across 6 time points (1, 2, 3, 4, 6, and 8 months), while 48 Malay mothers provided samples across 5 time points (colostrum, transitional milk, 2, 6, and 12 months). Samples were analysed for different ganglioside and phospholipid classes using HPLC-MS.

**Results:** Human breast milk consisted of both GM3 and GD3 gangliosides. GD3 was the dominant ganglioside in colostrum and transitional milk, while GM3 was the major ganglioside class in mature milk for both populations. Total ganglioside concentration was highest in colostrum and transition milk before dropping to a lower level during the start of the mature milk period. Over the mature milk period, both populations showed a gradual increase in average total ganglioside (GD3 +GM3) concentration from 14.6 mg/L to high of 24.5 mg/L, and from 14.8 to 25.3 mg/L for Chinese and Malay mothers respectively.

The phospholipids sphingomyelin (SM), phosphatidylcholine (PC), phosphatidylethanolamine (PE), phosphatidylinositol (PI) and phosphatidylserine (PS) were also measured. Total phospholipid (SM, PC, PE, PI and PS) concentrations were highest in colostrum, before dropping to lower levels at the start of the mature milk period. In the mature milk samples, the average total phospholipid concentration increased gradually over the lactational period for the Malay mothers, from 170 mg/L to 220 mg/L but the same was not observed with the Chinese mothers, where the levels remain relatively stable from 201 mg/L to 216 mg/L.

**Conclusion:** Using HPLC-MS techniques, we measured the ganglioside and phospholipid concentrations in breast milk from Chinese and Malay mothers across 8 and 12 month lactation periods, respectively. There were no significant differences in average total ganglioside and phospholipid concentrations in the mature milk between these two populations.

Human milk is the gold standard to which infant formulae are formulated. However, there is awareness that numerous bioactive lipid components are present in breast milk at significant levels that are at lower concentration in infant formula. These components may be important for normal growth and development of the infant immune system, visual performance and cognitive performance. Data from
this study may support the formulation of human milk replacers for use in situations where mothers are unable to breastfeed.
The nutritional management of hospitalized SGA late preterm infants: a multi-center survey in Beijing area

Zhenghong Li1, Danhua Wang1, Meiying Quan1, Ying Li2, Li Yang3, Xiaojing Xu4, Jing Zhu5, Jie Liu6, Xuanguang Qin7, Wenjing Li8, Xiaohui Fu9, Xin Zhang10

1Peking Union Medical College Hospital, Pediatric Department, Beijing, China
2Beijing Haidian District Maternal and Child Health Hospital, Pediatric Department, Beijing, China
3Beijing Tongzhou District Maternal and Child Health Hospital, Pediatric Department, Beijing, China
4Beijing Huaxin Hospital, Pediatric Department, Beijing, China
5Peking University Third Hospital, Pediatric Department, Beijing, China
6The People’s Hospital of Beijing University, Pediatric Department, Beijing, China
7Beijing Chaoyang Hospital, Pediatric Department, Beijing, China
8Beijing Obstetrics and Gynecology Hospital, Capital Medical University, Pediatric Department, Beijing, China
9Beijing Shangdi Hospital, Pediatric Department, Beijing, China
10Peking University First Hospital, Pediatric Department, Beijing, China

Objectives and study: To evaluate the nutritional management status of hospitalized small for gestational age (SGA) late preterm infants (infants with 34 to 36+6 weeks of gestational age and birth weight less than 10th percentile) and clinical practice difference with appropriate for gestational age (AGA) late preterm infants.

Methods: A cross-sectional survey, which continuously collected data of nutritional support and nutrition related complications of SGA and AGA late preterm infants, including baseline data at birth, enteral and parenteral nutritional support during hospitalization, time of achieving full enteral feeding, weight gain during hospitalization and the incidence of hyperbilirubinemia, anemia, neonatal infection, hypoglycemia and hyperglycemia.

Results: From October 2015 to March 2016, twenty-six hospitals and neonatal intensive care units in Beijing area participated in this clinical study, including 5 level II hospitals and 21 level III hospitals. A total of 751 late preterm infants were enrolled, with mean gestational age of 35.6±0.8 weeks. Seventy-four of them were SGA (9.9%) and 652 were AGA infants (86.8%). When compared with AGA infants, the hospital stay length for SGA late preterm infants was much longer (11.3±5.2 vs 8.7±4.6 days, p=0.000). SGA infants took a shorter time to reach the weight nadir (3.0±1.1 vs 3.5±1.6 days, p=0.005), but there was no statistically significant difference on time regained birth weight (5.4±2.5 vs 6.0±3.1 days, p=0.119). The exclusive breastfeeding rate for SGA was 5.4%, no statistically significant difference when compared with AGA infants (5.4% vs 3.2%, p=0.408), but the rates that using preterm formula was higher in SGA group (63.5% vs 46%, p=0.014). Infants who were given parental nutrition accounted for 68.9% in SGA group, while in AGA group, the rate of parenteral nutrition was 39.8%, which had statistical difference (p=0.000). When discharged, the energy from enteral nutrition (109.8±28.5 kcal/kg.d vs 91.9±29.9 kcal/kg.d, p=0.000) and enteral feeding volume (140.9±35.3 ml/kg.d vs 121.8±39.0 ml/kg.d, p=0.000) were higher in SGA late preterm infants group. The pertentages of infants could gain full enteral nutrition both were low in AGA and SGA group, but SGA infants had higher rate to gain full enteral feeding at discharge (32.4% vs 15.5%, p=0.004). However, SGA late preterm infants need longer time (10.8±4.2 vs 8.5±3.1 days, p=0.005) to gain full enteral feeding. The incidence of nutritional related complications, including hyperbilirubinemia, anemia, neonatal infection, hypoglycemia and hyperglycemia did not show ant difference between two groups.

Conclusion: SGA late preterm infants stayed in hospital longer than AGA counterparts, they had a better energy and enteral feeding level when discharged, with a little higher rate of infants who gaining full enteral feeding. However, the rate of exclusive breastfeeding and infants could gain full enteral feeding at discharge were still low. The nutritional management of late preterm infants, especially SGA should be laid emphasis among neonatologists.
Investigation on human milk collection and breastfeeding status of the infants hospitalized in NICU

Zhenghong Li¹, Changyan Wang¹

¹Peking Union Medical College Hospital, Pediatric Department, Beijing, China

Objectives and study: To investigate the factors on breastfeeding in NICU hospitalized infants, and to explore the strategies of promoting breastfeeding of NICU hospitalized infants.

Methods: By collecting the basic data and breastfeeding data of 70 cases from the NICU of Peking Union Medical College Hospital, we analyzed the factors influencing the human milk collection and feeding of NICU hospitalized infants.

Results: From July 2015 to December 2015, a total of 70 cases of NICU hospitalized patients were enrolled, including 24 cases of premature infants and 46 cases of full-term infants. In 70 cases, the total breastfeeding rate was 90%, while the rate of preterm infants was 95.83% and the exclusive breastfeeding rate of preterm infants was 45.75% before discharge. And the full-term infants breastfeeding rate was 86.95%. Maternal age, mode of delivery, gestational age and the prenatal breastfeeding guidance were not significantly correlated with the rate of breastfeeding. 56 mothers chose electric pump, while 12 of manual breast pump and 4 of manual milking, there was no correlation between the mode of milk expressing and the total milk volume of the third day and seventh day after delivery. The total milk expressing times everyday ranged from 3 to 10 times with an average of 6.28 ±5.13 times; and the night milk expressing times ranged from 0~3 with an average of 1.93 ±1.12 times. There was a significant difference in the total milk volume on day 7 after delivery between the group with the milk expressing times ≥5 and the group <5 (360.88ml vs 220.50ml, p<0.05); and there was also a significant difference in the total milk volume on day 7 after delivery between the group with the night milk expressing times ≥2 and <2 (198.00ml vs 360.88ml, p<0.05). 7 family had not sent human milk to NICU, one of which was an premature infant whose mother failed to breastfeed him due to taking immunosuppressive drugs; 4 of the full-term families couldn't send milk because of milk insufficiency and 2 of the full-term families because of the distance from home to the hospital and the short hospitalization time.

Conclusion: The breastfeeding rate in NICU of our hospital was as high as 90%, which was even higher in preterm infants than full-term infants. Compared with the mother's age, mode of delivery, mode of milk expressing and whether or not to accept breastfeeding guidance, the total milk expressing frequency and the frequency of milk expressing at night have a great significant impact on the total volume of human milk. Breast milk insufficiency was the main reason that leads to breastfeeding failure in NICU. Therefore, the hospital should offer more breastfeeding and milk expressing guidance to the NICU hospitalization patients' mothers, and help them build confidence in breastfeeding, especially guiding them to increase the frequency of milk expressing in order to increase the daily milk amount and improve the breastfeeding rate of NICU hospitalized infants.
The effect of gestational diabetes on macronutrients content

Dana Shapira¹, Ronit Lubetzky¹, Francis Mimouni², Dror Mandel³

¹Dana Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatrics, Tel Aviv, Israel
²Shaare Zedek Medical Center, Neonatology, Jerusalem, Israel
³Dana Dwek Children's Hospital, Tel Aviv Medical Center, Neonatology, Tel Aviv, Israel

Objectives and study: Little is known about the effect of gestational diabetes (GD) upon macronutrients content of human milk (HM). We thus aimed to study macronutrients (fat, lactose, protein) and caloric content in HM from women with GD compared to women with no GD.

Methods: Sixty two lactating mothers (31 with GD, 31 without GD) were recruited. Diagnosis of GD was made by using a 100-gram Glucose Tolerance Test. After manual expression, each mother contributed 3 samples of HM (during first 72 hours after labor (colostrum), after 7-days (transitional HM) and at 14 days post-partum (mature-HM). Immediately following expression, samples were stored at -20°C until thawed and analyzed using infrared transmission spectroscopy HM analyzer.

Results: Sixteen women (52%) in the GD group were treated by diet alone (48%) while 15 (48%) by pharmacotherapy. The two groups did not differ in terms of maternal age, maternal pre pregnancy weight, height, diet and weight gain during pregnancy, gestational age and infant birthweight. A total of 186 HM milk samples were collected. Macronutrients content in colostrum and transitional milk did not differ between the two groups. Fat and energy contents in mature HM were higher in the non GD samples than in the GD samples (p=0.07 and p<0.02, respectively). There were no differences in macronutrients content of samples of mother with diet treated GD compared to mother with pharmacotherapy treated GD.

Conclusion: Fat and energy contents of mature milk obtained from mothers with GD are lower compared to that of milk from mothers without GD. The mechanism and biological significance of our findings is yet to be determined.
Efficacy of the symbiotic combination of *Bifidobacterium longum* subsp *infantis* CECT7210 and a prebiotic type FOS versus *Salmonella Typhimurium* in a model of weaned piglet

Agustina Rodríguez-Sorrento\(^1\), Lorena Castillejos\(^1\), Paola López-Colom\(^1\), Gloria Cifuentes\(^2\), Susana María Martín-Orúe\(^1\), José Antonio Moreno\(^2\)

\(^1\)Universitat Autònoma de Barcelona, Servicio de Nutrición Y Bienestar Animal, Departament de Ciència Animal I Dels Aliments, Bellaterra, Spain

\(^2\)Laboratorios Ordesa, Basic Research Department, Sant Boi de Llobregat, Spain

Objectives and study: The study evaluated the efficacy of oral administration of *Bifidobacterium longum* subsp *infantis* CECT7210, a probiotic strain, combined with a prebiotic added at a dose of 5% in the feed, composed of inulin and oligofructose against *Salmonella Typhimurium*.

Methods: 72 piglets of 28 days were used, distributed in 24 pens in a 2x2 design: with or without symbiotic, and inoculated or not with the pathogen. Animals received the probiotic daily by oral route \((10^9\text{ ufc})\). After one week of adaptation, the animals were inoculated orally with *Salmonella Tiphymurium* \((10^8\text{ ufc})\). The consumption, the weight of the animals were recorded and fecal consistency and rectal temperature were evaluated, in addition to sampling feces. On days 4 and 8 post-inoculation (PI), one animal per pen was euthanized and samples of blood, digestive content and tissues were collected, *Salmonella* counts, fermentation product analysis, TNF-\(\alpha\), PigMAP in serum and ileal histomorphometry were performed.

Results: The inoculation produced a mild clinical picture with worsening of fecal consistency \((P <0.01)\) and fever \((P <0.01)\). Symbiotic treatment (SYM) numerically reduced *Salmonella* counts in feces at day 1 PI \((P = 0.14)\) and in caecum at day 8 PI \((P = 0.15)\). The weight gain in the PI period increased numerically with the symbiotic in challenged piglets and declined in the non-challenged piglets \((P = 0.25)\). The animals receiving SYM had a higher number of intraepithelial lymphocytes \((P = 0.03)\) and a lower index of mitosis at the ileal mucosa \((P <0.01)\) at day 8 PI.

Conclusion: The results suggest that the symbiotic can help to stimulate the immune response of the piglets to the pathogen and to reduce the damages in the intestinal villi caused by the pathogen.

Disclosure of interest: Gloria Cifuentes, Conflict with: is employee of Laboratorios Ordesa a Baby Food Company, José Antonio Moreno, Conflict with: is employee of Laboratorios Ordesa a Baby Food Company,
NUTRITION: Neonatal and infant nutrition

N-P-110

Hypoargininaemia and sepsis in very preterm infants receiving parenteral nutrition

Colin Morgan¹, Laura Burgess¹

¹Liverpool Women's Hospital, Neonatology, Liverpool, United Kingdom

Objectives and study: We have previously shown that very preterm infants (VPI) have low plasma arginine levels when receiving current parenteral nutrition (PN) amino acid (AA) formulations. Arginine is involved in several metabolic and inflammatory pathways including those affecting T-cell function. Hypoargininaemia is associated with necrotising enterocolitis (NEC). Arginine and glutamine share metabolic pathways. Glutamine also has a role in immune function and gut integrity.

Aim: to compare plasma arginine levels in VPI stratified according to whether positive (PS) or negative for sepsis (NS).

Methods: The RCT: Standardised Concentrated Additional Macronutrient Parenteral (SCAMP) nutrition study (1) stratified infants into to gestational bands and randomised to receive a standard or high protein/energy PN regimen. Our secondary analysis re-stratified VPI into PS or NS based on blood culture in the first 28 days of life using previously published sepsis criteria and outcomes (2). This process was repeated for a positive/negative diagnosis of confirmed NEC and the composite outcome of NEC or sepsis. Plasma arginine, glutamine and glutamate levels were measured in the second week of life using ion exchange chromatography.

Results: Of the 150 VPI (<29 weeks) randomised in the original study, AA data were available for 47/57 in the PS group and 77/93 in the NS group. Mean (sd) plasma arginine levels were lower in the PS group (Table 1) and lowest in the 24-26 wk gestation stratum. They were also lower in the substratum of all PS infants (n=21) with more than 1 episode of sepsis: 30 (15) µmol/l (p=0.02). Analysis was unchanged by excluding the 2 infants with early onset sepsis (day 1-3). There was no difference in plasma AA comparing NEC (n=19) and no NEC (n=105) groups. The composite outcome: NEC or sepsis is shown in Table.

Table: Mean (sd) plasma AA levels (µmol/l)

<table>
<thead>
<tr>
<th>Group (n)</th>
<th>Birthweight</th>
<th>PN age (d)</th>
<th>Arginine</th>
<th>Glutamine</th>
<th>Glutamate</th>
</tr>
</thead>
<tbody>
<tr>
<td>PS: all infants (47)</td>
<td>856 (148)</td>
<td>9 (3)</td>
<td>37 (18)</td>
<td>442 (114)</td>
<td>96 (32)</td>
</tr>
<tr>
<td>NS: all infants (77)</td>
<td>915 (180)</td>
<td>10 (3)</td>
<td>48 (30)</td>
<td>491 (161)</td>
<td>112 (65)</td>
</tr>
<tr>
<td>p</td>
<td>0.06</td>
<td>0.35</td>
<td>0.03</td>
<td>0.07</td>
<td>0.12</td>
</tr>
<tr>
<td>PS: 24-26 wks (27)</td>
<td>807 (114)</td>
<td>9 (2)</td>
<td>30 (11)</td>
<td>439 (120)</td>
<td>95 (29)</td>
</tr>
<tr>
<td>NS: 24-26 wks (32)</td>
<td>798 (162)</td>
<td>10 (3)</td>
<td>46 (36)</td>
<td>470 (167)</td>
<td>121 (82)</td>
</tr>
<tr>
<td>p</td>
<td>0.74</td>
<td>0.41</td>
<td>0.03</td>
<td>0.35</td>
<td>0.19</td>
</tr>
<tr>
<td>PS or NEC (59)</td>
<td>845 (157)</td>
<td>9 (3)</td>
<td>36 (19)</td>
<td>447 (131)</td>
<td>107 (46)</td>
</tr>
<tr>
<td>NS and no NEC (65)</td>
<td>932 (173)</td>
<td>10 (3)</td>
<td>50 (31)</td>
<td>493 (158)</td>
<td>105 (63)</td>
</tr>
<tr>
<td>p</td>
<td>&lt;0.01</td>
<td>0.25</td>
<td>&lt;0.01</td>
<td>0.08</td>
<td>0.88</td>
</tr>
</tbody>
</table>

Conclusion: Sepsis in the first 28 days of life is associated with low plasma arginine levels in VPI receiving PN.

References
Nutritional substrates’ use in very low birth weight infants at hospital discharge according to mode of feeding

Laura Morlacchi, Paola Roggero, Maria Lorella Ganni, Beatrice Bracco, Debora Porri, Camilla Menis, Fabio Mosca

1Neonatal Intensive Care Unit (Nicu), Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, University of Milan, Department of Clinical Science and Community Health, Milan, Italy

Objectives and study: Data concerning nutritional substrates’ use and how it can be influenced by the quality of nutrients’ intakes in very low birth weight (VLBW) infants at time of hospital discharge are still lacking. Aim of the study was to investigate nutritional substrates’ use in a cohort of healthy VLBW infants at discharge.

Methods: An exploratory pilot study was conducted. Inclusion criteria: healthy, orally fed and steadily growing VLBW infants, gestational age < 33 weeks. We excluded infants with clinical conditions/medications that could affect energy expenditure (EE). Infants were enrolled at time of hospital discharge. At enrollment, daily macronutrients’ intakes were calculated. Nutritional composition of human milk was determined by infrared spectroscopy (MIRIS® AB, Uppsala, Sweden) analysis. EE was measured using a prototype paediatric indirect calorimetry (Quark RMR, COSMED, Italy). Calorimetric measurements were performed for 3 hours after feeding. Protein oxidation was determined according to nitrogen balance standard method. Carbohydrate and fat oxidation were estimated from equations previously reported in literature.

Results: Thirteen infants were evaluated at 36 post-conceptional weeks. Eight infants were fed fortified human milk, five infants received preterm formula. Nutrients’ intakes complied protein and energy recommendations for preterm infants. Mean ± standard deviation of resting energy expenditure and macronutrients' oxidation rates are described in table 1. Protein oxidation contributed to 7% of energy expenditure, fat and carbohydrates to 23% and 70%, respectively. Carbohydrates oxidation was positively correlated (r 0.6, p 0.031) and fat oxidation inversely correlated (r = 0.68, p 0.010) with carbohydrate intake. In fortified human milk fed infants, protein storage was positively correlated (r 0.74, p 0.035) with the proportion of non-protein energy supplied as carbohydrates.

Table:

<table>
<thead>
<tr>
<th>Nutrient (g/kg/day)</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy expenditure</td>
<td>55 ± 7</td>
</tr>
<tr>
<td>Protein oxidation</td>
<td>1.0 ± 0.6</td>
</tr>
<tr>
<td>Carbohydrate oxidation</td>
<td>9.9 ± 3</td>
</tr>
<tr>
<td>Fat oxidation</td>
<td>1.4 ± 1.1</td>
</tr>
</tbody>
</table>

Conclusion: Our preliminary results provide data about the nutritional substrates’ use in preterm infants at the time of hospital discharge. In addition, they support the hypothesis that by modifying the quality of energy supply we could influence protein storage and define the adequate nutritional management for each preterm infant at discharge. Further larger studies are needed to confirm these findings.
Dietary sialyllactose influences diffusion tensor imaging measures in the corpus callosum of the young pig

Austin Mudd¹, Stephen Fleming², Maciej Chichlowski³, Brian Berg³, Sharon Donovan⁴, Ryan Dilger⁵

¹University of Illinois, Piglet Nutrition & Cognition Laboratory, Urbana, United States
²University of Illinois, Neuroscience Program, Urbana, United States
³Mead Johnson Pediatric Nutrition Institute, Evansville, IN, United States
⁴University of Illinois, Food Science & Human Nutrition, Urbana, United States
⁵University of Illinois, Animal Sciences, Urbana, United States

Objectives and study: Sialyllactose is an oligosaccharide composed of a sialic acid conjugated to a lactose molecule and is component in human, bovine and porcine milks. Studies in pre-clinical models have established a variety of biological effects associated with provision of dietary sialyllactose, including gut maturation, immune function and increasing brain sialic acid levels. This study aimed to examine the dose response effects of sialyllactose (Lacprodan SAL-10⁰; SL) on piglet brain development.

Methods: Beginning at 2 d of age, 38 (n = 9-10 per treatment) naturally-farrowed male piglets received one of four diets formulated to contain: control (CONT) [0 mg SL/L milk replacer], low (LOW) [130 mg SL/L], moderate (MOD) [380 mg SL/L], and high (HIGH) [760 mg SL/L]. All diets contained 4 g/L of a 1:1 mixture of polydextrose and galactooligosaccharides. At 32 or 33 d of age, piglets were subjected to magnetic resonance imaging (MRI) procedures to assess macrostructural and microstructural brain development. All outcomes were analyzed using a one-way ANOVA to assess differences between dietary treatments, significant outcomes were accepted at P ≤ 0.05 and trends at 0.05 < P < 0.10.

Results: Total brain volumes (i.e., absolute measures, mm³) were not different (P > 0.05) between dietary treatments. Moreover, assessment of ten individual brain regions did not yield differences (P > 0.05) due to diet in absolute or relative (i.e., percent total brain volume) volume measures. Axial, mean and radial diffusivity are used to assess white matter integrity and have been shown to change with age. This study assessed changes in these variables in different brain regions associated with feeding different levels of dietary SL. Diffusion tensor imaging revealed differences due to dietary treatment in measures of axial diffusivity (P = 0.002), mean diffusivity (P = 0.004), and radial diffusivity (P = 0.007) of the corpus callosum. In each of these outcomes, piglets provided the MOD diet exhibited the highest diffusivity measures compared with all other dietary treatments. Mean diffusivity (P = 0.075) and radial diffusivity (P = 0.051) in the left hippocampus tended to differ by dietary treatment, with piglets provided the MOD diet exhibiting the highest diffusivity measures.

Conclusion: Recent evidence in piglets suggests provision of SL resulted in increased corpus callosum sialic acid. While this study did not quantify sialic acid concentrations of the corpus callosum, our results corroborate recent evidence signifying sensitivity of the corpus callosum to provision of dietary SL. The differences in corpus callosum MRI measures in response to dietary SL merit future research to assess the impact of SL on specific aspects of corpus callosum development and associated functions.

Disclosure of interest: This project was funded by Mead Johnson Nutrition.
New adjustable human milk fortification to improve the growth of hospitalized preterm infants in China

Meiying Quan¹, Zhenghong Li¹, Lijuan Gou¹, Jingran Ma¹, Zhixing Sun¹, Yan Liu¹, Danhua Wang¹

¹Peking Union Medical College Hospital, Pediatric Department, Beijing, China

Objectives and Study: Exclusive breastfeeding is inadequate to maintain the incremental growth of postnatal preterm infants and human milk fortifier (HMF) is essential. But the composition of breast milk varies among mothers and even within the same mother at various times, standard commercial fortification may not appropriate for the growth of all preterm infants. This study is to test the hypothesis that infants fed according to the new adjustable fortification regimen have higher protein intakes and improved weight gain compared to infants fed according to current standard commercial fortification regimen.

Methods: This is a prospective randomized control study. Infants with birth weight between 800g and 1800g, gestational age (GA) <34 weeks, exclusive human milk feeding and without congenital malformation were eligible for this study. The adjustable fortification regimen encompasses increasing or decreasing the amount of fortifier and adding supplemental protein guided by periodic determinations of the protein concentration in human milk (PCHM) and body weight and blood urea nitrogen (BUN), from level -1 to level 3, the specific strategy was attached after the abstract(table 1). T test or χ²-square test had been used to compare the difference of nutrient intakes, growth rate, head circumference, biochemical parameters and length of NICU stay.

