Abstracts

25–28 May 2016

Athens · Greece
Megaron International Conference Centre

www.espghancongress.org
ESPGHAN would like to thank the following people for their services as Abstract Reviewers:

Nadeem Afzal
Carlo Agostoni
Jorge Amil Dias
Andras Arato
Henrik Arnell
Renata Auricchio
Irene Axelson
Ulrich Baumann
Mark Beattie
Marc Benninga
Beint Bentsen
Frank Bowedes
Christian Braegger
Efrat Broide
Jiri Bronsky
Pierre Broue
Stephan Buderus
Yoram Bujanover
Samy Cadranel
Jacoquin Calvo Lerma
Angelo Campanozzi
Cristina Campoy Folgoso
Gemma Castillejo
Christophe Chassard
Ania Chmielewska
Carla Colombo
Paula Crespo Escobar
Nick Croft
Salvatore Cucchiara
Lorenzo D’ Antiga
Gerard Damen
Barbara de Koning
Lissy De Ridder
Thierry De Preker
Dominique Debray
Tamas Decsi
Antal Dezsofi
Tietje Dijkstra
Jernej Dolinsk
Magnus Domellöf
Christoph Dupont
Ozlem Durmaz
Nick Embleton
Johanna Escher
Jackie Falconer
John Fell
Mary Fewtrell
Natasa Fileder Mis
Yigael Finkel
Bjorn Fischer
Kim Fleischer Michaelsen
Maria Fotoulaki
Esteban Frauca
Elvira George
Imke Goldschmidt
Isabel Goncalves
Emmanuel Gonzales
Frederic Gottrand
Olivier Goulet
Enke Grabhorn
Alfredo Guarino
Girish Gupte
Figen Gurakan

Nedim Hadzic
Jane Hartley
Corina Hartman
Almuthe Christine Hauer
Bruno Hauser
Olle Hernal
Loreto Hierro
Ilse Hoffman
Iva Hojsak
Roderick Houwen
Jean-Pierre Hugot
Jessie Hulst
Steffen Husby
Seamus Hussey
Warren Hyer
Oleg Jadresin
Joerg Jahn
Paloma Jara
Panayota Kafritsa
Nicolas Kalach
Ino Kanavaki
Thomas Karagiozoglou
Stavroula Kardy
Alejna Jaklin Kekez
Kathy Kennedy
Angelika Kindermann
Frank Kneepkens
Brigitte Kochavi
Henrik Köhler
Sanja Kolacek
Berthold Koletzko
Sibylle Koletzko
Bart Koot
Ilma Korponay-Szabo
Florence Lacaille
Alexandre Lapillone
Aron Lerner
Keith Lindley
Andrea Lo Vecchio
Thomas MacDonald
Sarah Macdonald
Giuseppe Maggiore
Claude Marcus
Patrick McKiernan
Valerie McLin
Luisa Mearin
Erasm Miele
Giorgina Mieli-Vergani
Walter Mihatsch
Zrinja Mišak
Christian Molgaard
Yael Mozer-Gassberg
Thomas Müller
Simon Murch
Antal Nemeth
Tena Nisette
Valerio Nobili
Andreas Nydegger
Giuseppina Oderda
Inger Ohlund
Rok Orel

Anders Paerregaard
Ioanna Panayotou
Alexandra Papadopolou
Joana Pawlowska
Noel Peretti
Eva Pfister
Alan Phillips
Isabel Polanco
Irit Poraz
Hildegard Przyrembel
Shimon Reif
Carmen Ribe
Edmond Rings
Eleftheria Roma
Frank Rümmele
Reene Scheenstra
Marco ScIVERES
Raanan Shamir
Eyal Shetey
Marco Silano
Francoise Smets
Piotr Socha
Johannes Spaling
Annmaria Staiano
Birgitta Strandvik
Ekkehard Sturm
Hania Szaewska
Laszlo Szonyi
Nikhil Thapar
Rut Anne Thomassen
Patrick Tounian
Riccardo Troncone
Dominique Turck
Dan Turner
Christos Tzivinikos
Vaidotas Urbonas
Pietro Vajo
Anemone van den Berg
Hans Van Goudoever
Indra Van Mourik
Patrick Van Rheenen
Myriam Van Winckel
Yvan Vandenplas
Gigi Veereman-Wauters
Gabor Veres
Henk-Jan Verkade
Batia Weiss
Zvi Weizman
Michael Wilschanski
David Wilson
Harland Winter
Heiko Witt
Ioannis Xini
Gitte Zachariassen
Aglaia Zellos
Noam Zevit
Matthias Zilbauer
Klaus-Peter Zimmer
GASTROENTEROLOGY: Inflammatory bowel disease

G-O-001

Early induction with Infliximab in Paediatric Crohn’s disease is associated with sustained primary response with less frequent need for dose intensification

Jessica Ling¹, Danika Buurman¹, Madhur Ravikumara², Cathy Mews², Kunal Thacker², Angela DeNardi², Zubin Grover²

¹Medical School University of Western Australia, Perth, Australia
²Princess Margaret Hospital for Children, Gastroenterology, Perth, Australia

Objectives and study: Loss of response (LOR) to Infliximab (IFX) in paediatric Crohns disease (CD) is frequent with almost 50%-60% requiring dose escalation within 3-5 years of commencement.(1,2) LOR is associated with longer disease duration, stricturing behaviour, and elevated post induction C-reactive protein (CRP). Our aims were to identify frequency and predictors of LOR to IFX.

Methods: In a retrospective single centre study, we reviewed children on scheduled IFX therapy over the last 5 years for predominant luminal CD. Only those with a successful primary response (drop in PCDAI by 15 points) and a minimum of 1 year follow up after commencing IFX were included. LOR was defined as symptomatic inflammatory relapse (elevated CRP or faecal Calprotectin and/or endoscopically or radiologically confirmed relapse) requiring IFX re-induction, dose escalation or interval shortening (4-6 weekly). Early IFX was defined as use ≤3months from diagnosis. Independent variables including age, disease behaviour and deep ulcers at diagnosis, perianal disease, first therapy, time to IFX, concurrent Immunomodulators, post induction CRP and time on IFX were analysed. Following univariate analysis, binary logistic regression was performed to predict LOR.

Results: 43 children received scheduled IFX for luminal CD and had a minimum of 1 year follow up. 15/43 initiated IFX ≤3 months from diagnosis, LOR was observed in 24/43(56%) over mean duration of 2.9 years (95% CI 2.5-3.3). 10/43(23%) discontinued IFX after failing dose escalation requiring second anti-TNF, surgical resection or both. Characteristics between groups with LOR vs. Sustained primary response (SPR) to IFX were differently only with a younger age at diagnosis (11.2 vs. 12.9, p=0.02), longer time to IFX (19.7 vs. 5.7 months p=0.002) and longer follow up (3.3 vs. 2.5 years, p=0.02) in those with LOR. Regression analysis confirmed that only early use of IFX was associated with reduction in LOR (OR 0.88, CI 0.79-0.98, p=0.01). Early (<3months) vs. late (>3months) use of IFX was associated with less frequent LOR (5/15, 33% vs. 19/28 68%), p=0.05.

Table: Table 1. Clinical characteristics between groups with LOR vs. SPR to IFX

<table>
<thead>
<tr>
<th></th>
<th>LOR(24)</th>
<th>SPR (19)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age</td>
<td>11.17</td>
<td>12.91</td>
<td>0.02</td>
</tr>
<tr>
<td>Mean CRP</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>32.54</td>
<td>26.37</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-IFX induction</td>
<td>25</td>
<td>32.2</td>
<td>NS</td>
</tr>
<tr>
<td>Mean PCDAI</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diagnosis</td>
<td>33.02</td>
<td>30.79</td>
<td>NS</td>
</tr>
<tr>
<td>Pre-IFX induction</td>
<td>29.37</td>
<td>32</td>
<td>NS</td>
</tr>
<tr>
<td>Complicating disease behaviour (B2/B3)</td>
<td>4 (16%)</td>
<td>2(11%)</td>
<td>NS</td>
</tr>
<tr>
<td>Perianal (Fistula)</td>
<td>5(21%)</td>
<td>5(26%)</td>
<td>NS</td>
</tr>
<tr>
<td>Deep ulcers on Colonoscopy</td>
<td>10(41%)</td>
<td>5(26%)</td>
<td>NS</td>
</tr>
<tr>
<td>First Induction Therapy</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CS</td>
<td>10</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>EEN</td>
<td>13</td>
<td>6</td>
<td>NS</td>
</tr>
<tr>
<td>Concomitant IM</td>
<td>20 (83%)</td>
<td>11(58%)</td>
<td>NS</td>
</tr>
<tr>
<td>IFX induction response</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical (PCDAI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>≤10</td>
<td>15(62%)</td>
<td>13(68%)</td>
<td>NS</td>
</tr>
<tr>
<td>≤30</td>
<td>9 (38%)</td>
<td>6 (32%)</td>
<td></td>
</tr>
<tr>
<td>Biochemical (CRP)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (&lt;5mg/dL)</td>
<td>16(67%)</td>
<td>9(47%)</td>
<td></td>
</tr>
<tr>
<td>Abnormal (&gt;5 mg/dL)</td>
<td>8 (33%)</td>
<td>10 (53%)</td>
<td></td>
</tr>
<tr>
<td>Mean Time from diagnosis to IFX (months)</td>
<td>19.68</td>
<td>5.62</td>
<td>0.002</td>
</tr>
</tbody>
</table>

**Conclusion:** Earlier introduction of IFX is associated with greater sustained primary response and less frequent relapse.

**Disclosure of interest:** Dr. Grover: received Lecture Fees by Janssen Australia, Others: None
Declared
Mucosa-associated ileal microbiota in new-onset pediatric Crohn’s disease

Amit Assa¹, James Butcher², Jennifer Li², Abdul Elkadri³, Phillip Sherman³, Aleixo Muise³, Alain Stintzi², David Mack⁴

¹Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, Petach Tikva, Israel
²Ottawa Institute of Systems Biology, Ottawa, Canada
³Cell Biology Program, Research Institute, Toronto, Canada
⁴Department of Paediatrics, Children’s Hospital of Eastern Ontario and University of Ottawa, Ottawa, Canada

Objectives and study: The composition of the intestinal microbiome appears relevant to the pathogenesis of Crohn’s disease (CD), with differences in both diversity and composition of the gut microbiota in CD patients compared to healthy individuals. However, there are still conflicting reports on the importance of various bacterial taxa in the pathogenesis of CD. The aim of this study was to characterize the composition of mucosa-associated intestinal microbiota in newly diagnosed pediatric CD patients.

Methods: Mucosa-associated bacteria were identified from ileal biopsy specimens obtained at colonoscopy of 10 patients with either ileal or ileo-colonic new onset CD and 15 controls without mucosal inflammation. Microbial composition was carried out by profiling the 16S rDNA V6 region using Illumina sequencing. Samples were analyzed for differences in alpha/beta diversity and also for differentially abundant taxa.

Results: The alpha diversity did not differ between the controls and CD cases or between CD subjects with localized ileal disease compared to those with more extensive disease. Controls also did not clearly separate from CD patients by principal coordinate analyses, however 117 operational taxonomic units (OTUs) were found to be differentially abundant between the two groups. In particular, numerous OTUs associated with Faecalibacterium prausnitzii species were observed to be increased in CD children.

Conclusion: These findings contribute to emerging evidence regarding dysbiosis in pediatric CD, and provide additional evidence challenging the protective role of Faecalibacterium prausnitzii in CD.

Disclosure of interest: The research or the authors have no conflict of interest to declare.

Amit Assa- None declared
James Butcher- None declared
Jennifer Li- None declared
Abdul Elkadri- None declared
Philip Sherman- None declared
Aleixo Muise- None declared
Alain Stintzi- None declared
David Mack- None declared
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-O-003

**Lower the threshold, a study of normal reference values of PH-impedance in children**

Taha Yousif¹, Osvaldo Borrelli¹, Nikhil Thapar¹, Keith Lindley¹, Mohamed Mutalib¹

¹Great Ormond Street Hospital for Children, Gastroenterology, London, United Kingdom

**Objectives and study:** Gastro-Oesophageal reflux (GOR) is a normal phenomenon that happens in children and adults after meals, mostly asymptomatic and lasting less than 3 minutes. The prevalence ranges between 50% at 3 months and 5% at one year of age. Currently the gold standard method for diagnosis is intra-luminal multi-channel pH Impedance (MII- pH) study. Reference values used now are based on expert opinions, as data is limited. We conducted this research to evaluate the normal values of MII-pH in children less than 16 years of age. These include acid exposure percentage via pH and impedance and number of acid and non-acid reflux episodes. We also performed subgroup analysis comparing infants less than 1 year old and older children.

**Methods:** Results of patients less than 16 years referred to Great Ormond Street Hospital Gastroenterology unit for assessment of GORD in the last 6 years were obtained from the electronic database. We excluded patients with any risk factor for GORD to calculate the normal values.

**Results:** Out of 1183 patients 849 patients’ reports were studied as the normal population with no underlying risk factor for GORD. As the data distribution for all variables were skewed we used the median and interquartile ranges. We found that our population’s median values are in general less than the currently used ones. Acid exposure percentage in our cohort was 1.7% versus 3%, number of reflux episodes 42 versus 70 in current accepted levels (see table).

**Table:**

<table>
<thead>
<tr>
<th>Variable</th>
<th>Number of observations</th>
<th>Mean</th>
<th>SD</th>
<th>Median</th>
<th>Lower Quartile</th>
<th>Upper Quartile</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage of Acid exposure pH</td>
<td>848</td>
<td>4.2</td>
<td>6.82</td>
<td>1.7</td>
<td>0.5</td>
<td>4.9</td>
</tr>
<tr>
<td>No. of acid reflux episodes (impedance)</td>
<td>848</td>
<td>27.30</td>
<td>27.33</td>
<td>20</td>
<td>8</td>
<td>38</td>
</tr>
<tr>
<td>No of non-acid reflux episodes (impedance)</td>
<td>849</td>
<td>1.80</td>
<td>10.64</td>
<td>0</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>No of all reflux episodes (impedance)</td>
<td>848</td>
<td>50.32</td>
<td>41.31</td>
<td>42</td>
<td>23</td>
<td>66</td>
</tr>
<tr>
<td>No of episodes &gt; 5 minutes</td>
<td>844</td>
<td>2.22</td>
<td>4.35</td>
<td>0</td>
<td>0</td>
<td>2.4</td>
</tr>
<tr>
<td>No of all proximal extent episodes</td>
<td>549</td>
<td>26.58</td>
<td>26.74</td>
<td>19</td>
<td>7</td>
<td>36</td>
</tr>
</tbody>
</table>

**Conclusion:** To our knowledge this is the largest data available on MII-pH in children. This study is limited by the nature of the population used although every effort was made to normalise the population of interest. We would recommend larger study on normal children to establish whether we should lower currently used values, this however will be faced by ethical dilemma in accepting normal children to be tested.

**Disclosure of interest:**
None Declared.
GASTROENTEROLOGY: Coeliac disease

G-O-004

Investigating the metabolic fingerprint of Celiac Disease – a prospective approach in the PreventCD cohort

Franca Kirchberg¹, Olaf Uhl¹, Luisa Mearin², Renata Auricchio³, Gemma Castillejo⁴, Ilma Korponay-Szabo⁵, Isabel Polanco⁶, Carmen Ribes Koninckx⁷, Sabine Vriezinga⁸, Katharina Werkstetter¹, Berthold Koletzko¹, Christian Hellmuth¹

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”, Dept. of Medical Translational Sciences and European Laboratory for the Investigation of Food-Induced Diseases, 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
⁷La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
⁸Leiden University Medical Center, Pediatrics, Leiden, Netherlands

Objectives and study: In the development of Celiac Disease (CD) both genetic and environmental factors play a crucial role. The Human Leukocyte Antigen (HLA)-DQ2 and HLA-DQ8 loci are strongly related to the disease, however, HLA-DQ2 and HLA-DQ8 are necessary but not sufficient for the development of CD. Therefore, rising interest lays in examining the mechanisms from the early beginning. Differences in serum and urine metabolic profiles between healthy individuals and CD patients have been reported previously¹. We aimed to investigate if the metabolic pathways were already altered in young infants, preceding the CD diagnosis.

Methods: Serum samples were available for 230 four months old infants of the PreventCD study, a multicenter, randomized, double-blind, dietary intervention study². They were all positive for HLA-DQ2 or HLA-DQ8 and had at least one first-degree relative diagnosed with CD. Amino acids were quantified after derivatization with liquid chromatography–triple quadrupole mass spectrometry (MS/MS) and polar lipid concentrations (lyso-phosphatidylcholines, phosphatidylcholines, and sphingomyelins) were determined with direct infusion MS/MS.

We investigated the association of the metabolic profile with (1) the development of CD up to the age of 8 years (yes/no), (2) with the HLA-risk groups as defined in Vriezinga et al. (2014), (3) with the age at CD diagnosis, using linear mixed models and cox proportional hazards models. Gender, intervention group, and age at blood withdrawal were included as potential confounder.

Results: By the end of 2014, thirty-three out of the 230 children (14%) were diagnosed with CD according to the ESPGHAN criteria. Median age of all children that time was 6.5 years (IQR, 5.9 - 7.1). The frequencies of the five HLA-risk groups (ranging from high to low risk) were: 30 (14%), 18 (8%), 116 (52%), 10 (5%), 50 (23%). Median age at diagnosis was 3.4 years (IQR, 2.4 - 5.2). Testing each metabolite for a difference in the mean between healthy and CD children (1), we could not identify a discriminant analyte or a pattern pointing towards an altered metabolism (Bonferroni corrected P > 0.05 for all). Metabolite concentrations (2) did not differ across the HLA-risk groups. When including the age of diagnosis using (3) survival models, we found no evidence for an association between the metabolic profile and the risk of a later CD diagnosis.

Conclusion: The metabolism of CD patients is not altered at young age. Our results suggest that pathways are affected only shortly before CD diagnosis and that furthermore the HLA-genotype does not influence the metabolic profile in young infants.


Disclosure of interest: None Declared
GASTROENTEROLOGY: Coeliac disease

G-O-005

Natural history of tissue transglutaminase autoantibodies in the TEDDY cohort

Satu Simell1, Ville Simell2, Hye-Seung Lee3, Alistair J. K. Williams4, Edwin Liu5, Kalle Kurppa6, William Hagopian7, Daniel Agardh8, Sibylle Koletzko9

1Turku University Hospital, Pediatric Gastroenterology, Turku, Finland
2Turku University Hospital, Turku, Finland
3Health Informatics Institute, Morsani College of Medicine., Department of Pediatrics, Tampa, Florida, United States
4Bristol University, Dept. of Diabetes & Metabolism, Bristol, United Kingdom
5Digestive Health Institute, University of Colorado, Denver, Colorado, United States
6University of Tampere and Tampere University Hospital, Centre for Child Health Research, Tampere, Finland
7Endocrinology, Diabetes and Metabolism, University of Washington, Washington, United States
8Skåne University Hospital, Department of Pediatrics, Malmö, Sweden
9Ludwig Maximilian’s University Munich Medical Center, Dr. von Hauner Children’s Hospital, Munich, Germany

Objectives and study: To investigate the natural history of tissue transglutaminase autoantibodies (tTGA) in children at genetic risk for celiac disease (CD).