Results: A total of 51 preterm infants were randomized to receive either a standard fortification regimen (n=27) or an adjustable fortification regimen (n=24). There is no statistical difference on demographic characteristics between standard group and adjustable group. The energy density (56.7±5.7kcal/100ml vs 62.0±7.7 kcal/100ml, p=0.008), protein (1.42±0.23g/100ml vs 1.58±0.23 g/100ml, p=0.028) and fat (2.87±0.45g/100ml vs 3.26±0.80g/100ml, p=0.035) content of human milk was higher in adjustable fortification group. The amount of HMF added in 100 ml human milk [2.6(2.8, 2.8) g/100ml vs 2.9(2.3, 3.1) g/100ml, p=0.052], blood BUN level (3.9±2.0 mmol/L vs 4.5±1.6 mmol/L, p=0.235) and prealbumin level (79.3±26.1 mg/L vs 88.5±18.1 mg/L, p=0.158) of the first week after enrollment had a higher tendency in adjustable group, but not significant difference between two groups. About 62.5% of infants in adjustable group were given additional protein supplement. Although the weight gain during hospitalization (18.5±3.5g/kg/d vs 18.3±3.1g/kg/d, p=0.057) did not show much difference in our study, adjustable group had a tendency of shorter time to gain weight of 1800g (24.0±9.3d vs 22.6±10.7d, p=0.626) and 2000g (30.3±9.2d vs 28.4±10.7d, p=0.504). The Z score for weight (-0.7±0.6 vs -0.4±1.4, p=0.368), length (-0.7±0.7 vs -0.3±1.1, p=0.142) and head circumference (-0.5±0.7 vs -0.1±1.0, p=0.158) at discharge also showed better tendency in adjustable group.
Table: Feeding schedule in adjustable fortification regimen group

<table>
<thead>
<tr>
<th>Body weight (g)</th>
<th>PCHM (g/100ml)</th>
<th>BUN (mmol/L)</th>
<th>Fortification level</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;1500</td>
<td>≥1.5</td>
<td>&gt;5.0</td>
<td>L0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.2 ~ 5.0</td>
<td>L1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;3.2</td>
<td>L2</td>
</tr>
<tr>
<td>≤1.4</td>
<td>&gt;5.0</td>
<td>L1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.2 ~ 5.0</td>
<td>L2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;3.2</td>
<td>L3</td>
<td></td>
</tr>
<tr>
<td>≥1500</td>
<td>≥1.5</td>
<td>&gt;5.0</td>
<td>L-1</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3.2 ~ 5.0</td>
<td>L0</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;3.2</td>
<td>L1</td>
</tr>
<tr>
<td>≤1.4</td>
<td>&gt;5.0</td>
<td>L0</td>
<td></td>
</tr>
<tr>
<td></td>
<td>3.2 ~ 5.0</td>
<td>L1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>&lt;3.2</td>
<td>L2</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: There is higher protein intake in adjustable fortification group. Infants in adjustable group had higher tendency of weight gain and shorter time to gain 1800g and 2000g, the sample size of our study limited the significant difference between standard and adjustable fortification group. Larger scale study should be carried out to prove above hypothesis.
Differences in composition of macronutrient and energy levels in preterm and full term human milk at first three weeks after delivery

Neti Nurani¹, Dessy Shinta², Sri Mulatsih¹

¹Dr. Sardjito General Hospital Faculty of Medicine Universitas Gadjah Mada, Pediatrics, Yogyakarta, Indonesia
²Dr Sardjito General Hospital, Pediatrics, Yogyakarta, Indonesia

Objectives and study: Background: Human milk’s macronutrients change dynamically and vary among mothers. Measurement of macronutrient content in human milk is required to improve nutritional management in preterm infants. Objectives to compare the macronutrient content in preterm and full term human milk at first three weeks after delivery.

Methods: We conducted a prospective study in 73 healthy mothers (15-45 years old) who delivered preterm and full term infants in Perinatology/NICU Division of Sardjito General Hospital between April and May 2016. Carbohydrate, fat, protein and energy levels were measured using human milk analyzer (MIRIS) every week for consecutive three weeks after delivery. Human milk samples were obtained by full expressed method and were collected in the morning.

Results: There were a wide variety of carbohydrate, fat, and protein levels in this study. Median protein levels (g/dl) in preterm and full term human milk were 2.0 and 1.70 (P=0.054) at first week, 1.50 and 1.60 (P=0.987) at second week, and 1.40 and 1.40 (P=0.87) at third week after delivery. Median energy levels (kcal/dl) 56 and 57 (P=0.12) at first week, 59 and 68 (P=0.97) at second week, 60 and 62 (P=0.51) at third week after delivery.

Table:

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pre term (N=36) Mean (Range)</th>
<th>Full term (N=37) Mean (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mothers age (year)</td>
<td>30.4 (17-41)</td>
<td>30.8 (20-41)</td>
</tr>
<tr>
<td>Parity</td>
<td>2 (1-4)</td>
<td>2 (1-4)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>34 (28-36)</td>
<td>39 (37-41)</td>
</tr>
<tr>
<td>Weight increment during pregnancy (kg)</td>
<td>9.3 (0.5-23)</td>
<td>10.6 (3-28)</td>
</tr>
<tr>
<td>Baby birth weight (g)</td>
<td>1744 (760-3000)</td>
<td>3029 (1980-4098)</td>
</tr>
<tr>
<td>Mothers Body Mass Index (kg/m²)</td>
<td>24 (17-32)</td>
<td>26 (17-34)</td>
</tr>
</tbody>
</table>

Conclusion: No significant differences of protein, fat, carbohydrate, and energy levels were found between preterm and full term human milk at first three weeks after delivery. Median protein levels in both group were highest at first week after delivery. Carbohydrate and energy levels in preterm and full term human milk were lower than published values.

Keywords: human milk, analysis, lactation, preterm, nutrition
Butyrate in human milk: a GEHM study of three global cohorts

Stephanie Shu¹, Judy Cundiff¹, Michael Gray¹, Beau Labhart¹, Sarah Maria¹, Shay Phillips¹, Ardythe Morrow²

¹Mead Johnson Nutrition, Pediatric Nutrition Institute, Evansville, United States
²Cincinnati Children’s Hospital Medical Center, The Perinatal Institute’s Center of Interdisciplinary Research in Human Milk and Lactation, Cincinnati, United States

Objectives and study: Butyrate (C4:0) is a short chain fatty acid (SCFA) found in human breast milk and is known to have beneficial physiological effects through interactions with infant gut microbiota; however, butyrate levels in human milk are not well established and believed to be influenced by both maternal diet and gut microbiota composition. As part of the Global Exploration of Human Milk (GEHM) collaboration, this study utilizes a newly developed analytical approach to investigate the total butyrate content of human milk collected at 4 weeks of lactation from mothers in three geographic regions.

Methods: Human milk was collected from mother-infant pairs participating in the GEHM study from three global populations in Shanghai, China, Mexico City, Mexico, and Cincinnati, United States (U.S.). For this butyrate investigation, 10 milk samples from each region at 4 weeks of lactation were analyzed for butyric acid (BA) using an internally developed gas chromatography-mass spectrometry (GC-MS) method. Development of an accurate BA analysis was a critical step in this study due to the volatile nature of SCFA and required the use of deuterated butyric acid (BA-D7) as an internal standard to improve recovery and precision. The method hydrolyzes bound butyrate to free BA using a nonspecific microbial triacylglycerol lipase (yeast), extracts the BA with ethyl acetate, and detects BA by a GC-MS equipped with a polar capillary column. This analytical approach was fully validated to ensure optimal precision and accuracy before evaluating human milk samples.

Results: The China cohort displayed an average BA level of 12.1 µg/mL with a range of 6.48 to 16.6 µg/mL. Mexico exhibited the lowest average BA concentration at 9.38 µg/mL with a range of 4.04 to 15.0 µg/mL. The U.S. milk yielded the largest BA range of 7.46 to 23.6 µg/mL and an average of 12.8 µg/mL.

Conclusion: This exploratory study presents a global glimpse into the butyrate content of human milk at 4 weeks lactation. Utilization of this novel method is planned for an expanded, longitudinal set of samples from the GEHM study representative of the first year of lactation. The data generated from the completed study may offer insights into the content and variability of butyrate in human milk from a global perspective.

Efficacy and safety of iron-containing parenteral nutrition for anemia in preterm infants: a randomized, double-blind and controlled study

Wu Qingqing¹, Weiping Wang², Qingya Tang¹

¹Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Clinical Nutrition, Shanghai, China
²Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Paediatric Intensive Care Unit, Shanghai, China

Objectives and study: To study the efficacy of iron-containing PN for prevention of anemia in preterm infants. To explore the effect of iron-containing PN on oxidant injury indexes. To supply evidences for prevention of anemia in preterm infants from clinical nutrition.

Methods: A prospective, controlled, randomized, unmasked trial. Preterm infants (gestational age < 37 weeks, 1500g ≤ Birth Weight ≤ 2000g) who were born in Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University and were admitted to Neonatal Intensive Care Unit, and duration of parenteral nutrition (PN without iron sucrose) was more than 7 days. The recruited infants were divided into five groups randomly: group-0 (PN), group-1 (PN with iron sucrose 100µg/kg/d), group-2 (PN with iron sucrose 200µg/kg/d), group-3 (PN with iron sucrose 300µg/kg/d), group-4 (PN with iron sucrose 400µg/kg/d). There are about 30 infants each group. Baseline values for all parameters were recorded. Collect the indexes of red blood cell parameters (red blood cell, hemoglobin), iron storage (total iron binding capacity, unsaturated iron binding capacity, ferritin) and oxidant injury (malondialdehyde and 8-isoprostane) before and after PN.

Results: There was no statistical difference between the baseline indicators. After the intervention, RBC and Hb were markedly decreased in five groups (P < 0.01). Ferritin was significantly increased (P < 0.05) except for group-1 (p=0.469) which tended to increase. Total iron binding capacity (TIBC) and unsaturated iron binding capacity (UIBC) were significantly decreased (P < 0.05) except for group-1 (P=0.519 and P=0.104) which tended to decrease. 8-isoprostane was markedly decreased (p=0.012) but malondialdehyde (MDA) tended to increase in group-4, and other groups were decreased in the two indexes. The rangeability of ferritin had statistical difference in 5 groups before and after intervention. It was significantly higher in group-3 than group-0 and group-1 (P=0.037 and P=0). And group-2 and group-4 were significantly increased compared with group-1 (P=0.19 and P=0.004). The decline of Hb in intervention groups was lower than group-0.

Conclusion: Iron-containing parenteral nutrition can improve iron storage indexes and slow down declined change of anemia indexes. It is safe in PN with iron sucrose 100µg/kg/d, PN with iron sucrose 200µg/kg/d and PN with iron sucrose 300µg/kg/d, but should be paid attention to PN with iron sucrose 400µg/kg/d in oxidant injury.
Incorporation of dairy fat in infant formula modifies microRNAs expression profiles in the cortex, liver and plasma as compared to vegetable formula: changes in microRNAs implicated in metabolic disorders

Anne Baroin-Tourancheau¹, Delphine Crepin¹, Hassina Ould-Hamouda¹, Bernadette Delplanque², Pascale le Ruyet³, Mohammed Taouis¹

¹University Paris-Saclay, Neuropsi Umr9197, Nmpa, Orsay, France
²Nmpa, Cnps, Universite Paris-Sud, Orsay, France
³Lactalis R&d, Nutrition, Retiers, France

Objectives and study: Achieving an appropriate omega3 status in the neonate is an important goal of neonatal nutrition impacting cognition and potentially protecting against metabolic disorders during adulthood. Infant formulas have been gradually replacing mother’s milk and are usually prepared with vegetal oils. Additionally, it is well known that omega 3 promote insulin responsiveness and exhibit a protective action against cardiovascular diseases through changes in the expression involved in insulin responsiveness. Recently, microRNAs (miRNAs), small non-coding RNAs (18-24 bases long), have emerged as one of the major post-transcriptional regulators involved in numerous biological processes. However, little is known concerning the impact of omega 3 status and dairy fat matrix on their expression especially early in life. To validate the potential replacement of vegetal fat with dairy fat in infant formulas, we used rats as a nutritional model to compare the effects of blends or pure fat based on dairy fat instead of vegetable sources (palm, rapeseed) supplemented or not with DHA. We evaluated the impact of dairy fat introduction on miRNAs expression profiles in the cortex, liver and plasma.

Methods: Seven groups of rats (6 males/group) were fed from weaning to 9 weeks of age with diets providing lipids from vegetable or dairy fat source. Three diets mimic infant formula FA composition, 2 resulting from classical vegetable blends (V1, V2, alphalinolenic acid ALA 1.7%), V 2 supplemented with DHA (0.2%) and the third one D1 from a blend of dairy and vegetable fat (2.3% ALA). The next 4 diets were prepared with pure fat: D2 and D3 from pure anhydrous dairy (D2: 0.8% ALA, D3=D2 supplemented with DHA), and from vegetable source: P (Palm ALA poor) and C ALA rich rapeseed (8% ALA). At the end of diet protocols, tissues and blood were collected and total RNAs were extracted. Total RNAs were size-fractioned on a 17% SDS-PAGE to yield a 14-40 bases small RNA fraction. Barcoded cDNA libraries were constructed using Truseq amplification primers. Reads >16 nucleotides were analyzed and normalized using sRNATool Box facilities and DESEQ-R program.

Results: We have performed 21 differential expression analyses (2 groups of samples) in cortex, liver and plasma. We focused on the most striking differences that are related to lipid metabolism and insulin responsiveness. Here, we show in the cortex that V2 as compared to D1 exhibits a higher expression of miR-15a-5p, miR-184 and miR-486 that are associated to hepatic steatosis, insulin resistance and vulnerability to coronary artery, respectively. Furthermore, in V2 liver a higher expression of miR-148a was found as compared to D1, which is associated to elevated LDL level by downregulation of LDL receptor. We have extended our analysis to D1, D2 and D3 where the expression of the following miRNAs is downregulated : let-7g-5p, miR-770-5p, miR-370, miR-183, miR-455 that are associated to type 2 diabetes, insulin resistance, increased liver lipogenesis, decreased insulin signaling and increased adipogenesis, respectively.

Conclusion: Taken together, our results show for the first time, to our knowledge, that the supplementation of dairy fat modifies miRNAs expression profile in the cortex, liver and plasma, and more importantly down regulates some miRNAs that are implicated in metabolic disorders. These results need to be confirmed by directly measuring the identified miRNAs by qRT-PCR to validate the Truseq analysis.

Granted by Lactalis.
Using a symptom scoring tool to aid diagnosis and management of cow's milk protein allergy

Lynda Rigley, Emma Cribb

Doncaster & Bassetlaw Hospitals NHS Foundation Trust, Paediatric Dietetics, Doncaster, United Kingdom

Objectives and study:

Many infants present with symptoms that can be related to the intake of cow’s milk. However Cow’s Milk Protein Allergy (CMPA) is often not considered as a diagnosis mainly due to the lack of a specific diagnostic marker. CoMiSS™ (Cow’s Milk-related Symptom Score) is an awareness tool developed by clinicians experienced in managing children with GI problems and/or atopic diseases (1). It combines many common cow’s milk related symptoms. It may aid earlier diagnosis and be used to evaluate and quantify symptoms during therapeutic intervention. The CoMiSS™ tool was evaluated in a District General Dietetic Department as a way of monitoring dietetic intervention and outcomes.

Methods:
The CoMiSS tool was completed on initial contact with 58 patients under the age of one year referred for suspected CMPA. If the child had already been started on a speciality formula, parents were asked to reflect on symptoms prior to treatment. All patients were offered an appropriate formula irrespective of the score. Patients were reviewed at least 6 weeks later and re-scored. Dietitians using the tool were asked to evaluate it.

Results:
The mean CoMiSS™ score was 16.5 (range7-29). Twenty eight (48%) were started on an extensively hydrolysed formula (EHF), 19(32%) on an amino acid (AAF) formula. Three were breastfed and mothers were advised to follow a milk free diet. Two babies (over 6months) stayed on soya formula. The remaining 6 stayed on a formula not recommended by current guidelines. Five on lactose free (LF) and one on preterm formulas. The mean age at initial contact was 20.3 weeks (range 3-48 weeks).

All patients received advice and review. After a period of at least 6 weeks the CoMiSS™ was re-scored. All patients had a reduction in their score and an improvement in their symptoms. The mean re-score was 3.4 (range 0-15). Scores only remained above 12 in 2 patients both of these declined an EHF and chose to remain on LF formula. All of their symptoms improved but they continued to have eczema. One patient had no improvement with an EHF but symptoms resolved with anti-reflux medication.

Parents were advised that as symptoms had improved they could now challenge with milk to confirm the diagnosis. All families except two chose not to perform the challenge. For those that were challenged, symptoms returned.

The tool took 5-10 minutes to complete with the family; all found it easy to use. Dietitians commented the scores enabled them to discuss possible diagnosis of CMPA with more confidence. On patient review it provided quantitative data that could be discussed with parents to confirm the need for ongoing dietary management and reassure parents of an improvement.

Conclusion: Our data supports the use of the CoMiSS™ as an awareness tool. This tool is also useful in Secondary care for measuring clinical outcomes. It is a quick and easy to use tool that combines the vast range and variability of clinical symptoms associated with CMPA. It was observed that infants were referred for dietetic advice much later as most parents stated infants had suffered with the symptoms from birth. The use of the CoMiSS™ tool in the Primary care setting could improve patient care. It could lead to quicker diagnosis, reduced number of GP visits, and reduce the need for referrals to Secondary care.

Reg. Trademark of Société des Produits Nestlé SA
Impact of fortification in the osmolality of different human preterm milk

Amandine Ligneul¹, Anne Laure Sérandour², Sylvie Rohou³, Marie Cécile Andro-Garçon⁴, Jennifer Chauvel⁵, Pierre Dupas⁶, Catherine Fressange-Mazda⁷, Pascale le Ruyet¹, Alain Dabadie⁷, Anne Sauret⁸

¹Lactalis R&d, Nutrition, Retiers, France
²Slb Pharma, Rennes, France
³Eurosafe, Rennes, France
⁴Ch Yves Le Foll, Lactarium, St Brieuc, France
⁵Ch Yves Le Foll, Neonatology, St Brieuc, France
⁶Lactalis, Nutrition Euroe, Torcé, France
⁷Chu Rennes, Pediatric Gastroenterology, Rennes, France
⁸Chu Rennes, Lactarium, Rennes, France

Objectives and study: Preterm infants have specific nutrient needs regarding nitrogen, micronutrients and energy in order to catch up their growth retardation. Adding human milk fortifier is essential and currently use in neonatologist units but, such supplementation induce an increased osmolality. Current guidelines recommend that the osmolality should not exceed 450 mOsm/kg in order to minimize the risk of necrotizing enterocolitis and feed intolerance. A commercial human milk supplement, Supplétine®, was developed to fortify preterm human breast milk by increasing protein, mineral and DHA content. However, its impact on osmolality has not been systematically studied, therefore we investigated the effects of this fortification on preterm human milk (HM) osmolality.

Methods: The study was declared and accepted by the CH Rennes ethical comity of in June 2016 (n°16.77). From July to December 2016, 24 samples of expressed HM stored at 4°C, were provided by the Human milk bank of CH Yves Le Foll (St Brieuc, France) and CHU de Rennes - Hôpital Sud (Rennes, France). To cover the variability of mother’s milk composition, we used milk from mothers of preterm babies born before 28 weeks of gestation and after 1 to 2 weeks or 3 to 4 weeks of delivery or between 29-31 weeks of gestation and after 1 to 2 weeks or 3 to 4 weeks of delivery. Osmolality was measured in triplicate by the Gonotec Osmomat 030 (Eurosafe Laboratory, St Grégoire, France) in a 2 ml sample of HM. The total osmolality of HM solutions, expressed in mOsm/kg H2O, was determined by measuring the freezing point of the solutions compared to pure water. Fresh or pasteurised HM was measured at baseline, immediately after adding HM fortifier Suppletine® (HMF) at 3%, 4%, 4.5% and 5% (w/v) and after 24 hours stored at 4°C.

Results: The osmolality of fresh HM (n=16) ranged from 280 to 304 mOsm/kg. The fortifier added at 3%, 4%, 4.5% and 5% increased the osmolality respectively to 404 mOsm/kg (n=6, range 396-418 mOsm/kg), 439 mOsm/kg (n=15, range 409-487 mOsm/kg), 468 mOsm/kg (n=2, range 464-472 mOsm/kg) and 473 mOsm/kg (n=10, range 440-502 mOsm/kg). Thus, the fortifier impacts the osmolality by 32 mOsm/g of added powder.

Conclusion: Adding up to 4% of Suppletine® to fortify preterm milk is safe, whatever the origin and quality of milk and hospital practices. A 4% HMF Suppletine® increases the nutritional quality of human milk without increasing osmolality beyond 450 mOsm/kg.

Disclosure of interest: Pierre Dupas Conflict with LACTALIS; Catherine Fressange-Mazda Conflict with LACTALIS; Pascale Leruyet Conflict with LACTALIS; Amandine Ligneul Conflict with LACTALIS

Vol. 64, Supplement 1, April 2017 960
Looking for a correlation between serum leptin values and leptin receptor polymorphism A668G in healthy infants

Francesco Savino¹, Allegra Sardo², Di Stasio Liliana³, Paola Montanari⁴, Ilaria Galliano⁴, Rossi Lorenza⁴, Massimiliano Bergallo⁴

¹Città Della Salute e Della Scienza Di Torino, S.A.P.I. Children Hospital Regina Margherita, Turin, Italy
²University of Turin, Pediatria, Turin, Italy
³University of Turin, Department of Agricultural, Forest and Food Sciences, Torino, Italy
⁴University of Turin, Department of Public Health and Pediatrics, Torino, Italy

Objectives and study: Leptin, a hormone released by adipocytes, regulates energy metabolism and it is found in breast milk. The primary function of this hormone is to inhibit food intake and to promote energy expenditure. Leptin exerts its actions through its receptor, Ob-R, which is found in neurons in arcuate nucleus in the hypothalamus. Higher serum leptin values are related to lower BMI in infancy, suggesting that this hormone could be a protector against obesity. Leptin and receptor genes and their polymorphisms play a central role in determining obesity. Several studies, conducted on adults, investigated the association between these factors and serum leptin values and BMI. In infancy, few studies have been carried out on this topic and results are controversial.

The aim of this study was to evaluate the correlation between leptin receptor polymorphism (LEPR A668G) and healthy infants’ serum leptin values.

Methods: Between June 2015 and October 2016, we enrolled 105 healthy infants from ten days to six months of life at “Pediatria 1U Lattanti” – Regina Margherita Hospital, Città della Salute e della Scienza di Torino, Turin, Italy. We measured infants’ anthropometric parameters and serum leptin values with a Radioimmunoassay method (RIA). For each infant, we evaluated the genotype of the LEPR A668G polymorphism, with an especially processed for this study technique, the Amplification Refractory Mutation System-Mismatch Amplification Mutation Assay real-time PCR (ARMS-MAMA). Statistical analysis was performed using χ² test and ANOVA. We set statistical significance at p<0.05.

Results: We didn’t find any difference in anthropometric parameters (p>0.05) and the analyzed cohort was homogeneous. The median leptin concentration was 3.08 (0.76) ng/ml in infants with AA-genotype (n=43), 4.04 (0.59) ng/ml in AG-genotype children (n=27) and 7.66 (0.86) ng/ml in infants with GG-genotype (n=35). We found higher leptin levels in GG-genotype infants for LEPR A668G (p<0.001), suggesting a link.

Conclusion: This is the first study to evaluate the influence that leptin receptor gene polymorphisms could exert on infant growth. We found higher serum leptin levels in infants with GG genotype for LEPR A668G. According to the results, it seems that the genotype GG could be a protector against obesity development in infancy and adulthood. What is more, these data confirm that not only leptin variations, but also its receptor ones could play a role in the gain of weight in early infancy. Further studies are needed to evaluate the role of genetics and early environmental factor in the predisposition of obesity later in life.
Objective and study: Oligosaccharides in milk act as soluble decoy receptors and prevent pathogen adhesion to the infant gut. Milk oligosaccharides reduce infectivity of a porcine rotavirus strain; however, the effects on human rotaviruses are less understood. In this study, we determined the effect of specific and abundant milk oligosaccharides on the infectivity of two globally dominant human rotavirus strains.

Methods: Four milk oligosaccharides: 2′fucosyllactose (2′FL), 3′sialyllactose (3′SL), 6′sialyllactose (6′SL) and galacto-oligosaccharides (GOS) were tested for their effects on the infectivity of human rotaviruses, G1P[8] and G2P[4] through fluorescent focus assays on MA104 cells. Oligosaccharides were added at different time points in the infectivity assays. Infections in the absence of oligosaccharides served as controls.

Results: All oligosaccharides significantly reduced the infectivity of both human rotavirus strains in vitro; however, virus strain-specific differences in effects were observed. The greatest reduction for G1P[8] was seen with 2′FL when added after the onset of infection (62%), while the greatest effect for G2P[4] was seen with the mixture of 3′SL and 6′SL when added during infection (73%). 3′SL+6′SL combination in the same ratio as present in breast milk was more potent in reducing G2P[4] infectivity than when used individually. For all oligosaccharides, the reduction in infectivity was mediated by an effect on the virus and not on MA104 cells.

Conclusion: Milk oligosaccharides can act as soluble decoy receptors and reduce the infectivity of human rotaviruses. While breast-fed infants are directly protected, the addition of specific oligosaccharides to infant formula can confer these benefits to formula-fed infants.

Disclosure of interest: Vassilis Triantis: Employee of FrieslandCampina
Ruud Schoemaker: Employee of FrieslandCampina
**NUTRITION: Neonatal and infant nutrition**

N-P-122

**Weight gain in the first month of life as a predictor of high growth rate during the first year of life of exclusively breastfed infants**

Igor Kon¹, Maria Gmoshinskaya², Nataliya Shilina³, Vladimir Furtzev⁴, Elena Budnikova⁴, Tatyana Abramova²

¹Federal Research Center of Nutrition and Biotechnology, Moscow, Russian Federation
²Federal Research Center of Nutrition and Biotechnology, Age-Related Nutritiology, Moscow, Russian Federation
³Institute of Nutrition, Age-Related Nutritiology, Moscow, Russian Federation
⁴Krasnoyarsk State Medical University Named after Professor V.F. Voyno-Yasenetskii of Ministry of Health, Krasnoyarsk, Russian Federation

**Objectives and study:** High weight gain in infancy – a risk factor of later obesity – has been observed not only in formula fed but also in exclusively breast-fed infants. Paediatrician has to consult parents on the breastfeeding tactics for infants at risk for accelerated weight gain. At the same time there is a very limited number of informative, available in daily practice predictors that indicate the possibility of elevated growth rate in exclusively breastfed infants. The aim was to identify informative predictors of accelerated weight gain in exclusively breastfed infants on the basis of the study of their physical development trajectories during the first year of life.

**Methods:** The work was performed at child outpatient’s clinics of Moscow and Krasnoyarsk in 2011-2012. The study protocol was approved by the local ethical committees of the Federal Research Center of Nutrition and Biotechnology and Krasnoyarsk state medical university. All women gave their informed consent. We questioned 280 women with infants being breast-fed at least 12 months and exclusively breast-fed for 4 months, with the birth weight >2500 g and birth length >47 cm. The anthropometric measurements at 1, 2, 3, 6, 9 and 12 months of life taken during infants visits to outpatient’s clinics and fixed in their cards were investigated using WHO Anthro, 2005. Statistical analysis was performed by SPSS 9.0 (Χ², Student’s t-test, non-parametric Mann-Wynny test). The differences were considered as statistically significant at p<0.05.

**Results:** Depending on the weight gain in the first month of life, infants were divided into 3 groups: the 1ˢᵗ group – infants with weight gain < 500 g (n=25), the 2ⁿᵈ group - weight gain 501-1000g (n=124), the 3ʳᵈ group - weight gain > 1000 g (n=131). Birth weight of infants in the 1ˢᵗ, 2ⁿᵈ and 3ʳᵈ groups was 3374±85 g, 3495±39 g and 3345±33g, respectively (p₂-₃=0.003). Infants of the 3ʳᵈ group showed significantly higher body weight gain compared to infants of the 1ˢᵗ and 2ⁿᵈ groups over the first 3 months of life (2273±167 g, 2625±58 g, 3157±53 g in infants of the 1ˢᵗ, 2ⁿᵈ and 3ʳᵈ groups, respectively), and over the first 6 months of life (4041±301 g, 4309±88g, 4866±83 g, pANOVA=0.000) and a trend towards a higher body weight gain over the first 12 months of life (6710±305 g, 6685±107 g, 6927±91 g, p₂-₃=0.085). At the age of 1(pANOVA=0.012), 2, 3, 6 (pANOVA=0.000) and 9 (p₂-₃=0.035) months the body weight of infants of the 3ʳᵈ group was significantly higher than the body weight of infants in two other groups without significant differences in infants body length.

**Conclusion:** Thus, the body weight gain over 1 kg in the first month of life is associated with a higher growth rate in the first 3 and 6 months of age and a higher body weight during the first year of life, and can therefore serve as a predictor of increased weight gain in exclusively breastfed infants. It also indicates the need to pay attention to the regime of breast-feeding for these infants eliminating any possibility of indiscriminate feeding and overfeeding.
Macronutrient composition of human milk from mothers of preterm infants

Anup Thakur¹, Neelam Kler¹, Pankaj Garg¹, Priya Gandhi¹

¹Sir Ganga Ram Hospital, Neonatology, New Delhi, India

Objectives and study: Studies focusing on the macronutrient content of human milk fractions from Indian mothers delivering premature neonates are scarce and show conflicting results. The objective of the study was to analyze human milk of mothers delivering preterm infants (<37 weeks) for their macronutrient content (protein, fats and calories) in the first week of lactation.

Methods:

- **Study design:** Observational study.
- **Study population:** Mothers aged 18-45 years of age giving birth to premature infants [between 25 – 36] weeks of gestation, having enough milk for their infants were enrolled.
- **Analysis of Macronutrients in Breast milk through MIRIS machine [Human Milk Analyzer]**- Individual milk samples were collected from each participant between 8 am and 12 pm on 7th day of life (± 2 days). Mother’s one breast was emptied by a breast pump and the milk samples was collected in plastic containers. 2 ml of left over expressed breast milk after feeding the infant was used for analysis. For uniformity human milk was obtained from mother’s left breast. The Human Milk Analyzer (HMA), produced by MIRIS uses infrared transmission spectroscopy to measure the macronutrients in milk against a known reference library included with the machine.

Results: A total of 24 samples of mothers delivering preterm babies were analyzed. The mean (SD) gestation and weight of infants were 33(3.02) wks and 1825.50(733) g. Human milk was collected on 5.8(0.9) days. The mean (SD) content of fats, carbohydrates, crude protein, true protein and energy in the samples were 2.2(1.23) g, 5.44(0.65) g, 2.13(0.45) g, 1.97(1.08) g and 53.58(13.18) k/cal.

Conclusion: The protein and fat content of human milk of mothers delivering preterm neonates is lower than reported in other Indian studies done using US milkoscan. This needs to be confirmed in larger gestation specific studies.
Treatment of non-IgE mediated cow’s milk allergy with a partially hydrolyzed rice infant formula: a prospective study

Ramón Tormo1, Guillermo Cárdenas2, Hegoi Segurola2

1Via Augusta Clinic. Quiron Hospital ., Pediatric Gastroenterology and Nutrition Unit, Barcelona, Spain
2Via Augusta Clinic, Pediatric Gastroenterology and Nutrition Unit, Barcelona, Spain

Introduction: Non–IgE-mediated cow’s milk protein allergy in infants is a frequent cause of colic, intense crying, irritability, malabsorption, and failure to thrive. Fecal fat levels are generally increased in these patients.

Objective: To verify a hydrolyzed rice protein–based formula effect in non–IgE-mediated cow’s milk protein allergy children.

Material and methods: Our study population comprised 30 infants (age< 12 months) fed on cow’s milk protein–based formulas (with or without lactose) or extensively hydrolyzed formulas and soy formulas with symptoms suggestive of non–IgE-mediated cow’s milk protein allergy. Non–IgE-mediated cow’s milk protein allergy was diagnosed through Fecal Near Infra-Red method (FENIR). Prick test were negative in old infants.

Results: Fecal fat levels were over 5 g/100 g of feces. All the children were switched to a hydrolyzed rice protein–based formula. After 1 month, fat levels returned to normal values (<5 mg/100 g) and symptoms improved: crying and irritability disappeared, and the patients reached their normal weight and height. In addition, the taste was well accepted by the infants.

Conclusions: In infants with non–IgE-mediated cow’s milk protein allergy, feeding with a hydrolyzed rice protein–based formula is an adequate and safe alternative, leading to improvement of symptoms and reduction of steatorrhea.
The human milk oligosaccharide 2'-fucosyllactose modulates metabolism of the infant intestinal microbiota

Enrique Vazquez1, Pieter Van den Abbeele2, Massimo Marzorati2, maria RAMIREZ1, Jomay Chow3, Ricardo Rueda1, Rachael Buck3

1Abbott Nutrition, Strategic R&d, Granada, Spain
2Prodigest Bvba, Gent, Belgium
3Abbott Nutrition, Strategic R&d, Columbus, United States

Objectives and study: Human milk contains all the nutrients necessary to support infant growth and development, including a rich repertoire of human milk oligosaccharides (HMO). The HMO fraction is unique in its diversity, quantity and complexity. 2'-fucosyllactose (2'-FL) is the most abundant HMO in a majority of human milk, with a concentration of up to 4.65 g/L. In contrast, trace amounts of oligosaccharides are present in mature bovine milk and in milk-based infant formulas. Accumulating evidence indicates that HMO consumption benefits the infant in multiple ways. Perhaps, the best known benefit of HMO is its role as a prebiotic. Although the composition of bacterial communities varies across the length of the gastrointestinal tract, and microbiota-derived host benefits may depend on the presence of specific bacterial species in a particular location within the gut, little is known about the effects of 2'-FL on microbial metabolism in the different regions of the colon. The aim of this study was to investigate the potential prebiotic properties of 2'-FL on gut microbiota activity in the proximal and distal colon.

Methods: Stool samples from 6-month-old infants (n=3) were maintained in the Simulator of the Human Intestinal Microbial Ecosystem (SHIME®) in the presence or absence of 2'-FL (2g/L). Microbial metabolic activity assessed by measuring gas, lactate, short-chain fatty acids (SCFA) and NH4+ production in the proximal and distal regions of the colon.

Results: Treatment with 2'-FL resulted in a marked increase in fermentation as shown by greater gas production and microbiota-induced acidification of the luminal content (as measured by base-acid consumption). Moreover, 2'-FL stimulated the production of acetate, propionate and total SCFA levels in the distal colon for all three donors (p<0.05). Treatment with 2'-FL also resulted in reduced lactate (P<0.05) in the distal colon from all three. 2'-FL decreased NH4+ levels in the proximal colon of all three donors (p<0.05), but reduced NH4+ in the distal colon of only one donor (p=0.019). 2'-FL had a negligible effect on branched-chain fatty acid levels, with the exception of decreased levels in the proximal colon of donor 3 (p=0.007). Remarkably, even though 2'-FL was fermented in the proximal colon, significant fermentation of 2'-FL occurred in the distal colon as reflected by total SCFA levels.

Conclusion: Our results indicate that 2'-FL treatment exerted beneficial effects on infant gut microbiota and that its effects were generally consistent among the three donors tested. 2'-FL promoted greater fermentation as reflected by increased gas and SCFA production. Finally, 2'-FL had little effect on BCFA levels; however, reduced NH4+ levels were detected, especially in the distal colon.

Disclosure of interest: The following authors, EnriqueVvazquez, Maria Ramirez, Ricardo Rueda, Jomay Chow and Rachael Buck are Abbott Nutrition employees
The human milk oligosaccharide 2'-fucosyllactose modulates infant intestinal microbiota in luminal and mucosal ecosystems

Enrique Vazquez¹, Pieter Van den Abbeele², Massimo Marzorati², maria Ramirez¹, Jomay Chow³, Ricardo Rueda¹, Rachael Buck³

¹Abbott Nutrition, Strategic R&d, Granada, Spain
²Prodigest Bvba, Gent, Belgium
³Abbott Nutrition, Strategic R&d, Columbus, United States

Objectives and study: A distinguishing feature of human milk is its large quantity and great diversity of unconjugated and complex glycans compared to those of other mammals. Differences in the amount and variety of oligosaccharides also set human milk apart from bovine milk, which forms the base for most infant formulas. Over 200 oligosaccharides have been identified in human milk (HMOs), with 2'-fucosyllactose (2'-FL) being the most abundant with levels up to 4.65 g/L. Accumulating evidence indicates that HMOs provide multiple benefits to infants, and their role as prebiotics is perhaps the best-known benefit. The human gut has different ecological niches that harbor specific microbial communities. Because microbiota-derived benefits may be driven by the presence of specific microbial species, it is important to know how nutrition may impact the microbial composition in the different intestinal ecosystems. To date, little is known about the impact of 2'-FL on the microbial profile within the different intestinal ecosystems. Aim: To investigate the potential prebiotic properties of 2'-FL on the gut microbiota composition of the lumen and mucosa, in both the proximal and distal colon.

Methods: Stool samples from 6-month-old infants (n=3) were maintained in the Simulator of the Human Intestinal Microbial Ecosystem modified for mucosal compartment (M-SHIME®) in the presence or absence of 2'-FL (2g/L). Microbiota profiles were assessed via qPCR and 16S-targeted Illumina sequencing in samples from luminal and mucosal compartments, in both distal and proximal regions of the colon.

Results: 2'-FL treatment tended to increase luminal Proteobacteria and Bacteroidetes levels and reduce Firmicutes levels. Mucosal abundances were less drastically affected. By using qPCR, we showed that while the levels of total bacteria, Firmicutes and Bacteroidetes were relatively stable throughout the experiment, a specific increase of Bifidobacteriaceae was observed upon 2'-FL treatment.

Conclusion: Treatment with 2'-FL resulted in strong and immediate bacterial modulation in luminal and mucosal bacterial communities. The increase of Proteobacteria and Bacteroidetes upon 2'-FL administration concur with recent findings that both phyla contain members that are capable of cross-feeding on human milk oligosaccharides, meaning that they are not necessarily primary degraders of 2'-FL but rather that they benefit from degradation products of 2'-FL that are generated by other microbes.

Disclosure of interest: The authors Enrique Vazquez, Maria Ramirez, Jomay Chow, Ricardo Rueda and Rachael Buck are Abbott Nutrition employees
Impact of malnutrition on weight after surgery in children hospitalised for digestive, urologic or plastic surgery

Camille Wallon¹, Arnaud De Luca², Karine Bernardo², Anne Le Touze¹, Véronique Lesage¹, Marc Laffon¹, Hubert Lardy¹, Regis Hankard²

¹Chu Tours, Tours, France
²Inserm U1069, Tours, France

Objectives and study: To assess the impact of malnutrition on the weight after surgery. Our hypothesis was that the weight loss was more important for malnourished-children than for well-nourished children after surgery. The secondary aim was to find factors associated to the variation of the weight.

Methods: Every child hospitalised for a surgery more than 4 days between the 7th of July 2015 and the 26th of December 2015 and every child from 27th of December 2015 to 18th march 2016. Children were splitted into two groups whether they were malnourished or not. Malnutrition was determined according to the guidelines of the French Pediatric association and included abnormal nutritional indices.

Results: 165 patients were included, among them 27 were malnourished. The variation of weight was higher in malnourished children than in well-nourished children (0.43±0.20 vs. -0.11±0.15kg, p=0.02). Fasting duration was 13.9±9.6h before and 25.3±28.6h after surgery. Age was the only factor associated with gain weight (OR 1.1 per year, p<10⁻⁴), (multivariate logistic regression).

Conclusion: Nutritional status did not worsen in malnourished children at admission, nonetheless it did not improve. Multidisciplinary approach associating surgeons, anaesthetists and paediatricians is wanted to better take into account the nutritional status in the global care plan.
Dietary practices and beliefs among parents of children with inflammatory bowel disease: preliminary results

Aleksandra Pituch-Zdanowska¹, Piotr Albrecht¹, Alicja Stawicka¹, Elżbieta Jarocka-Cyrta², Aleksandra Banaszkiewicz¹

¹Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland ²University of Warmia and Masurian, Department of Pediatrics, Gastroenterology and Nutrition, Olsztyn, Poland

Objectives and study: Patients with inflammatory bowel disease (IBD) often worry about a diet and they make links to certain foods in order to prevent disease flare. So far, dietary practices and beliefs were investigated in adult patients with IBD. The purpose of the study was to evaluate dietary beliefs and behaviors among parents of children and adolescents with IBD.

Methods: This prospective study was conducted in two University-affiliated hospitals for children in Poland (cities of Warsaw and Olsztyn) between March and November 2016. Parents of children with IBD diagnosed according to Porto criteria were asked to filled in questionnaire that consisted of two parts. The first part consisted of a few questions regarding age, sex and diagnosis of patient. In the second part of the questionnaire, parents were asked about dietary beliefs and practices regarding their children.

Results: A total of 66 parents of children and adolescents with IBD participated in the survey. Mean age of children was 14.1±3.5 years, 52% girls, 45% Crohn's disease. 28% (n = 19) of respondents believed that diet could initiate the disease, while 69% (n = 46) believed that food could trigger a flare. About 72% (n=48) reported not eating foods that child usually like, in order to prevent relapse and around 38% (n=25) felt uncomfortable with outdoor dining because of the disease. 50% (n=33) of respondents reported that the disease had changed the pleasure of eating. 31% (n=21) of patients did not share the same menu as the other members of the family. Above 80% of respondents declared avoiding fast food, hot spices and soft and blue cheeses. 77% reported avoiding soft drinks and salty snacks, and above 60% reported avoiding milk (boiled milk - 47%), legumes and fried foods. A half of respondents declared avoiding chocolate and other sweets. Majority of parents (65%; n=43) believed that their child with IBD requires nutritionist care and 47% (n=31) of them received nutrition advice by dietitian. 13% of patients has not received any nutrition advice ever.

Conclusion: Preliminary results of our study showed that majority of parents of children with IBD hold beliefs concerning to the role of diet in IBD that result in avoidance of certain foods.
Nutritional Status and clinical characteristics of paediatric patients with cerebral palsy in Turkey

Kursad Aydin1, Turkish Cerebral Palsy Study Group none2, Jennifer Williams3, Aysugul Alptekin Sarioglu4

1Gazi University Medical Faculty, Istanbul, Turkey
2Turkish Cerebral Palsy Study Group, Istanbul, Turkey
3Abbott Nutrition, Columbus, United States
4Abbott Laboratories, Istanbul, Turkey

Objectives and study: The study was conducted to evaluate the prevalence of malnutrition and aetiology of cerebral palsy (CP) among paediatric patients in Turkey.

Methods: This was a cross-sectional, non-interventional survey study with data from 1108 paediatric CP patients collected between October 2015 and July 2016. Male or female children with CP aged ≥1 and <19 years who were current paediatric neurology outpatients were enrolled from 20 sites in Turkey. Genetic disorders, CP-unrelated chronic diseases, CP of postnatal origin and other concomitant diagnoses were exclusion criteria. The study was approved by an Institutional Review Board. All subjects and/or guardians provided signed informed consent.

Results: Of the children, 451(40.7%) were female, and mean age was 7.2 ± 0.1 years. Mean age for CP diagnosis was 30.6 ± 0.9 months. 586 (52.9%) of the children were delivered via Caesarean section, parental consanguinity was a factor in 286 (25.8%) of the patients, 105 (9.5%) of the patients were a multiple birth, and number of patients having a CP sibling was 49 (4.4%). Mean gestational age was 35 weeks. The three most common CP aetiologies were asphyxia (62.5%), low birth weight (45.6%), and prematurity (44.5%); most common CP types were spastic (87.5%), dyskinetic/dystonic (6.0%), and ataxic-hypotonic (4.1%); and, finally, affected parts of the body for these patients were quadriplegic (54.0%), diplegic (31.2%) and hemiplegic (13.7%). Mean z-scores for weight-for-age, height-for-age, head circumference-for-age, using Neyzi growth standards, at birth were -2.11 ± 0.07, -1.28 ± 0.14, and, -0.83 ± 0.24; whereas, at the time of enrolment, mean z-scores were -1.95 ± 0.07, -1.7 ± 0.07, and -2.83 ± 0.07, respectively.

According to physician questionnaires, 634 (57.2%) of sampled paediatric CP patients were malnourished, and the physicians considered nutritional management a priority.

Conclusion: This survey provided valuable information about malnutrition and paediatric cerebral palsy patients in Turkey. This data may be utilized for future proactive strategies in the prevention and treatment of malnutrition in this population.

Disclosure of interest: Employees of sponsor Abbott Nutrition: Jennifer A. Williams and Aysugul Alptekin.Investigators under sponsor Abbott Nutrition: Kursad Aydin and Turkish Cerebral Palsy Study Group
Is there a time to perform the Nissen fundoplicatio procedure in SMA type 1 patients?

Tommaso Bellini1, Federica Trucco2, Maria Grazia Faticato3, Marina Pedemonte2, Arrigo Barabino1, Serena Arrigo1, Claudio Bruno2, Girolamo Mattioli3, Carlo Minetti2, Paolo Gandullia1

1Gaslini Children Hospital, Pediatric Gastroenterology and Endoscopy Unit, Genoa, Italy
2Gaslini Children Hospital, Pediatric Neurology and Muscular Diseases Unit, Genoa, Italy
3Gaslini Children Hospital, Pediatric Surgery Unit, Genoa, Italy

Objectives and study: spinal muscular atrophy type I (SMA 1) is rare, progressive autosomal recessive neuromuscular disease and is usually fatal in the first year of life. SMA 1 leads to progressive muscle weakness, dysphagia and swallow difficulties within the first months of life. Therefore, SMA 1 patients require early supportive enteral nutrition. However, both nasogastric tube (NGT) and percutaneous endoscopic gastrostomy (PEG) do not prevent gastroesophageal reflux (GER) and/or aspiration pneumonia, which can be overcome by Nissen fundoplicatio procedure with surgical gastrostomy (NFP). Aim of our study is to establish a possible therapeutic window to perform NFP in SMA type 1 patients.

Methods: we used our database to collect all patients who need enteral or parenteral supportive nutritional care. We retrospectively enrolled all patients with a genetically confirmed SMA 1 presented at our department between 2009 and 2015. NFP was proposed on the basis of radiologically confirmed aspiration pneumonia episodes or on the evidence of GER with an upper gastrointestinal series (with barium given by NGT, UGS).

Results: twenty-five SMA 1 patients were enrolled. Sixteen patients suffered at least one aspiration pneumonia episode; of these, eight (8/25, 32%) performed a UGS with evidence of GER. Nine patients performed a UGS and presented GER, with no history of aspiration pneumonia. UGS is a safe procedure and no complications were observed. First aspiration pneumonia episode occurred at a median age of 8.3 months (range between 2 and 18 months). UGS was performed at a median age of 18 months (range between 4 and 48 months). NFP has been proposed to all 25 families and it was performed in 21 patients (4 refused). All patients did not present further episodes of aspiration after the procedure; no postoperative complications have been reported. Patients underwent NFP at a median age of 22.4 months (range between 3 and 56 months). Three of the four patients who refused the procedure presented other aspiration pneumonia episodes. The fourth patient was lost at follow-up.

Conclusion: our study shows that in SMA1 patients, the first aspiration pneumonia and/or GER occur frequently within the first year of life. Therefore, we suggest to take in consideration a UGS test and subsequently a preventive anti-GER NFP before the respiratory and digestive symptoms occur.
Effectiveness of iron fortified infant cereals on hemoglobin levels of children aged 12-24 months: a cross-sectional study in New Delhi India

Arun Fotedar\textsuperscript{1}, Jasjit Bhasin\textsuperscript{2}

\textsuperscript{1}Metro Hospital and Cancer Institute, New Delhi, India
\textsuperscript{2}B L Kapur Super Speciality Hospital, Dept of Neonatal, Paediatric & Adolescent Medicine, New Delhi, India

Objectives and study: Iron deficiency anemia represents third largest disease burden, with an estimated annual cost of US$23.8 billion per annum of future production losses and 6.9 billion Disability Adjusted Life Years (DALYs). Commercial Iron-fortified cereals (CIFIC) can contribute substantially in preventing iron deficiency anemia and maintaining an adequate body iron status. Hence with the objective to assess the effectiveness of intake CIFIC along with other complementary food’s on the hemoglobin level of children from 12-24 months of age the study was conducted.