Methods: A total of 8,676 genetic susceptible children for CD carrying HLA DR3-DQ2 and/or DR4-DQ8 were recruited from the general population between 2004 and 2010 at six centers in Sweden, Finland, Germany, and US and followed from birth in the ongoing prospective longitudinal The Environmental Determinants of Diabetes in the Young (TEDDY) study. Participants were screened annually for tTGA using radioligand binding assays (cut off <1.3 U/L). If a child turned tTGA positive, all available serum samples taken three-monthly until 4 years and six-monthly thereafter were tested and analyzed until end of follow up or start of gluten free diet (GFD) (“stop”). Children were categorized into 4 groups: 1. all samples negative (G1); 2. final positive, i.e. positive sample(s) until stop (G2); 3. Transient positive, i.e. positive sample(s) followed by negative sample(s) at stop (G3); fluctuating positive, i.e. at least one positive sample followed by negative and positive sample(s) with negative or positive result at stop (G4). CD risk factors previously identified in the cohort (homozygous for DR3-DQ2, female sex, having a first degree relative (FDR) with CD or living in Sweden) as well as tTGA titers (first, maximum, last) were compared between the groups using Fisher’s exact test or Wilcoxon rank sum test. Statistical significance was considered <0.01.

Results: A total of 6672 children were screened for tTGA (48.8% females, median age at stop 72 months [range 8-129], 490 started a GFD). Of those, 1276 (19%) had at least one tTGA positive, all available serum samples taken three-monthly until 4 years and six-monthly thereafter were tested and analyzed until end of follow up or start of gluten free diet (GFD) (“stop”). Children were categorized into 4 groups: 1. all samples negative (G1); 2. final positive, i.e. positive sample(s) until stop (G2); 3. Transient positive, i.e. positive sample(s) followed by negative sample(s) at stop (G3); fluctuating positive, i.e. at least one positive sample followed by negative and positive sample(s) with negative or positive result at stop (G4). CD risk factors previously identified in the cohort (homozygous for DR3-DQ2, female sex, having a first degree relative (FDR) with CD or living in Sweden) as well as tTGA titers (first, maximum, last) were compared between the groups using Fisher’s exact test or Wilcoxon rank sum test. Statistical significance was considered <0.01.

<table>
<thead>
<tr>
<th>Variable</th>
<th>G1 n=5396</th>
<th>G2 n=724</th>
<th>G3 n=349</th>
<th>G4 n=203</th>
<th>p-value G2 vs G3</th>
<th>p-value G2 vs G4</th>
<th>p-value G3 vs G4</th>
</tr>
</thead>
<tbody>
<tr>
<td>HLA DR3-DQ2/DR3-DQ2 (%)</td>
<td>15.4</td>
<td>45.4*</td>
<td>37.5*</td>
<td>36.5*</td>
<td>0.0149</td>
<td>0.0248</td>
<td>0.9268</td>
</tr>
<tr>
<td>Female (%)</td>
<td>47.1</td>
<td>60.0*</td>
<td>48.1</td>
<td>55.2</td>
<td><strong>0.0002</strong></td>
<td>0.2260</td>
<td>0.1540</td>
</tr>
<tr>
<td>FDR with CD (%)</td>
<td>2.1</td>
<td>8.7*</td>
<td>5.2*</td>
<td>6.9*</td>
<td>0.0478</td>
<td>0.4734</td>
<td>0.5681</td>
</tr>
<tr>
<td>Sweden (%)</td>
<td>29.4</td>
<td>38.5*</td>
<td>37.0*</td>
<td>36.0</td>
<td>0.6388</td>
<td>0.5141</td>
<td>0.8535</td>
</tr>
<tr>
<td>Age at 1st tTGA+, median (mo)</td>
<td>-</td>
<td>39</td>
<td>42</td>
<td>33</td>
<td>0.483</td>
<td><strong>&lt;0.0001</strong></td>
<td><strong>&lt;0.0001</strong></td>
</tr>
</tbody>
</table>

Vol. 62, Supplement 1, May 2016 8
The frequencies of the four risk factors for CD were higher in tTGA positives (G2-G4), compared to negatives (G1), but did not differ between G2-G4, except for female sex being more frequent in final positives (G2). Children with fluctuating titers (G4) were younger at seroconversion compared to G2 and G3. The first, maximal and last positive titers were markedly lower in children with negative seroconversion during follow up (G3, G4) compared to those who remained tTGA positive (G2).

**Conclusions:** Almost 20% of children with genetic predisposition for CD develop tTGA positivity identified by screening. Spontaneous seroconversion to negative tTGA results occurs in 43% of them, with the majority having only low tTGA levels. Our data suggest that screening detected children with low tTGA titers should be followed on a normal diet without gluten restriction and retested before they are evaluated with duodenal biopsies.

**Disclosure of interest:** none

| First tTGA+ level, median (U) | - | 20.4 | 3.7 | 4.8 | <0.0001 | <0.0001 | 0.0335 |
| Max. tTGA+ level, median (U) | - | 73.5 | 5.7 | 11.8 | <0.0001 | <0.0001 | <0.0001 |
| Last tTGA+ level, median (U) | - | 56.7 | 2.3 | 2.0 | <0.0001 | <0.0001 | 0.1991 |

*p<0.0001, §p<0.001, #p<0.005 compared to G1
GASTROENTEROLOGY: Coeliac disease

G-O-006

Oats in the Diet of Children with Celiac Disease: a Double-Blind, Randomized, Placebo-Controlled Multicenter Trial

Elena Lionetti1, Simona Gatti2, Nicole Caporelli2, Tiziana Galeazzi2, Ruggiero Francavilla3, Salvatore Cucchiara4, Paola Roggero5, Basilio Malamisura6, Giuseppe Iacono7, Andrea Budelli8, Rosaria Gesuita9, Carlo Catassi2

1University of Catania, Department of Pediatrics, Catania, Italy
2Marche Polytechnic University, Department of Pediatrics, Ancona, Italy
3University of Bari Aldo Moro/Department of Interdisciplinary Medicine, Bari, Italy
4Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
5Neonatal Intensive Care Unit (NICU), Department of Clinical Science and Community Health, Fondazione Ircs “ca’ Granda” Ospedale Maggiore Policlinico, University of Milan, Italy
6S. Maria Dell’olmo Hospital, Cava De’ Tirreni, Italy
7“G. Di Cristina” Children Hospital, Palermo, Italy
8Heinz Italia S.P.A, Latina, Italy
9Marche Polytechnic University, Department of Epidemiology, Biostatistics and Medical Information Technology, Ancona, Italy

Objectives and study: The inclusion of oats in the gluten-free diet (GFD) for treatment of celiac disease (CD) is controversial. We aimed to evaluate in a 15-month, randomized, double-blind, placebo-controlled multicenter trial clinical, serological and mucosal safety of pure oats in the treatment of pediatric patients with CD.

Methods: This is a non-inferiority clinical trial with a crossover design. Sample size was estimated using intestinal permeability test (IPT) as primary response variable and considering a clinical difference between the two diets of 0.01 as maximum. We randomly assigned 306 children with a biopsy-proven diagnosis of CD on a GFD for at least 2 years to receive a treatment AB (6 months of diet “A”, 3 months of standard GFD, 6 months of diet “B”), or BA (6 months of diet “B”, 3 months of standard GFD, 6 months of diet “A”). A and B diets included gluten-free products (flour, pasta, biscuits, cakes and crisp toasts) with either pure oats or placebo. The amount of oats was 15 gr/day for children aged 4-6 years, 25 gr/day for 7-10 years, and 40 gr/day for 11-14 years. Clinical [Body Mass Index (BMI), class of BMI, Gastrointestinal Symptoms Rate Scale (GSRS) score], serological [IgA anti-transglutaminase antibodies (TGA), IgA and IgG anti-deamidated gliadin peptides (AGA), and IgA anti-avenin] and IPT data were measured at basal and after six months of diet in the first period, after three months of washout at the beginning of the second period to obtain measurements at the second basal and after six months of diet. First and second-order carry-over effect (θ, λ) and direct treatment effect (τ) were evaluated by a non-parametric approach using medians as summary statistic.

Results: After exclusion of 129 patients who dropped out, the cohort included 177 children (79 in group A and 98 in group B). There were 124 girls (70%), and the median age of the cohort was 8.9 years (range, 6.9 to 11.2). Differences in treatment carry-over at the time of the second baseline measurement (θ) and differences in treatment carry-over at the time of the second treatment measurement (λ) and direct treatment effect (τ) were found not statistically significant for all clinical, serological, and mucosal variables studied. The upper limit of 95% confidence interval of IPT direct treatment effect was found lower than the highest difference considered clinically relevant. Results from crossover analysis are shown in table.
**Table:** First order carry-over effect, direct-by-period interaction, direct treatment effect according to the sequences AB, BA.

<table>
<thead>
<tr>
<th></th>
<th>$\theta$</th>
<th>$\lambda$</th>
<th>$\tau$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median (1-(\alpha)/2 %CI)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BMI</td>
<td>0.084 (-0.05; 0.20)</td>
<td>0.05 (-0.15; 0.20)</td>
<td>-0.5 (-0.12; 0)</td>
</tr>
<tr>
<td>BMI Class</td>
<td>0.50 (-1.0; 1.50)</td>
<td>0.50 (-1.0; 2.0)</td>
<td>-0.25 (-1.0; 0.25)</td>
</tr>
<tr>
<td>GRSR Score</td>
<td>0 (0; 0)</td>
<td>0 (-0.5; 0)</td>
<td>0 (-2.5; 0)</td>
</tr>
<tr>
<td>IgA Aga</td>
<td>0.29 (-0.35; 0.90)</td>
<td>0.14 (-0.70; 1.05)</td>
<td>-0.15 (-0.50; 0.25)</td>
</tr>
<tr>
<td>IgG Aga</td>
<td>0.29 (-0.35; 0.90)</td>
<td>0.15 (-0.70; 1.05)</td>
<td>-0.15 (-0.50; 0.25)</td>
</tr>
<tr>
<td>TGA</td>
<td>0.4 (-0.05; 0.95)</td>
<td>0.30 (-0.25; 0.80)</td>
<td>-0.02 (-0.25; 0.23)</td>
</tr>
<tr>
<td>IPT</td>
<td>0.001 (-0.01; 0.01)</td>
<td>-0.003 (-0.014; 0.007)</td>
<td>0.004 (-0.0002; 0.0089)</td>
</tr>
<tr>
<td>IgA Anti-avenin</td>
<td>0.0005 (-0.0005; 0.0014)</td>
<td>-0.0005 (-0.0019; 0.0005)</td>
<td>-0.0002 (-0.0007; 0.0003)</td>
</tr>
</tbody>
</table>

**Conclusion:** Addition of non-contaminated oats in the treatment of children with CD does not determine significant changes in nutritional parameters, clinical symptoms, serological markers, and intestinal permeability.

**Disclosure of interest:** All authors have conflict of interest with Heinz Italy s.p.a. Carlo Catassi has conflict of interest with Dr Shaer, and Menarini Diagnostics.
The Impact of "Crohn's Disease-TReatment-with-EATing" Diet (CD-TREAT Diet) and Exclusive Enteral Nutrition on Healthy Gut Bacteria

Vaios Svolos¹, Richard Hansen², Katie Hughes¹, Umer Zeeshan Ijaz³, Christopher Quince⁴, Daniel Gaya⁵, Richard Russell², Konstantinos Gerasimidis⁶

¹Human Nutrition, School of Medicine, College of Mvls, University of Glasgow, Glasgow Royal Infirmary, United Kingdom
²Department of Paediatric Gastroenterology, Hepatology and Nutrition, Royal Hospital for Children, Glasgow, United Kingdom
³School of Engineering, University of Glasgow, United Kingdom
⁴Warwick Medical School, University of Warwick, United Kingdom
⁵Department of Gastroenterology, Glasgow Royal Infirmary, Glasgow, United Kingdom
⁶Human Nutrition, School of Medicine, College of Medical, Veterinary and Life Sciences, University of Glasgow, Glasgow Royal Infirmary, United Kingdom

Objectives and study: We have recently demonstrated an extensive modulation of gut microbiome in children with Crohn's disease on induction treatment with exclusive enteral nutrition (EEN) (1,2). This observation offers clues about the potential mode of EEN action and advocates towards the development of novel therapies through dietary manipulation of the gut microbiota. This cross-over, RCT compared the effect of a novel "ordinary" food based diet (CD-TREAT diet) and EEN on healthy gut microbiota.

Methods: Healthy adults followed two experimental diets for seven 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 content, fatty acid composition, lactose and gluten free content). Participants were randomly allocated to start with EEN or CD-TREAT first. Fresh faecal samples were collected before and after each dietary intervention (4 different time points) and faecal short chain fatty acids (SCFA), pH, ammonia and sulphide were measured.

Results: 100 samples were collected from 25 healthy subjects. Faecal concentration of total SCFA, acetic, propionic, butyric and caproic acid significantly decreased during both dietary interventions (ΔMedian μmol/g, EEN: -167.27, -135.61, -15.47, -21.01, -2.02 vs CD-TREAT: -165.18, -68.92, -25.5, -34.99, -1.36, all p<0.01). Proportional ratio (% of total SCFA) was significantly reduced for butyric and caproic acid (ΔMedian %, EEN: -2.92%, -0.47%, CD-TREAT: -5.04%, -0.21%, all p<0.01); while did not change for the other SCFA. Faecal concentration of iso-butyric and iso-valeric acid was significantly increased after EEN only (ΔMedian μmol/g, EEN: 2.33, 2.59), while their proportional ratio increased after both diets (ΔMedian %, EEN: 1.95%, 2.13%, CD-TREAT: 0.72%, 0.88%, all P<0.001). Faecal pH significantly changed from a neutral baseline level to the alkaline range (ΔMedian pH units, EEN: 1.39 vs CD-TREAT: 0.97, both p<0.001). Likewise, total sulphide significantly increased during both diets (ΔMedian μmol/g, EEN: 3.1, CD-TREAT: 0.92, both p<0.001). Faecal ammonia and free sulphide concentration did not differ between the 4 time points.

Conclusion: We have developed an "EEN composition alike" food based diet which induces similar effects on gut microbial metabolites with EEN. Further analysis including high-throughput deep sequencing techniques will provide additional scientific evidence before we move this novel dietary treatment towards a subsequent clinical trial in people with active CD.


Disclosure of interest: None Declared
The availability of calcineurin inhibitors and infliximab in acute severe colitis have reduced colectomy rates in 283 children admitted during 1990-2012

Sapir Choshen\(^1\), Helen Finnamore\(^2\), Marcus KH Auth\(^3\), Tali Bdolah-Abram\(^3\), Eyal Shteyer\(^4\), David Mack\(^5\), Jeffrey Hyams\(^6\), Neal Leleiko\(^7\), Anne Griffiths\(^8\), Turner Dan\(^4\)

\(^1\)Shaare Zedek Medical Center, Pediatrics, Jerusalem, Israel  
\(^2\)Alder Hey Children's NHS Foundation Trust, Liverpool, United Kingdom  
\(^3\)The Hebrew University of Jerusalem, Israel  
\(^4\)Shaare Zedek Medical Center, The Juliet Keidan Institute of Pediatric Gastroenterology and Nutrition, Jerusalem, Israel  
\(^5\)University of Ottawa, Children's Hospital of Eastern Ontario Ibd Centre and Department of Pediatrics, Ottawa, Canada  
\(^6\)Connecticut Children's Medical Center, Hartford, United States  
\(^7\)Hasbro Children's Hospital/Rhode Island Hospital, Alpert School of Medicine at Brown University, Providence, United States  
\(^8\)Sickkids Hospital, Toronto, Canada

Objectives and study: One third of children admitted with acute severe colitis (ASC) fail intravenous corticosteroids (IVCS) and require salvage therapy. While colectomy was originally the only available salvage treatment, cyclosporine and then tacrolimus (Cys/Tac) have been introduced since 1996, followed by infliximab (IFX) in 2004, as second line medical treatment prior to colectomy. However, no data to date have shown whether these interventions actually managed to reduce colectomy rates, during the admission or thereafter.

We aimed to explore trends in colectomy rate in pediatric ASC before and after the introduction of Cys/Tac and IFX, using the largest pediatric cohort of ASC to date.

Methods: 283 children treated with IVCS for ASC during 1990-2012 were included (from the prospective (n=128) and retrospective (n=99) OSCI studies and another 55 retrospectively reviewed patients from Jerusalem and Liverpool). Patients were followed for 1 year (46% males, age 12.1±3.9 years, disease duration 2 (IQR 0-14) months, baseline PUCAI 69±13 points). Data accrual were similar in the 3 cohorts, collected using the same standardized case report forms at admission, 3 days and 5 days thereafter, at discharge and at 1 year. Colectomy rates were compared between 3 periods: 1990-1996 (era1: pre medications; n=68), 1997-2004 (era2: Cys/Tac and colectomy; n=45), 2005-2012 (era3: IFX, Cys/Tac and colectomy; n=170). No child in our cohort has been treated with IFX prior to 2005.

Results: Total 1-year colectomy rates were 40/68 (59%) during era1, 17/45 (38%) during era2, and 31/170 (18%) during era3 (P<0.001). Since IVCS failure rates was different between the eras, we then focused on those failing IVCS. Of the 283 children, 89 children (31%) failed IVCS treatment and required second line therapy during admission (44 primary colectomy, 9 Cys/Tac and 22 IFX; total colectomy 56). The 3 era groups were similar in 12 pre-treatment basic variables at admission (e.g. PUCAI, CRP, albumin, disease duration etc.) except for age and ESR. The rate of colectomy in those requiring salvage therapy during the admission was significantly reduced from 100% (51/51) in era 1, to 62% (8/13) in era2 and 33% (14/42) in era3 (p<0.001). At 1 year after discharge, 123 children (43%), were treated with second line therapy (44 primary colectomy, 12 Cys/Tac and 53 IFX; total colectomy 88). The rate of colectomy was again significantly reduced from 100% (40/40) of children requiring salvage therapy in era1 to 77% (17/22) in era2 and 51% (31/61) in era3 (p<0.001).

Conclusion: We show for the first time that the introduction of Cys/Tac and then infliximab sharply reduced the need for colectomy during admission and 1-year thereafter in pediatric ASC.