Methods: A cross sectional study was carried out over a period of 4 months (Nov 2015 – Feb 2016) in three pediatric outpatient clinics of New Delhi, India. A predesigned questionnaire was used to elicit information on socio-demography, complementary feeding, and intake of CIFIC from 66 mother and child pair. Child’s anthropometric measurement and hemoglobin levels were recorded by pediatrician.

Results: Out of 66 children, 60.6% were boys. The prevalence of anemia (hb <11g/dl) was 42.4%. Multiple logistic regression analysis revealed that the children in CIFIC group were protected against anemia (Adj OR: 0.007, 95% CI: 0.001-0.079, p<0.001). On the contrary, boys (Adj OR:11.6, 95% CI: 1.23-108.9, p=0.032) and children with low birth weight  (Adj OR:11.7, 95% CI:1.23-111.76, p=0.032) the associated with anemic status.

Table: Comparison of CIFIC* and Non- CIFIC groups across various study variables attending selected pediatric clinics in New Delhi, India, Nov 2016 – Feb 2017 (N=66)

<table>
<thead>
<tr>
<th>Study variable</th>
<th>CIFIC group (n=36)</th>
<th>Non- CIFIC group (n=30)</th>
<th>t</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>SD</td>
<td>Mean</td>
<td>SD</td>
</tr>
<tr>
<td>Age (months)</td>
<td>16.1</td>
<td>3.3</td>
<td>13.4</td>
<td>4.5</td>
</tr>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>12.5</td>
<td>1.2</td>
<td>10.2</td>
<td>1.0</td>
</tr>
<tr>
<td>Birth weight (kg)</td>
<td>2.9</td>
<td>0.4</td>
<td>2.8</td>
<td>0.5</td>
</tr>
<tr>
<td>Present weight (kg)</td>
<td>10.4</td>
<td>1.4</td>
<td>9.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Height/length (cm)</td>
<td>78.9</td>
<td>3.7</td>
<td>75.7</td>
<td>7.3</td>
</tr>
<tr>
<td>BMI for age (kg/m(^2))</td>
<td>16.68</td>
<td>1.49</td>
<td>16.14</td>
<td>1.83</td>
</tr>
</tbody>
</table>

*Commercial Iron fortified infant cereals; *statistically significant

Conclusion: Intake of CIFIC (minimum 1-2 serving/day) was associated with lesser chance of anemia by maintaining an adequate body iron status in children of 12-24 months. However, gender and low birth weight were also associated with anemia. CIFIC may have a role in mass fortification programs with a positive public health impact by limiting DALYs and other costs. However, due to limited geographic location and small sample size, further larger and controlled studies are recommended to confirm this hypothesis.
Early administration of prebiotics protects from respiratory infections and atopy by modifying intestinal microbial structure

Vittoria Buccigrossi1, Giusy Ranucci1, Maria Grazia Felisi2, Luigi Cantarutti3, Federica Visentin4, Daniela Piacentini5, Maria Immacolata Spagnuolo1, Carlo Giaquinto4, Alfredo Guarino1

1University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
2Consorzio Valutazioni Biologiche e Farmacologiche, Pavia, Italy
3Pedianet Project, Padova, Italy
4University of Padova, Padova, Italy

Objectives and study: Intestinal microbiota affects the development of immunologic tolerance and defense from infections. Prebiotics may change gut microbiota structure. Aim of this study was to investigate the potential relationships between gut microbiota composition and respiratory infections (RI) or atopic dermatitis (AD) in infants fed prebiotics-enriched formula.

Methods: A total of 345 infants were enrolled in a prospective, double blind, randomised, 24 months study and randomly assigned to receive either a standard infant formula (SF) or GOS/PDX formula until 48 weeks of life if or from when breast milk was insufficient. Further control were infants on exclusive mother milk until 6 months. Blinded family paediatricians monitored the incidence and features of primary outcomes. A microbiological substudy was conducted collecting stool samples of infants at basal time (before intervention) and at 9 months of life (after almost 3 months of intervention). For microbiological analysis patients were divided in groups as follows: infants with RI (at least one episode/9 months; n=97) and controls (No RI n=44) and infants with (n=65) or without AD (No AD n=76). FISH technique was applied to quantitatively detect Bifidobacteria, Bacteroides, Firmicutes/Bacteroidetes ratio (F/B), F. prausnitzii and Clostridium cluster I/II and IX. The correlation between microbial structure and feeding pattern was also investigated.

Results:

Microbial structure and Respiratory Infections

Infants with RI had significantly lower bacterial load of Bifidobacteria compared with No RI group (10.74±10.46 vs 18.44±10.77 n°bacteria x109/ml; p<0.001). GOS/PDX were associated with increased load of Bifidobacteria compared with the other groups (n° bacteria x109/ml: 17.83±10.93 GOS/PDX, 12.62±11.01 SF and 11.85±13.64 BF group; p=0.011 between groups). The prevalence of RI was lower GOS/PDX formula than in breastfed or SF infants (33% GOS/PDX, 41% in BF and 48% in SF infants; p=0.074 between all groups; p=0.026 between GOS/PDX and SF).

Microbial structure and Atopic Dermatitis

Infants that developed AD had a significantly higher F/B ratio (0.97±3.99 AD vs 0.23±0.84 No AD; p=0.012) and a significantly lower colonization of Clostridium cluster I/II than No AD group (1.24±2.04 AD vs 3.77±9.07 No AD; p=0.022). AD was reduced in GOS/PDX and in breastfed infants compared with SF (37% GOS/PDX, 39% BF and 43% SF). Clostridium cluster I/II colonization increased over time in GOS/PDX group while decreased in control group and BF one.

Conclusion: Early administration of prebiotic-enriched formula affects microbial structure. This in turn exerts a functional effects and protects from RI and AD. Namely, bifidogenic effects protects from RI whereas Clostridium cluster I/II is associated with prevention of AD.

Conflict of interest: The study was supported by Mead & Johnson Foundation.

Disclosure of interest: Conflict of interest: The study was supported by Mead & Johnson Foundation.
Long-chain polyunsaturated fatty acids, but not folate, supplementation during pregnancy is related with weaker brain connectivity in children at 10 years of age

Juan Verdejo Román¹, Cristina Martínez Zaldívar¹, Francisco Jose Torres Espinola¹, Andrés Catena², Cristina Campoy Folgoso³

¹Euristikos Excellence Centre for Paediatric Research, University of Granada., Granada, Spain
²University of Granada, Mind, Brain and Behaviour International Research Centre (Cimcyc), Granada, Spain
³University of Granada, Centre of Excellence for Paediatric Research Euristikos, Granada, Spain

Objectives and study: Recent studies have shown that maternal supplementation with folate and long-chain polyunsaturated fatty acids (contained in fish oil) during pregnancy, have an important effect on children’s brain development.

We aimed at examining whether children born from mothers supplemented with fish oil (FO) or 5-methyltetrahydrofolate (5-MTHF) had different resting state connectivity at 10 years of age.

Methods: Fifty-seven children (33 girls; mean age 9.71 ± 0.22) enrolled in the NUHEAL project (NUtraceuticals for a HEALthier life; registration no. NCT01180933) underwent a six minute resting state functional Magnetic Resonance Imaging (fMRI) session. They were classified into four groups on the basis of their prenatal supplementation (i.e: FO, 5-MTHF, FO+5-MTHF, and placebo). To test the effect of FO supplementation, we classified participants into two groups: (i) 33 children supplemented with FO or FO+5-MTHF, (ii) 24 supplemented with 5-MTHF alone or placebo. To examine the effect of folate supplementation, they were divided in (i) 24 children supplemented with 5-MTHF or FO+5-MTHF and (ii) 33 children supplemented only with FO or placebo.

Analysis was carried out using the Probabilistic Independent Component Analysis [Beckmann, 2004] as implemented in MELODIC (Multivariate Exploratory Linear Decomposition into Independent Components) Version 3.14, part of FSL (FMRIB’s Software Library, www.fmrib.ox.ac.uk/fsl). Pre-processed data were whitened and projected onto a 40-dimensional subspace using Principal Component Analysis. A dual regression method as implemented in FSL, followed by two-groups t-tests was used to compare maps across groups. Results were Bonferroni corrected for multiple comparisons.

Results: Children born to mothers supplemented with FO (alone or FO+5-MTHF) showed weaker functional connectivity in the default mode network (angular gyrus) and the sensorimotor network (motor and somatosensory cortices) compared to the placebo and the 5-MTHF groups (P_{FWE}<0.05).

We found no significant differences in brain networks during resting state between children supplemented with or without 5-methyltetrahydrofolate.

Conclusion: Long-chain polyunsaturated fatty acids, but not folate, supplementation during pregnancy is linked to decreased functional connectivity of children’s brain networks at 10 years of age old. Further research is needed to understand how fish oil supplementation is related with less children brain connectivity.

This study has been funded by European Commission: 6FP EARNEST European Project FOOD-CT-2005-007036; and, 7FP NUTRIMENTHE European Project KBBE-2007-1 – GA No: 212652.
Health related quality of life in children (0-7 years old) with avoidant restrictive food intake disorder

Hilde Krom1, Liesbeth v.d. Sluijs Veer2, Marie-Anne Otten3, Suzanne van Zundert4, Marc Benninga1, Lotte Haverman2, Angelika Kindermann1

1Academic Medical Center/Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Academic Medical Center/Emma Children’s Hospital, Psychosocial Department, Amsterdam, Netherlands
3Academic Medical Center/Emma Children’s Hospital, Department of Rehabilitation, Amsterdam, Netherlands
4Academic Medical Center/Emma Children’s Hospital, Department of Dietetics, Amsterdam, Netherlands

Objectives and study: The diagnosis ‘avoidant restrictive food intake disorder (ARFID)’ describes an eating/feeding disturbance (e.g. lack of interest in eating/food; avoidance based on the sensory characteristics of food; concern about aversive consequences of eating) as manifested by persistent failure to meet appropriate nutritional/energy needs associated with ≥1 of the following: significant weight loss/failure to achieve expected weight gain/faltering growth in children, significant nutritional deficiency, dependence on enteral feeding/oral nutritional supplements, or a marked interference with psychosocial functioning (see DSM-5 for the full criteria). Studies are lacking evaluating the health related quality of life (HRQOL) in this specific group of children. Therefore, the aim of this study was to assess the HRQOL in young children with ARFID.

Methods: A cross-sectional study was conducted in all children fulfilling the ARFID criteria (0-7 years) at our tertiary paediatric feeding clinic (September 2014 - July 2016). The multidisciplinary feeding team, consisting of a paediatric gastroenterologist, psychologist, dietician and speech language pathologist, prospectively collected socio-demographic, paramedical, and medical parameters through standardized consultation. Before consultation, parents of all patients were asked to complete questionnaires to determine the HRQOL: the TNO-AZL Preschool Children Quality of Life (0-5 years), and the ‘Pediatric Quality of Life Inventory’ (6-7 years). T-tests, Mann-Whitney U tests, and Fischer’s Exact tests were used to compare socio-demographic, paramedical, and medical parameters of ARFID patients with and without completed questionnaires. ARFID patients with completed questionnaires were included for the analyses. The HRQOL of this group was compared to both a healthy as a chronically ill Dutch norm population using Mann-Whitney U tests. Differences of p<0.01 were defined as statistical significant.

Results: The prevalence of ARFID in patients visiting our feeding clinic was 64% (95% Bs CI 54.1-73.3) of whom 75.4% (n=46) completed all questionnaires and were included. No significant differences considering socio-demographic, paramedical, and medical parameters were found between in- and excluded ARFID patients. The HRQOL of ARFID patients aged 0-5 years (n=37) was significantly lower on 6/12 scales (appetite, lungs, stomach, motor functioning, positive mood and liveliness) compared to healthy controls (p<0.01), and on 4/12 scales (appetite, stomach, motor functioning, and liveliness) compared to chronically ill controls (p<0.01). The ARFID patients scored higher on the problem behaviour scale (less behaviour problems) compared to both healthy and chronically ill controls (p<0.01). Children with ARFID aged 6-7 years (n=9) had lower scores in 3/6 scales (total score, psychosocial health, and school functioning) compared to healthy controls (p<0.01), and no significant different scores compared to chronically ill controls.

Conclusion: Considering the HRQOL of young children with ARFID is decreased on multiple scales, the effect on HRQOL should be incorporated in clinical practice, and customized care should focus on the affected scales. Furthermore, clinical studies should add HRQOL as an outcome measure.

NUTRITION: Nutrition and health outcomes

N-P-135

Short-term effects of supplementation with omega-3 fatty acids in children with attention deficit/hyperactivity disorder

Ana Checa-Ros¹, Isabel Seiquer², Cristina Campoy Folgoso³, Ana Haro², Antonio Molina-Carballo⁴, José Uberos⁴, Antonio Muñoz⁴

¹Faculty of Medicine. University of Granada, Department of Paediatrics, Granada, Spain
²Spanish Research Council, Department of Physiology and Biochemistry of Animal Nutrition (Eez-Csic), Granada, Spain
³University of Granada, Centre of Excellence for Paediatric Research Euristikos, Granada, Spain
⁴Hospital Clínico Universitario San Cecilio, Department of Paediatrics, Granada, Spain

Objectives and study: Positive effects of omega-3 polyunsaturated fatty acids (ω-3 PUFAs) on cognition and learning might make them a helpful treatment in children with Attention Deficit/Hyperactivity Disorder (ADHD). However, the choice of the most appropriated doses and combinations of these fatty acids is still controversial. A short-term, open-label clinical trial was conducted with the following aims: 1) to investigate the influence of exogenous intake of ω-3 PUFAs over the general lipid profile, fatty acid categories (saturated fatty acids SFAs, monounsaturated fatty acids MFAs and polyunsaturated fatty acids PUFAs) and the values of PUFA/SFA and ω-6/ω-3 indices; 2) to report the tolerability and safety profile; and 3) analyse the short-term cognitive effects.

Methods: Children and adolescents newly diagnosed with ADHD according to the criteria established by the 5th revision of the Diagnostic and Statistical Manual of the American Psychiatric Association (DSM-5) were included. Each of them was administered a therapeutic combination of methylphenidate (MPH) and ω-3 fatty acids (eicosapentaenoic acid EPA 70 mg + docosahexaenoic acid DHA 250 mg). Serum fatty acid profiles were analysed by gas chromatography. As well, attention levels were measured in relation to the results obtained in a specific scale of visual attention (Magallanes Scale of Visual Attention). One-way analysis of variance (ANOVA) with Least Significant Difference (LSD) method investigated differences in fatty acid profiles before and 1 month after treatment, whereas Student t test was used to analyse differences in attention levels. Written informed consent signed by parents or tutors was required to participate in the study. All procedures were carried out in accordance with the Helsinki Declaration as revised in 1998.

Results: 38 ADHD patients were enrolled at start of intervention period (28 boys; mean age 10.42 ± 2.41 years; range 7-15 years). In relation to serum fatty acid profile, the total sum of SFAs significantly increased after supplementation with EPA/DHA (from 32.80 ± 0.60 to 35.38 ± 0.36, p < 0.0005). In consequence, PUFA/SFA index significantly decreased (p < 0.028). Some values barely changed before and after treatment, as it was with MUFA and PUFA total values. However, several ω-6 fatty acids significantly decreased, like arachidonic acid (from 12.44 ± 1.28 to 9.25 ± 0.57, p < 0.026). EPA and DHA concentrations increased by 27% and 3% respectively (p > 0.05). Thereupon, total ω-3 fatty acid levels increased by 13% and ω-6/ω-3 index decreased (8%), although these differences were not statistically significant (p > 0.05) (Table 1). Results of visual attention scale showed a significant improvement of quality of attention percentile after 1 month of treatment (from 32th percentile to 51th percentile, p < 0.026). An overall improvement of core symptoms of ADHD was reported by parents and teachers. Medication was well-tolerated and no severe side effects appeared.

Conclusion: These findings suggest that ω-3 fatty acids represent a possible adjuvant therapy in children with ADHD and may enhance the effects of MPH with an adequate safety profile. Further long-term follow-up studies are required to confirm these initial findings.
Prevalence and cumulative incidence of eczema in infants fed goat or cow milk based formula

Elizabeth Carpenter¹, Colin Prosser¹

¹Dairy Goat Co-Operative Ltd, Hamilton, New Zealand

Objectives and study: Eczema is an intermittent non-infective inflammatory skin disease inflicting between 15 and 20% of children in developed countries. Eczema can be extremely distressing in babies and parents, affecting quality of life through chronic sleep disturbance. It often leads to exclusion of certain foods on the basis that they are thought to exacerbate the symptoms of eczema. The objectives of this study were to (i) describe the prevalence and cumulative incidence of eczema in a group of unselected infants in Australia followed prospectively from within 2 weeks of birth to the age of 12 months and (ii) to evaluate the association with type of feeding in first 4 months.

Methods: This was a post-hoc analysis of data from a multi-centre, double blind, controlled feeding trial in Australia (Australia and New Zealand Clinical Trials Registry ACTRN12608000047392). Healthy term infants were randomly allocated to goat milk or cow milk formula before they were 2 weeks of age (Br J Nutr. 2014;111:1641). The goat milk infant formula (goat IF) was manufactured by Dairy Goat Co-operative (NZ) Ltd using whole goat milk without added whey proteins, with a blend of milk fat and vegetable oils. The control cow infant formula (cow IF) contained skimmed cow milk and whey proteins, with vegetable oils as the sole source of fat. Infants were fed study formula to at least 4 months of age, with no other liquids or solids. A reference group of exclusively breastfed infants was included. A study nurse, trained to diagnose visible symptoms of eczema, assessed the babies at 1,2,3,4,6 and 12 months of age. Eczema severity was also assessed using SCORing Atopic Dermatitis (SCORAD) in all children with visible eczema.

Results: A total of 285 infants had eczema assessments; 94, 91 and 100 in the goat IF, cow IF and breast-fed groups, respectively. The prevalence of infants with any symptoms of eczema were 1.8%, 3.9%, 9.6%, 11.7% and 7.9% at 2,3,4,6 and 12 months. The cumulative incidence of eczema over the 12 months was 14%, 23% and 21% in the goat IF, cow IF and breast-fed groups, respectively. The incidence of eczema with SCORAD above 10 (to exclude those with trivial rash only) were 7%, 16% and 14% in the goat IF, cow IF and breast-fed groups, respectively. A family history of atopy (mother, father and/or siblings) was found in 73% of subjects.

Table: The association between types of feeding in first 4 months and eczema expressed as odds ratio with 95% confidence interval (CI) and after adjusting for family history of allergy were

<table>
<thead>
<tr>
<th>Group comparison</th>
<th>Adjusted Odds Ratio (95% CI)</th>
<th>Adjusted p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cow IF/Goat IF</td>
<td>2.04 (0.92, 4.52)</td>
<td>0.08</td>
</tr>
<tr>
<td>Cow IF/breastfed</td>
<td>1.21 (0.60, 2.45)</td>
<td>0.59</td>
</tr>
<tr>
<td>Goat IF/breastfed</td>
<td>0.59 (0.27, 1.29)</td>
<td>0.19</td>
</tr>
</tbody>
</table>

Conclusion: This study is important in providing evidence regarding the prevalence and cumulative incidence of skin complaints such as eczema in infants in the first 12 months of life after fed formula made from goat milk or cow milk. The prevalence of eczema appears to peak at 4-6 months of age. By 12 months fewer infants exhibited any symptoms of eczema. While the number of infants with eczema was insufficient to accurately determine the relative risk of eczema of goat milk compared to cow milk, these data suggest there is a trend for a lower incidence in the goat whole milk formula group, compared to the cow formula group. This observation should be tested in a larger, adequately powered randomised controlled trial.
NUTRITION: Nutrition and health outcomes

N-P-137

7th annual Paediatric Nutrition Week: e-Pinut 2016

Arnaud De Luca¹, Camille Guidon², Michel Fischbach³, Guimber Dominique⁴, Noel Peretti⁵, Piloquet Hugues⁶, Regis Hankard⁷

¹Inserm U1069, Tours, France
²University Hospital Centre, Tours, France
³Chu, Pédiatrie I, Strasbourg, France
⁴Chu Lille, Reference Center for Congenital and Malformative Esophageal Disease (Cracmo), Division of Gastroenterology, Hepatology and Nutrition , Lille, France
⁵Hcl Inserm, Université Claude Bernard Lyon 1, Faculté de Médecine Lyon-Est, Inserm U1060, Carmen Laboratory, Lyon, France
⁶Nantes University Hospital, Nantes, France
⁷Inserm U1069, University of Tours, Tours, France

Objectives and study: In the literature of the last 30 years, the prevalence of protein-energy malnutrition (PEM) remains stable (10-15%) in Paediatric wards. New approaches are needed to address this issue. Involvement of caregivers in PEM management is not well known and could be helpful. Our 7th annual survey of systematic nutritional assessment in hospitalised children aimed to assess the role of caregivers and the evolution of PEM during hospitalisation.

Methods: This two-week cross-sectional observational survey included patients below 18 years, admitted in participating centres. All hospitalised children were weighed and measured at admittance and at discharge. Children below the 3rd centile of body mass index for age and sex had full diagnostic procedure, according to the 2012’s guidelines of the French Paediatric Society. Nutritional support was recorded. Data were recorded using e-Pinut web-based tool (www.epinut.fr). A questionnaire regarding the role of caregivers in PEM management was recorded for malnourished children.

Results: Six countries (Algeria [n=28], Belgium [n=63], Democratic Republic of the Congo [n=84], France [n=1583], Gabon [n=17], and Ivory Coast [n=20]) were involved, including 58 centres. Among the 1926 collected observations, 1781 were analysed (mean age: 6.1±5.3 years). A weight-for-height z-score <-2SD (compatible with PEM) was present in 8% of cases. Nutritional support was present in 26% of cases, of which 52% had artificial nutrition. Fifteen % of malnourished children did not have nutritional support. Twenty-one centres returned 147 questionnaires for the role of caregivers. Childcare assistants and nurses had a major role in measurements (85%), meal delivery (66%) and nutritional support delivery (53%). Dieticians played a key role in nutritional plan (42%), diet counselling (50%), and nutritional support explanations (57%). Nutritional management was perceived as increasing care in 41% of cases, notably for nurses (19%) and caregivers assistants (10%) but only for 2% of parents. Weight at discharge was recorded in 707 patients. Weight loss >2.5% affected 15% of patients hospitalised for ≥3 days (n=388), and weight loss >5% affected 4% of children.

Conclusion: All caregivers are involved in the management of PEM with a pivotal role in measurements and delivery of nutritional support for nurses and childcare assistants, and a major therapeutic role for dieticians. Substantial weight loss during hospitalisation is frequent and requires monitoring. Since 7 years, the large number of participating centres shows a lasting mobilisation promoting awareness in nutritional assessment in Paediatric wards.

Disclosure of interest: A. de Luca: Research support from Nutricia Nutrition Clinique-France
Oral status in overweight children and adolescents from a tertiary hospital

Gabriela Ferreira¹, Inês Ferreira², Irene Pina-Vaz², Henedina Antunes³

¹Faculty of Engineering of University of Porto, Doctoral Programme in Biomedical Engineering, Oporto, Portugal
²Faculty of Dental Medicine of University of Porto, Oporto, Portugal
³Hospital de Braga, School of Health Sciences of University of Minho, Icvs/3b's and 2ca Braga, Paediatric Gastroenterology, Hepatology and Nutrition Unit, Braga, Portugal

Objectives and study: Considering that overweight and oral diseases have many etiologic factors in common, this study aimed to assess the oral status in overweight children and adolescents in a tertiary hospital in Portugal, comparing to the data of National Study of Prevalence of Oral Diseases (NSPOD).

Methods: This cross-sectional study included fifty-one (n = 51) subjects with mean age 14.2 (± 1.9), obesity patients of a Gastroenterology, Hepatology and Paediatric Nutrition Unit. Anthropometric measures (weight and height) were carried out by trained nurses according to standardized routines. Overweight/obesity was determined based on the WHO (World Health Organization) cut-off points for BMI. Oral status it was determined by clinical examination by one calibrated examiner, using dental mirror and metal periodontal probe, under artificial illumination. The decay activity and experience was determined by calculating the DMFT index (decayed, missing and filled teeth) according to WHO recommendations. The periodontal condition was evaluated by bleeding on probing (BOP) examination and severity of periodontal disease was categorized into absent (%BOP = 0), mild (0 < %BOP < 10%), moderate (10% ≤ %BOP < 50%) and severe (%BOP ≥ 50%). Rest salivary flow rate was obtained after subjects expel in a test-tube during 5 minutes and expressed in mL/min. The rate lower than 0.7 mL/min are considered in high risk category in caries risk assessment. Descriptive and inferential analysis were performed using IBM SPSS 20.0. This research was approved by the Braga Hospital Ethics Committee for Health.

Results: The sample was mostly male (70.6 %) and urban residents (54.9%). The mean of tooth brushing was 1.4 (± 0.7) times per day. Concerning to caries experience, 49% of individuals were caries free (DMFT = 0) and DMFT index ranged from 0 to 8 (median = 1). Comparing the data of children with 12 years-old (n = 8, median = 1.5) to the NSPOD (1.5), there were no statistical significance between the values. Regarding to 15 years-old-group (n=6, median = 2), caries prevalence was lesser than the observed in Portugal for the same age (DMFT = 3.4). It was obtained mean of 22.5% (± 13.9%) in bleeding on probing evaluation, which can be considered moderate status of periodontal disease. Concerning to salivary flow rate, the mean observed was 0.4 mL/min (± 0.2 mL/min).

Conclusion: It was found low rates of salivary secretion and moderate status of periodontal disease in this sample of overweight children and adolescents, which should alert paediatricians, nutritionists and dentists to the possibility of higher risks of dental caries in this condition. In contrast, as expected high prevalence of caries due to more consumption of sweets in the obesity population, the observed less prevalence of caries in the population of obesity children than in generally paediatric population perhaps is explained by the health care with repeated recommendations to brushing tooth.
Nutritional screening in preschool-aged children

Laura Trandafir¹, Mihaela Moscalu², Doina Azoicai³, Otilia Frasinariu⁴

¹“Sant Mary” Clinical Emergency for Children Hospital, Pediatric Department, Iași, Romania
²University of Medicine and Pharmacy “grigore T. Popa”, Preventive Medicine and Interdisciplinarity Department, Iasi, Romania
³University of Medicine and Pharmacy Grigore T Popa Iasi, Iasi, Romania
⁴University of Medicine and Pharmacy Grigore T Popa Iasi, Paediatrics Department, Iasi, Romania

Objectives and study: Nutritional assessment in preschool aged children is a base for further preventive and interventional programs in children obesity and malnutrition. In this study, we assess the prevalence of nutritional disorders among preschool-aged children from Northeast Romania.

Methods: The study cohort consists of 165 children from kindergartens in two district of Northeast Romania, 86 boys (52.1%) and 79 girls (47.9%), aged to years 63.9±13.5SD mean age year. Based on the weight and height measurement, body mass index (BMI) was calculated. Obesity and overweight was defined according to CDC recommendations. WC percentile were calculated using database from Fernandez et al., 2005 and abdominal obesity was defined like WC above 90th percentile. Continuous variables with normal distribution were expressed as mean ± standard deviation, and and continuous variables without normal distribution were expressed as median (min-max). The categorical variables were expressed as absolute frequency and relative frequency. Data were analyzed using SPSS V.21 software (IBM Statistical Package for the Social Sciences, Chicago, Illinois).

Results: Nutritional screening revealed a prevalence of malnutrition of 12.1%, 7.27% of overweight and 9.1% obesity, while 71.5% of children were normal weight. The study showed no significant association between nutritional status and gender of children (χ² = 9.15, p = 0.0574, 95% CI). The girls had normal weight with increased frequency (78.5% vs. 65.1%), while nutritional disorders were more prevalent in males (underweight: 16.3% -male; 7.6% female). The results showed a significant association between the area of origin and nutritional status (χ² = 8.68, p = 0.03384). In rural areas the frequency of malnutrition was 18%, while in urban areas was 5.3%, overweight was 10.5% in urban and 4.5% in rural areas, and obesity presented a higher rate in rural areas (10.1% vs. 7.9%). We observed an increased risk of malnutrition in the 2-4 years age group (exp (β)-OR = 3.28, 95% CI: 1.09-6.84, p = 0.034), while obesity had not a statistical significant risk (exp (β) - OR = 3.83, 95% CI: 1.15-5.73, p = 0.028) in this age group.

Conclusion: The prevalence of overweight and obesity is high in preschool-aged children, especially in urban areas. These results are part of a nutritional screening study conducted in kindergarten to identify children and adolescents with overweight and obesity.
Quality of life and associated factors in overweight and obese children

Valeria Novikova¹, Anna Guseva², Margarita Gurova³

¹V.A. Almazov Federal North-West Medical Research Centre, Pediatric, St. Petersburg, Russian Federation
²Regional Children Hospital, Department of Gastroenterology, Kursk, Russian Federation
³Belgorod National Research University, Department of Pediatrics, Belgood, Russian Federation

Objectives and study: Obesity is common metabolic disorder in children, but little information is available about quality of life (QoL) and other aspects of their well being. To study quality of life and range of psychological parameters in overweight and obese children

Methods: For this purpose we assessed QoL, the level of personal, reactive anxiety and depression in obese and overweight children. Results were compared with healthy control children. All children were asked to complete the adopted SF-36 questionnaire, the Scales of personal (PA) and reactive anxiety (RA) and Depression Scale.

Results: We studied 60 obese children – the 1st group (body mass index (BMI) 27.5 ± 1.24) and 65 overweight children – the 2nd group (BMI 23.6 ± 1.09). 30 children were taken as a control group (BMI 18.4 ± 1.41). QoL in overweight and obese children were significantly lower as compared to healthy children (56.04±18.13 – 1 group and 52.96±23.32 – 2 group vs. 86.92±11.8, p<0.01). The more important deviations were found in terms of impairment in emotional and physical role functioning in obese children, whereas in overweight children – in social functioning. The mean values of scale in PA and RA anxiety were higher in children with metabolic disorders than in healthy ones and increase with increasing BMI: PA 46.45±9.95 (1 group) and 42.74±9.17 (2 group) vs. 32.59± 8.03, p< 0.001 and 41.79±9.05 vs 38.04±7.75 vs 218±7.26 (p< 0.001). The same tendency was found according to the Depression Scale (52.66±7.07 and 50.59±5.99 vs. 32.54 ± 8.02, p< 0.001).

Conclusion: Quality of life of children with metabolic disorders (overweight and obesity) is significantly reduced as compared to healthy children and associated with persistent psychological problems. Normalization of psychological parameters may improve the efficacy of current therapeutic strategies of these groups of patients and restore the quality of life.
N-P-141

Do malnutrition screening tools and body composition measurements predict surgical site infections in patients after scoliosis surgery?

Aikaterini Kakotrichi1, Nara Elizabeth Lara Pompa2, Jane Williams3, Sarah Macdonald3, Kathy Kennedy2, Katherine Fawbert4, Vanessa Shaw4, Jane Valente4, Jonathan Wells2, Mary Fewtrell2, Susan Hill5

1Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom
2Ucl Institute of Child Health, Childhood Nutrition Research Centre, London, United Kingdom
3Great Ormond Street Hospital for Children, NHS Foundation Trust, London, United Kingdom
4Great Ormond Street Hospital for Children, London, United Kingdom
5Great Ormond Street Hospital for Children, Paediatric Gastroenterology, Division of Nutrition, Intestinal Failure and Rehabilitation, London, United Kingdom

Objectives and study: Malnutrition screening tools (MSTs) are often used in the paediatric setting, with the aim of identifying malnourished patients or those at risk of becoming so, to intervene at an early stage. However, whilst MSTs can predict length of hospital stay, there is a lack of data on their ability to predict clinical outcomes in specific patient groups. We investigated the ability of MSTs and body composition (BC) measurements to predict a specific clinical outcome - surgical site infection (SSI) - in patients with diverse diagnoses and spinal pathology, admitted for elective spinal surgery.

Methods: Data on SSI were collected retrospectively in post-operative children aged ≥5 years, who had undergone spinal surgery from January 2014-March 2015. Anthropometry, information on diagnoses (3 groups; neuromuscular diseases, syndromic conditions and idiopathic scoliosis) and BC (bioelectrical impedance, BIA) were collected prospectively, within 48 hours of admission (BodyBasics Study). STAMP, STRONGkids, PYMS and the GOSH nutrition screening flowchart were completed, classifying patients as low, medium or high risk; these were later re-categorised as “low-medium” risk and “high” risk, since high-risk group patients are referred for dietetic input. Data on patient activity, daily intake and feeding patterns (3 categories; “fully orally fed, independently”, “fully orally fed, with help of carer” or “artificially fed”, i.e. partial enteral feeding and/or parenteral nutrition) were collected. Definitions for SSI and surveillance periods were established as per the “Protocol for the Surveillance of Surgical Site Infection” by Public Health England, and classified as present or absent.

Results: 32 patients (12 males; 37.5%) were included with median age 14.49 years (IQR 4.0); 31.3% (10) in the “neuromuscular group”, 40.6% (13) the “syndromic diseases” group, and 28.1% (9) the “idiopathic scoliosis group”. Mean weight SD score was -1.16 (SD 1.67), median BMI z-score was -0.065 (IQR 1.97) and mean lean mass (LM, from BIA) SD score was -1.84 (SD 1.30). 7 (21.9%) of the patients developed SSI. STAMP, STRONGkids and PYMS risk categories (either as 3 or 2 groups) and LMSDS were not significantly associated with SSI (p>0.05). The relative risk of developing SSI was 1.4 times higher for children with a more complex diagnosis (RR 1.44, 95%CI [1.1, 1.9]) compared to those with idiopathic scoliosis. Patients who were orally, independently fed had a significantly lower risk of SSI compared to those orally fed with help, or with artificial nutrition (p 0.01 & 0.02 respectively); this effect was also observed when LMSDS and STRONG (“low-medium”, “high”) or GOSH flowchart risk categories were included in multivariate analysis (p 0.01 & 0.03 for STRONG, p 0.04 & 0.03 for GOSH flowchart).

Conclusion: STAMP, STRONGkids and PYMS MSTs and lean mass measurements did not predict SSI, in this specific patient group. “Simpler” variables such as underlying diagnosis and feeding independently were related to SSI and may better identify patients at risk in this group, although this needs confirmation in a larger sample.
Nutritional status and prevalence of malnutrition in hospitalized children: a single center experience

Miray Karakoyun¹, burcu kumru², Esra Pekpak³, Burcu Hismi⁴, Ayhan Yaman⁵, Yeliz Cagan Appak¹

¹Tepecik Training and Research Hospital, Department of Paediatric Gastroenterology, Izmir, Turkey
²Gaziantep Cengiz Gökçek Obstetrics and Pediatric Hospital, Nutrition and Diet, Gaziantep, Turkey
³Cengiz Gokcek Gynecology, Obstetric and Children Hospital, Department of Pediatric Hematology, Gaziantep, Turkey
⁴Tepecik Training and Research Hospital, Department of Inborn Errors of Metabolism, Izmir, Turkey
⁵Cengiz Gokcek Gynecology, Obstetric and Children Hospital, Department of Pediatric Intensive Care, Gaziantep, Turkey

Objectives and study: Malnutrition can be defined as a state of nutrition in which deficiency or excess of energy, protein, and other nutrients causes measurable adverse effects on tissue, body form and function and the clinical outcome. It is associated with increased morbidity and mortality, poor growth and delayed mental and psychomotor development. Clinical findings vary depending on the duration and severity of malnutrition. We aimed to determine the prevalence of malnutrition and nutritional status among children.

Methods: 2999 children between >1 month and <18 months old, who presented and hospitalized in our center were included in the study. Measurements of height, body weight, height by age, body weight by height, the upper and middle arm circumference, and height by age, body mass index, triceps skin fold thickness at the time of admission were conducted by the same person and devices. The malnutrition assessment was performed according to the WHO classification based on the SDS values. Children with a height by age below 2SDS was considered to be chronic; those with BMI > 2 SDS were obese. Children between 0 and 5 years of age with a height by age < -2SDS, children between 5 and 10 years of age with a weight by age or BMI <-2SDS and children above 10 years of age with a BMI < -2SDS were considered to have acute malnutrition.

Results: There were 1688 males (56.3%) and 1311 females (43.7%), included in the trial. The mean age was 2.3 years; the mean birth weight was 3061 grams. The rate of acute malnutrition was 19.7%; chronic malnutrition was 12.1% and the obesity was 6%. Acute malnutrition and obesity most commonly occurred between 0 and 5 years of age while chronic malnutrition was most commonly observed ≥ 10 years of age. Evaluating patients with respect to the correlation between breastfeeding, weight of birth and malnutrition, we detected higher incidence of chronic malnutrition among those who were not breastfed. Immigrant patients were particularly detected to have a markedly higher rate of chronic malnutrition.
Table: Rates of gender and malnutrition among patients

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>1688</td>
<td>56.3</td>
</tr>
<tr>
<td>Female</td>
<td>1311</td>
<td>43.7</td>
</tr>
<tr>
<td><strong>Acute Malnutrition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2509</td>
<td>80.3</td>
</tr>
<tr>
<td>Yes</td>
<td>614</td>
<td>19.7</td>
</tr>
<tr>
<td><strong>Chronical Malnutrition</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2745</td>
<td>87.9</td>
</tr>
<tr>
<td>Yes</td>
<td>378</td>
<td>12.1</td>
</tr>
<tr>
<td><strong>Obesity</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>2937</td>
<td>94.0</td>
</tr>
<tr>
<td>Yes</td>
<td>186</td>
<td>6.0</td>
</tr>
</tbody>
</table>

Conclusion: Malnutrition is a very important cause of mortality and morbidity. Therefore, assessment of malnutrition and supply of support to these patients is important among inpatients apart from the indication of hospitalization. Following assessment of the nutritional status in patients, medical nutrition treatment should be started, thereby ensuring intake of necessary energy, macronutrients and micronutrients. Training of the parents on the importance of breastfeeding and healthy nutrition by healthcare professionals is effective in preventing malnutrition. In addition, the rate of chronic malnutrition was observed to be quite high in immigrant patients. Living conditions need to be improved, increased access to food and better hygiene conditions need to be ensured in these patients.
Intestinal failure in paediatric inpatients: a five year audit at a tertiary children’s hospital in New Zealand

Amy Kostrzewski¹, Kim Herbison¹, Kaajal Dijkstra², Rebecca Dean², Briar McLeod², Helen Evans³

¹Starship Child Health, Auckland, New Zealand
²Auckland City Hospital, Auckland, New Zealand
³Starship Child Health, Department of Paediatric Gastroenterology, Auckland, New Zealand

Objectives and study: The aim of this audit was to identify incidence, aetiology and outcomes of inpatients with intestinal failure (IF) admitted to the only tertiary children’s hospital in New Zealand. The New Zealand National Intestinal Failure Service (NZ NIFS) was established in 2015 to identify the extent of IF and current practices for managing IF in infants, children and adults. This audit will be a useful comparative baseline with development and direction of this service.

Methods: A retrospective review of intravenous nutrition (IVN) records was undertaken to identify all IF patients aged 0 – 18 years excluding NICU patients, over a five year period between 1st July 2010 and 30th June 2015. IF was defined as patients receiving IVN ≥ 21 days as an inpatient as per the NZ NIFS criteria for patient notification.

Scanned medical records of IF patients were reviewed to identify diagnosis, indication for IVN, biochemical markers for intestinal failure-associated liver disease (IFALD) and clinical outcome. Indication for IVN was defined as per NZ NIFS pathological classifications for diagnoses (adapted from 2016 ESPEN guidelines for chronic intestinal failure in adults): extensive small bowel mucosal disease; mechanical obstruction; intestinal dysmotility; short bowel syndrome; intestinal fistula and other. IFALD was defined as any liver function test (bilirubin, alkaline phosphatase, gamma-glutamyl transferase, aspartate transaminase, alanine transaminase) elevated to > 1.5 times the upper limit of the reference range, for at least 2 weeks, in the absence of another cause.

Clinical outcome and IFALD with consideration to indication for IVN and patient diagnosis were analysed using a Fisher’s exact test.

Results: There were 572 children that required IVN during the five year period. Nineteen percent (109/572) of patients were classified as having IF. The most frequent indications for IVN in IF patients were extensive small bowel mucosal disease (51%), short bowel syndrome (19%) and mechanical obstruction (12%).

IFALD occurred in 17% of IF patients (19/109) and was more common in those with extensive small bowel mucosal disease, although this was not statistically significant (p = 0.21).

Sixty-four percent (70/109) had successful intestinal rehabilitation to enteral autonomy. Patients with extensive small bowel mucosal disease were likely to achieve enteral autonomy (p = 0.045). Seven percent (8/109) required establishment of home IVN with 1% (1/109) referred for intestinal transplantation overseas. Readmission of existing home IVN patients accounted for 18% (19/109) of IF admissions. No mortality related to IFALD was identified; however 10% (11/109) died from their underlying diagnosis. Patient survival was 90% (98/109).

Conclusion: This audit shows the incidence of IF in our patient population is similar to a recent report in the United Kingdom. A high proportion of IF patients within our group had the indication of extensive small bowel mucosal disease. Whilst the majority of our IF patients achieved enteral autonomy, this audit has illustrated the chronic burden of home IVN patients to inpatient services.
Objectives and study: Feeding disorders are becoming a growing problem recently more frequently reported by the parents and recognized by doctors. The feeding problems may originate from disturbed parent-child relationship or sensory integration disabilities but are also based on serious medical problems.

We aimed to analyze the feeding difficulties reported by parents of children with feeding disorders in good general health and with underlying serious medical problems and their expectations related to the therapy.

Methods: We performed a prospective study in children with feeding disorders referred to our hospital based on questionnaires completed by the parents before starting therapy (n=136). Most of the children with feeding disorders did not have additional serious health problems (n=73; aged 21 ±17 months; HBD 38±2.7 weeks) and the others (n=63; aged 21 ±17; HBD 36±4.8) presented with various health problems: brain damage, congenital abnormalities, seizures, epilepsy, mental retardation, Autism Spectrum Disorders, vision/hearing disorders, asthma, chronic bronchitis or recurrent pneumonia. We analyzed the following problems/components: the lack of appropriate weight gain (1), lack of hunger (2), the reluctance to touch the food (3), choking during feeding (4) vomiting related to eating (5), holding food in mouth and refusal to swallow (6). We also looked at expectations of the parents related to the proposed therapy: increasing the amount of food digested by the child (7), increased diversity of food consumed (8), changing the texture of food (9), increasing the desire of the child to touch and explore the taste and smell of new food (10), improvement of eating behaviors (11). We compared problems and expectations of parents between the group of healthy children and those with serious medical problems by chi square test.

Results: The frequency of problems and expectations reported by caregivers of healthy children with feeding disorders and caregivers of children with serious medical problems and feeding disorders were as follows: (1) 41/56 vs 40/54; (2) 23/72 vs 13/63; (3) 29/72 vs 25/60; (4) 23/73 vs 24/63; (5) 16/73 vs 16/63; (6) 20/73 vs 16/63; (7) 51/73 vs 40/63; (8) 43/73 vs 25/63; (9) 28/73 vs 25/63; (10) 23/73 vs 18/63; (11) 34/73 vs 31/63, respectively in 1 and 2 group. No statistically significant differences were found between two groups in components analyzed.

Conclusion: Expectations and problems reported by parents regarding feeding disorders are the same in a group of healthy children and with medical problems.
**Nutrition and Health Outcomes**

**N-P-145**

**b-defensin level changes over time in children under three years of age receiving cholecalciferol**

Victoria Kuryaninova¹, Svetlana Dolbnya¹, Anna Kasyanova¹, Anastasiya Yagupova¹, Irina Zakharova², Leonid Klimov¹, Georgiy Anisimov³, Dmitriy Bovrishev³

¹Stavropol State Medical University, Stavropol, Russian Federation
²Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation
³North-Caucasus Federal University, Stavropol, Russian Federation

**Objectives and study:** was to analyze changes over time in the levels of calcidiol, $\beta_1$- and $\beta_2$-defensins in children under three years of age receiving one-month course of treatment with therapeutic doses of cholecalciferol.

**Methods:** One hundred and seven children aged from 1 month to 3 years were enrolled in the study. Fifty (46.7%) children were under 12 months of age, 29 (27.1%) – from 12 to 24 months years of age, and 28 (26.2%) - from 24 to 36 months of age. Cholecalciferol doses were selected based on the initial level of calcidiol: if this level was <20 ng/mL, then the dose of 3,000 IU/day was used (32 children); the doses of 2,000 IU/day and 1,000 IU/day were prescribed if the initial levels were 20-30 ng/mL (40 children) and >30 ng/mL (35 children), respectively. The duration of therapy was 30 days. The tests performed included determination of serum levels of calcidiol (25(OH)D, $\beta_1$- and $\beta_2$-defensins before and after one-month course of treatment with cholecalciferol.

**Results:** Following one-month course of administration of cholecalciferol at therapeutic doses, the level of 25(OH)D increased from 24.8 [17.6-32.5] to 49.1 [39.7-69.8] ng/mL (p<0.001). The baseline serum level of $\beta_2$-defensins in children, who had been receiving preventive doses of vitamin D (500 IU/day) before the study, was 335.8 [116.0-767.4] pg/mL. This level in children who had not been receiving cholecalciferol was 159.2 [74.1-581.6] pg/mL (p<0.05). The differences between the levels of $\beta_1$-defensin among children treated and not treated with preventive doses of cholecalciferol were found to be insignificant - 3.32 [2.4-5.9] pg/mL and 3.28 [2.0-5.8] pg/mL, respectively (p>0.05). The average levels of $\beta_1$-defensin in breastfed and formula-fed children were 7.1 [2.2-7.2] pg/mL and 3.2 [1.3-3.4] pg/mL, respectively (p<0.05). The levels of $\beta_2$-defensins were found to be different in breastfed and formula-fed children and comprised 870.4 [359.1-1139.6] pg/mL and 116.0 [79.1-353.8] pg/mL, respectively (p<0.001). Use of a therapeutic dose of cholecalciferol resulted in a insignificant increment of the level of $\beta_1$-defensin and in a significant increment of the level of $\beta_2$-defensin. The level of $\beta_1$-defensin increased from 3.3 [2.2-5.9] pg/mL to 3.65 [2.3-6.3] pg/mL (p<0.05). The levels of $\beta_2$-defensin in subjects receiving therapeutic doses of vitamin D increased from 244.6 [90.0-782.1] to 514.2 [344.1-1038.8] pg/mL (p<0.001).

**Table:** $\beta_2$-defensin increments following one-month course of cholecalciferol

<table>
<thead>
<tr>
<th>Cholecalciferol daily dose</th>
<th>$\beta_2$-defensin level, pg/mL</th>
<th>Before treatment Me (25Q – 75Q)</th>
<th>After treatment Me (25Q – 75Q)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1,000 IU/day (n=35)</td>
<td>165.4 [88.3–300.2]</td>
<td>452.5 [357.7–634.8]</td>
<td>&lt;0.005</td>
<td></td>
</tr>
<tr>
<td>2,000 IU/day (n=40)</td>
<td>233.0 [52.2–527.6]</td>
<td>505.20 [264.8–1034.1]</td>
<td>&lt;0.01</td>
<td></td>
</tr>
<tr>
<td>3,000 IU/day (n=32)</td>
<td>386.2 [106.6–889.2]</td>
<td>823.3 [363.6–1072.4]</td>
<td>&lt;0.05</td>
<td></td>
</tr>
</tbody>
</table>

Correlation between the daily dose of cholecalciferol and the increment of the $\beta_2$-defensin level in infants and toddlers comprised r=0.34 (p<0.001).

**Conclusion:** The levels of $\beta$-defensins, and particularly $\beta_2$-defensin, in infants and toddlers depend on saturation with vitamin D. In children with vitamin D deficiency and insufficiency, one-month course of cholecalciferol administered at therapeutic doses (1,000 - 3,000 IU/day) is associated with dose-dependent increase in $\beta_2$-defensin levels.
Neglected malnutrition: micronutrient deficiencies

Ovgu Kul Cinar1, Gulnaz Cig2, Ethem Erginöz2, Tufan Kutlu3, Tulay Erkan3, Murat Bolayırlı4

1Istanbul University Cerrahpasa School of Medicine, Department of Pediatrics, Istanbul, Turkey
2Istanbul University Cerrahpasa School of Medicine, Department of Public Health, Istanbul, Turkey
3Istanbul University Cerrahpasa School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
4Istanbul University Cerrahpasa School of Medicine, Department of Clinical Biochemistry, Istanbul, Turkey

Objectives and study: Micronutrients are vitamins and trace elements. In spite of being required in very small amounts, they are involved in fundamental functions of the body; such as growth, neurological development, regulation of immune system. Micronutrient deficiencies can occur as complications in children with various chronic diseases. Because of acceleration of growth in childhood period, micronutrient deficiencies are common in the children. It is known that untreated micronutrient deficiencies are a strong cause of childhood morbidity and mortality.