Disclosure of interest: None Declared
**GASTROENTEROLOGY: Inflammatory bowel disease**

**G-O-009**

**Early immunization and increased risk of serious adverse events during Infliximab mono-versus combotherapy.**

Bénédicte Pigneur¹, Cécile Talbotec², Solène Artru², Hélène Lengline², Lorenzo Norsa³, Olivier Goulet¹, Frank Ruemmele¹

¹Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, and Genius Group, Paris, France
²Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
³Hopital Necker Enfants Malades, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France

**Objectives and study:** Anti-tumour necrosis factor (TNF) agents have improved the prognosis of IBD and are widely used in adult and pediatric IBD patients. The risk of immunization against infliximab is well known and over time loss of response occurs in up to 40% of patients. There is some evidence that combotherapy of infliximab associated to an immunosuppressor (Azathioprine AZA) seems to reduce this risk of immunization. On the other side, there are registry data indicating that combo-therapy of AZA and anti-TNF agents increase the risk for adverse events, particularly infections and malignancies. There is ongoing discussion on the role of anti-TNF treatment for young male patients receiving AZA in the development of a rare but often lethal form of lymphoma, hepatosplenic T cell lymphoma. Due to these risks of combo-therapy many pediatric patients start anti-TNF medication as monotherapy. The objectives of our study were to compare the rate of early immunization against infliximab in a paediatric cohort comparing mono to a combo-therapy scheme of infusions.

**Methods:** Thirty-seven pediatric patients followed for Crohn's disease (onset <17 years) at Necker hospital who initiated their anti-TNF therapy between 01/01/2014 and 01/08/2015 were prospectively included in this study. 15 patients received IFX (REMICADE®) monotherapy and 22 received IFX in association with Azathioprine. The main indication of anti-TNF monotherapy was perianal Crohn's disease (7/15 patients) and severe growth retardation (4/15 patients). For each patient were collected at each visit the disease activity score (wPCDAI), biological parameters, a dosage of infliximab trough levels and antibodies to Infliximab (ATI). Infliximab was administered intravenously with a regimen that included an induction phase at weeks 0, 2 and 6 (5mg/kg/infusion) followed by a maintenance treatment every 8 weeks.

**Results:** After induction treatment, before the infusion of the maintenance phase (Week 14), all patients were in clinical remission (wPCDAI<12.5). IFX trough levels were numerically lower in patients on monotherapy (4.2 ± 4.4 mg/ml) compared to AZA-IFX combo-therapy (7.1 ± 4.7 mg/ml, NS). Immunisation reflected as positive anti-IFX antibodies was observed at W14 7 of 15 patients (46%) on mono- compared to 2/22 patients (9%) on combo-therapy (p <0.05). Antibodies were first detected at the second perfusion and increased over time. More serious adverse events occurred in the monotherapy group with 3 patients having an anaphylactic shock (20%) compared to 1 patient on combotherapy (4.5%, p<0.05) at the third infusion. The secondary addition of AZA in immunized patients, allowed to make disappear anti-IFX antibodies within six months in 2/15 patients and Infliximab trough levels increased.

**Conclusion:** Infliximab monotherapy has a higher risk of early immunization during the induction scheme with subsequent lower treatment efficacy and increased risk of serious adverse effect. The choice of monotherapy regimen or combination with another immunosuppressive therapy should be discussed for each patient establishing an individual risk-benefit profile.

**Disclosure of interest:** None Declared
Early detection of necrotizing enterocolitis and late onset sepsis by intestinal microbiota analysis

Tim de Meij¹, Berkhout Daan², de Groot Evelien², van Weissenbruch Mirjam³, Anton van Kaam³, Hendrik Niemarkt⁴, Peter Andriessen⁴, Andries Budding²

¹Vu University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
²Vu University Medical Center, Amsterdam, Netherlands
³Academic Medical Center, Amsterdam, Netherlands
⁴Maxima Medical Center, Veldhoven, Netherlands

Objectives and study:

Necrotizing enterocolitis (NEC) is the most common severe gastro-intestinal disease in very low birth weight infants. Currently available biomarkers lack accuracy to detect NEC in pre-clinical stage. Furthermore, clinical symptoms of NEC are usually indistinguishable from sepsis, leading to delay in initiation of NEC-therapy, worsening its prognosis. Alterations of intestinal microbiota are considered an essential factor in the pathogenesis of NEC and late onset sepsis. We hypothesized that intestinal microbiota analysis allows for early detection of NEC and sepsis.

Methods:

In six neonatal intensive care units in the Netherlands and Belgium, fecal samples of infants born at gestational age ≤ 30 weeks were collected daily, up to the 28th day of life. Included infants were allocated in three subgroups: NEC, sepsis and matched controls. Five time-intervals were defined; (a) T-4 (four days before diagnosis of NEC or sepsis); (b) T-3 (three days before diagnosis); (c) T-2 (two days before diagnosis); (d) T-1 (one day prior to diagnosis) and (e) T0 (day of diagnosis of NEC or sepsis). Fecal samples were analyzed by IS-pro, a clinically applicable PCR-based microbiome profiling technique.

Results:

So far, fecal samples of 385 subjects (35 NEC; 105 sepsis; 245 controls) were collected through time. Currently, fecal samples of 53 subjects (13 NEC; 20 sepsis; 20 controls) have been analyzed by IS-pro. Preliminary results showed that the three subgroups could statistically significant be differentiated from each other based on their microbiota profiles, up to four days prior to clinical onset of NEC and sepsis. Cumulative profiles differed between the subgroups at each defined time interval, but showed a fairly stable pattern through time. In NEC subjects, a gradually increase of the species Citrobacter koserii and Clostridium perfringens was observed in the days prior to NEC. The sepsis-group showed a significantly lower diversity of the Proteobacteria compared to the NEC subgroup and controls, at all time-points (all p<0.0001). The predictive accuracy of the PLS-DA model by ROC curves for NEC versus controls and NEC versus sepsis were high, especially for the Proteobacteria..

Conclusion:

Microbiota composition of NEC subjects differed from sepsis and controls already up to four days prior to onset of NEC and sepsis, underlining the crucial role of the intestinal microbiome in the development both diseases. Our observations suggest that microbiota profiling might select a subgroup of neonates already in early stage who are at increased risk for development of NEC and sepsis. Detailed understanding of disease-specific microbial shifts may lead to development of novel targeted, individualized therapeutic strategies in the prevention and treatment of NEC and sepsis.

Disclosure of interest: None Declared
Objectives and study: In a 12-week, open-label, multicentre safety and pharmacodynamics study, presented elsewhere, teduglutide 0.05 mg/kg/day reduced the volume of and the days per week on parenteral support (PS; parenteral nutrition and/or intravenous fluids) and advance enteral nutrition (EN; oral and/or tube feeding) in children with short bowel syndrome (SBS). Here we report the safety and tolerability results from this study.

Methods: Patients were aged 1–17 years with SBS ≥12-month duration who required PS for ≥30% of caloric and/or fluid/electrolyte needs and who showed minimal/no advance in EN feeds for ≥3 months before baseline. Patients enrolled sequentially into 3 teduglutide cohorts (0.0125 mg/kg/day [n=8], 0.025 mg/kg/day [n=14], 0.05 mg/kg/day [n=15]) or received standard of care (SOC; n=5). Safety data were collected at all scheduled study visits. ClinicalTrials.gov: NCT01952080; EudraCT: 201300458830.

Results: There were no reported deaths or discontinuations due to treatment-emergent adverse events (TEAEs). All patients experienced ≥1 TEAE; most were mild (95% teduglutide, 100% SOC) or moderate (57% teduglutide, 60% SOC). Patients with TEAEs occurring in ≥10% of the combined teduglutide vs SOC groups were vomiting (12 [32%] vs 0), upper respiratory tract infection (10 [27%] vs 2 [40%]), catheter-related complication (9 [24%] vs 1 [20%]), pyrexia (9 [24%] vs 2 [40%]), cough (7 [19%] vs 1 [20%]), abdominal pain (6 [16%] vs 1 [20%]), reduced blood bicarbonate (5 [14%] vs 2 [40%]), fatigue, headache, and nausea (5 [14%] vs 0 each), central line infection (4 [11%] vs 0), diarrhoea (4 [11%] vs 1 [20%]), and increased faecal volume (4 [11%] vs 0). There were no reports of AEs related to fluid overload, intestinal obstruction, hepatobiliary complications, or colon polyps. Serious TEAEs reported in ≥5% of the combined teduglutide vs SOC groups were central line infection (4 [11%] vs 0), pyrexia (4 [11%] vs 2 [40%]), catheter-related complication (3 [8%] vs 1 [20%]), and parainfluenzae virus (2 [5%] vs 0). None were considered related to study drug. No patient developed neutralising antibodies to teduglutide. One patient was positive for non-neutralising anti-teduglutide antibodies at the study follow-up visit (Week16) but was negative at 3-month follow-up.

Conclusion: Data from this study indicate that as well as improving intestinal function, teduglutide has a generally good safety profile and is well tolerated. Most TEAEs were related to gastrointestinal complaints and/or central line–related issues.

Disclosure of interest: Drs Hill, Carter, Horslen, Kocoshis, and Venick have served as study investigators for and received research support from NPS Pharmaceuticals, Inc. Dr Li is an employee of NPS Pharmaceuticals, Inc. This study was supported by NPS Pharmaceuticals, Inc. Bedminster, NJ, a wholly owned subsidiary of Shire plc.
**GASTROENTEROLOGY: Inflammatory bowel disease**

G-O-012

**Reference values of fecal calgranulin C (S100A12) in school aged children and teenagers**

Anke Heida¹, Anneke Muller Kobold², Lucie Wagenmakers², Koos van de Belt², Patrick van Rheenen¹

¹University Medical Center Groningen, Pediatric Gastroenterology and Nutrition, Groningen, Netherlands
²Department of Laboratory Medicine, University of Groningen, University Medical Center Groningen, Netherlands

**Objectives and study:** Fecal calprotectin is a frequently used screening test to identify children who are most likely to need endoscopy for suspected inflammatory bowel disease (IBD), but the number of false positive test results is considerable. Calgranulin C (S100A12) is a marker of intestinal inflammation that is potentially more specific for IBD, as it is exclusively released by activated granulocytes. We established a cutpoint for Calgranulin C in healthy children. Additionally, we investigated if Calgranulin C levels can discriminate children with IBD from healthy controls.

**Methods:** In a prospective community-based reference interval study we collected stool samples of children aged 6 to 18 years. A total of 110 healthy individuals and 40 children with suspected IBD (who were later confirmed by endoscopy to have IBD) sent a feces sample to the hospital laboratory of the University Medical Centre in Groningen. Levels of Calgranulin C were measured in duplo with a sandwich ELISA (Inflamark®). The lower limit of detection was 0.2 µg/g. The upper reference limit was calculated using the 97.5th percentile of observations in healthy children. Measurements of Calgranulin C in healthy children and those with IBD were combined to calculate the sensitivity, specificity and receiver operating characteristic (ROC) curve.

**Results:** The upper reference limit in healthy children was 0.86 µg/g (bootstrapped 95% confidence interval: 0.30-1.40), corresponding with a sensitivity of 87.5% and specificity of 98.2%. Median Calgranulin C levels were significantly higher in patients with IBD (9.26 µg/g (interquartile range (IQR) 2.66-11.87)) compared to healthy controls (<0.20 µg/g (IQR <0.20 - 0.20); P<0.001). The best cutoff point based on the ROC curve is 0.32 µg/g, corresponding with 97.5% sensitivity and 96.3% specificity.

**Conclusion:** Children and teenagers with newly diagnosed IBD have significantly different Calgranulin C results than healthy individuals. Calgranulin C shows diagnostic promise under ideal testing conditions. Future studies need to address whether Calgranulin C better discriminates those with IBD from a cohort of suspected patients than the established fecal marker calprotectin.

**Disclosure of interest:** This study was supported by a grant from CisBio Bioassay (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.
A prospective 24-week mucosal healing and deep remission assessment of small bowel and colonic Crohn’s disease as detected by colon capsule endoscopy

Salvatore Oliva¹, Stanley Cohen², Fortunata Civitelli¹, Marina Aloi¹, Franca Viola¹, Emanuele Casciani³, Francesca Maccioni⁴, Paola Papoff⁵, Cesare Hassan⁶, Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
²Children’s Center for Digestive Health Care, Atlanta, United States
³Sapienza University of Rome, Rome, Italy
⁴Sapienza University of Rome, Radiological Sciences, Oncology, and Pathology, Rome, Italy
⁵Nuovo Regina Margherita Hospital, Gastroenterology, Rome, Italy

Objectives and study: Data on small bowel (SB) mucosal healing (MH) and deep remission (DR) in children with Crohn’s disease (CD) are rare. Recently, colon capsule endoscopy (CCE) has been proved effective as “pan-endoscopy” in pediatric CD. This is the first study to prospectively assess MH and DR on the entire GI tract by performing two subsequent CCE over 24 weeks in children with CD in comparison with biomarkers, magnetic resonance enterography (MRE) and SB contrast ultrasonography (SICUS).

Methods: Children with known CD were prospectively recruited and underwent imaging studies followed by CCE, at baseline and after 24 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.

Results: Forty-eight patients (pts) were recruited, 22 with clinical and biomarker activity and 26 in remission. At baseline CCE confirmed significant inflammation (either in SB or colon) in 18 (82%) of 22 pts with clinical and/or biomarker disease activity, while showed mild lesions and/or normal mucosa in 4 (18%). MRE and SICUS did not demonstrate active disease in 5/18 (23%) with lesions at CCE, but it found nonspecific findings in 2 of 4 with negative CCE. Biomarker levels were elevated with FC in 13 (59%); CRP levels in 10 (45%) and either biomarker in 15 (68%). In the 26 pts with remission, CCE showed SB lesions in 13 (50%) and colonic lesions in 6 (23%). Complete MH and DR were observed in 10 (39%). Imaging studies found lesions only in 2 of 4 with negative CCE. Biomarker levels were elevated with FC in 13 (59%); CRP levels in 10 (45%) and either biomarker in 15 (68%). In the 26 pts with remission, CCE showed SB lesions in 13 (50%) and colonic lesions in 6 (23%). Complete MH and DR were observed in 10 (39%). Imaging studies found lesions only in 7 (27%, p<0.05). At 24-week follow-up, CCE identified DR only in 8/20 (36%) of the active group; while in 12/20 (54%) showed a partial MH. In inactive pts, CCE revealed that only 7/10 pts maintained DR. Of 16 pts in remission and with lesions at baseline, CCE showed that 9 (56%) achieved DR and 5 (44%) a partial MH after a change of therapy. MRE and SICUS had a good concordance in evaluating DR (14/17, 82%) in both groups, but did not identify partial MH (only 8/17, 47%, p<0.05). FC and CRP were not able to accurately evaluate DR in either group.

Conclusion: This study shows for the first time that CCE is effective for monitoring DR and MH of the entire GI tract and in directing therapy for pediatric patients with CD.

Disclosure of interest:
2nd author name, Conflict with: Covidien.
Utility of proposed modified simple endoscopic score in upper gastrointestinal Crohn’s disease

Oren Ledder1, Peter Church2, Anne Griffiths2, Javier Martin de Carpi3, Johanna Escher4, Luisa Mearin5, Batia Weiss6, Raanan Shamir7, Baruch Yerushalmi8, Ron Shaoul9, George Alex10, Daniel Lemberg11, Dan Turner12

1Shaare Zedek Medical Center, Pediatric Gastroenterology, Jerusalem, Israel
2The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
3Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain
4Erasmus MC, Holland, Netherlands
5Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
6Edmond and Lily Safra Children’s Hospital, Sheba Medical Center, Tel-Hashomer, Israel
7Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel
8Soroka Hospital, Bershova, Israel
9Rambam Hospital, Pediatric Gastroenterology, Haifa, Israel
10Royal Children’s Hospital, Melbourne, Australia
11Sydney Children’s Hospital, Sydney, Australia
12Shaare Zedek Medical Center, Genius Group, Jerusalem, Israel

Objectives and study: With more frequent performance of upper endoscopy (EGD), upper gastrointestinal (UGI) inflammation in Crohn’s disease (CD) patients has become increasingly recognized. UGI CD is associated with earlier onset and more severe disease. Recognition of UGI CD may assist in predicting disease course and directing appropriate therapy. Descriptive colonoscopy findings in CD are well standardized, however this is not so in the UGI. Lack of standardization limits the ability to implicate clinical significance of UGI CD. We empirically applied the Simple Endoscopic Score for CD (SES-CD) in the UGI for the first time, using the same indices as that for colonoscopy. The study aimed to assess the utility of the UGI SES-CD and its clinical significance in pediatric CD.

Methods: We used prospectively recorded data of pediatric CD patients collected for the ongoing ImageKids study. All patients underwent an EGD during the enrollment phase with a full clinical assessment within 2 weeks of the EGD. SES-CD items were scored in real time during upper endoscopy at each region (esophagus, stomach body, antrum and duodenum) with maximum total UGI SES-CD of 48. Demographics, clinical findings, biochemical markers, weighted Pediatric Crohn’s Disease Activity Index (wPCDAI) and physician global assessment (PGA) were also recorded.

Results: 94 children were enrolled at time of analysis (52 male; mean age 11.4 years ±3.0; range 3.3-17.3 years). Mean time from diagnosis to enrollment and endoscopic assessment was 2.4 years (±2.1; range 0.8-8.2). Mean wPCDAI 17.2 (±14.3; range 0-52.5). Median UGI SES-CD was 0 ± 3 (range 0-17). 44% had UGI SES-CD score ≥1, the majority of whom had endoscopic pathology identified in the duodenum (32%) with the least frequently involved region being the esophagus (9%). The major contributor to overall score in the esophagus, stomach body and antrum was “affected area” with less contribution from ulcer scores. In the duodenum these scoring features occurred in comparable frequencies. Narrowing was not identified in any region. There was a poor but significant correlation of UGI SES-CD with ESR and wPCDAI (r=0.2, r=0.2 P<0.05). There was no correlation between UGI SES-CD and age of diagnosis, clinical manifestations (including abdominal pain), other biochemical markers or specific Crohn’s therapy used. Patients with perianal CD had higher UGI SES-CD score [Median (IQR) 3 (±5) vs 0 (±3); p=0.01].
**Conclusion**: UGI SES-CD is an easily reported objective scoring system which may standardize reporting of endoscopic features of UGI CD.

UGI findings were present in almost half of patients in this cohort.

There is a lack of correlation between UGI findings and symptomatology, further supporting the recommendation of routine UGI endoscopy at IBD diagnosis rather than limiting EGD to patients with UGI symptoms.

**Disclosure of interest**: The ImageKids study is funded by an IIS grant from Abbvie. The authors declare no conflict of interest relating to this work.
GASTROENTEROLOGY: Coeliac disease

G-O-015

Validation of small intestine digital histomorphometry for celiac disease

Alina Popp¹, Juha Taavela², Jorma Isola³, Markku Mäki²

¹Tampere 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
²University of Tampere and Tampere University Hospital, Centre for Child Health Research, Tampere, Finland
³Institute of Biosciences and Medical Technology, University of Tampere, Tampere, Finland

Objectives and study: Digital image analysis of small intestinal biopsies, allowing quantitative villus height crypt depth ratios measurements (VH:CrD) and CD3-positive cell counts, holds promise in celiac disease research. We validated our morphometric procedures using virtual microscopy of small intestinal biopsy sections and compared the results to those of conventional microscopy.