In our study, we wanted to see the correlation between micronutrient deficiency and chronic disorders of childhood. We also aimed to compare the results of chronically ill children with healthy children.

Methods: We conducted a prospective clinical trial among 268 children who were 1-18 years of age. The chronically ill group consisted of 140 children, and the healthy control group consisted of 128 children. All patients were assessed with a standard nutrition questionnaire. Anthropometric measurements were obtained. A blood specimen was drawn for determination of vitamin A, vitamin D, vitamin B6, vitamin B12, folate, iron, zinc and selenium status. Hemoglobin (Hb) levels, mean corpuscular volume (MCV), red cell distribution width (RDW), total iron-binding capacity and transferrin saturation ratio values were recorded.

Results: The findings revealed that while body mass index-for age percentile below 5 percentile was 7.9% of chronically ill children group, it was 1.6% of healthy control group. While 77.9% of ill children have meat in their daily dietary intake, the percentage was 92.2% in the healthy group (p<0.05). The situation was similar at daily dietary intakes of vegetables and fruits, milk and milk products, fish and seafood, legumes and eggs.

The results clearly indicated that the levels of serum vitamin A, vitamin D, iron, zinc and selenium were significantly lower in chronically ill children (Table).

The categorization of children on the basis of degree of anemia showed that 11.7% of children were anemic (Hb<11 g/dl) totally. In the chronically ill children group the percentage of anemia (Hb<11 g/dl) was 20.3%, while in the control group it was 2.4% (p<0.05). The blood iron status of ill children was 64.2± 40.9 µg/dl, while in the healthy group it was 77.6± 35.2 µg/dl. Besides that, red cell distribution width (RDW) mean values of chronically ill children (mean: 15.2% ± 2.8%) were elevated compared to healthy group (mean: 13.8% ± 1.08%); transferrin saturations of chronically ill children (mean: 20.7% ± 11.8%) were lower than healthy group (mean: 22.5% ± 11.05%), which are also correlated with iron deficiency anemia.
Conclusion: Micronutrient deficiency which is called ‘hidden hunger’ is widespread globally and has received increased attention. The main finding of this study indicate that chronically ill children have lower serum levels of vitamin A, vitamin D, iron, zinc and selenium. Hemoglobin levels of chronically ill children are also lower. It should be emphasized that iron deficiency anemia is still the most challenging public health problem and is also more common among chronically ill children. Since micronutrient deficiencies increase morbidity and mortality, it is essential to provide adequate intake of micronutrients.

**Key words:** iron deficiency anemia, micronutrient deficiency, neglected malnutrition.

### Table:

<table>
<thead>
<tr>
<th>Patient Group</th>
<th>Values</th>
<th>Vitamin A (μg/L)</th>
<th>Vitamin D (ng/mL)</th>
<th>Iron (μg/dL)</th>
<th>Zinc (μg/dL)</th>
<th>Selenium (μg/L)</th>
<th>Hemoglobin (g/dL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n=140)</td>
<td>Mean</td>
<td>388,50</td>
<td>30,22</td>
<td>64,28</td>
<td>88,99</td>
<td>44,57</td>
<td>12,28</td>
</tr>
<tr>
<td></td>
<td>Median</td>
<td>351,05</td>
<td>23,80</td>
<td>60,50</td>
<td>84,70</td>
<td>43,48</td>
<td>12,30</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>204,66</td>
<td>24,2</td>
<td>40,92</td>
<td>30,81</td>
<td>12,91</td>
<td>1,67</td>
</tr>
<tr>
<td>Control Group</td>
<td>Mean</td>
<td>434,55</td>
<td>32,96</td>
<td>77,64</td>
<td>89,84</td>
<td>40,67</td>
<td>12,78</td>
</tr>
<tr>
<td>(n=128)</td>
<td>Median</td>
<td>400,34</td>
<td>28,31</td>
<td>73,00</td>
<td>92,00</td>
<td>40,55</td>
<td>12,60</td>
</tr>
<tr>
<td></td>
<td>Standard Deviation</td>
<td>254,17</td>
<td>19,97</td>
<td>35,24</td>
<td>24,90</td>
<td>12,22</td>
<td>1,07</td>
</tr>
</tbody>
</table>
Growth pattern analysis of Korean infants and young children based on the Korean National Health Examination Survey

Yeoun Joo Lee\(^1\), Jin Soo Moon\(^2\)

\(^1\)Pusan National University School of Medicine, Pediatrics, Yangsan, Korea, Rep. of South
\(^2\)Seoul National University College of Medicine, Department of Pediatrics, Seoul, Korea, Rep. of South

**Objectives and study:** There is almost no study available for growth pattern of infants and young children in Korea. We aimed this study to evaluate the growth pattern of Korean infant and young children by using nationwide growth data of Korean National Health examination program for infants and children.

**Methods:** We collected birth weight from birth registration of Statistics Korea between 1997 and 2014. In addition, body weight, length/height and head circumference from Korean National Health Examination Program for infants and children between 2007 and 2014 were also collected. Among the data, we disregarded weight and length/height data exceeding 99% or under 1%, assumed as data error. Birth weight, weight, length/height and head circumference were compared by 2006 WHO growth standard.

**Results:** Mean standard score of birth weight comparing 2006 WHO growth standard was decreasing over time of -0.062, -0.077, -0.133, and -0.207 in 1997, 2002, 2007, and 2014 year, respectively. Mean standard score of body weight was 0.733 and 0.703 in 4-7 month breastfed infants and all infants, respectively, the differences were decreasing of 0.565 in 9-13 month, 0.384 in 18-25 month, and 0.168 in 54-61 month. Mean standard score of length/height was 0.608 and 0.683 in 4-7 month breastfed infants and all infants, respectively, and also the differences were decreasing of 0.548 in 9-13 month, 0.220 in 18-25 month, and -0.208 in 54-61 month. Mean standard score of head circumference was 0.230 and 0.260 in 4-7 month breastfed infants and all infants, and showed similar pattern of 0.263 and 0.275 in 9-13 month and 18-25 month, respectively.

**Conclusion:** Average birth weight in Korea was decreasing over the time observed. Mean standard score of weight and length/height was higher in 4-7 month compared to WHO growth standard. However, the gap was decreasing and getting closer to the mean of WHO growth standard in 54-61 month. Head circumference was similar with WHO growth standard. To validate these results, we need further study whether to identify that it is the distinct characteristics or comes from disqualified systematic errors. We consider we need further prospective data collection by using standardized sampling survey.

**Disclosure of interest:** Jin Soo Moon. Conflict with: This work was supported by the Research Program funded by the Korea Centers for Disease Control and Prevention (2016-E34004-00).
Addition of dairy lipids and probiotic Lactobacillus fermentum CECT 5716 in infant formula programs gut microbiota, epithelial permeability, immunity and GLP-1 secretion in adult minipigs

Marion Lemaire, Gaëlle Boudry, Stéphanie Ferret-Bernard, Isabelle Nogret, Michèle Formal, Armelle Cahu, Laurence Le Normand, Gwénaëlle Randuineau, Sylvie Guérin, Véronique Romé, Moez Rhimi, Pascale le Ruyet, Isabelle Cuinet, Charlotte Baudry, Philippe Gérard, Sophie Blat, Isabelle Le Huërou-Luron

1Inra, Nutrition & Digestive, Nervous and Behavioural Adaptations, Saint-Gilles, France
2Inra, Agroparistech, Université Paris-Saclay, Micalis Institute, Jouy-En-Josas, France
3Lactalis R&d, Nutrition, Retiers, France
4Lactalis R&d, Retiers, France

Objectives and study: Postnatal nutrition may have long-lasting metabolic and physiologic impacts in adulthood. Gut microbiota has been identified as a key actor of this nutritional imprinting, able to induce long-lasting changes on intestinal functions. Addition of dairy lipids (DL) in infant formula (IF) has been associated with benefits on infant microbiota composition, digestion and gut physiology in a piglet model. Clinical studies showed that IF supplementation with Lactobacillus fermentum CECT 5716 (Lf), a probiotic strain isolated from human milk, modulates infant microbiota composition and prevents infections. If positive effects have been observed in childhood, evidence on long-term effects of IF lipid composition and Lf supplementation on microbiota and host metabolism and physiology is still scarce. The objective of this study was therefore to investigate, in a Yucatan minipig model, the long-term effects of DL and Lf addition in IF on adult gut microbiota, intestinal barrier and endocrine functions, as well as metabolic and immunologic status.

Methods: Twenty-six piglets received from postnatal day 2 to 28 a formula containing either: only plant lipids (PL), a half-half mixture of PL and DL (DL), a half-half mixture of PL and DL supplemented with Lf (DL+Lf). After weaning, pigs were fed a standard diet for 1 month and then challenged with a hyperenergetic diet for 3 months. Gut microbiota metabolism (short-chain fatty acids, faecal metabolome) and composition (16S RNA sequencing) were evaluated in 5-month-old minipigs. Their intestinal permeability (Ussing chambers), immunity (cytokine secretion of ileal explants challenged with LPS) and endocrine function (density of GLP-1 secreting cells and plasma level), as well as their entero-insular axis (meal test, pancreas anatomy) and metabolism (lipid profile, glucose tolerance (IVGTT)) were also assessed.

Results: Acetate concentration in caecum tended to increase (P = 0.06) in adult DL minipigs compared to PL. Faecal metabolome was also modified by the IF composition. Relative abundances of operational taxonomic units (OTUs) such as Eubacterium coprostanoligenes and Rikenellaceae RC9 gut group were higher in DL+Lf compared to PL whereas that of Citrobacter genus was lower. Relative abundance of Eubacterium coprostanoligenes and Blautia genus were higher in DL compared to PL. An increased ileal trans- and paracellular permeability was observed in DL+Lf compared to PL. Conversely, intake of DL+Lf during early life decreased LPS passage in jejunum and modified LPS-induced cytokine secretion by decreasing the pro-inflammatory (TNF-α and IL-8) responses of ileal explants compared to PL. DL+Lf also increased the entero-insular function through an increased GLP-1 secretory capacity (both basal and meal-stimulated) but had no effect on GLP-1 secreting cell density and pancreas anatomy. Metabolic dysfunctions (dyslipidemia and insulin resistance) induced by the hyperenergetic diet were not different between groups. Neither were the growth and the food intake.

Conclusion: This study highlights a long-term programming effect of DL and Lf addition in IF on gut microbiota, epithelial barrier, immune orientation and endocrine function. Current analysis of the same intestinal parameters in formula-fed piglets would provide reliable information on the potential mechanisms through which early-life experiences may lead to the observed long-term effects.

Disclosure of interest: This study was supported by Lactalis. The authors whose names are listed below report a conflict with Lactalis: M. Lemaire, P. Le Ruyet, I. Cuinet and C. Baudry.
The interrelationship between IL-6, 25-OH vitamin D, hepcidine and anemia in children with acute infectious disease

Hadar Lev¹, Dror Mandel², Shlomi Cohen³, Yosef Weisman⁴, Varda Deutsch⁵, Amit Ovental², Ronit Lubetzky³

¹Dana Dwek Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Tel Aviv, Israel
²Dana Dwek Children’s Hospital, Tel Aviv Medical Center, Neonatology, Tel Aviv, Israel
³Dana-Dwek Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology, Hepatology and Nutrition Unit, Tel Aviv, Israel
⁴Dana Dwek Children’s Hospital, Tel Aviv Medical Center, Pediatrics, Tel Aviv, Israel
⁵Tel Aviv Sourasky Medical Center, Hematology Laboratories, Tel Aviv, Israel

Objectives and study: Hepcidin is the master regulator of iron metabolism. Upregulation of hepcidin expression is triggered by proinflammatory cytokines and it is considered being a major cause of anemia of inflammation. Recently it has been shown that vitamin D suppresses hepcidin expression. We aimed to examine the interrelation between hepcidin, vitamin D status and anemia in children with acute infection.

Methods: Ninety one patients (45 girls, 46 boys, mean age 7.3±5 years) were enrolled after admission to the pediatric ward. Sixty two patients had infectious disease (30 without anemia and 32 with anemia). Twenty-eight patients were hospitalized for non-infectious causes. Blood was obtained for measurements of CBC, 25 (OH) D, hepcidin, IL-6, iron and ferritin and compared between the 3 groups.

Results: Data is depicted in table 1. Hepcidin and IL-6 were significantly higher in the anemic infectious group compared to non-anemic infectious and control patients. We found vitamin D deficiency in 6 patients with infection and anemia, 2 in the infectious and no anemia and none in the control group. Mean 25 (OH) D levels were significantly lower among infectious and anemic patients. Correlation analyses found significant associations between hepcidin levels and ferritin (R² =0.47, P<0.001) and transferrin (R²=0.57, p<0.001), but not between hepcidin and vitamin D.
### Table: Laboratory data of participants.

<table>
<thead>
<tr>
<th></th>
<th>Infect no Anemia n=30</th>
<th>Infect &amp; Anemia n=32</th>
<th>Control n=28</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hgb (g/dL)</td>
<td>12.2±0.9 (11.1-14.9)</td>
<td>10.16±0.5* (8.7-11)</td>
<td>12.72±1.4 (10-16.6)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hct (%)</td>
<td>37.6±3.14 (25-35)</td>
<td>31.5±2.2* (33-48)</td>
<td>38.5±3.8 (33-49)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Ferritin (ng/mL)</td>
<td>117.8±95.9 (31-481)</td>
<td>142.43±124.5*** (26-510)</td>
<td>63.72±64.7 (5-244)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hepcidine (ng/mL)</td>
<td>23.9±18.5 (0-76)</td>
<td>41.2±41.2* (1.5-151.2)</td>
<td>17.8±21.1 (0-76)</td>
<td>0.009</td>
</tr>
<tr>
<td>Log IL-6</td>
<td>1.7±1 (0.7-42)</td>
<td>2.7±1.1** (1.5-229.5)</td>
<td>1.73±1.4 (0-95)</td>
<td>0.03</td>
</tr>
<tr>
<td>25 (OH)D (ng/mL)</td>
<td>26.4±6.7 (11-43)</td>
<td>24±7.6*** (9-41)</td>
<td>31.28±12.5 (17-66)</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*Difference between the anemic infectious patients to both the infectious with no anemia and control
**Difference between anemic infectious to infectious with no anemia.
***Difference between 3 groups.

**Conclusion:** We suggest that higher IL-6 and lower 25 (OH)D leads to higher hepcidin level and subsequently anemia of acute infection in pediatric population.
Immune protective effects of Lactobacillus rhamnosus GG-derived soluble mediators in a pneumonia co-infection model

Saskia van Selm¹, Sarmauli Manurung², Gabriele Gross², Tim T. Lambers², Eric A.F. Van Tol², Marien de Jonge¹

¹Radboudumc, Department of Pediatrics, Laboratory of Pediatric Infectious Diseases, Nijmegen, Netherlands
²Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands

Objectives and study: Respiratory tract infections are an important cause of morbidity and mortality, especially in young children. Serious acute symptoms that require hospitalization are often linked to viral and bacterial co-infections. Viral respiratory infection may increase the susceptibility for subsequent bacterial infections in the lung and thereby lead to more severe disease outcomes. Oral administration of Lactobacillus rhamnosus GG (LGG) soluble mediators have previously been demonstrated to modulate immune responses and reduce allergic airway inflammation and bacterial gastrointestinal infection. In this study we determined the protective effects of the same LGG soluble mediator preparations in an in vivo co-infection mouse model.

Methods: C57BL/6J mice were nasally infected with influenza A virus 20 days after the start of nutrient intervention, followed 5 days later with sub-lethal S. pneumoniae bacterial infection. Body weight was monitored at 0, 24, 48, and 72 hours relative to the time point of the S. pneumoniae infection. Nose lavage fluid and whole lung homogenates were collected at 24 h and 72 h post bacterial infection for bacterial counts and immune marker measurements. Started at weaning, two LGG soluble mediator preparations (LEGa and LEGb) or unconditioned bacterial culture (reference) medium were administered by oral gavage on alternate days for 24 days. The LEGa and LEGb preparations were both obtained from LGG culture supernatant, underwent identical downstream processes, differing only in desalting method (LEGa: column chromatography, LEGb: ultrafiltration). Each administration contained an average of 5*10⁸ CFU equivalent/animal (or a corresponding amount of unconditioned culture medium). The control groups (both infected and non-infected) received water without any supplementation.

Results: Mice supplemented with LEGb showed lower pneumococcal counts in the nose 24 h after bacterial infection than infected control animals (p = 0.0079). IL-6, IFN-β and chemoattractant protein MCP-1 in the lung were significantly reduced compared to the infected control group. Furthermore, the effect of LEGb was sustained up to 72 h, indicated by higher levels of IL-10 (p = 0.016) in the lung as compared to mock-treated controls. Overall, infected animals displayed rapid weight loss (up to 16%) after the influenza virus and S. pneumoniae co-infection, a proxy for disease severity. However, animals receiving LEGb supplementation showed significantly reduced weight loss (p = 0.0189) at 72 h compared to infected controls. Supplementation of LEGa resulted in overall less pronounced protective effects. Importantly, animals supplemented with unconditioned medium responded similar to infected animals receiving water, indicating the beneficial effects of LEGb to be caused by bioactive components originating from L. rhamnosus GG cells.

Conclusion: The current results indicate that LGG-derived soluble mediators induce early immune protective effects leading to reduced severity of pneumococcal pneumonia in a co-infection rodent model.

Disclosure of interest: S. van Selm: No
S. Manurung: employee of Mead Johnson Nutrition
G. Gross: employee of Mead Johnson Nutrition
T.T. Lambers: employee of Mead Johnson Nutrition
E.A.F. van Tol: employee of Mead Johnson Nutrition
M.I. de Jonge: No
The effect of Channa striata extract supplementation on asymmetric dimethylarginine (ADMA) and physical fitness of Indonesian short stature children

Maria Mexitalia¹, Anindita Soetadji¹, Mohammad Syarofil Anam¹, Sudigdo Sastroasmoro², Hertanto Wahyu Subagio³

¹Faculty of Medicine Diponegoro University/Dr. Kariadi Hospital, Pediatrics, Semarang, Indonesia
²Faculty of Medicine The University of Indonesia/Dr. Ciptomangunkusumo Hospital, Pediatrics, Jakarta, Indonesia
³Faculty of Medicine Diponegoro University/Dr. Kariadi Hospital, Nutrition, Semarang, Indonesia

Objectives and study: Asymmetric dimethylarginine (ADMA) is an endogenous inhibitor of L-arginine (Arg)-derived nitric oxide (NO). Increasing ADMA levels are associated with reducing NO synthesis as assessed by impaired endothelium-dependent vasodilation. Children with short stature have altered arginine / nitric oxide pathway which hypothesized as having correlation with physical fitness through endothelial dysfunction. The objectives of the study is to evaluate the beneficial effect of Channa striata extract (CSE) enriched arginine on physical fitness by reducing ADMA.

Methods: Double-blind randomized controlled was conducted to 141 short stature healthy children (male 82; female 59) aged 9-12 years in rural area of Central Java Indonesia. Short stature was defined as the height less than 2 height/age Z score based on WHO 2005 growth chart standard. Subjects consisted of 72 children giving supplementation of CSE 500 mg/day (supplementation group/SG) and 69 giving placebo (placebo group/PG). CSE contained 3.36 g protein, 2.17 g albumin, 0.77 g total lipid, glucose 0.07 g, Zn 3.34 mg; Cu 2.34 mg and Fe 0.20 mg. Physical fitness was measured by modified Harvard step test as stated as VO2max, physical activity by 7 days physical activity record and stated as physical activity level (PAL), food intake by 3 days food recall and ADMA level was measured by ELISA method using Human ADMA (CLIA Kit Elabscience), Statistical analysis was done by unpaired t-test and spearman correlation.

Results: The mean weight was 22.4 kg and the mean height was 122.5 cm. After 6 months supplementation, the children showed the high level of VO2 max i.e. 42.5(7.25) ml/min on SG and 41.34(5.45) ml/min on PG (p=0.284). All children revealed active category on physical activity level (PAL) i.e. 1.76 (0.13) on SG and 1.77 (0.12) on PG. By food recall it showed that the food intake was not different between the group, i.e. on SG were 1319 (312.6) kcal, 41.27(10.44) g protein and 2.7(0.7) g arginine, meanwhile on PG revealed 1333 (326.7) kcal, 42.02(11.07) g protein and 2.7(0.8) g arginine respectively. The ADMA level was 3.21(1.03) µmol/L on SG; meanwhile on PG was 3.11(0.95) µmol/L (p=0.575). There was correlation between physical activity and physical fitness both of the groups; SG r=0.297 and PG r=0.195 (p<0.05), but there was no correlation between physical fitness and ADMA level.

Conclusion: There was correlation between physical activity and physical fitness but there was no correlation between ADMA and physical fitness. It has been considered that Channa striata extract enriched arginine supplementation might not influence the endothelial dysfunction measured by ADMA on active short stature healthy children age 9-12 years.
Concordance on nutritional classification between the World Health Organization standards and Colombian growth standards

Claudia Granados¹, Lina Paola Montaña¹, Fabián Armando Gil¹

¹Pontificia Universidad Javeriana, Bogotá D.C., Bogota, Colombia

Objectives and study: Growth statistics are often used as direct measures of physical development or as proxies for socio-economic status. Its importance is highlighted with as part of the major development goals of the United Nations Development Millennium Goals. In Colombia there are two proposed standards: the Colombian Growth Standards (CGS) and the World Health Organization (WHO) standards. But so far there are no comparative studies to determine their differences in nutritional classification.

The aim of this study was to evaluate the degree to which the nutritional classification of Colombian children under 18 years differs when using WHO and CGS growth standards. We also compared the WHO and CGS categorizations to a new set of labels for categories introduced by the Colombian health ministry (Resolution 2465, June 2016 and Resolution 2121, June 2010). This new labelling replaces the category 'overweight' with 'risk of overweight', the category 'obesity' with 'overweight', and the category 'severe obesity' with 'obesity' for children younger than 5 years old.

Methods: We used a concordance study to evaluate the agreement between the classifications of two growth standards with the kappa coefficient.

Nutritional classification of 272 children were compared. They were chosen randomly from a database according to the following nutritional indicators: weight for age (W/A), height for age (H/A) and body mass index for age (BMI/A), using the WHO and CGS standards. Changes in nutritional classification regarding BMI classifications between old 2010 and new 2016 Colombian health ministry resolution are reported.

Results: Kappa coefficient had substantial agreement in W/A, H/A, BMI, for children under 5 years old. For children, older than 5 years, the H/A had an almost perfect agreement of 0.919 (95% CI between 0.876 and 0.949) and the BMI for this age group had moderate agreement with 0.54 (95% CI between 0.521 a 0.62).

Changes in BMI classification by WHO standards of obese children went from 8% under 2010 classification to 1% using 2016 classification. For this same age group in the CGS the percentage went down from 4% to 1%.

Table:
BMI Nutritional risk stratification under old 2010 and new 2016 Colombian health ministry resolution for the 272 selected children.

**Conclusion:** Knowing the validity in methodology of the CGS process, our analysis supports its reliability, which probably better reflects the Colombian population. We found that the parameter weight for height is not included in the CGS program, yet it is important for the classification of acute weight loss. Finally, the new health resolution’s classification (2465) under-estimates overweight and obese diagnosis by introducing the new label “risk of overweight”.
Nutritional status of school children 3-12 years old in Madrid (Spain) during the economic crisis

José Manuel Moreno1, Miguel Saenz-De-Pipaon-Marcos2, Ana Moráis3, Felix Sanchez Valverde4, Juan Diaz5

1“12 de Octubre” Hospital, Infant Nutrition Unit. Comité DE Nutrición Aep, Madrid, Spain
2Hospital LA Paz, Neonatology, Madrid, Spain
3“La Paz” University Hospital, Pediatric Nutrition AND Metabolic Diseases, Madrid, Spain
4Hospital Virgen del Camino, Pediatric Gastroenterology Unit, Pamplona, Spain
5Hospital Universitario Central de Asturias, Pediatric Gastroenterology and Nutrition, Oviedo, Spain

Objectives and study: The increase in childhood obesity in Spain is worrisome, mainly in low socioeconomic classes. The recent economic crisis may have modified the pattern of nutritional status, even with the appearance of malnutrition in lower ages. In order to study the nutritional status of school-children in public schools in the City of Madrid, in cooperation with the local Council a wide observational study was performed in 2014.