Methods: Standard H&E stained biopsy specimens (n=142) from adult celiac disease patients and non-celiac disease controls were scanned and analyzed using a dedicated virtual microscopy platform-Celiac Slide Viewer. The specimens, which comprised different grades of mucosal injury, were evaluated morphometrically on computer screen by two accredited evaluators. Specimens with tangential cutting were included. The intraobserver and interobserver variations for VH:CrD and CD3+ densities (IELs/100 epithelial cells) were analyzed by the Bland-Altman method and intraclass correlation.

Results: Both observers measured 93 samples out of 142 (65 %) for VH and CrD readings. The rejected samples were evaluable neither for morphometry measurements, nor for Marsh-Oberhuber classes because of tangential biopsy cuttings. CD3+ stained specimens were available from 108 patients. The intraobserver analysis of VH:CrD showed a mean difference of -0.0325 with limits of agreement from −0.520 to 0.455; the standard deviation (SD) was 0.249. The mean difference in interobserver analysis was -0.0401, limits of agreement −0.802 to 0.722, and SD 0.389. The intraclass correlation coefficient in intraobserver variation was 0.977 and that in interobserver variation 0.935. CD3+ IEL density showed a SD of 19.4% and an intraclass correlation coefficients of 0.968.

Conclusion: The results indicate that digital morphometry is a powerful tool for measuring even small injury changes of small intestinal mucosa. Virtual microscopy allow image sharing via internet, saving and tracking of measurements. A conversion table between Marsh-Oberhuber grouped classification and quantitative morphometry will be presented.

Disclosure of interest: None Declared.
A noninvasive follow-up of pediatric ulcerative colitis by using colon capsule endoscopy and ultrasonography

Salvatore Oliva1, Fortunata Civitelli1, Marina Aloi1, Franca Viola1, Anna Dilillo1, Paola Papoff1, Salvatore Cucchiara1

1Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy

Objectives and study: The management of ulcerative colitis (UC) is mostly based on the evaluation of colonic mucosa status as assessed by the endoscopy. Unfortunately, repeated colonoscopies are not well accepted by children and adolescents. Recently, colon capsule endoscopy (CCE) and colonic ultrasonography (US) have been proved highly accurate and well tolerated in evaluating mucosal changes of large bowel in pediatric UC. A novel noninvasive approach, including CCE, US and fecal calprotectin (FCP), was compared with standard colonoscopy for diagnostic accuracy in pediatric UC; safety and tolerability were also evaluated.

Methods: We prospectively enrolled 32 consecutive pediatric patients (15 males, 17 females, mean age 13.2±3.2 years) with known UC (mean duration of colitis: 38.3±28.8 months) and candidates for colonic endoscopy. Only patients able to swallow the capsule were evaluated. Patients underwent FCP and US at day 0, CCE at day 1 followed by colonoscopy in the late afternoon or at day 2. Disease activity was assessed according to the Mayo score and US parameters of activity, thus patients were classified into 3 categories: 0 = normal or inactive disease; 1 = mild; >2 = moderate-to-severe. Statistical analysis was applied with calculation of specificity, sensibility, PPV and NPV of the different techniques and their combination.

Results: Sensitivity of CCE to detect colonic inflammation was 95% and specificity was 100%. The positive and negative predictive values of CCE for colonic inflammation were 100% and 92%, respectively. US showed a sensibility of 85% and specificity of 92%, with PPV and NPV of 94% and 79%, respectively. The combination of CCE, US and FCP reached 95% and 100% of sensibility and specificity, with PPV and NPV of 100%. The overall tolerability was higher in the noninvasive approach (p<0.05). No serious adverse event related to any procedure or preparation was reported.

Table:

<table>
<thead>
<tr>
<th>Diagnostic accuracy</th>
<th>SE, (95% CI)</th>
<th>SP, (95% CI)</th>
<th>PPV, (95% CI)</th>
<th>NPV, (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FCP</td>
<td>80 (62-91)</td>
<td>83 (65-94)</td>
<td>89 (72-97)</td>
<td>71 (53-85)</td>
</tr>
<tr>
<td>US</td>
<td>85 (67-95)</td>
<td>92 (75-98)</td>
<td>94 (79-99)</td>
<td>79 (60-90)</td>
</tr>
<tr>
<td>CCE</td>
<td>95 (79-99)</td>
<td>100 (87-100)</td>
<td>100 (87-100)</td>
<td>92 (76-98)</td>
</tr>
<tr>
<td>FCP+US+CCE</td>
<td>95 (79-99)</td>
<td>100 (87-100)</td>
<td>100 (87-100)</td>
<td>92 (76-98)</td>
</tr>
</tbody>
</table>

Conclusion: This new noninvasive approach by using FCP, US and CCE is highly accurate and more tolerated than standard colonoscopy in the follow-up of pediatric UC. The introduction of such noninvasive tools in the clinical practice facilitates the management of children with UC and may lead to future revision of current guidelines.

Disclosure of interest:
None Declared
Brain responses to uncertainty about upcoming visceral pain in quiescent Crohn’s disease – a fMRI study

Amandine Rubio¹, Sonia Pellissier², Lukas Van Oudenhove³, Huynh Giao Ly³, Jan Tack³, Chantal Delon-Martin⁴, Bruno Bonaz⁵

¹Grenoble University Hospital, Pediatric Gastroenterology and Nutrition, Grenoble, France
²Université de Savoie, Chambery, France
³University of Leuven, Department of Clinical and Experimental Medicine, Translational Research Center for Gastrointestinal Diseases, Leuven, Belgium
⁴Inserm U836, Grenoble Institut of Neurosciences, Grenoble, France
⁵Grenoble University Hospital, Clinique Universitaire D'hépato-Gastroenterologie, Grenoble, France

Objectives and study: Patients with Crohn’s disease (CD) in remission are exposed to chronic cognitive and emotional distress, linked to the constant risk of relapse. This permanent situation of anticipation and uncertainty can lead to anxiety, which may, in turn, trigger relapse. We aimed to investigate the effects of uncertainty on behavioral and brain responses to anticipation of visceral discomfort in quiescent CD patients.

Methods: Barostat-controlled rectal distensions at individually titrated discomfort and pain thresholds were preceded by cued uncertain or certain anticipation in 9 adult CD patients and 9 matched healthy volunteers. Brain responses across the different anticipation conditions in “pain neuromatrix” regions were measured using fMRI and compared between CD and controls. The influence of anxiety-related psychological variables on cerebral anticipatory activity was also analyzed. The study protocol was approved by the local Ethics Committee. All participants gave written informed consent in compliance with the Declaration of Helsinki and received a compensation for their participation.

Results: During uncertainty about upcoming visceral pain, CD patients had significantly greater activations than controls in the cingulate cortex, insula, amygdala and thalamus with trends in the hippocampus, prefrontal and secondary somatosensory cortex. In CD patients, brain responses to uncertainty in the majority of pain neuromatrix regions correlated positively with gastrointestinal symptom-specific anxiety and, to a lesser extent, trait anxiety and intolerance of uncertainty.

Conclusion: In the context of uncertainty regarding the occurrence of uncomfortable visceral sensations, CD is associated with excessive reactivity in brain regions known to be involved in sensory, cognitive and emotional aspects of pain processing and modulation as well as conscious threat appraisal. Our findings contribute to a better understanding of the role emotional and cognitive factors in CD, which may in turn inform the development of new (psycho)therapeutic approaches for management of symptoms and the related anxiety in these patients.

Disclosure of interest: None Declared
**GASTROENTEROLOGY: Inflammatory bowel disease**

G-O-018

**Genetic polymorphism in cannabinoid receptor 2 contributes to the risk of pediatric IBD**

Caterina Strisciuglio1, Giulia Bellini2, Erasmo Miele3, Massimo Martinelli3, Sabrina Cenni3, Alessandra Vitale2, Carlo Tolone2, Annamaria Staiano3, Emanuele Miraglia del Giudice2, Francesca Rossi2

1Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy
2Second University of Naples, Department of Woman, Child and General and Specialized Surgery, Naples, Italy
3Federico II University, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy

**Objectives and study:** Recent evidence suggests that endocannabinoids may limit intestinal inflammation via CB1 and/or CB2 receptor activation; however, their mechanistic role in inflammatory bowel disease (IBD) has not been clearly defined yet. In the present study we aimed to establish the role of common missense variant of CNR2, encoding for the CB2 receptor, in the risk of developing IBD in a well-characterized Italian cohort of pediatric IBD patients.

**Methods:** We evaluated the association of CNR2 variant in 114 Crohn's disease (CD), 107 ulcerative colitis (UC), and 600 controls, by direct sequencing and confirmed the results by Taqman assay. The disease activity was measured with Pediatric Crohn Disease Activity Index and Pediatric Ulcerative Colitis Activity Index for CD and UC, respectively. Additional data were collected from clinical records on patients' demographics, age at symptom onset and diagnosis, disease location, extraintestinal manifestations, therapy, clinical relapses, and need of surgical intervention.

**Results:** We found a significant allele and genotype association in CD patient \( p = 0.02 \) and \( p = 6 \times 10^{-5} \) respectively; whereas in UC we found a significant association only for genotype frequencies \( p=0.05 \). In particular, the GG/GG genotype (RR homozygous subjects) was highly prevalent in IBD children resulting in a frequency of about 50% compared to the 32% in controls with an increased susceptibility for RR homozygous subjects to develop a kind of IBD, in particular CD (odds ratio = 1.794 at CI 95%; \( p = 3.5 \times 10^{-4} \) for general IBD; odds ratio = 2.02 at CI 95%; \( p = 10^{-3} \) for CD; odds ratio = 1.57 at CI 95%; \( p = 0.03 \) for UC). Moreover, considering the presence of the GG allele alone (homozygous RR plus heterozygous QR subjects vs QQ subjects) the risk for developing Crohn was significantly higher (OR = 7.048 at C.I. 95%; \( p = 0.2 \times 10^{-5} \)). Upon genotype-phenotype evaluation, an increased frequency of moderate-severe disease activity was found in both CD and UC carrying the CNR2 rs35761398 risk genotype.

**Conclusion:** The rs35761398 polymorphism contributes to the risk of pediatric IBD, in particular CD. It is also associated with a more severe phenotype in both UC and CD. Taken together, our data suggest the involvement of CB2 in the pathogenesis and in the clinical features of pediatric IBD.

**Disclosure of interest:** None Declared.
Cyclic enteral nutrition for the maintenance of remission in pediatric Crohn’s Disease patients

Sara Nóbrega¹, Bénédicte Pigneur², Frank Ruemmele²

¹Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatiques, Paris, France
²Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, and Genius Group, Paris, France

Objectives and study: Enteral nutrition (EN) is a well-established treatment in pediatric Crohn’s disease (CD) for induction of remission and flares with similar efficacy compared to steroid therapy and no side effects. There are reports of EN as maintenance therapy, but usually on top of other treatment or after surgically induced remission. The aim of our study was to test feasibility and efficacy of cyclic exclusive EN as sole maintenance therapy.

Methods: Nine patients with active luminal paediatric Crohn’s disease, L1 (n=2) or L3 (n=7), followed at Necker Hospital between 2012 and 2014 were included in this prospective pilot study. After 8 weeks of exclusive EN with Modulen IBD, patients who came into complete CRP-negative remission were proposed to continue on cyclic EEN therapy as sole treatment in an open manner. Cyclic EEN consists of a 6 weeks phase of normal feeding followed by a 2 weeks phase of exclusive EN, without any concomitant CD-related medication. Patients were followed on a fixed scheme (3 months visits) with collection of anthropometric, clinical and biological data. T0 refers to time of study inclusion when diagnosis of CD was made, T1 end of induction of remission, T2 3 months after induction of remission and T3 9 months after induction of remission. Friedman test was used and a level of significance α=0.05 was considered.

Results: At the end of the induction of remission period, all patients were in deep remission (CRP-negative). At month 3 and 9 follow-up visit, 67% of patients were on clinical remission, with wPCDAI 8.1 (SD=8.7) and 6.7 (SD=8.8), respectively. Concomitant to the clinical response, biological scores markedly improved with mean sedimentation rate 31 mm/h (SD=14.2) at T0 and 12.7 mm/h (SD=8.4) at T3 (p=0.014) and albumin normalization with 33.8 g/l (SD=3.8) at T0 vs 41 g/l (SD=4.9) at T3 (p=0.014). Patients presented catch up growth with improvement of their anthropometric measurements at T1 and stabilization thereafter. (Table)

Table:

<table>
<thead>
<tr>
<th></th>
<th>T0 (n=9) Mean (SD)</th>
<th>T1 (n=9) Mean (SD)</th>
<th>T2 (n=9) Mean (SD)</th>
<th>T3 (n=6) Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Z-score weight</td>
<td>-0.89(SD=0.91)</td>
<td>-0.37(SD=0.97)</td>
<td>-0.43(SD=0.96)</td>
<td>-0.48(SD=1.18)</td>
</tr>
<tr>
<td>Z-score height</td>
<td>-0.23(SD=0.89)</td>
<td>-0.11(SD=0.80)</td>
<td>-0.11(SD=0.86)</td>
<td>-0.12(SD=0.66)</td>
</tr>
<tr>
<td>Z-score BMI</td>
<td>-1.09(SD=0.66)</td>
<td>-0.38(SD=0.89)</td>
<td>-0.58(SD=0.83)</td>
<td>-0.57(SD=1.19)</td>
</tr>
</tbody>
</table>

Conclusion: This study demonstrates for the first time prolonged clinical, biological remission and improved growth in pediatric CD patients treated only with cyclic enteral nutrition. Cyclic EN can be an efficacious non pharmacological treatment of Crohn’s disease patients potentially acting ahead of the inflammatory cascade in the intestinal mucosa. A sufficiently power randomized controlled trial is currently conducted by the GETAID pédiatrique to confirm these pilot data.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Inflammatory bowel disease

G-O-020

Enteral nutrients delay onset, reduce severity and promote recovery of induced colitis via calcium-sensing receptor

Sam Cheng¹, Lieqi Tang¹

¹University of Florida, Gainesville, United States

Objectives and study: Total enteral nutrition (TEN) is an effective 1st line therapy for children and adolescents with inflammatory bowel disease (IBD). In addition to reducing epithelium injury, TEN promotes mucosa healing that corticosteroid therapy does not, yet the mechanism of its action remains elusive. The extracellular calcium-sensing receptor (CaSR) is a unique family C G protein-coupled receptor and is activated by calcium, polyamine and amino acid/peptide, constituents of TEN. Highly expressed in the gut particularly epithelium lining mucosa of gastrointestinal tract, CaSR is a key molecule that contributes to preservation of epithelial barrier integrity and maintenance of gut immune balance; disruption of CaSR results in intestinal inflammation (Cheng, et al. FEBS Lett'14;588:4158-66). We hypothesize that intestinal CaSR may mediate therapeutic effects of enteral nutrients via interactions with calcium, polyamine, and amino acid.

Methods: To test this, dextran sodium sulfate (DSS) colitis rodent model of IBD was employed, and effects of calcium, spermine and tryptophan, added to diet, were examined and compared with that of cinacalcet, a specific pharmacological CaSR agonist as well as FKS06, a known anti-inflammatory agent. DSS (1.5-5%) was administered to animals via drinking water for 7 consecutive days to induce "acute" colitis or for two cycles of 5 day-on and 2 day-off to induce "chronic" colitis. Changes in stool consistency, stool blood, and body weight were recorded daily to monitor onset, severity and recovery of induced colitis. At end of experiment, animals were sacrificed either immediately after DSS treatment to assess colonic mucosal injury or were allowed to recover 1-3 days before sacrifice in order to assess colonic epithelial cell migration and healing. Colon tissues were also collected and assayed for changes in CaSR expression and transepithelial electrical resistance (TEER).

Results: CaSR was more abundantly expressed in colitic than normal colonic mucosa of high calcium (5x EMR (estimated minimal requirement)) diet-fed than control diet-fed rats. Compared to control diet-fed rats, high calcium diet-fed animals had more protected mucosal barrier as reflected by higher TEER, lower crypt damage scores, and more accelerated mucosal healing as reflected by faster colonic epithelial cell migration (re-epithelialization) rates following mucosal injury, with histopathological changes on colitis severity scores comparable to that of FKS06. As a result, onset of colitis in high calcium diet-fed animals was delayed, severity reduced, and recovery hastened. Similar therapeutic effects were also observed for high tryptophan (5x EMR), high spermine (10x EMR) diet, and in animals receiving cinacalcet. In contrast, relative to wild type mice, mice lacking intestinal CaSR had earlier onset, more severe colitis and delayed recuperation following DSS challenge, in further support of active protective roles by intestinal CaSR.

Conclusion: Our results suggest that intestinal CaSR may be a target of TEN. The ability of calcium, spermine, tryptophan and cinacalcet to effectively delay onset, reduce severity and promote recovery of induced colitis suggests that activating CaSR, either nutritionally or pharmacologically, may represent a new approach to prevent and/or treat bowel inflammatory disorders including IBD.

Disclosure of interest: None Declared.
Complications and disease recurrence after primary ileocecal resection in pediatric Crohn’s disease: a multicenter cohort analysis

Kay Diederent, Lissy de Ridder, Patrick van Rheenen, Victorien Wolters, Luisa Mearin, Gerard Damen, Tim de Meij, Herbert van Wering, Laura Tseng, Matthijs Oomen, Justin de Jong, Marc Benninga, Angelika Kindermann

1 Academic Medical Center, Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2 Erasmus MC-Sophia Children’s Hospital, Rotterdam, Netherlands
3 University Medical Center Groningen, Pediatric Gastroenterology and Nutrition, Groningen, Netherlands
4 University Medical Center Utrecht, Netherlands
5 Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
6 Radboud University Medical Center, Nijmegen, Netherlands
7 VU University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
8 Amphia Hospital, Breda, Netherlands
9 Academic Medical Center, Amsterdam, Netherlands
10 Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Up to 25% of pediatric-onset Crohn’s disease (CD) patients undergo surgical resection before adulthood. Limited data are available on the complications and long-term outcome of surgery in children with CD. Therefore, we aimed (I) to investigate the complication and disease recurrence rate after primary ileocecal resection for pediatric CD and (II) to identify predictors for complications and disease recurrence.

Methods: A retrospective cohort analysis was performed of all children (aged <18 years) who underwent primary ileocecal resection for CD between 1990 and 2015 at seven tertiary hospitals in the Netherlands. Severe complications, defined as requiring surgical, endoscopic or radiological intervention, and associated risk factors were assessed. Time to clinical recurrence, defined as active disease requiring a step up in medical treatment, and surgical recurrence, defined as disease recurrence requiring intra-abdominal surgery, was analyzed using Kaplan-Meier estimates. Postoperative maintenance therapy was defined as mesalazines, thiopurines, methotrexate, or anti-TNF agents started within 3 months after ileocecal resection. Multivariate logistic and Cox regression analyses of risk factors were performed for severe complications and recurrence, respectively.

Results: We identified 122 children with CD who underwent primary ileocecal resection [52% male; mean age at surgery 15.2 years (SD 1.6)] for stenosis (61%), therapy refractory inflammation (27%) and intra-abdominal fistulae or abscesses (11%). The majority of patients (57%) had isolated ileal disease. Median time from diagnosis to surgery was 11 months (IQR 3–31) and median follow up after surgery was 4 years (IQR 1–10). Sixteen patients (13%) developed a severe postoperative complication, 8 of whom (7%) had an anastomotic leak. Concurrent colonic disease [OR 4.82 (95% CI 1.38-16.90) p=0.014] was an independent risk factor for a severe complication. Clinical and surgical recurrence rates after 1, 5 and 10 years were 18%, 46%, 69% and 3%, 10%, 23% respectively.

Conclusion: Ileocecal resection is a very effective treatment for pediatric CD. However, children should be carefully monitored, since the severe postoperative complications rate is relatively high. Ileocolonic disease is a risk factor for severe postoperative complications. Moreover, postoperative maintenance therapy was a protective factor for both clinical and surgical recurrence.

Disclosure of interest: None Declared
Rapid infliximab infusion in children: a multicenter cohort study

Raffi Lev-Tzion¹, Amit Assa², Baruch Yerushalmi³, Avishay Lahad⁴, Oren Ledder¹, Dan Turner¹

¹Shaare Zedek Medical Center, Jerusalem, Israel
²Schneider Children’s Medical Center, Petach Tikva, Israel
³Soroka University Medical Center, Beersheva, Israel
⁴Edmond and Lily Safra Children’s Hospital, Sheba Medical Center, Tel Hashomer, Ramat-Gan, Israel

Objectives and study: A significant drawback of infliximab administration is the length of infusion time. While a number of adult studies have found rapid infusion to be safe, pediatric data continues to be scarce. We report our experience with a 1-hour rapid infusion protocol, prescribed in four pediatric IBD units over a period ranging from 6-20 months.

Methods: 1-hour infliximab infusions were administered to children with IBD who fulfilled the following criteria: 1) They had received at least 4 standard duration infusions with no infusion reactions; 2) There was no recent dose increase; 3) No more than 10 weeks had elapsed since the previous infusion. Standard duration infusions were administered over the course of approximately 3 hours for the first 3 infusions, and approximately 2 hours for subsequent infusions. Premedication administration was left to the discretion of each individual center. Patients were followed prospectively and all infusion reactions were recorded in patients' charts.

Results: 85 children with IBD received infliximab infusions (69 CD, 9 UC and 7 IBD-U); mean age 15.4±2.9 years, 55.3% males, and median disease duration 23 (IQR 48-12) months. 50 children qualified for the rapid infusion protocol. 448 standard duration infusions and 311 rapid infusions were administered. 57/85 (67%) patients received concomitant immunomodulators. 7 infusion reactions (1.6%) occurred during standard duration infusions and 3 (0.96%) occurred during rapid infusions (p=0.54).

Conclusion: Consistent with adult data, our results indicate that 1-hour infliximab infusions in selected pediatric IBD patients offer a safe alternative to traditional 2-3 hour infusions. By decreasing the time patients and their parents need to spend in the infusion center, rapid infliximab infusion can mitigate an important obstacle to patient acceptance of infliximab therapy.

Disclosure of interest: D.T.: Research grants, speaker's remuneration and consultation fee from Abbvie, Takeda and Janssen. Other authors: no conflicts of interest declared.
New trends in biologic use in paediatric IBD in the UK: significantly less co-immunosuppression, milder disease and more patients!

Rafeeq Muhammed¹, Kajal Mortier², L Williams³, Marcus Auth⁴, Nicholas Croft⁵, Robert Mark Beattie⁶, John Fell⁷, Sabari Loganathan⁸, Charlie Charlton⁹, Anthony Akobeng⁹, Mary-Anne Morris¹⁰, Anne Willmott¹¹, Babu Vadamanayan¹², Franco Torrente¹³, Sally G Mitton¹⁴, Assad Butt¹⁵, Huw Jenkins¹⁶, Astor Rodrigues¹⁷, John Punts¹⁸, Fevronia Kiparissi¹⁹, Mark Furman²⁰, Michael Cosgrove²¹, Susan Bunn²², Anna Pigott²³, Warren Hyer²⁴, David C Wilson²⁵, Richard K Russell²⁶

¹Birmingham Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom
²Royal College of Physicians, London, United Kingdom
³Alderhay Children's Hospital, Liverpool, United Kingdom
⁴Royal London Hospital, London, United Kingdom
⁵Southampton University Hospital NHS Trust, Southampton, United Kingdom
⁶Chelsea and Westminster Hospital, London, United Kingdom
⁷Aberdeen Royal Infirmary, Aberdeen, United Kingdom
⁸Nottingham University Hospital NHS Trust, Nottingham, United Kingdom
⁹Manchester Children's Hospital, Manchester, United Kingdom
¹⁰Norfolk and Norwich University Hospital NHS Trust, Norwich, United Kingdom
¹¹University Hospital of Leicester, Leicester, United Kingdom
¹²King's College Hospital, London, United Kingdom
¹³Addenbrooke's Hospital, Cambridge, United Kingdom
¹⁴St George's Hospital, London, United Kingdom
¹⁵Brighton and Sussex University Hospital NHS Trust, Brighton, United Kingdom
¹⁶University Hospital of Wales, Cardiff, United Kingdom
¹⁷John Radcliffe Hospital, Oxford, United Kingdom
¹⁸Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom
¹⁹Great Ormond Street Hospital, London, United Kingdom
²⁰Royal Free London NHS Hospital Trust, London, United Kingdom
²¹Singleton Hospital, Swansea, United Kingdom
²²Great North Children's Hospital, Newcastle Upon Tyne, United Kingdom
²³University Hospital of North Midlands, Stoke on Trent, United Kingdom
²⁴St Mark's Hospital, London, United Kingdom
²⁵Royal Hospital for Sick Children, Edinburgh, United Kingdom
²⁶Royal Hospital for Children, Glasgow, United Kingdom

Objectives and study: The national clinical audit of biological therapies for Inflammatory Bowel Disease (IBD) was started in 2011. Paediatric patients started on biological therapy for the treatment of IBD between September 2011-February 2015 are included in this analysis. Methods: Paediatric IBD centres in the UK submitted real time data to the audit web tool. Additional data from the Personalised Anti-TNF alpha Therapy in Crohn's Disease Study (PANTS) have also been included. We ascertained the % of new paediatric IBD (PIBD) biological starters in UK by comparing data from the biologics audit to the data from the national audit of the PIBD service provision (September 2014).

Results: 696 patients are included (579 with Crohn’s disease (CD), 92 with ulcerative colitis (UC) and 25 with IBD unclassified (IBDU)) 609 directly via the audit and 87 from PANTS. The number of patients entered into the web tool has increased from 191 patients in 2012 to 235 patients in 2015. 63% of patients with CD were male with median diagnostic age of 13 years with median interval to biologic initiation of 1 year. The indication for starting biological therapy was active luminal CD in 463/570 (81 %) patients. 551/579 (95%) of CD patients were treated with Infliximab. The audit now covers the majority of new starters in paediatrics (62%). There is a trend for treating milder disease with the median PCDAI score at the initiation of treatment being 25 (IQR 18-38). 119/197 (60%) of these patients received concomitant immunomodulatory therapy and 25/197 (13%) were receiving steroids at the initiation of biological treatment; compared to the 1st audit period the rates of co-immunosuppression and steroid usage at initiation are significantly lower 56/67 (84%) cf. 60% (119/197), p<0.001 and 24% (16/67) cf. 13% (25/197), p<0.05 respectively.
There have been no changes in safety data. Of the 92 UC patients, 88 (96%) received Infliximab. Median PUCAI score at the time of initiation of biological therapy was 35 dropping to 15 at 3 months follow up. Pre treatment PUCAI score is lower compared to previous years. Patient related outcome measures (PROM) were assessed using IMPACT-III questionnaire. Median IMPACT-III score at the initiation of biological therapy was 116 (IQR 102-137) and this had significantly improved to 132 at 3 months follow up (IQR 93-146).

**Conclusion:** The increase in participation of IBD biological audit demonstrates the value of the audit. The audit suggest that biologics are being used to treat milder Crohn’s disease compared to previous years, as evidenced by the lower PCDAI score and lower use of steroids at initiation of treatment. The surprising trend of reduced prescription of co-immunosuppressants was seen in this audit; however this is not clearly related to any changes in safety signal.

**Disclosure of interest:** Dr Rafeeq Muhammed, first author, conflict with MSD Immunology, Abbvie, Dr Falk, Tillotts Pharma, Nestle, Takeda and Pfizer. Dr Nicholas Croft, 5th author, conflict with Abbvie, Abbot, Shire, MSD Immunology, Schering Plough. Dr John Fell, 7th Author, conflict with Dr Falk and Nestle. Dr David Wilson, 26th Author, conflict with Pfizer and MSD Immunology. Dr Richard Russell, 27th Author, conflict with MSD Immunology, Nestle, Abbvie, Dr Falk, Takeda, Napp, Mead Johnson, Nutricia, 4D pharma. Other authors have no conflict of interests to declare.
**Distressed behavior and GER in infants: new insights**

Silvia Salvatore¹, Federica Pagliarin², Koen Huysentruyt³, Kris Van de Maele⁴, Yvan Vandenplas⁵

¹University of Insubria, Varese, Italy
²University of Insubria, Pediatrics, Varese, Italy
³Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Pediatrics, Brussels, Belgium
⁴Uz Brussel, Paediatrics, Brussels, Belgium
⁵Uz Brussel, Department of Pediatrics, Brussels, Belgium

**Objectives and study:** The relation between gastroesophageal reflux (GER) and distressed behavior, expressed as crying in infants is still unclear. Parents are often very anxious and preoccupied when their infant is crying and distressed, which are often interpreted as pain. Management of these pain episodes is a major concern. The "Face, Legs, Activity, Cry, Consolability (FLACC)" scale is a validated measurement used to assess pain for infants and young children. The objective of this study was to assess the relation between GER and the FLACC score.

**Methods:** We conducted a prospective study (jan - nov 2015) consecutively including infants submitted to multichannel intraluminal esophageal impedance (MII) (Sleuth®, Sandhill Scientific, Inc; Highland Ranch, CO, USA) and pH-monitoring for suspected GER-disease (GERD) who presented episodes of crying during the investigation. The technique, methodology and analysis of MII-pH monitoring and GER events were defined according to published criteria. Symptoms were considered as temporally associated with GER if occurred within a 2-minutes period of time. All MII-pH tracings were analyzed by a single author (SS) who was blind to the result of the FLACC score. Parents were instructed to fill in a symptom diary and the FLACC scale during episodes of crying. The scale was scored in a range of 0–10 with 0 representing no pain and 2 the maximum pain expression for any of the five categories as reported in previous reports. The medians of the total FLACC score were considered according to the presence/absence, duration, kind and extension of GER events.

Statistical analysis was performed using Kruskal-Wallis (test H) and t test when appropriate.

**Results:** We recruited 75 subjects (age 10 days -21 months, mean age 3.8, SD 3.7, median age 2.5 months; 37 males and 38 females). During the investigation 973 episodes of crying were reported, in 466 (48%) of which the FLACC scale was completed and analyzed. Among them, 319 (68%) episodes of crying were not associated with GER. GER occurred before crying in 91 episodes (FLACC median value 6), simultaneously in 31 (FLACC 2) and after crying in 24 (FLACC 5.5)(p=0.001). The median values of FLACC were not significantly different between episodes with (FLACC 5) or without (FLACC 4) GER, proximal (FLACC 6) or only distal (FLACC 5) GER, or between subjects with (median FLACC 3) or without (median FLACC 4) abnormal acid exposure. Neither younger age or duration of GER were significantly correlated with high values of FLACC (P=0.15). Weakly acidic reflux (n:xx) presented a significant higher value of FLACC compared to acid reflux events (FLACC 6 vs 4, Test H di Kruskal-Wallis: P=0.0002).

**Conclusion:** In infants, most episodes of crying were not associated with GER. The presence, kind, temporal sequence, duration, extension of concomitant GER could not be predicted by the FLACC scale. In infants, weakly acidic reflux was perceived more painful compared to acid reflux episodes, suggesting that volume may be more painful than acid.

**Disclosure of interest:** None Declared
GASTROENTEROLOGY: GI motility, GERD and functional GI disorders

G-O-025

Laryngeal inflammation and gastroesophageal reflux: two sides of the same or two different coins?

Fabio Meneghin 1, Martina Rossano 2, Elena Albani 3, GianVincenzo Zuccotti 4, Silvia Salvatore 2

1 Ospedale Sacco, Milano, Italy
2 University of Insubria, Varese, Italy
3 Ospedale Sacco, Pediatrics, Milano, Italy
4 Ospedale Sacco, Univerity of Milan, Pediatrics, Milano, Italy

Objectives and study: The correlation between gastroesophageal reflux (GER) and laryngeal inflammation is unclear and needs to be clarified because many children started acid inhibitors based only on laryngoscopic findings. The aim of the study was to examine the correlation between laryngeal findings and esophageal impedance -pH monitoring (MII-pH) results.

Methods: This is a two-center prospective study consecutively including all children with respiratory symptoms who underwent flexible laringoscopy and multichannel esophageal intraluminal impedance (MII)-pH monitoring (Sleuth®, Sandhill Scientific, Inc; Highland Ranch, CO, USA) for suspected laryngeal and GER-disease (GERD). Exclusion criteria were: esophageal or laryngeal previous surgery, lap between the two investigations above 2 months, reflux treatment started between the investigations, artifacts on MII-pH, incomplete laryngoscopy or laryngeal report. The technique, methodology and analysis of MII-pH and GER events were defined according to published criteria. Statistical analysis was performed using Mann-Whitney test U, chi square, Fisher, Kruskal-Wallis and t test when appropriate. Laryngoscopy was considered as positive if it showed erythema and/or edema of arytenoids or postcricoid or vocal cord region or nodules. The Reflux finding Score (RFS) at laryngoscopy was also considered. MII-pH was considered pathological when total percentage of acid exposure (Reflex Index, RI) was >5% for children and >10% for infants or when symptom association probability (SAP) was ≥95% as previously reported.

Results: 78 children (range 0.5-181 months, median age 57 months) were analyzed. The most common symptoms were chronic cough, recurrent wheezing and dysphonia in children and ALTE/apnea and regurgitation in infants. Most patients were referred by the ENT specialist to the gastroenterologist because of laryngeal abnormality. In 52 (67%) laryngoscopy was reported as positive but we did not find any significant correlation with percentage of acid exposure, total number of GER, proximal GER episodes, or positive SAP at MII-pH. Laryngeal erythema and/or edema of arytenoids were the most common laryngeal abnormalities reported in our patients but were not associated with a significantly different esophageal RI. The value of RFS was also similar in patients with or without pathological MII-pH.

Conclusion: Recurrent respiratory symptoms and laryngeal inflammation are frequently reported in children. We did not find a correlation between laryngeal erythema or edema or RFS and GER. A validated and reliable laryngeal score still needs to be identified for pediatric patients. In children, acid inhibitors should not be started based only on laryngoscopic findings.

Disclosure of interest: None Declared

Vol. 62, Supplement 1, May 2016
Influence of percutaneous endoscopic gastrostomy on gastro-esophageal reflux disease

Madeleine Gottrand¹, Lalanne Arnaud¹, Guimber Dominique¹, Coopman Stéphanie¹, Turck Dominique¹, Michaud Laurent¹, Gottrand Frédéric¹

¹Chu Lille, Reference Center for Congenital and Malformative Esophageal Disease (Cracmo), Division of Gastroenterology, Hepatology and Nutrition, Lille, France

Objectives and study: The influence of percutaneous endoscopic gastrostomy (PEG) on gastro-esophageal reflux disease (GERD) is a matter of debate. Whereas most pH(impedance)metry studies showed that PEG does not precipitate GERD on the short term, the influence of PEG on GERD on the long term is unknown. Following our previous study showing that GERD is not caused/aggravated by PEG (Pediatrics. 1996; 97:726–8), the policy in our center is not to perform antireflux surgery at the time of PEG placement unless preexisting GERD is not controlled. The aim of this study was to assess the outcome of GERD on long term follow-up in children undergoing PEG placement and to identify factors associated with the occurrence/aggravation of GERD after PEG placement.

Methods: Using an ad hoc questionnaire, data of children (n = 368) who underwent PEG in our center were recorded, retrospectively between 1990 and 1999 and prospectively between 1999 and 2003. GERD was defined by at least one of the followings: clinical manifestations requiring antisecretory or prokinetic treatment; presence of peptic esophagitis; need for anti-reflux surgery. Aggravation of GERD in a child presenting GERD before PEG was defined by at least one of the followings: occurrence of peptic esophagitis; need for increasing antisecretory treatment; need for antireflux surgery. PEG was placed by the same team of pediatric gastroenterologists using the standard pull technique. Multivariate analysis was used to identify factors favoring GERD after PEG placement. A survival analysis without antireflux surgery was also performed.

Results: 326 patients (56% with neuromuscular disability (ND)) were studied with a median follow-up of 3.5 years (range 2 to 13.5). Eighteen patients (5.5%) underwent fundoplication before PEG placement and were excluded from the analysis. The most common indication for PEG placement was feeding difficulties (63%) with or without failure to thrive. GERD was present in as many as 74% of patients at the time of PEG placement. After PEG placement, GERD occurred in 11% of patients free of GERD before and aggravated in 25% of those with preexisting GERD. Factors associated with GERD aggravation after PEG placement were presence of neuromuscular disability (OR = 2.89; IC95%: 1.63–5.14) and presence of GERD before PEG placement (OR = 7.27; IC95%: 4.03-13.10). After PEG placement only 52 patients (16%) required antireflux surgery of whom 22 (42%) during the first year following PEG placement. The only factor significantly associated with the need for antireflux surgery was neuromuscular disability (OR = 1.98; IC95%: 1.10-3.56).

Conclusion: GERD is frequent in children requiring PEG but is most often controlled by medical treatment after PEG placement. Risk factors for GERD aggravation after PEG placement are underlying neuromuscular disability and preexisting GERD. Systematic antireflux surgery at the time of PEG placement is unjustified.

Disclosure of interest: None Declared.
Neuroglioplastic changes induce functional repercussions in the remaining ‘healthy’ bowel in Hirschsprung disease.