Methods: 290,111 children, 3-12 years old, attend public schools in Madrid. A stratified sample taking into account age (grade), city district, and school was designed. 32 schools were selected, and two classes (3-6 year, Primary School; 6-12 Secondary School) in each were included in the survey. The questionnaire included weight and height (auto-reported), dietary report (weekly frequency of intake), as well as socioeconomic variables (country of origin, both for parents and children, socioeconomic status, employment, number and characteristics of the family). Quantitative data were presented as mean and standard deviation and qualitative as percentage and range. Undernutrition was defined if weight for height was < -2 SD; overweight if BMI was > +1, and obesity if > +2, according to OMS growth standards (2006). A qualitative survey was also performed with the local pediatricians.

Results: 1211 questionnaires were recruited (1208 valid). 55% of the parents were born in Spain, and 45% abroad. Undernutrition was present in 5.0% of the sample and excess of weight (overweight + obesity) in 36.7%. Undernutrition was present in 5.0% of the sample and excess of weight (overweight + obesity) in 36.7%. Undernutrition was higher in children under 6 (9.1%), with no differences within genders. We could not find any relationship between undernutrition and the characteristics of families, or the perception of having money problems at the end of the month, but slightly higher in those families where both parents were unemployed. Excess of weight was higher in children with non-Spaniard parents (44% vs 32%), as well as in those families with economic problems (41% vs 31%). There is a trend in increased excess of weight with age, both in boys and in girls. In the survey answered by the pediatricians, 17% reported to have visited at least one case of undernutrition in the last year.

Conclusion:

1. 5.0% of the sample was undernourished, while the excess of weight was present in 1 every 3 children (36.7%), higher in boys (40%) and in older ages, in siblings of foreign couples (44%) and in monoparental families (43%).

2. Obesity is more often present in families with economic difficulties (41% vs 31%).

3. It seems that economic crisis has increased the burden of excess of weight in those vulnerable families.
Feeding habits of school-children 3-12 years old in the city of Madrid (Spain) during the economic restraints

Miguel Saenz-De-Pipaon-Marcos¹, José Manuel Moreno², Mercedes Gil-Campos³, Victor Manuel Navas López⁴, Miguel Angel Sanjose-Gonzales⁵, Susana Redecillas Ferreiro⁶

¹Hospital La Paz, Neonatology, Madrid, Spain
²12 de Octubre” Hospital, Infant Nutrition Unit. Comité DE Nutrición Aep, Madrid, Spain
³Hospital Universitario Reina Sofia, Córdoba, Spain
⁴Hospital Materno Infantil, Málaga, Spain
⁵Comité DE Nutrición Aep, Lugo, Spain
⁶Hospital Vall D’hebron, Nutrition Unit, Barcelona, Spain

Objectives and study: Spain has one of the highest rates of childhood obesity in Europe, especially in low income classes. The recent economic restraints may have modified the feeding patterns and, therefore, may influence the rate of obesity. In order to study the nutritional status as well as the feeding habits of school-children in public schools in the City of Madrid, in cooperation with the local Council, an observational study was performed in 2014.

Methods: 290,111 children, 3-12 years old, attend public schools in the city of Madrid (Spain). A stratified sample taking into account age (grade), city district, and school was designed. 32 schools were selected, and two classes (3-6 year, Primary School; 6-12 y Secondary School) in each center were included in the survey. The questionnaire included weight and height (auto-reported), dietary report (weekly frequency of intake), as well as socioeconomic variables (country of origin, both for parents and children, socioeconomic status, employment, number of members and characteristics of the family). Quantitative data were presented as mean and standard deviation and qualitative as percentage and range. Undernutrition was defined if weight for height was < -2 SD; overweight if BMI was > +1, and obesity if > +2, according to OMS growth standards (2006). A qualitative survey in the local pediatricians was also performed.

Results: 1,211 questionnaires were recruited (1,208 valid). 55% of the parents were born in Spain, and 45% abroad. 96% of the sample had breakfast daily, but only 88% in children from families where one of parents was unemployed. A whole breakfast (grains, dairy and fruits) was taken only by 40%. 2/3 of school children in public schools have lunch at school (63%), but a higher percentage (63%) in monoparental families as well as in families with economic difficulties. Only for meat, grains and dairy, the weekly intake was close to the recommendations (80% of the sample followed recommendations). On the contrary, weekly intake of soda or soft drinks was clearly above recommendations: 2.3 times/w. This intake was higher in siblings of foreign couples (2.42), and in siblings from families where the father was unemployed (2.51), as well as in those with obesity in the anthropometric evaluation (2.42). 75% of surveyed pediatricians considered that economic restraints had modified feeding habits, mainly decreasing the intake of fruits, vegetables and fish.

Conclusion:

1. The quality of the diet was worse in siblings of families with unemployment in one or two parents, and in those families with economic difficulties.

2. The most concerning facts were: low intake of fish, vegetables and fruits, and higher than recommended of soft drinks.

3. Having lunch at school during working days may have a major impact in the quality of the diet.
Elearning to improve parenteral nutrition skills in pediatric: pilot study in 2 university's hospital

Laetitia Marie Petit¹, Pauline Le Pape², Nadia Bajwa¹, Ino Kanavaki³, Luca Garzoni⁴, Valérie McLin⁵, Caroline Fonzo-Christe², Pascal Bonabry², Dominique Belli⁶

¹Hopitaux Universitaires de Geneve, Pediatrics, Geneva, Switzerland
²Hopitaux Universitaires de Geneve, Pharmacy, Geneva, Switzerland
³Geneva University Hospitals, Gastroenterology Unit, Department of Children and Adolescents, Geneva, Switzerland
⁴Hopitaux Universitaires de Geneve, Gastroenterologie, Hepatologie et Nutrition Pediatrqiues, Geneva, Switzerland
⁵University Hospitals Geneva, Pediatrics, Geneva, Switzerland
⁶Hopitaux Universitaires de Geneva, Geneva, Switzerland

Objectives and study: Education and training may improve prescription of paediatric parenteral nutrition (PN). In hospitals, prescription of pediatric PN may be performed by physicians or clinical pharmacists. Delayed prescription may be due to lack of ability, but is at risk of disregard in nutritional intervention for malnourished patients. To assess and compare in two hospitals the impact of a self-made E-learning module designed to teach prescription of paediatric PN, on the ability of physicians to manage theoretical clinical cases focused on detection of malnutrition and prescription of PN.

Methods: Two university hospitals (HOSP1: prescribing physicians, HOSP2: non-prescribing physicians, clinical pharmacists in charge of PN prescription). Physicians who accepted to participate were randomized into two groups in each hospital. All participants completed a pre-test to establish baseline knowledge at inclusion, one month before randomization in the 2 groups.

- Intervention-group: E-learning module (45 minutes) followed by a post-test, one month after pre-test. Satisfaction of the E-learning module evaluated on a standardized questionnaire.
- Control-group: post-test one month after pre-test only.

Pre- and post-test were developed on Survey Monkey and included 3 clinical cases (total score range: 0 to 250).

Six months after the first test, only the participants of HOSP1 passed another test, to evaluate persistence of prescription skills.

Outcome: E-learning impact was evaluated by comparing the scores’ differences between pre- and post-test between both groups, globally and in the two hospitals.

Results: 65 physicians participated (36 in HOSP1 (mean post-graduate years of experience ± standard deviation: 4.0 ± 2.8) and 29 in HOSP2 (3.1 ± 2.6)). Initial knowledge scores were higher in HOSP1 (pre-test scores 180±29 vs 133±24, p<0.001). No significant E-learning impact was observed globally (mean difference +15.1 points, 95% CI [-8.3 to 38.4], p>0.05) or in either hospital even if the improvement of knowledge by the E-learning group was higher in HOSP2 (+24 points, 95% CI [-10.3 to 59]) than in HOSP1 (+8 points, 95% CI [-21 to 37], p>0.05). At the six month test, participants of HOSP1 showed persistence of knowledge without significant improvement compared to pre-test scores in all participants. Satisfaction with the E-learning tool was very high: in both centers, 100% of participants estimated that the E-learning module met their needs and would recommend it to their colleagues.

Conclusion: In this pilot study, there was no impact of an E-learning module on the knowledge of physicians about pediatric PN. However, the direct responsibility on PN prescription appears to be in relationship with the results of initial knowledge tests, participants of prescribing hospital having scores’ results being significantly higher. Persistence of ability to prescribe PN could be due to participation in the study, which serves as training tool in that hospital. The high level of satisfaction with this new pedagogic tool is a sign to keep on assessing how to use it optimally in post-graduate medical education.
Factors associated with the advanced bone age in obese children

Min-su Oh¹, Sorina Kim¹, Juyeon Lee¹, Mu Sook Lee², Ki-Soo Kang¹

¹Jeju National University Hospital, Department of Pediatrics, Jeju, Korea, Rep. of South
²Jeju National University Hospital, Department of Radiology, Jeju, Korea, Rep. of South

Objectives and study: In the obese children, an excessive advancement of bone age may occur. The authors aimed to study the correlation between factors associated with child obesity and advanced bone age.

Methods: We prospectively enrolled 232 patients, who visited a pediatric obesity clinic and was more than 85 percentile of body mass index (BMI), from May 2015 to December 2015. Factors associated with child obesity included the percentile of anthropometric data, obesity degree based on the percentage over standard weight per sex, metabolic syndrome and the degree of nonalcoholic fatty liver disease (NAFLD). The degree of obesity based on the standard weight was classified into the overweight (10~20%), mild (20~30%), moderate (30~50%), and severe (≥50%). The degree of NAFLD was graded to the normal, mild, moderate, and severe. In these factors, the rate of ‘normal bone age group’ and the rate of ‘advanced bone age group’ were analyzed. ‘Advanced bone age group’ was defined as the patients who had a difference between the bone age and the chronological age more than 2 standard deviation (SD). The statistical analysis was done by t-test and χ² test of SPSS 18.0.

Results: ‘Normal bone age group’ was 185 (79.1%) patients and 10.1±2.0 years-old (mean±SD). ‘Advanced bone age group’ was 49 (20.9%) patients and 10.1±2.0 years-old (mean±SD). The rate of ‘advanced bone age group’ was significantly higher than the rate of ‘normal bone age group’, as the percentile of height (P=0.000), weight (P=0.001), BMI (P=0.034), waist circumflex (P=0.009), and systolic blood pressure (P=0.013) changed to be higher. BMI z-score was higher in ‘advanced bone age group’ than in ‘normal bone age group’ (2.43±0.52 vs 2.10±0.46; P=0.000). However, the rate of two groups was not different according to the change of the percentile of weight for height (P=0.307) and degree of obesity based on standard weight (P=0.299). In ‘advanced bone age group’ compared to ‘normal bone age group’, the level of insulin (27.80±26.13 vs 18.65±12.33; P=0.034), homeostatic model assessment–insulin resistance (HOMA-IR 6.56±6.18 vs 4.43±2.93; P=0.037) were significantly higher. However, HDL-cholesterol was lower in ‘advanced bone age group’ than in ‘normal bone age group’ (43.88±9.98 vs 48.95±10.50; P=0.005). The rate of ‘advanced bone age group’ was higher in the obese child with metabolic syndrome than in whom without metabolic syndrome (28.2% vs 14.7%; P=0.016). The rate of ‘advanced bone age group’ was higher in the child with more severe degree of NAFLD (11.6% in the normal, 27.7% in the mild degree, 29.2% in the moderate degree, 35.0% in the severe degree; P=0.004).

Conclusion: The rate of ‘advanced bone age group’ was higher in the child with more severe degree of obesity and accompanied by complications of obesity. Therefore, an appropriate management for obesity may help to delay the abnormal progression of bone age in children.
Is gastrostomy feeding with pureed food as effective as enteral formula in treatment of severely malnourished patients with neurologic impairment?

Anija Orel¹, Nataša Fidler Mis¹, Matjaz Homan², Rok Orel³, Rok Blagus⁴

¹University Children’s Hospital Ljubljana, Ljubljana, Slovenia  
²University Children’s Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia  
³University Children’s Hospital Ljubljana, Department of Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia  
⁴Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia

Objectives and study: The use of commercial enteral formulas is generally recommended for gastrostomy feeding in patients with severe neurologic impairment (NI), however homemade pureed foods are still very popular amongst some groups of patients. Therefore we decided to compare the effectiveness of enteral formulas and pureed feeds for treatment of severe malnutrition that is extremely common in patients with severe neurologic impairment.

Methods: 37 severely malnourished patients (2-26 years) with severe NI (GMFCS grade V) and gastrostomy were divided in 2 groups, enteral formula (n=17) and pureed food (n=20) and taken into 6 month intervention. Anthropometric measurements were taken to monitor their nutritional status and body composition before and after intervention. Needs for energy, macro- and micronutrients were calculated individually in the same way for patients in both groups. Gastrointestinal (GI) symptoms and rate of infection were evaluated with questionnaires.

Results: Both weight-for-age and BMI-for-age z-scores increased more in enteral formula vs. pureed food group (2.07 vs. 0.70, p=0.0012 and 3.75 vs. 0.63, p=0.0014), respectively. Enteral formula group patients increased in lean body mass expressed as fat-free mass index (0.70kg/m²), while patients in pureed food group did not (-0.06kg/m²) (P=0.0487). We did not find any significant differences in frequency of GI symptoms and rate of infection between the two groups.

Conclusion: Enteral formula is more suitable and effective than pureed food for treatment of NI patients with severe malnutrition. Even when quantity and composition of pureed food is calculated and designed professionally, the effect on the nutritional status of this group of patients can be unsatisfactory.
**NUTRITION: Nutrition and health outcomes**

**N-P-159**

**Association of RANKL-OPG ratio with left ventricular hyperthrophy in obese children and adolescents**

Lucia Pacifico, Simona Zampetti, Giuseppe Campagna, Paolo Versacci, Antonio De Merulis, Raffaella Buzzetti, Claudio Chiesa

1 Sapienza University of Rome, Rome, Italy
2 University of Rome, Rome, Italy
3 National Research Council, Rome, Italy

**Objectives and study:** Over the last few decades obesity has reached epidemic proportions in both children and adults in developed countries, and more recently in developing countries. It is well-known that obesity in the adult population is strongly associated with cardiovascular structural and functional alterations such as increased carotid intima-media thickness, left ventricular (LV) hypertrophy, LV diastolic and systolic dysfunction. Cardiac changes in LV structure and function have also been described in obese children and adolescents. In recent years, the receptor activator of nuclear factor kappa B ligand/RANK/osteoprotegerin (OPG/RANK/RANKL) axis has been hypothesized as a potentially mediator of left ventricular hypertrophy (LVH). The aim of the present study was to explore in overweight/obese children and adolescents the association of RANKL/OPG ratio with early signs of morphological cardiac changes.

**Methods:** We determined the serum levels of RANKL and OPG by commercially available enzyme-linked immunosorbent assays in 188 overweight/obese children and adolescents (mean age ± standard deviation, 10.4 ± 3.0; 104 boys, and 84 girls). LV mass index (LV mass/height$^{2.7}$), and relative wall thickness (RWT) (interventricular septal thickness at end-diastole + LV posterior wall thickness at end-diastole / LV dimension at end-diastole) were estimated using M-mode echocardiography. LV hypertrophy (LVH) was defined by the 95th percentile of the normal distribution, as proposed by Khoury et al., using age- and gender-specific quantiles. High levels of RWT were defined using a cut-point of 0.375. LV geometry was defined as: normal geometry (normal LV mass and RWT), eccentric LVH (LVH and normal RWT), LV concentric remodeling (increased RWT and absence of LVH), concentric LVH (increased RWT and LVH).

**Results:** OPG and RANKL levels were higher in females than in males [median (interquartile range) 1.74 (1.64-1.87) and 3.29 (1.91-6.36) pmol/L, respectively, vs 1.69 (1.61-1.81) and 2.13 (1.53-3.75) pmol/L; P< 0.05 and P< 0.001, respectively], but the OPG/RANKL ratio was lower [0.53 (0.27-0.88) vs 0.79 (0.27-0.88) pmol/L; P< 0.01]. In gender-specific multivariate linear regression analyses, OPG/RANKL ratio was significantly associated with LV mass, LV mass indexed to height, and RWT in male children but not in female subjects, after adjustment for anthropometric and cardiometabolic confounders such as age, body mass index-standard deviation score (BMI-SDS), waist circumference (WC), blood pressure (BP), high density cholesterol (HDL-C), triglycerides and glucose (or insulin resistance). To further investigate the association of OPG/RANKL ratio with LV hypertrophy we performed a multiple logistic analysis. OPG/RANKL ratio was significantly associated with concentric remodelling, eccentric and concentric LV hypertrophy, after adjustment for age, BMI-SDS, WC, as well as high BP, high triglycerides, low HDL cholesterol and impaired glucose in males but not females.

**Conclusion:** Our study provides evidence that OPG/RANKL ratio is independently associated with indices of LVH in male but not female overweight/obese children and adolescents. Future longitudinal studies in a large pediatric population will be required to further elucidate whether the OPG/RANKL system is likely to be a pathophysiological mediator or merely an epiphenomenon.
The effectiveness of a feeding intervention protocol on improving feeding difficulties in children seen in a tertiary hospital outpatient multi-disciplinary feeding clinic

Christine Grace Pasana¹, Mary Jean Guno¹

¹The Medical City, Department of Pediatrics, Pasig City, Philippines

Objectives and study: Feeding difficulties are noted in approximately 20-50% of normally developing children and 70-89% of children with developmental disabilities. A standardized feeding protocol involving effective behavioral interventions will guide pediatricians in the diagnosis and management of feeding difficulties encountered in clinical practice. This study aimed to determine if the Identification and Management of Feeding Difficulties [IMFeD®]-based feeding intervention protocol improves feeding difficulties in pediatric patients in terms of weight, food variety, compliance, and parental satisfaction.

Methods: This is a retrospective study conducted in an outpatient multi-disciplinary feeding clinic in a tertiary hospital in the Philippines. Charts of one hundred thirty-one (131) patients who have undergone the [IMFeD®]-based feeding intervention from April 2012 to May 2014 were reviewed. Baseline demographics, weight, and variety of food intake were obtained. Thirty-three (33) caregivers consented to a structured follow-up interview conducted via telephone call. Changes in weight and variety of food intake were compared post-intervention. Compliance to feeding guidelines and parental satisfaction were also measured.

Results: A statistically significant increase in weight was noted post-intervention (p<0.001). Food variety increased in majority of patients but the increase was significantly lower in vegetables than in grains (p<0.001, x²=17.2) and meat (x²=22.7, p=0.002). All caregivers reported moderate to high compliance to the feeding guidelines, with significantly better compliance in children >2 years of age compared to infants aged 5 months to 2 years (x²=4.991, p=0.025). Parental satisfaction was reported at 66.7%.

Conclusion: The findings of this study support the use of the [IMFeD®]-based intervention in the improvement of feeding difficulties in patients seen in an outpatient feeding clinic.
Analysis of causes of enteral nutrition disruption and prognosis of sepsis and severe sepsis in PICU

Suyun Qian¹, Boliang Fang¹

¹Beijing Children’s Hospital, Capital Medical University, Pediatric Intensive Care Unit, Beijing, China

Objectives and study: To describe the interruptions to enteral nutrition (EN) and it’s relationship to prognosis in children with sepsis and severe sepsis in pediatric intensive care unit.

Methods: Daily EN intake and reasons for EN interruptions were prospectively observed and recorded in children with sepsis and severe sepsis who admitted in our PICU from 2012.11 to 2013.4. Clinical prognosis was compared between children with and without EN interruptions.

Results: Total 60 consecutive children were included, median age 9.67 (5.36, 37.0) months. 50 children suffered EN interruptions, while 10 children didn't. Median time to EN initiation was 2.59 (1.53, 3.67)h; EN was interrupted in 83.3%(50/60) children, for a total of 108 times and 696 h, the most common reasons were fibrobronchoscopy and radiology procedures. Children spent 0.04(0.02,0.08) of their total observational period without EN nutrition due to EN interruptions, and was not correlated with PCIS (P=0.38, r=0.12). Children with EN interruptions suffered longer PICU duration(11.88±7.06 vs 6.8±4.42, P=0.03), but there was no difference in the 28th hospital day’s mortality between these two groups(12% vs 10%, P=1).

Conclusion: EN were frequently interrupted due to multiple reasons in children with sepsis and severe sepsis, the majority were procedures need fasting and EN intolerance. EN interruptions may have something to do with prolonged PICU length of stay, but the relationship need to be examined in future studies.
Galacto-oligosaccharide/polydextrose enriched formula prevents respiratory infections and modifies history of all allergy in a population of infants at risk of atopy: the pipa birth cohort study

Giusy Ranucci¹, Vittoria Buccigrossi¹, Paola Baiardi², Eleonora Borgia³, Stefania Zanconato³, Eugenio Baraldi³, Maria Immacolata Spagnuolo¹, Carlo Giaquinto³, Alfredo Guarino¹

¹University of Naples Federico II, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
²Consorzio Valutazioni Biologiche e Farmacologiche, Pavia, Italy
³University of Padova, Padova, Italy

Objectives and study: There is a growing evidence of a protective effect by prebiotics on the risk of atopy and infections through modification of microbiota. Our aim was to evaluate whether early feeding with a galacto-oligosaccharide/polydextrose (GOS/PDX)-enriched formula prevents infections and atopic dermatitis (AD) in infants born to allergic parents (Prebiotic in prevention of Atopy – PIPA cohort study).

Methods: A total of 345 infants were enrolled in a prospective, double blind, randomised, 24 month study and assigned to either a standard infant formula (SF) or a GOS/PDX formula until 48 weeks of life if or from when breast milk was insufficient. Further control were infants on exclusive mother milk (BF) until 6 months. Blinded family paediatricians monitored the incidence and features of atopy and infections.

Results: The incidence of respiratory infections and wheezy bronchitis was reduced in the GOS/PDX group compared to SF (p:0.023 and p:0.04, respectively) during the assumption period. In addition within 96 weeks of age a significantly lower number of children used antibiotics more than 3 times in GOS/PDX than SF group (p: 0.05). The total number of RI episodes was lower in the GOS/PDX group than SF (p:0.04). Mean duration of RI episodes and parents workdays lost at 96 weeks was not different between the three groups. Gastroenteritis incidence was slightly lower in the GOS/PDX than SF group (p:0.06); it was significantly reduced in breast fed infants (p:0.03).

According to raw hazards by Cox analysis the rate of atopic dermatitis was reduced by 35% in GOS/PDX group. The cumulative incidence of AD at 48 and 96 weeks was not different in children fed prebiotic versus SF. The incidence of AD at 36, 48 and 96 weeks was similar in GOS/PDX group and BF. The SCORAD scores in all groups were progressively reduced in growing infants with the same pattern in the three groups. AD drug use, total number of AD episodes and mean duration of AD was not different between the three groups. The cumulative incidence of AD at 36, 48 and 96 weeks was significantly lower in infants who received a total amount of prebiotic formula above the median than either those below the median as well as those breastfed (respectively p:0.032, p:0.034; p:0.04). No differences in the cumulative incidence of AD was observed in infants introducing formula feeding before or after 2 months of life. However the first AD episode was slightly delayed in infants fed prebiotic compared to standard formula or breast milk. GOS/PDX had an excellent safety profile and good nutritional adequacy, with a normal growth pattern and tolerance. No major side effects were reported during the entire observation period.

Conclusion: Early nutrition with GOS/PDX prevents respiratory infections. The effect on atopy that appears dose-related needs to be confirmed.

Disclosure of interest: The study was supported by Mead & Johnson Foundation.
Hormones and adipokines in children 7-10 years of age with overweight and obesity

Elena Roslavtseva\textsuperscript{1}, Vera Skvortsova\textsuperscript{1}, Tatiana Borovik\textsuperscript{1}, Leila Namazova-Baranova\textsuperscript{2}, Malokhat Khodzhieva\textsuperscript{3}

\textsuperscript{1}Scientific Center of Children's Health, Healthy and Sick Child Nutrition Department, Moscow, Russian Federation
\textsuperscript{2}Federal State Autonomous Institution "Scientific Center of Children's Health" of the Ministry of Health of the Russian Federation, Moscow, Russian Federation
\textsuperscript{3}Scientific Center for Children's Health, Healthy and Sick Child Nutrition Dep, Moscow, Russian Federation

**Objectives and study** To compare the levels of certain hormones and adipokines in primary school aged children being overweight/obese and those with normal body weight.