Anne Darie1, Tony Durand2, Lucie Gryenberg1, Etienne Suply1, Marc-David Leclair1, Hugues Piloquet3, Jean-François Mosnier4, Pierre-Antoine Grohard5, Philippe Aubert6, Catherine Le Berre-Scoul7, Philine de Vries5, Guillaume Levard9, Véronique Couvrat6, Guillaume Podevin7, Françoise Schmitt7, Sabine Irtan8, Thierry Villemagne8, Hubert Lardy9, Cécile Muller10, Erik Hervieux10, Louise Galmiche11, Sabine Sarnacki10, Hélène Boudin9, Pascal Derkinderen9, Michel Neunlist12

1University Hospital of Nantes, Pediatric Surgery, Nantes, France
2University Hospital of Nantes, Inserm U913, Nantes, France
3University Hospital of Nantes, Pediatric Gastroenterology, Nantes, France
4University Hospital of Nantes, Pathology, Nantes, France
5University Hospital of Brest, Pediatric Surgery, Brest, France
6University Hospital of Poitiers, Pediatric Surgery, Poitiers, France
7University Hospital of Angers, Pediatric Surgery, Angers, France
8University Hospital of Trousseau, Pediatric Surgery, Paris, France
9University Hospital of Tours, Pediatric Surgery, Tours, France
10University Hospital of Necker Enfants Malades, Pediatric Surgery, Paris, France
11University Hospital of Necker Enfants Malades, Pathology, Paris, France

Objectives and study: In Hirschsprung disease (HD), the only current treatment is the complete removal of the aganglionic bowel with the transition zone and anastomosis to the ganglionic bowel considered as ‘healthy’. However the postoperative course remains unpredictable. Enterocolitis occurs in one third of these patients and intestinal dysmotility, especially severe constipation, in half of them. There is currently a lack of biomarkers to predict evolution of the disease as well as a precise understanding of the pathophysiological mechanisms involved in HD postoperative complications. The aim of this study was therefore to characterize the enteric nervous system (ENS) phenotype in the ‘healthy’ ganglionic zone of resected colon samples in HD patients.

Methods: After ethical board approval, we initiated a multicenter, translational and prospective study, which included full term neonates with HD and control patients (anorectal malformation) during their first year of life. Samples of resected bowel were collected at the time of surgery. Whole mounts of colonic myenteric plexus were stained with antibodies against calretinin, neuronal nitric oxide synthase (nNOS), and HuC/D (pan-neuronal marker). The expression level of the glial marker GFAP (glial fibrillary acidic protein) was analyzed by western blot. To determine the functional repercussion of the neuroplastic changes on neuromuscular transmission, functional ex vivo analysis of motility were performed on fresh muscular strips. Colonic contractile response induced by electrical field stimulation (EFS) was investigated in organ chambers in absence or presence of N-nitro-L-arginine methyl ester (L-NAME) (inhibitor of NO production) and/or atropine (cholinergic receptor antagonist).

Results: During one year, 11 HD patients without stoma and 7 control patients were included with a comparable median age of 77 days and 136 days respectively. The density of ENS structures (ganglia and interganglionic fiber strands) was significantly lower in the ‘healthy’ bowel in HD as compared to control (p=0,01) and the neuronal area tended to be larger in HD (p=0,08). In addition, the number of HuC/D neurons per ganglia was lower (p=0,02), especially for nNOS-immunoreactive (IR) neurons (p=0,0008) but not for calretinin-IR neurons as compared to control. GFAP expression was significantly lower in the ‘healthy’ bowel in HD (p=0,02), and was interestingly correlated to the number of nNOS-IR neurons per ganglia (p=0,003). EFS-induced contractile responses were similar in HD as compared to control. However, the L-NAME sensitive component of EFS induced response tended to be reduced in the ‘healthy’ bowel in HD in comparison to control (p=0,06), but no difference was reported for the atropine sensitive one.
**Conclusion:** This pilot study suggests that the remaining ‘healthy’ bowel in HD is not probably as healthy as thought. Our data suggest the occurrence of neuroplastic changes in specific neuronal subpopulations. In particular, reduced NOS expression could reflect ENS immaturity and contribute to dysmotility observed in HD patients. Therefore, approaches aimed at enhancing NOS pathways in HD could be of therapeutical interest for treatment and/or prevention of postoperative complication in HD.

**Disclosure of interest:** None declared.
A new formulation of oral viscous budesonide in treating of pediatric eosinophilic esophagitis: a pilot study

Salvatore Oliva¹, Danilo Rossetti¹, Paolo Rossi¹, Sara Isoldi¹, Paola Papoff¹, Simone Frediani¹, Tullio Frediani¹, Sandra Lucarelli¹, Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy

Objectives and study: Oral Viscous Budesonide (OVB) is a recent therapeutic option for Eosinophilic Esophagitis (EoE) versus dietary restriction and inhaled steroids. This pilot study aims to evaluate the efficacy and safety of a new oral viscous budesonide suspension in children and adolescents with EoE.

Methods: We treated with OVB 36 children (29 male; median age 12 years) with EoE diagnosed according to ESPGHAN guidelines (JPGN 2014;58:107). Patients <150 cm and >150 cm height received 2 mg and 4 mg OVB daily, respectively, for 12 weeks. Upper GI endoscopy was performed at baseline, after 12 weeks of therapy and 6 months after the end of therapy. Baseline and post-treatment scores were calculated for symptoms, endoscopy and histology (from Dohil R, Gastroenterology 2010,139:418). All patients underwent multichannel intraluminal impedance (MII-pH). Serum cortisol was performed at baseline, 12, 36 weeks.

Results: At the end of OVB trial, endoscopy showed macroscopic and histological remission in 32 patients (88.9%), while median pre- and post-treatment peak eosinophil count/HPF markedly decreased from 42 (range: 15-100) to 5 (range: 0-30), respectively. Moreover, mean symptom and histology scores impressively improved vs baseline (p<0.01); 7/36 children (19.4%) with positive MII-pH were treated also with proton pump inhibitors. Interestingly, 6 months after end of OVB therapy, endoscopy showed esophageal relapse in 21 patients (58.3%), whereas 15 (41.7%) were in remission. No significant difference between pre-/post- treatment morning cortisol levels occurred.

Conclusion: OVB is an effective and safe treatment for pediatric EoE, determining a meaningful improvement of symptoms, endoscopic and histological features. The disease recurrence after OVB cessation raises the question whether treatment should be prolonged in some subsets of patients with a tendency to relapse.

Disclosure of interest: ITC Farma Srl provided the entire drug supply.
Prevalence of functional gastrointestinal disorders in young Belgian, Dutch and Italian children

Nina Steutel1, Elena Scarpato2, Rossella Turco2, Hessel Nijenhuis3, Yvan Vandenplas3, Miranda Langendam1, Merit Tabbers1, Marc Benninga1, Annamaria Staiano2

1Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Federico II University, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy
3Uz Brussel, Department of Pediatrics, Brussels, Belgium
4Academic Medical Center, Department of Clinical Epidemiology, Bioinformatics and Biostatistics, Amsterdam, Netherlands

Objectives and study: Paediatric functional gastrointestinal disorders (FGIDs) are a common problem worldwide. So far, epidemiologic data about FGIDs with respect to infants and younger children in Belgium, Italy and The Netherlands are limited. In this prospective, multicenter study we aim to determine the prevalence of FGIDs in young children in these countries.

Methods: We have enrolled infants and children aged between 0 and 4 years, who attended a well-baby clinic, in The Netherlands, or a general paediatrician, in Belgium and Italy, 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, and 3) socio-demographic information on the family and exposure to stressful life events. FGIDs were defined according to the Rome criteria. After oral informed consent, questionnaires were completed at the site of inclusion. Parts 1 and 2 were completed by interviewing parents, part 3 was completed by parents themselves.

Results: So far, a total of 783 children has been included: Group 1 consisted of 286 children aged between 0 and 6 months (Belgium n = 10, Italy n = 45, The Netherlands n = 231), whilst Group 2 consisted of 497 children aged between 7 months and 4 years of age (Belgium n = 20, Italy n = 72, The Netherlands n = 405). According to the Rome III criteria, the prevalence of FGIDs in children between 0 and 6 months of age was 20.3%, while in children aged between 7 months and 4 years the prevalence of FGIDs was 10.1%. Specifically, the most common FGIDs in children from Group 1 were infant regurgitation (5.9%) and infant colic (5.9%), whereas in children from Group 2 the most common FGID was functional constipation (7.2%).

Data regarding the prevalence of all FGIDs in each age group are summarised in the Table.

<table>
<thead>
<tr>
<th>Group</th>
<th>0 – 6 months; n = 286 (%)</th>
<th>7 months – 4 years; n = 497 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>159 (55.6%)</td>
<td>Male 236 (47.5%)</td>
</tr>
<tr>
<td>Female</td>
<td>127 (44.4%)</td>
<td>Female 261 (52.5%)</td>
</tr>
<tr>
<td>Cyclic vomiting syndrome</td>
<td>1 (0.3%)</td>
<td>6 (1.2%)</td>
</tr>
<tr>
<td>Functional diarrhoea</td>
<td>N/A</td>
<td>5 (1%)</td>
</tr>
<tr>
<td>Functional constipation</td>
<td>3 (1%)</td>
<td>36 (7.2%)</td>
</tr>
<tr>
<td>Rumination syndrome</td>
<td>11 (3.8%)</td>
<td>4 (0.8%)</td>
</tr>
<tr>
<td>Infant regurgitation</td>
<td>17 (5.9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Infant dyschezia</td>
<td>14 (4.9%)</td>
<td>1 (0.2%)</td>
</tr>
<tr>
<td>Infant colic</td>
<td>17 (5.9%)</td>
<td>N/A</td>
</tr>
<tr>
<td>Any FGID</td>
<td>58 (20.3%)</td>
<td>50 (10.1%)</td>
</tr>
</tbody>
</table>

N/A: not applicable; FGID: functional gastrointestinal disorder

Conclusion: This community sample, collected in 3 European countries, demonstrated that FGIDs are common in young children. Prevalence of FGIDs tends to be higher in the first months of life. This study will further examine the relationship between early life events and FGIDs in young children.

Disclosure of interest: None declared.
**GASTROENTEROLOGY: Coeliac disease**

G-O-030

**Mode of delivery and risk of celiac disease in at-family-risk infants prospectively investigated from birth: the CELIPREV study**

Elena Lionetti\(^1\), Stefania Castellaneta\(^2\), Ruggiero Francavilla\(^3\), Alfredo Pulvirenti\(^4\), Alessio Fasano\(^5\), Carlo Catassi\(^6\)

\(^1\)University of Catania, Department of Pediatrics, Catania, Italy
\(^2\)San Paolo Hospital, Department of Pediatrics, Bari, Italy
\(^3\)University of Bari Aldo Moro/Department of Interdisciplinary Medicine, Bari, Italy
\(^4\)University of Catania, Department of Clinical and Molecular Biomedicine, Catania, Italy
\(^5\)Massgeneral Hospital for Children and the Celiac Program, Division of Pediatric Gastroenterology and Nutrition and Center for Celiac Research, Boston, United States
\(^6\)Marche Polytechnic University, Department of Pediatrics, Ancona, Italy

**Objectives and study:** The relationship between the risk of celiac disease (CD) and the mode of delivery is unclear. To determine whether the mode of delivery is associated with the risk of CD in genetically predisposed children within the Risk of CD and Age at Gluten Introduction (CELIPREV) trial.

**Methods:** We recorded information by telephone interview on the mode of delivery of children participating the CELIPREV, a multicenter, prospective intervention trial that compared early and delayed introduction of gluten in infants with a familial risk of CD. 832 newborns with a first-degree relative with CD were enrolled. The HLA genotype was determined at 15 months of age, and serologic screening for CD was evaluated at 15, 24, and 36 months and at 5, 8, and 10 years. Patients with positive serologic findings underwent intestinal biopsies. The final study group included 553 children who were positive for HLA-DQ2, HLA-DQ8, or both. The primary outcome of the current study was the prevalence of CD autoimmunity and overt CD among the children at 5 years of age according to the mode of delivery. Secondary outcome was the interplay between the mode of delivery and nutritional and genetic variables studied (breast-feeding, age at gluten introduction, genotype, gender, CD-affected first-degree relative, intestinal infections) in influencing the risk of CD.

**Results:** We obtained data on the mode of delivery from 431 children of the 553 with a standard-risk or high-risk-HLA genotype. At 5 years of age, there was no difference between children born by cesarean or vaginal delivery for autoimmunity (24% and 19%, P=0.2) or overt disease (19% and 14%, P=0.2). None of the variables studied was associated with the development of CD, with the exception of HLA genotype: the risk of CD autoimmunity was higher among children with high-risk HLA than among those with standard-risk HLA (42% vs. 19%, P<0.001), as was the risk of overt CD (29% vs. 15%, P=0.02).

**Conclusion:** The mode of delivery did not modify the risk of CD. The HLA genotype is the only known risk factor for CD development.

**Disclosure of interest:** Elena Lionetti has conflict of interest with Heinz Italy, s.p.a. Carlo Catassi has conflict of interest with Heinz Italy s.p.a, Dr Shaer, and Menarini Diagnostics.
GASTROENTEROLOGY: Coeliac disease

G-O-031

Accuracy of three commercially available point-of-care tests in monitoring celiac disease

Sabine Vriezinga¹, Bram van der Geest¹, Kristel van Roessel¹, Anneloes Boers¹, Hein Putter², Edmond Rings³, Rama Wahab¹, Luisa Mearin¹

¹Leiden University Medical Center, Pediatrics, Leiden, Netherlands
²Leiden University Medical Center, Medical Statistics, Leiden, Netherlands
³Leiden University Medical Center and Sophia Children’s Hospital Erasmus University Medical Centre, Pediatrics, Leiden and Rotterdam, Netherlands

Objectives and study: To evaluate and compare 3 different commercially available point-of-care (POC) tests for anti-tissue transglutaminase (TG2A) in children with treated celiac disease (CD) against results of conventional TG2A at the laboratory with ELISA.

Methods: Cross-sectional study, evaluating 3 different POC tests (X, Y and Z*) on 142 blood samples from IgA competent CD patients aged ≤18 years, attending the paediatric gastroenterology outpatient clinic of Leiden University Medical Center, the Netherlands. Results were evaluated blinded to the outcome of conventional TG2A assessment (EliA™ Celikey™ IgA test) 10 and 30 minutes and 1 day after performing the test (T10, T30 and T1d respectively). Sensitivity and specificity with 95% confidence intervals (CI) were calculated, as well as negative and positive predictive value. Performance of tests was acceptable if the sensitivity was ≥90%.

Results: Serum TG2A was positive in 47/142 samples. Test Y test had a greater sensitivity than the other 2 evaluated tests (89% [95% CI 0.81-0.98] versus test X: 34% [95% CI 0.20-0.48] and Z: 55% [95% CI 0.41-0.70]), and its sensitivity was 96% [95% CI 0.90-1.0] when results were read 1 day after the test was carried out. Prolonging the reading time from T10 to T30 significantly improved the performance of tests X and Z in case of positive serum TG2A (sensitivity test X 62% [95% CI 0.48-0.76], p<0.001; and test Z 70% [95% CI 0.57-0.83], p=0.016) but for test Z this was associated with a drop in specificity.

Conclusion: The studied POC tests have different sensitivities for the relatively low positive TG2A in treated coeliac disease patients. Performance of the tests may improve when reading time is prolonged. For implementation of POC tests in the follow-up of treated CD patients we recommend to use tests that have been validated in this specific group of patients.

Disclosure of interest: None Declared.

* X = BIOCARD™, Celiac Test for IgA TG2A (Ani biotech Oy, Vantaa, Finland); Y = BIOHIT, Celiac quick test for IgA, IgG and IgM TG2A (Biohit Oyj, Helsinki, Finland); Z = Eurospital, Xeliac Test Professional for IgA and IgG TG2A (Eurospital SpA, Trieste, Italy).
Degradation of immunogenic gluten epitopes from wheat by sourdough lactobacilli.

Roberta Moretti¹, Gloria Raimondi², Giorgia Borrelli², Flavia Indrio¹, Fernanda Cristofori³, Ruggiero Francavilla¹, Marco Gobetti⁴, Maria De Angelis⁵

¹Dipartimento Interdisciplinare DI Medicina, Sezione DI Pediatria. Università DI Bari, Italy
²Scuola DI Specializzazione in Pediatria. Università DI Bari, Italy
³Uoc Pediatria. P.O. Centrale Santissima Annunziata Taranto. Bari, Italy
⁴Department of Soil; Plant and Food Sciences; Università DI Bari, Italy

Objectives and study: Celiac disease is an immune-mediated enteropathy driven by ingested gluten and the intestinal damage is mediated by immune response (IFNγ, IL-2, IL-10). To assess if a pool of lactobacilli is able to hydrolyze gluten in an environment that simulates the gastrointestinal digestion.

Methods: 10 probiotic strains were studied (L. casei BGP93, L. bulgaricus SP5, L. paracasei BGP1; BGP12, L. plantarum BG112; BGP12; LP35; LP40; LP47, L. rhamnosus SP1). Gliadin extracted from wheat were hydrolyzed by pepsin and trypsin to simulate in vivo digestion and mixed with the probiotics. PT-digest of T. aestivum was the positive control. The proteolytic activity of lactobacilli was monitored through chromatographic techniques, mass spectrometry and immunological assays (R5-ELISA). Intestinal biopsies of celiac patients on gluten-free diet were obtained and cultured with PT-digest detoxified with lactobacilli. IFNγ, IL-2 and IL-10 genes were amplified by real time PCR and their expression evaluated by the T-test. Biopsies cultured with RPMI-1640 medium alone were used as negative control.

Results: The probiotic pool were able to: a) decrease the gluten content (from 1,220,000 ppm to 10,582 ppm; p<0.001) and to b) suppress the production of IFNγ that showed a tissue concentration similar to that of the negative control (16.4 pg/ml vs. 23.7 pg/ml; p=NS).

Conclusion: Our data shows that a mixture of probiotic strains is able to decrease the gluten content of wheat and to decrease the gluten mediated production of inflammatory cytokines.

Disclosure of interest: Roberta Moretti, None Declared; Gloria Raimondi, None Declared; Giorgia Borrelli, None Declared; Flavia Indrio, None Declared; Fernanda Cristofori, None Declared; Ruggiero Francavilla, None Declared; Marco Gobetti, None Declared; Maria De Angelis, None Declared.
Role of the gluten-free diet on neurological-EEG findings and sleep disordered breathing in children with celiac disease

Chiara Maria Trovato¹, Pasquale Parisi², Monica Montuori¹, Caterina Anania¹, Alessandro Ferretti², Maria Arena², Francesco Valitutti¹, Salvatore Cucchiara¹, Maria Pia Villa²

¹Sapienza-University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
²Sapienza-University of Rome, Pediatrics, Rome, Italy

Objectives and study: Celiac disease (CD) is a systemic disorder affecting many systems, among which the nervous system. In 2013, Diaconu et al. studied the incidence of neurologic manifestations in children with CD, showing that one-third of children presented one or more neurologic symptoms as the onset manifestation of CD. Status epilepticus and encephalopathy in the absence of profound GI symptom can be a symptom of a celiac crisis. A meta-analysis of the few evidence-based data available on these disorders in children showed that the relative risk of epilepsy in individuals with CD, and of CD in individuals with epilepsy, compared with the general population, was 2.1 and 1.7, respectively. In the vast majority of these patients, wakefulness EEGs revealed focal abnormalities, mainly localized in one or both occipital regions. To assess whether celiac children are at risk for EEG- and sleep disordered breathing (SDB), and whether an appropriate gluten-free diet (GFD) may influence these disorders.

Methods: We consecutively enrolled 22 children (18 females and 5 males, mean age at diagnosis 9.51 ± 4.17 DS years, range 3–16 years) with a new biopsy-proven celiac disease (CD) diagnosis. At CD diagnosis and after 6 months of GFD, each patient underwent a general and neurological examination, an electroencephalogram, a questionnaire investigating neurological features, and a validated questionnaire about SDB: OSA (obstructive sleep apnea) scores < 0 predict normality; values > 0 predict OSA.

Results: At CD diagnosis, 8 of 22 (36.4%) patients complained headache and 3 of 22 had presented febrile seizures. 21 children filled OSAS test (mean OSAS score: 3.4 ± 2.1 DS). Abnormal EEG findings were observed in 11 of 22 (50%) children. The EEG examinations revealed abnormal finding, such as focal or generalized sharps and/or spikes and spike-waves, in 11 children (50%). 1 child had abnormal finding in frontal region, 3 in occipital region, 2 in parietal region and 5 children showed diffuse aberration. (Table1). After 6 months of GFD, we analyzed data of 9 children: headache disappeared in 72% of children and EEG abnormalities in 78%; all children showed negative OSA score.

Table:

<table>
<thead>
<tr>
<th>Age at CD diagnosis</th>
<th>EEG abnormalities (cerebral regions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 7,42</td>
<td>Frontal</td>
</tr>
<tr>
<td>2 10,33</td>
<td>Occipital</td>
</tr>
<tr>
<td>3 14,16</td>
<td>Diffuse</td>
</tr>
<tr>
<td>4 3,16</td>
<td>Diffuse</td>
</tr>
<tr>
<td>5 16,16</td>
<td>Diffuse</td>
</tr>
<tr>
<td>6 8,67</td>
<td>Diffuse</td>
</tr>
<tr>
<td>7 9,75</td>
<td>Occipital</td>
</tr>
</tbody>
</table>
Table 1: description of cases including age at diagnosis and location of cerebral aberration.

**Conclusion:** According to our preliminary data, in the presence of unexplained EEG abnormalities and/or other neurological disorders/SDB in newly diagnosed CD diagnosis, is likely to be disease-related and respond to GFD over 6-month time.

**Disclosure of interest:** No conflict of interest
Presence of gluten immunogenic peptides in the urine of celiac patients: A novel method to monitor Gluten Free Diet

Maria de Lourdes Moreno¹, Ángel Cebolla², Alba Muños-Suano², Carolina Carrillo³, Isabel Comino¹, Ángeles Pizarro³, Francisco León⁴, Alfonso Rodriguez-Herrera⁵, Carolina Sousa¹

¹Faculty of Pharmacy, Microbiology and Parasitology, Seville, Spain  
²Biomedal S.L., Seville, Spain  
³Hospital Universitario Virgen del Rocío, Unidad Clínica de Aparato Digestivo, Seville, Spain  
⁴Celimmune, Bethesda, United States  
⁵Instituto Hispalense de Pediatria, Unidad de Gastroenterología Y Nutrición, Sevilla, Spain

Objectives and study: Available methods to assess GFD compliance are insufficiently sensitive to detect occasional dietary transgressions that may cause gut mucosal damage. We aimed to develop a method to determine gluten intake by detection of gluten immunogenic peptides (GIP) and evaluate its correlation with mucosal damage in order to monitor GFD compliance in patients with CD.

Methods: Urine samples of 76 healthy subjects and 58 patients with CD subjected to different gluten dietary conditions were collected. A total of 69 adults (>16 years of age) and 65 children were included. A lateral flow test (LFT) with the highly sensitive and specific G12 monoclonal antibody for the most dominant GIP and a LFT reader were used to quantify GIP in solid-phase extracted urines. For the adult arm of the study an intestinal endoscopic biopsy was taken to match with urine sampling.

Results: We detected the presence of GIP in concentrated urines from healthy individuals subjected to different dietary conditions as early as 4-6 h after single gluten intake, and remained detectable for 1-2 days. The sensitivity of the assay was high, with detection of consumption of as little as >25 mg of gluten in processed bread. The urine assay revealed infringement of the GFD in about 50% of the patients. Analysis of duodenal biopsies of adult with CD revealed that most of them (89%) with no villous atrophy had no detectable GIP in urine, while all patients with quantifiable GIP in urine showed incomplete mucosal healing.

Conclusion: GIP are detected in urine after gluten consumption, enabling a new and non-invasive method to monitor GFD compliance and transgressions. The method was sensitive, specific and simple enough to be convenient for clinical monitoring of patients with CD as well as for basic and clinical research applications including drug development.

Disclosure of interest: AC and FL own stock in Biomedal SL. Other authors have declared no conflict of interest. The method of this manuscript was included in a patent application by MLM, CS, AR-H and AC as inventors with the assigned number P201400569.
**GASTROENTEROLOGY: Coeliac disease**

G-O-035

**Serum hepcidin levels are not increased in anemic children with celiac disease**

Elzbieta Jarocka-Cyrta\(^1\), Monika Kowalczyk-Kryston\(^2\), Miroslawa Uscinowicz\(^2\)

\(^1\)University of Warmia and Masuria, Department of Pediatrics, Gastroenterology and Nutrition, Olsztyn, Poland
\(^2\)Medical University of Bialystok, Department of Pediatrics, Gastroenterology and Allergology, Bialystok, Poland

**Objectives and study:** Anemia is a common extraintestinal manifestation of celiac disease (CD), but its exact mechanisms are unknown. A central player in iron homeostasis is hepcidin, synthesized as a prohormone (prohepcidin). Hepcidin decreases iron gut absorption and controls its tissue distribution in response to iron stores, erythropoietic demand and inflammation. Increased hepcidin production is an established cause of anemia in chronic inflammatory disorders, with IL-6 playing a key role in this upregulation. Previous studies suggest that the etiology of anemia in CD is multifactorial and chronic inflammation of the small intestine may be one of the causes.

**Aim:** The aim of this study was to evaluate hepcidin and prohepcidin plasma levels in anemic and non-anemic children with CD.

**Methods:** The study included 138 consecutive children with newly diagnosed CD according to ESPGHAN criteria, treated in one academic center. The median age was 9.75 years, (range: 1.5-17), 32% were girls. Patients were divided into two groups: anemic (ACD) and non-anemic (NACD), according to WHO criteria. The control group (CG) consisted of 50 children (median age 12.1, range 9.08-14.67, 25 girls) with functional gastrointestinal disorders, in whom CD and anemia were excluded. Patients with infections, chronic inflammatory disorders or treated with iron or red blood cell transfusion within 6 months prior to study were excluded. For each patient, hematology parameters and serum biomarkers were measured including high-sensitive C-reactive protein (hs-CRP), ferritin and IL-6. Serum hepcidin and prohepcidin levels were assessed using a commercially available ELISA kit (Peninsula Lab, USA and DRG, Germany).

**Results:** Anemia was diagnosed in 32 patients (23%), at a median age of 10.43 year, more commonly in girls (23 girls). The ACD and NACD groups did not differ with respect to age and BMI. ACD patients compared to NACD had significantly lower Hb levels (p=0.0001), ferritin (p=0.0009), MCV (p=0.0001), Tsat (0.0001) and increased platelet count (p=0.0104). Interestingly, NACD showed significantly lower hematology parameters compared to CG: Hb (p=0.0369), MCV (p=0.0004), erythrocytes (p=0.0001), platelet count (p=0.0014) and ferrityn (p=0.0006). IL-6 and hs-CRP concentrations were similar in ACD, NACD and CG. No significant differences in serum hepcidin levels were found between ACD and NACD patients (p=0.88) and between both CD groups and controls (ACD vs CG p=0.88, NACD vs CG p=0.659). Hepcidin levels did not correlate with age, sex, prohepcidin levels or any of the examined inflammatory or hematologic parameters. Serum prohepcidin levels were similar in the three studied groups.

**Conclusion:** Our study demonstrates for the first time that anemia in celiac disease is not accompanied by increased serum levels of hepcidin. These findings suggest that anemia in celiac disease does not directly result from chronic inflammation.

**Disclosure of interest:** None Declared.
The role of Myo5B and Syntaxin 3 in cargo-selective apical exocytosis in Microvillus Inclusion Disease

Georg-Friedrich Vogel¹, Katharina MC Klee², Andreas Robert Janecke¹, Thomas Müller¹, Michael WHess³, Lukas A Huber⁴

¹Medical University Innsbruck, Paediatrics I, Innsbruck, Austria
²Medical University Innsbruck, Division of Cell Biology, Innsbruck, Austria
³Medical University Innsbruck, Division of Histology and Embryology, Innsbruck, Austria

Objectives and study: Microvillus inclusion disease (MVID) is a rare, fatal autosomal recessive enteropathy. This life-threatening, severe watery diarrhea is due to a disrupted brush border of enterocytes of the small intestine. The ultrastructure of patients’ enterocytes displays loss or immature formation of microvilli and the occurrence of so-called microvillus inclusions. Recently mutations in the MYO5B and STX3 gene, coding for the actin motor protein Myo5B and the apical target SNARE protein Syntaxin 3, respectively, have been shown to be causal for the observed clinical phenotype [1,2,3]. Myo5B is involved in important intracellular trafficking pathways. Myo5B, together with the small Rab GTPases Rab8a, Rab11a and Rab25, orchestrates recycling and transcytosis of membrane proteins and is crucial for correct polarization of epithelial cells (e.g. enterocytes).

Methods: Myo5B and Syntaxin 3 were deleted by genome-editing in polarized CaCo2 cells as enterocyte model, in order to analyze their role in the establishment of epithelial polarity and apical cargo transport.

Results: The loss of Myo5b or Syntaxin 3 disrupts enterocyte polarity, recapitulating the phenotype of MVID in-vitro. Biochemical analysis of SNARE couplings revealed a specific apical cargo trafficking route depending on Myo5B, Synaptotagmin-like protein 4a, Munc18-2, Vamp7 and Syntaxin 3. This route, furthermore, proofed to be cargo-specific as some apical cargo proteins (e.g. NHE3, GLUT5 and CFTR) mislocalised whereas others (e.g. DPPIV, SI and AminopeptidaseN) still properly localized at the apical plasma membrane [4].

Conclusion: Together, these findings outline the role of Myo5B and Syntaxin 3 in cargo-selective apical exocytosis and shed new light on the pathophysiology of MVID.

Acknowledgements: The Austrian Research Funds (FWF) within the MCBO program supported this work.

References:

Disclosure of Interest: None declared.
Effectiveness of double-balloon enteroscopy-facilitated polypectomy in paediatric patients with Peutz-Jeghers syndrome

Dalia Belsha¹, Arun Urs¹, Mike Thomson¹

¹Sheffield Children's Hospital NHS Foundation Trust, Sheffield, United Kingdom

Objectives and study: Sizable small-bowel (SB) polyps in Peutz-Jeghers syndrome (PJS) pose a high risk for intussusception, often necessitating laparotomy and intraoperative-enteroscopy (IOE). Our aim is to examine the effectiveness of double-balloon enteroscopy (DBE) facilitated polypectomy as an alternative therapeutic option for pediatric patients with PJS.

Methods: Prospective analysis of collected data (6 years) on all patients with PJS referred for DBE-facilitated SB polypectomy at a pediatric tertiary-referral center in the UK.

Results: Between August 2009 to June 2015, 14 patients with PJS (8 males, median age thirteen and a half years; range: 8-16 years) were referred for SB polypectomy by DBE (Figure 3). All patients had at least 1 pre-DBE evaluation by SBCE or diagnostic imaging or both. Four (26%) patients had a history of SB surgery following intussusception. A total of 21 DBE procedures were performed with the number of procedures required per patient ranging from 1 (n=8) to 3 (n=1). Five patients required 2 procedures each. 11 DBE procedures were performed via the oral route and anal route, 10 via the oral route only. Estimated mean depth of insertion was 239(120-420) cm post-pylorus and 69(50-140) cm proximal to the ileo-cecal valve for oral and rectal procedures, respectively. In two patients, pan-enteroscopy was confirmed by visualization of the ileo-cecal valve via the trans-oral route. Mean duration for DBE via the oral and anal routes was 82(range 45-240) minutes and 57(30-70) minutes respectively.

The aim at DBE was to attempt polypectomy of all significant polyps found (as detected by SBCE and/or SB radiology) in all patients. One patient did not undergo polypectomy at DBE as the polyps were considered non-significant due to likely overestimation of size at SBCE. Therefore 13 patients were considered suitable for DBE-facilitated polypectomy. Of these, 10/13 patients (77%) underwent successful polypectomy by DBE alone or else (13%) by Lap-DBE facilitated polypectomy (n=3; patients 1, 2, 12) for large, sessile duodenal polyps that were deemed high-risk for polypectomy by DBE alone. On average, 3(range 1-7) polypectomies per patient were performed. A total of 43 polyps were resected; the majority of them were pedunculated (86%) while the remainder, were semi-pedunculated or sessile. The median diameter of excised polyps was 22mm (range: 10-45mm). Distribution: 14% were duodenal in origin; 69% of polyps were located within the jejunum; and 14% were located within the ileum. The histopathology of all retrieved polyps confirmed their hamartomatous nature.

The only complication identified in the series, occurred in a patient after successful polyp clearance by Lap-DBE (patient 1) who suffered a pelvic abscess related to an infected laparoscopy-port wound which responded well to conservative management and drainage.

At a median follow-up period of 26 months (range: 1-60 months) all patients remain well and have not required further intervention having undergone 2-3 year surveillance by SBCE and/or MRE. During that period, 6 patients had repeated DBE for further polyp.

Conclusion: This series demonstrates that DBE-facilitated polypectomy is an effective alternative to IOE in selected pediatric patients with PJS. DBE offers a less invasive approach and should be considered as an alternative therapeutic option at an early age where possible.

Disclosure of interest: None Declared.
The role of anatomic anomalies of pancreatic duct in pediatric chronic pancreatitis

Grzegorz Oracz¹, Karolina Wejnarska¹, Elwira Kolodziejczyk¹, Jaroslaw Kierkus¹, Jozef Ryzko¹

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: The etiology of chronic pancreatitis (CP) in children is varied and includes gene mutations, anatomic anomalies (AA), metabolic disorders and others. The reported pediatric experience with CP is small and the role of AA of pancreatic duct is not well elucidated. The aim of this study was to evaluate the role of anatomic anomalies of pancreatic duct as a cause of chronic pancreatitis in children.

Methods: 292 children with CP, hospitalized since 1988 to 2015, were enrolled to the study. The medical records of these patients were reviewed for etiological factors, data on the presentation, diagnostic findings and endoscopic treatment.

Results: Anatomic anomalies were found in 47 patients (16.1%) (25 girls and 22 boys; mean age 9.5 years, range: 2.5-17 years). We detected pancreas divisum in 32 patients (11%), ansa pancreatica in 8 patients (2.7%), anomalous pancreaticobiliary union (APBU) in 4 patients (1.4%). Three patients had other rare anomalies of pancreatic duct (1%). In 15 patients (47%) with pancreas divisum we found gene mutations (SPINK1-7 pts [2 homozygous]; CFTR-5 pts; PRSS1-3 pts; CTRC-2 pts; CPA1-1 pt). Five patients (62.5%) with ansa pancreatica had gene mutations (SPINK1-3 pts [1 homozygous]; CFTR-1 pt; PRSS1-1 pt). Three patients (75%) with APBU had gene mutations (SPINK1-1 pt; CFTR-2 pts). Two children with other rare AA (66%) had gene mutations (1-SPINK1 homozygous; 1-CTRC).

Sphincterotomy of papilla minor was done in 30 children (94%) with pancreas divisum, whereas pancreatic duct stenting via papilla minor was done in 21 patients (66%). Surgery was performed in 8 children (17%) with AA of pancreatic duct.

Conclusion:
1. In the pediatric CP pancreas divisum is more frequent than in population.
2. We should be aware of coexisting AA of pancreatic duct and other etiological factors of CP, as gene mutations.
3. Endoscopic therapeutic procedures are often performed in patients with CP and pancreas divisum.

Disclosure of interest: None Declared.
Nasogastric or nasojejunal tube feeding in pediatric acute pancreatitis: a clinical, randomized pilot study

Jingan Lou¹, Hong Zhao¹, Jindan Yu¹, Youyou Luo¹, Feibo Chen¹, Jie Chen¹
¹Children’s Hospital Zhejiang University School of Medicine, Gastroenterology, Hangzhou, China

Objectives and study: Recent clinical studies have shown that nasogastric tube feeding is safe in the majority of adult patients with acute pancreatitis. But the safety and efficiency of nasogastric tube feeding in pediatric acute pancreatitis has not been investigated. This study aims to compare the safety and efficiency between nasogastric feeding and nasojejunal feeding in children with acute pancreatitis.

Methods: The study design was a randomized controlled trial. Children with acute pancreatitis were fed via NG (candidate) or NJ (comparative) route within 72 hours after admission. The primary outcome was tolerance of enteral nutrition support. Secondary end points were duration of hospital stay, duration of tube feeding, occurrence of any complication (tube-associated, infections, feeding-associated).

Results: A total of 33 children with acute pancreatitis were recruited into this study and were randomized to NG group (16) or NJ group (17). Age, gender, pediatric acute pancreatitis scores, CTSI scores and gastrointestinal symptoms or abdominal pain did not significantly differ between the two groups. 81% (13/16) of NG group and 94% (16/17) of NJ group can tolerate with tube feeding (P>0.05). The duration of hospital stay was 18.9±4.7 d for NG group and 18.3±6.3 d for NJ group. For duration of tube feeding were 16.8±7.4 d and 15.8±4.4 d separately. One children of NJ group has tube-associated complication. 5 patients of NJ group and 2 of NG group have feeding-associated complications such as diarrhea, vomit and abdominal pain. None of all patients has complication of any infection.

Conclusion: NG tube feeding appears effective and safe for acute pediatric pancreatitis comparing with NJ tube feeding. Before recommendation to clinical practice, further high qualified, large scale, randomized controlled trials are needed.

Disclosure of interest: None Declared.
Helicobacter pylori infection in children with Coeliac disease.