**Methods:** The study involved 80 children (boys 37, girls 43) aged 7-10 years. Weight and height of children recorded according to standard methods were expressed as standard deviation scores (z-scores) adjusted for age and gender using WHOAnthroPlus program 2009 (weight-for-age, WAZ; body mass index (BMI)-for-age, BAZ). The study group (n = 40) were children with overweight and obesity with median Z-score BAZ = 2.29 (+1.96 - +2.9). The comparison group (n = 40) included healthy children with normal weight with median Z-score BAZ = 0.30 (-0.43 - +0.72). The serum levels of 5 hormones: ghrelin, insulin, glucose-dependent insulinotropic polypeptide (GIP), glucagon-like peptide-1 (GLP-1) and glucagon: C-peptide (proinsulin fragment) and 6 adipokines (adiponectin, adipisin, leptin, plasminogen activator inhibitor-1 (PAI-1), resistin, visfatin) were assessed by flow fluorimetry using as solid phase fluorescent labeled microparticles platform dual beam laser analyzer Bio-Plex 200 (Bio-Rad, USA) equipped with a program Bio-PlexManager, version 5.0, using ready-made multiplexed test systems by the same manufacturer (Bio-PlexHumandiabet panel).

**Results:** The levels of all five studied hormones, C-peptide, resistin and leptin in study group group were significantly higher than in control group (table).

Correlation analysis revealed direct correlation between Z-score BAZ and levels of hormones (ghrelin, insulin, GIP, GLP-1 and glucagon), C-peptide and adipokines (leptin, resistin, visfatin).

The overweight/obese children had high levels of most of the studied substances at the age of 7-8 years. The levels of all 5 hormones as well as C-peptide and adipokines leptin, plasminogen activator inhibitor-1 (PAI-1), resistin and visfatin was significantly higher compared with their peers with normal body weight (p <0.031). The same differences persisted at the age of 9-10 years.
Table:

<table>
<thead>
<tr>
<th>Hormones, adipokines ng/ml</th>
<th>Study group (n = 40) Me (5;95)</th>
<th>Control group (n = 40) Me (5;95)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Leptin</td>
<td>265 (131-389)</td>
<td>41 (20.5-93.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Resistin</td>
<td>38 (30-52)</td>
<td>22 (16.5-39.5)</td>
<td>0.008</td>
</tr>
<tr>
<td>Ghrelin</td>
<td>45 (39-52)</td>
<td>38 (31.5-44)</td>
<td>0.003</td>
</tr>
<tr>
<td>Insulin</td>
<td>14 (11-20)</td>
<td>10 (8-12.5)</td>
<td>0.000</td>
</tr>
<tr>
<td>GIP</td>
<td>9 (8-10)</td>
<td>7 (6-8)</td>
<td>0.000</td>
</tr>
<tr>
<td>GLP-1</td>
<td>16 (14-19)</td>
<td>13 (11.5-15)</td>
<td>0.001</td>
</tr>
<tr>
<td>Glucagon</td>
<td>18 (16-19)</td>
<td>16 (14-17)</td>
<td>0.008</td>
</tr>
<tr>
<td>C-Peptide</td>
<td>12 (10-18)</td>
<td>9 (7-11)</td>
<td>0.005</td>
</tr>
</tbody>
</table>

**Conclusion:** The obtained data suggest the significant changes in metabolism of overweight/obese children at the age of 7-10 years. High levels of hormones and adipokines at the age of 7-8 years suggest that the violations occur early enough, and some biochemical indicators can serve as markers of metabolic disorders.
The study of rs9939609 of FTO, rs4994 of ADRB3 and rs1801123 of MTHFR gene polymorphisms association with body mass index and weight gain in pregnant women and birth weight of their infants in the Caspian region of Russia

Nataliya Shilina¹, Anvar Dzhumagaziev², Irina Malysheva², Elena Sorokina³, Dina Bezrukova², Ludmila Dikareva², Lyutsya Akmaeva², Olga Makurina³, Ekaterina Netunaeva³, Igor Kon³

¹Institute of Nutrition, Age-Related Nutritiology, Moscow, Russian Federation
²Astrakhan State Medical University, Astrakhan, Russian Federation
³Federal Research Center of Nutrition and Biotechnology, Moscow, Russian Federation

Objectives and study: Obesity in women increases the risk of pregnancy and delivery complications and has negative effects on both mother and infants health. Genetic factors play a significant role in obesity development. However there is a limited number of studies on the association of obesity-related genetic polymorphisms with the body mass index (BMI) of pregnant women in different regions of Russia, their weight gain during pregnancy and infants birth weight. The aim of the study was to evaluate the association of some single nucleotide polymorphisms (rs9939609 of FTO, rs4994 of the β3 adrenoreceptor /ADRB3/ and rs1801123 methylenetetrahydrofolatereductase /MTHFR/ genes) with the BMI of pregnant women in the Caspian region of Russia (Astrakhan city), their weight gain during pregnancy, and the birth weight of infants.

Methods: The anthropometric indices were evaluated in 88 pregnant women of 20 to 40 years of age of which 40 were obese (BMI>30 kg/m²) and 48 were not obese (BMI 18,5-29,9 kg/m²), and in their newborns. All participants gave their informed consent. Genetic polymorphisms were studied using real time polymerase chain reaction. Statistical analysis was performed by the SPSS 20. The differences were considered statistically significant at p<0.05.

Results: The frequency of the obesity risk allele A of rs9939609 polymorphism of FTO gene in Astrakhan women was 39.8 %, which is lower than in Europe and other parts of Russia (42.3-47.8%) but higher than in China and Japan (16-20%). The frequency of risk allele C of rs4994 polymorphism of ADRB3 gene was 10.2 %. The frequency of risk allele T of rs1801123 polymorphism of MTHFR gene in Astrakhan women was 30.1%, of allele C 69.9%. The association of all polymorphisms studied with the BMI was positive but it was significant for rs4994 polymorphism of ADRB3 (OR= 5,4 CI (1,05- 28,1), p=0,036) and for (AT+AA) genotypes of rs9939609 polymorphism of FTO (OR = 4,4 CI (0,99-19,4), p=0,046) genes only in women older than 30. The weight gain during pregnancy was 14,0±1 kg, 11,8±0,9 kg and 10,0±1,6 kg (p<0.05) for TT, TA and AA genotypes of rs9939609 polymorphism of FTO gene, respectively. There were no significant differences in pregnancy weight gain for different genotypes of two other gene polymorphisms studied. There were no differences in infants’ birth weight as well as percentage of macrosomia in them according to polymorphisms studied.

Conclusion: Our results regarding genotypes and alleles frequencies of gene polymorphisms studied are in accordance with the results of the studies conducted in Europe and America with the exception of the lower frequency of the obesity risk allele A of rs9939609 polymorphism of FTO gene. The association of polymorphisms studied with women’s BMI becomes evident in older age than in other regions of Russia. The genotype AA of rs9939609 polymorphism of FTO gene was not associated with high weight gain in pregnant women in Astrakhan. This finding needs in further investigation and confirmation.
Parental and children's drinking behaviour; results of the Toybox study

Piotr Socha1, Zbigniew Kulaga2, An-Sofie Pinket3, Marieke De Craemer4, Greet Cardon4, Odysseas Androutsos5, Katarzyna Szott1, Berthold Koletzko6, Luis Moreno7, Vileta Iotova8, Yannis Manios5

1The Children's Memorial Health Institute, Gastroenterology, Hepatology, Nutritional Disorders and Pediatrics, Warsaw, Poland
2The Children's Memorial Health Institute, Public Health, Warsaw, Poland
3Ghent University, Department of Public Health, Gent, Belgium
4Ghent University, Department of Movement & Sports Sciences, Ghent, Belgium
5Harokopio University, School of Health Science and Education, Athens, Greece
6Dr. von Hauner Children's Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
7University of Zaragoza, Faculty of Health Sciences, Zaragoza, Spain
8Umhat "St. Marina, Clinic of Endocrinology, Varna, Bulgaria

Objectives and study: We have earlier documented that volumes of different kinds of drinks are related to each other in preschool children based on the Toybox project and in this study we analyzed associations of caregivers drinking habits and drinking behaviour of their children.

Methods: ToyBox study (www.toybox-study.eu) participants were four to six years old preschool children from European countries: Belgium, Bulgaria, Germany, Greece, Poland, and Spain. There were 6794 children whose parents/caregivers provided data on their and their children drinking patterns together with data on age, body weight, height and parental educational attainment and whose data was biologically/physiologically plausible. We evaluated associations of child’s and their parents' beverages intake. Consumed beverages were grouped into: 'Healthy' Drinks (HD)- water, pure fruit juice, tea without sugar, plain milk, light soft drinks and Calorically Sweetened Beverages (CSB)- soft drinks, pre-packed/bottled fruit juice, sugared and chocolate milk, smoothies and tea with sugar. Due to non-normal distribution of dependent variables stepwise multiple quantile regression was applied with SAS statistical package.

Results: Child's HD consumption was significantly positively associated with parental daily HD consumption ($\beta=0.56$) and significantly negatively associated with parental daily CSB drinks consumption ($\beta=-0.42$). Maternal and paternal education level and age were not associated with HD consumption by their child. Female sex ($\beta=-1.5$), child’s age ($\beta=-4.78$) and BMI SDS ($\beta=-1.77$) were independent predictors of lower consumption of 'healthy' drinks.

CSB consumption was significantly negatively associated with parental daily HD consumption ($\beta=-0.07$) and significantly positively associated with parental daily CSB drinks consumption ($\beta=0.97$). Maternal education level and paternal age were not associated, whereas paternal education and maternal age were independently, significantly negatively associated with CSB consumption by their child. Female sex was independent predictor of lower consumption of CSB, whereas child’s age and BMI were not predictors of CSB consumption. Maternal education level and paternal age were not associated, whereas paternal education and maternal age were independently, significantly negatively associated with CSB consumption by their child.

Conclusion: Children's drinking habits are independently associated with their parents' drinking habits. Still, given the cross-sectional nature, the present study did not aim to show causal interference between health behaviours of caregivers and their children in preschool age.

The ToyBox-study is funded by the Seventh Framework Programme (CORDIS FP7) of the European Commission under grant agreement n° 245200.
The range of oral feeding among children fed by gastrostomy or nasogastric tube

Ewa Winnicka¹, Maciej Dadalski¹, Magda Sokolek¹, Małgorzata Matuszczyk¹, Michal Szczepanski¹, Elżbieta Banaś², Jarosław Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
²The Children Memorial Health Institute, Pediatrics, Nutrition and Metabolic Disease, Warsaw, Poland

Objectives and study: Inability of safe and efficacious oral feeding in children is a multifactorial problem. Home Enteral Nutrition (HEN) is a system of nutritional care for patients enterally fed by gastrostomy or nasogastric tube at least in 50% of daily need. But the maintenance of oral feeding is the crucial factor of swallowing rehabilitation and social adaptation. The aim of this study was to compare ability to maintain oral feeding in children with neurological impairment compared to children with other feeding and swallowing problems.

Methods: The group of patients with neurological impairment (n=52, aged 116±61 months, mean body weight 24±11kg) was compared to children with other medical problems (incl. genetic, metabolic, gastrologic, cardiologic; n=62, aged 120±176 months, body weight 22±11kg). There were no significant differences in demographic data. The oral feeding data was obtained with a questionnaire during routine visit with involvement of a gastroenterologist and a dietician. The number of patient with sustained oral feeding was established in both groups, and in these subgroups we investigated amount of oral feeding as follows: 1. Taste stimulation and trophic feeding; 2. Up to 30% daily need; 3. 30% to 50% daily need. Oral fluid intake was categorized as follows: 1. Minimal intake; 2. Up to 50ml/24h; 3. Over 50ml/24h. The frequency of daily feeding and watering was also categorized to be: 1. Occasionally; 2. Once daily; 3. More than once daily. The data was analyzed with chi-square test with appropriate modifications.

Results: 11 out of 49 patients with neurological impairment had oral feeding sustained vs. 31 out of 59 in the group with other medical problems [p<0.005]. 16 out of 50 patients with neurological impairment had oral watering maintained vs. 34 out of 58 in the group with other medical problems [p<0.005]. The volume of water intake was also higher in the second group. Please copy and paste the corresponding text here.

Conclusion: Neurological impairment as a reason of inability of oral feeding in children is a specific and significant risk factor of oral feeding and watering cessation in this group of patients.
The educational program for management of cow's milk allergy has improved day-by-day practice of paediatricians in Russia

Aleksandra Surzhik\textsuperscript{1}, Svetlana Makarova\textsuperscript{1}, Leila Namazova-Baranova\textsuperscript{1}, Gennadiy Novik\textsuperscript{2}, Elena Vishneva\textsuperscript{1}, Tatiana Lavrova\textsuperscript{3}

\textsuperscript{1}Federal State Autonomous Institute “Scientific Center of Children’s Health” The Ministry of Health of the Russian Federation, Nutricia Russia, Moscow, Russian Federation
\textsuperscript{2}Saint-Petersburg State Pediatric Medical University, St.Petersburg, Russian Federation
\textsuperscript{3}Nutricia Russia, Scientific, Moscow, Russian Federation

Objectives and study: Today food allergy (FA) is one of the most common chronic diseases in children. The incidence among children is 4-8%. And unfortunately, there is disappointing dynamics during the last 10 years. Cow’s milk protein is the most significant allergen in early childhood. So every paediatrician should understand the principles of management cow’s milk allergy (CMA).

Published in 2014 EAACI recommendations as well as the recommendations of ESPGHAN (2012), and based on these documents National Guideline of the Union of pediatricians of Russia clearly prescribed algorithms for management of CMA, which, however, are not always followed. Breastfeeding with adequate mother’s diet is the first priority of prevention and treatment of CMA, in other cases the infants with CMA should receive eHF or AAF. Data of audit of clinics showed that very often nutrition recommendation did not match guideline’s rules.

The aim of this work was to assess the compliance of the daily practice to international and national Guidelines of management of CMA and create educational program for implementation guideline’s principles into day-by-day work.

Methods: Unanimous survey of pediatricians by phone provided by independent agency was done in March 2015 (n=1988) and in September 2016 (n=2453). For deeper understanding of main mistakes the allergists from 8 regions of Russia fulfilled the special form for assessments of pediatricians and GPs behavior before allergist visit (n=1185).

For implementation guideline the educational program was launched in 2015 under the auspices of the Russian Union of Pediatricians. The program included two parts: round-tables for allergists with cases analyze and interactive seminars for pediatricians.

Results: Education program has given good results (Fig.1)

Results of allergist survey showed that recommendations for food correction before visiting allergist received 57% of formula-fed infants with FA, while only in 21% of cases the diet therapy was adequate (eHF or AAF). The most often mistakes are in table (tab.1). 1/3 of infants used 2-3 formula before allergist visit.

The debut of the various manifestations of the FA was observed at a mean age of 3.42 months [SD 2.06]. Age appeals to the allergist averaged 5.28 months [SD 2.72]. Infants with GI symptoms isolated reliably later were sent for consultation allergist than infants with skin symptoms (6.79 mo. vs. 5.27 mo, \( p = 0.035 \))

During period from April’2015 till September 2016 education program covered more than 1500 pediatricians and allergist. The best coverage was in Volga region - more than 40% from all participants. In September 2016, the level of the right management of CMA was 43%, it is higher than average national level.
Table:

<table>
<thead>
<tr>
<th>Formula</th>
<th>% of recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extensive hydrolyze formula or amino acid formula</td>
<td>21</td>
</tr>
<tr>
<td>Partial hydrolyze formula</td>
<td>22,1</td>
</tr>
<tr>
<td>Switch to other regular formula</td>
<td>5,5</td>
</tr>
<tr>
<td>Goat milk formula</td>
<td>3,5</td>
</tr>
<tr>
<td>Lactose Free formula</td>
<td>3,3</td>
</tr>
<tr>
<td>AR formula</td>
<td>1,6</td>
</tr>
</tbody>
</table>

Conclusion: Experience shows that pediatricians do not pay enough attention to diet therapy does not explain to parents the importance of this component of treatment, and make many mistakes in the appointment of specialized products. Guidelines is rules for day-by-day practice only for part of pediatrics, but started educational program has proven its effectiveness and can be a good tool for guideline implementation.

Disclosure of interest: A.Surzhik is the employee of Nutricia Russia, but there isn't conflict of interest with this work, T.Lavrova is the employee of Nutricia Russia but there isn't conflict of interest with this work,
Resting energy expenditure associated with metabolic disorders in Chinese obese children

Ran Wang\textsuperscript{1}, Li Qing\textsuperscript{1}, Lu Ting Peng\textsuperscript{1}, Xiaonan Li\textsuperscript{1}

\textsuperscript{1}Department of Children Healthcare, Nanjing Children’s Hospital Affiliated to Nanjing Medical University, Nanjing, China

Objectives and study: To study the characteristics of Resting Energy Expenditure (REE) and evaluate the association between REE and glucose or lipid metabolism in obese children and adolescents.

Methods: Recruited children and adolescents were from the department of child healthcare in Nanjing children’s hospital during July, 2015 to Sept, 2016. REE was measured by indirect calorimetry (IC). Body composition was assessed by bioelectrical impedance. Puberty status was determined by Tanner staging. The homeostasis model assessment of insulin resistance (HOMA-IR) was used to evaluate the degree of insulin resistance. The association between REE and anthropometric parameters or metabolism indexes were performed using statistics analysis. The study was approved by the ethics committee of Nanjing children’s hospital.

Results: One hundred and ninety-six obese children (143 boys and 53 girls) aged 7–16 years were recruited (BMI SDS: 2.90±0.85). REE was expressed per kg of body weight (REE/Wt). REE/Wt was related negatively to age (r=-0.520, p<0.001), BMI SDS (r=-0.175, p=0.014), fat mass (FM) (r=-0.590, p<0.001), fat free mass (FFM) (r=-0.571, p<0.001) and decreased significantly during puberty (r=-0.440, p<0.001). Moreover, REE/Wt was associated with fasting blood insulin (r=-0.158, p=0.027), HOMA-IR (r=-0.179, p=0.012) and postprandial blood insulin (r=-0.238, p=0.002). REE/Wt was lower in insulin resistant group (25.6±4.3) compared to normal insulin group (28.3±5.6, p<0.001). All above associations or difference remained after adjusted for age, FM and FFM. However, there were no relationships between REE and blood pressure, serum glucose, high density lipoprotein, triglyceride and total cholesterol.

Conclusion: The REE/Wt in obese children and adolescents was negatively correlated with age and the degree of insulin resistance. Puberty development and the dysfunction of insulin target tissues especially heat production organs may mediate the decrease of REE/Wt in obese children and adolescents. The regulation mechanism of insulin on REE deserves further investigation.
NUTRITION: Nutrition and health outcomes

N-P-170

Reticulocyte hemoglobin content - accurate indicator of iron deficiency in adolescents

Irina Zakharova1, Irina Tarasova2, Elena Machneva1

1Federal State Budgetary Educational Institution of Further Professional Education "Russian Medical Academy of Continuous Professional Education" of the Ministry of Healthcare of the Russian Federation, Moscow, Russian Federation
2Federal State Budgetary Institution "Federal Research Center of Pediatric Hematology, Oncology and Immunology N.A. D. Rogachev" of the Ministry of Health of the Russian Federation, Moscow, Russian Federation

Objectives and study: Nowadays there is an objective of finding new more sensitive, specific and economically beneficial iron deficiency indicators (ID) in adolescents under outpatient treatment. Reticulocyte hemoglobin content (CHr or Ret-He) can be one of these indicators. We studied the accuracy of CHr for ID diagnostics in adolescents.

Methods: 337 adolescents aged 11-17 (median age is 15 y.o.) – the students of middle and senior forms of Moscow general education schools, who didn’t have any signs of acute and chronic inflammatory disease, were included in our study. Clinical blood analysis with the use of automatic hematology analyzer with hemoglobin (Hb) and hematocrite (Ht) content, red blood cell count (RBC), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and CHr determination were performed in all the included adolescents, biochemical parameters (transferring saturation – SAT%) were determined. ID criterion was taken as SAT ≤16%. Sensibility (Se), specificity (Sp), test accuracy (E), Youden index (J), area under curve (AUC) with 95% confidence interval (CI), cut-off point were calculated and determined for each hematological characteristic. Accuracy/efficacy of the indicator was estimated according to AUC.

Results: The largest AUC indicative of maximum indicator efficacy was achieved for CHr – in cut-off point (32.1 pg). AUC was equal to 0.733, sensibility – 61.3%, specificity – 82.1%.

Table: Hematological indicators accuracy for ID diagnostic in adolescents

<table>
<thead>
<tr>
<th>Indicator</th>
<th>AUC (95% ДИ)</th>
<th>ρ</th>
<th>Cut-off point</th>
<th>Se, %</th>
<th>Sp, %</th>
<th>J</th>
<th>E, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb</td>
<td>0.724 (0.658–0.790)</td>
<td>0.000</td>
<td>125.5 g/L</td>
<td>41.3</td>
<td>92.7</td>
<td>34</td>
<td>81.3</td>
</tr>
<tr>
<td>Ht</td>
<td>0.695 (0.626–0.763)</td>
<td>0.000</td>
<td>39.1 %</td>
<td>57.3</td>
<td>71.4</td>
<td>28.7</td>
<td>68.2</td>
</tr>
<tr>
<td>RBC</td>
<td>0.583 (0.511–0.656)</td>
<td>0.028</td>
<td>4.53× 10^{12}/L</td>
<td>44</td>
<td>71.8</td>
<td>15.8</td>
<td>65.6</td>
</tr>
<tr>
<td>ЦП</td>
<td>0.725 (0.656–0.794)</td>
<td>0.000</td>
<td>0.86</td>
<td>58.7</td>
<td>74</td>
<td>32.7</td>
<td>70.6</td>
</tr>
<tr>
<td>MCV</td>
<td>0.648 (0.573-0.723)</td>
<td>0.000</td>
<td>82 fl</td>
<td>44</td>
<td>83.2</td>
<td>27.2</td>
<td>74.5</td>
</tr>
<tr>
<td>MCH</td>
<td>0.729 (0.660–0.797)</td>
<td>0.000</td>
<td>28.6 pg</td>
<td>62.7</td>
<td>71.8</td>
<td>34.5</td>
<td>69.7</td>
</tr>
<tr>
<td>CHr</td>
<td>0.733 (0.659–0.806)</td>
<td>0.000</td>
<td>32.1 pg</td>
<td>61.3</td>
<td>82.1</td>
<td>43.4</td>
<td>77.4</td>
</tr>
</tbody>
</table>

Conclusion: Our study showed that CHr was the most accurate among all the traditionally used hematological indicators of ID in adolescents. In the case of 32.1 pg cut-off point test sensibility was equal to 61.3%, specificity – 82.1%, AUC – 0.733. CHr can be used for ID diagnostic in adolescents under outpatient treatment.
Current evidence on duration of exclusive breastfeeding and growth in infancy: a systemic review

Bernadeta Patro-Gołab¹, Bartlomiej Zalewski¹, Anna Polaczek¹, Hania Szajewska¹

¹Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland

Objectives and study: Growth patterns of breastfed infants differ from those of formula-fed infants. However, the effect of breastfeeding duration on early growth, which has known long-term implications, remains unclear. We aimed to systematically evaluate current evidence on the association between duration of exclusive breastfeeding and different growth parameters in infancy.

Methods: In this systematic review, we searched MEDLINE, EMBASE and additional sources of data from January 2011 up until August 2016. Only cohort studies and randomized controlled trials (RCTs) were eligible for inclusion.

Results: A total of 7 cohort studies and 2 RCTs that overall recruited infants representing the general population met our inclusion criteria. Identified studies were clinically and methodologically heterogeneous. In the setting of developed countries, the majority of observational studies showed that longer duration of exclusive breastfeeding was modestly inversely associated with infant weight (4 studies) and length (3 studies). Body mass index (BMI) was assessed in 3 studies in this setting. Based on the estimated BMI growth curves (from 1 to 19 months of age), longer duration of exclusive breastfeeding was significantly associated with an earlier peak in infant BMI and a lower prepeak velocity in 1 study. Another cohort study showed no association of duration of exclusive breastfeeding with BMI z-score for age at 1 year after adjustment for relevant confounders. Finally, no effect of exclusive breastfeeding for 4 months versus 6 months on early growth patterns (weight, length and BMI for age) was observed in a single RCT. Inconsistent results on the association between exclusive breastfeeding duration and both linear growth and weight gain were found in 3 cohort studies conducted in developing countries.

Conclusion: Although longer duration of exclusive breastfeeding tended to be associated with lower length and weight gain in some observational studies, a potential protective effect against rapid weight gain has not been confirmed in experimental studies.

Disclosure of interest: The research leading to these results has received funding from the European Union's Seventh Framework Programme (FP7/2007-2013), project EarlyNutrition under grant agreement n°[289346].