Nevzat Aykut Bayrak¹, Engin Tutar², Burcu Volkan³, Esra Polat⁴, Gunsel Kutluk⁴, Birol Öztürk², Deniz Ertem²

¹Diyarbakır Children's Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
²Marmara University School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
³Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
⁴Kanuni 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.

Methods: Children who underwent endoscopy between January 2012 and December 2015 in four pediatric gastroenterology centers were included in the study. The presence of Hp infection was confirmed by both histopathology and the rapid urease test. 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 2396 endoscopies performed in the study period, 1840 cases were eligible for the study. A total of 374 CD patients (mean age: 9.54±4.5 years, 57.2% girls) and 1466 controls (mean age: 9.84±4.7 years, 54% girls) were included into the study. Hp infection rate was significantly lower in CD group (29.1% vs 48.2%, χ²: 43.6, OR: 2.25 95% CI: 1.76-2.88, p<0.01). There was no correlation between Hp infection and modified Marsh scores in CD patients (r²: -0.082, 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, compared to the controls. Hp infection might have a protective role in the development of CD.

Disclosure of interest: None Declared
First report of a lethal infantile autosomal recessive ITGB6V343M disorder correlating with impaired integrin αVβ6 receptor dimerization in intestinal epithelia

Rhea Willems¹, Patrick Philipp Weil¹, Thomas Ziegenhals², Stefan Juranek², Philipp Schreiner², Daniel Dödde¹, Silvia Vogel¹, Daniel Pembaur¹, Meike Röper¹, Wirth Stefan¹, Andreas Jenke³, Jan Postberg⁴

¹Helios Medical Centre Wuppertal, Witten/Herdecke University Hospital, Wuppertal, Germany
²University of Würzburg, Germany
³Evangelisches Krankenhaus Oberhausen, Germany
⁴Helios Medical Centre Wuppertal, Witten/Herdecke University Hospital, Paediatrics Research, Wuppertal, Germany

Objectives and study: We report on a patient with undiagnosed intractable diarrhea in whose family tree several comparable cases occurred. By means of whole exome sequencing we identified an autosomal recessive nonsynonymous single nucleotide polymorphism (SNP) in the integrin beta-6 gene (ITGB6G1312A) as the most feasible causative mutation. Due to structural simulations we hypothesize that the resulting amino acid substitution (ITGB6V438M) leads to impaired receptor dimerization. Our goal is to test our hypothesis and to elucidate the biological consequences of ITGB6V438M on the αVβ6 integrin receptor function and its relevance for a pathomechanism. Since a connection between αVβ6 and wound healing was proposed, it seems plausible that loss of ITGB6 function might affect tissue differentiation in the fetus as well as wound healing in chronically inflamed epithelia.

Methods: To test we performed pedigree analyses and genotyping by pyrosequencing on further family members. Structural consequences of ITGB6V438M were assessed using Swiss PDB viewer and 4U8M. The distribution of αVβ6 and ITGB6 was compared between the patient's gut epithelia and matched controls. We are currently performing biophysical measurements of ITGAV/ITGB6 dimerization (leading to the αVβ6 receptor) using recombinant wt and mutated proteins. A role of ITGB6 in wound healing and consequences of ITGB6V438M are currently being tested in zebra fish.

Results: Pedigree analyses revealed that 5 out of 16 (31.25%) infants died earlier than 9 months after birth. We identified heterozygous carriers of ITGB6G1312A and homozygous wildtypes in symptomless individuals of the family. Immunohistochemistry revealed that equal levels of ITGB6 can be detected between the affected patient and controls, but less dimeric αVβ6 could be detected in the gut epithelia of the index patient.

Conclusion: Current results suggest that ITGB6V438M can indeed lead to impaired αVβ6 dimerization. Our ongoing studies will elucidate more molecular details with respect to this previously unknown SNP in the etiological context of intractable diarrhea.

Disclosure of interest: None declared
GASTROENTEROLOGY: Coeliac disease

Use of vitamin D, omega-3 fatty acids, and iron supplements during pregnancy is not associated with the risk of celiac disease in offspring: the TEDDY Study

Jimin Yang1, Roy Tamura1, Ulla Uusitalo1, Carin Andrén Aronsson2, Åke Lernmark2, Marian Rewers3, William Hagopian4, Jin-Xiong She5, Olli Simell6, Jorma Toppari7, Anette G. Ziegler8, Beena Akolkar9, Jeffrey Krischer1, Jill M. Norris10, Suvi M. Virtanen11, Daniel Agardh2

1Health Informatics Institute, Morsani College of Medicine, University of South Florida, Tampa, United States
2Department of Clinical Sciences, Lund University, Malmö, Sweden
3Barbara Davis Center for Childhood Diabetes, University of Colorado School of Medicine, Aurora, United States
4Pacific Northwest Diabetes Research Institute, Seattle, United States
5Medical College of Georgia, Georgia Regents University, Augusta, United States
6Department of Pediatrics, University of Turku and Turku University Hospital, Turku, Finland
7Department of Pediatrics, University of Turku and Turku University Hospital; Department of Physiology, Institute of Biomedicine, Turku, Finland
8Institute of Diabetes Research, Helmholtz Zentrum München and Forschergruppe Diabetes, Klinikum Rechts der Isar, Technische Universität München and Forschergruppe Diabetes e.V, Munich, Germany
9National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, United States
10Department of Epidemiology, University of Colorado Denver, Colorado School of Public Health, Aurora, United States
11National Institute for Health and Welfare; School of Health Sciences and Center for Child Health Research, University of Tampere and Tampere University Hospital, Helsinki; Tampere, Finland

Objectives and study: Environmental factors besides gluten exposure have been postulated to influence the risk of developing celiac disease (CD) among individuals with genetic predisposition. Few data exist regarding maternal exposures during pregnancy and the risk of CD in offspring. This study aimed to investigate the association between maternal intake of vitamin D, omega-3 fatty acids (n-3 FAs), and iron supplements during pregnancy and risk of developing celiac disease autoimmunity (CDA) and CD in the offspring.

Methods: Children carrying HLA genotypes associated with increased risk for type1 diabetes and CD are followed from birth in Finland, Germany, Sweden and the US in the prospective The Environmental Determinants of Diabetes in The Young (TEDDY) Study. Participants who had persistently positive tissue transglutaminase autoantibodies (tTGA) on two consecutive visits were defined as having CDA and were further evaluated for CD. Diagnosis of CD was defined as having a biopsy showing a Marsh score >1 or having high tTGA levels >100 U/mL if a biopsy was not performed. The duration and frequency/dose of vitamin D, n-3 FAs, and iron supplements during pregnancy was recalled using a questionnaire at 3-4 months postpartum. Cumulative intakes of supplemental vitamin D and n-3 FAs were calculated, and the median intake of each type of supplements was used to create ordinal variables (1: no supplementation, 2:<median intake, 3:≥median intake) that were used in Cox proportional hazards models to calculate the hazard ratios.

Results: A total of 6608 participants were included in the analysis. CDA was confirmed in 1037 children at a median age of 3.1 years (range 0.9-9.0 years) and CD diagnosis was biopsy-confirmed in 381 children at a median age of 3.8 years (range 1.2-9.9 years). Across all participating countries, 38% of the mothers took iron supplements. Vitamin D supplements were used by 66% of the mothers at a median cumulative intake of 1400 mcg (IQR 1842 mcg). The n-3 FAs were taken by 17% of the mothers at a median cumulative intake of 60 g (IQR 57 g). Vitamin D intake (below and above median intake, HR=1.03, 95% CI 0.95, 1.13, p=0.45) or n-3 FAs intake (HR=0.93, 95% CI 0.83, 1.04, p=0.20) did not predict CDA, after adjusting for country, child’s HLA-genotype, sex, having a first degree relative (FDR) with CD, duration of breastfeeding, and household crowding. Similarly, the risk of CD was not associated with supplemental vitamin D (HR=1.06, 95% CI 0.92, 1.22, p=0.43) or n-3 FAs (HR
= 0.95, 95% CI 0.77, 1.16, p=0.61); neither after adjustment for country, child’s HLA genotype, sex, and celiac disease in FDR nor when the cumulative intakes were analysed as binary variables. The use of iron supplements did not show an association with the risk of CDA (HR = 0.93, 95% CI 0.81, 1.07, p=0.30) or CD (HR = 1.01, 95% CI 0.80, 1.26, p=0.96) after adjusting for the same aforementioned variables.

Conclusion: This study found no association of vitamin D or omega-3 fatty acids or iron supplementation during pregnancy and risk of developing CDA or CD in the offspring.

Disclosure of interest: None declared.
Gluten Free diet leads to an obesogenic life style

Eyal Shteyer, Neriya Levran, Jessica Livovsky, Edna Shachar, Michael Wilschanski

1Shaare Zedek Medical Center, Pediatric Gastroenterology Institute, Jerusalem, Israel
2Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Objectives and study: Initiation of life long gluten free diet in children with celiac disease (CD) influences the child’s life in many aspects. In addition to the psychological effects, several studies among children with CD reported a high prevalence of overweight and obesity. The effects of the diet on the child’s family were scarcely studied. The aim of this study was to assess the influence of GFD on the child and his/her family’s eating habits and lifestyle behaviors.

Methods: Children and their parents filled out the Family Eating and Activity Habits Questionnaire (FEAHQ) at the time of diagnosis of CD and at least 5 months after initiation of GFD. The FEAHQ assess physical activity, exposure to various food such snacks and candies, eating related to hunger and eating styles. In addition questions assessing symptoms related to CD and adherence to diet was also given.

Results: Forty families were studied; twenty females, aged from 4 to 15.7 years (median age 7.4 years± 2.8 years). All presenting symptoms of CD improved significantly after GFD. Most patients improved their height and weight z scores (64% and 62% respectively). Overweight and obesity slightly increase after GFD (7.5% and 10%). When assessing physical activity the patients had increased activity (p=0.04), whereas the parents showed decreased activity (p=0.4). After GFD the family ate more snacks and candies (p=0.05), with the significant change reported by the children and fathers (p=0.001 and 0.03 respectively). Finally, parents and patients reported increased in obesogenic eating styles (p values: mothers 0.001, fathers 0.02 and children 0.02).

Conclusion: Our study shows that initiation of GFD in children with CD leads to changes in eating habits and staple food eating that may lead to a more obesogenic environment. As obesity is increasing in the general population and in CD it is crucial for the gastroenterologist to be aware and of this side effect of GFD and to identify and educate families towards a more healthy life style and diet.

Disclosure of interest: None Declared
Industrial food additive microbial transglutaminase is immunogenic in children with celiac disease

Torsten Matthias¹, Patricia Jeremias¹, Sandra Neidhöfer¹, Aaron Lerner²
¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel

Objectives and study: Microbial transglutaminase (mTg) is capable of cross-linking numerous molecules. It is a family member of human tissue transglutaminase (tTg), involved in CD. Despite declarations of mTg safety, direct evidence for immunogenicity of the enzyme is lacking.

Methods: The serological activity of mTg, tTg, gliadin complexed mTg (mTg neo-epitope) and gliadin complexed tTg (tTg neo-epitope) were studied in: 95 pediatric celiac patients (CD), 99 normal children (NC) and 79 normal adults (NA). Sera were tested by ELISAs, detecting IgA, IgG or both IgA and IgG: AESKULISA® tTg (tTg), AESKULISA® tTg New Generation (tTg neo-epitope (tTg-neo)), microbial transglutaminase (mTg) and mTg neo-epitope (mTg-neo). Marsh criteria were used for the degree of intestinal injury.

Results: Comparing pediatric CD patients with the 2 normal groups: mTg-neo IgA, IgG and IgA+IgG antibody activities exceed the comparable mTg ones (p<0.0001). All mTg-neo and tTg-neo levels were higher (p<0.001). tTg IgA and IgG+IgA were higher than mTg IgA and IgA+IgG (p<0.0001). The levels of tTg-neo IgA/IgG were higher than tTg IgA/IgG (p<0.0001). The sequential antibody activities reflecting best the increased intestinal damage were: tTg-neo IgG ≥ mTg-neo IgG > mTg-neo IgA+IgG > tTg-neo IgA. Taken together, mTg-neo IgG and tTg-neo IgG correlated best with intestinal pathology (r²=0.989, r²=0.989, p<0.0001, p<0.0001, respectively).

Conclusions: mTg is immunogenic in children with CD and by complexing to gliadin its immunogenicity is enhanced. Anti-neo-epitope mTg antibodies correlate with intestinal damage to the same degree as anti-tTg. Further studies are needed to explore the pathogenic potential of anti-mTg antibodies in CD.

Disclosure of interest: TM is the head of Aesku.Kipp Institute. PJ, SN are employed by Aesku.Kipp Institute.
AL, “none declared”
Results of the ESPGHAN Endoscopy Training Survey

Ilse Broekaert¹, Jörg Jahnel², Marta Tavares³, Nicolette Moes⁴, Hubert van der Doef⁵, Christos Tzivinikos⁶

¹University of Cologne, Pediatrics, Cologne, Germany
²Medical University Graz, Austria
³University Hospital Porto, Portugal
⁴University Medical Center Groningen, Pghn, Groningen, Netherlands
⁵University Medical Center Groningen, Groningen Transplant Center, Dept. Pediatrics, Groningen, Netherlands
⁶Alder Hey Children’s Hospital, Paediatric Gastroenterolpogy, Liverpool, United Kingdom

Objectives and study: Endoscopy training is an essential part of pediatric gastroenterology, hepatology and nutrition (PGHN) fellowship as specified in the ESPGHAN training syllabus. The aim of this study was to evaluate the endoscopy training among fellows and young professionals in PGHN. The recently published ESPGHAN syllabus suggests a minimum of 100 esophagogastroduodenoscopies (EGDs) and 50 colonoscopies for certification (D’Antiga et al., 2014).

Methods: 84 PGHN fellows participated in an electronic survey called by ESPGHAN between 2/2014 and 9/2015. The survey comprised 32 questions on general information, number of endoscopies performed, specific endoscopic procedures, supervision and certification, and endoscopy training.

Results: Among 84 participants 28 (33 %) have already finished their training and 42 (50 %) are still in training. 53 fellows (63%) reported to be enrolled in an official PGHN fellowship program leading to a subspecialty certification. 32 (38 %) devote their entire time to PGHN training and 34 (40 %) between 50 and 99 % of their time. 66 PGHN fellows (79 %) are trained in endoscopy during their fellowship. Of all fellows, 29 (35 %) are trained by an adult gastroenterologist and 6 (7 %) by surgeons. 30 (36 %) follow the ESPGHAN syllabus.

Concerning the numbers of endoscopic procedures, PGHN fellows have completed 207 EGDs, 67 colonoscopies, 11 polypectomies, 10 variceal bandings and 20 PEG changes/ insertions on average. The terminal ileum is intubated in 29 % most of the time (>90 %).

63 fellows (75 %) enjoy continuous supervision, 65 fellows (77 %) keep an endoscopy logbook, and 28 (33 %) have formal assessments (paper or online) during and 47 (56 %) at the end of their training.

During their training 54 fellows (64 %) have attended basic skills endoscopy courses and 43 fellows (51%) have completed endoscopy simulator trainings. 79 fellows (94%) wish participation in future ESPGHAN endoscopy summer schools and 75 fellows (89%) would like to attend basic endoscopy skills courses. Fellows feel that their upper GI endoscopy training will allow practicing as consultant in 86 % and their colonoscopy training in 67 %. 59 fellows (70 %) would like ESPGHAN to be responsible for the accreditation of endoscopy centers.

Conclusion: This survey shows that endoscopy training differs among fellows in Europe regarding accomplished procedures, the training program including supervision and certification and specific endoscopy courses. Only 36% have followed the ESPGHAN training syllabus and only 86 %, respectively 67%, feel skilled enough to perform EGDs and colonoscopies when practicing as a consultant. We encourage all European GI centers to follow the ESPGHAN training syllabus to harmonize endoscopy training during PGHN fellowship throughout Europe, eventually leading to better endoscopy skills of young consultants.

Disclosure of interest: None Declared.
Self-administered telemedicine reduces number of outpatient visits and days of absence from school in paediatric and adolescent patients with inflammatory bowel disease

Katrine Carlsen¹, Christian Jakobsen¹, Lars Folmer Hansen¹, Anders Paerregaard¹, Lene Buhl Riis², Pia Susanne Munkholm³, Vibeke Weer¹

¹Hvidovre Hospital, Department of Paediatrics, Hvidovre, Denmark
²Herlev Hospital, Department of Pathology, Herlev, Denmark
³North Zealand Hospital, Department of Gastroenterology, Frederikssund, Denmark

Objectives and study: Paediatric patients with Inflammatory Bowel Disease (IBD) face a life of repeated hospitalizations and frequent outpatient visits, which may affect social activities and increase absence from school and potentially reduce educational possibilities. Our aim was to optimize care by a novel telemedicine application and thereby allocating the patients’ time and hospital resources to periods of active disease.

Methods: IBD patients 10-17 years were prospectively randomized to an open label case-control telemedicine intervention for 2 years with an inclusion period of 8 months. Patients in the telemedicine (web) group used the web-application young.constant-care.com in which the disease burden was estimated by a patient-reported symptom score and faecal calprotectin (FC). The IBD-care team monitored the patients by weekly web-rounds and beside one annual pre-planned visit, further outpatient visits were scheduled on demand in case of increased disease burden. The control group continued standard care by outpatient visit every third month including FC.

Results: 53 patients (32 ulcerative colitis (UC), 21 Crohn’s Disease (CD)) were included (27 web, 26 control); median duration of participations: web 86 weeks (IQR 36), control 92 weeks (IQR 20).

Adherence using the telemedicine program was 80 % (total 355 actual of 444 expected entries). Number of on demand outpatient visits in addition to the annual visit in the web group and the quarterly visits in the control group, showed no difference; mean web 1.6 (SEM 0.5 CI 95% 0.6;2.5) mean control 1.4 (SEM 0.4 CI 95% 0.6;2.1). Numbers of total outpatient visits were 74 (2.7 per patient) in the web and 172 (6.6 per patient) in the control group. This difference reflects a total outpatient-cost difference in Denmark of 10,022 Euro.

No difference was found in time to first on demand visit and time to step-up in treatment intensity. Numbers of hospitalizations in the web group were 1 (in total 5 days) versus 7 (in total 18 days distributed at 5 patients) in the control group (no significant difference). No differences were observed regarding extra doctor and nurse telephone call or nurse consultations.

Significant difference was observed in number of IBD related absence days from school between the web (mean 1.4 days per patient, SEM 0.5) and control group (mean 15.7 days per patient, SEM 4.5 P=0.002).

Conclusion: Telemedicine in children and adolescence with IBD reduces the number of needed outpatient visit and hospitalizations without increasing the risk of step-up in medical treatment. Furthermore, the web-group had significant lower IBD related absence days from school.

Disclosure of interest: None Declared
Risk of serious infection in pediatric inflammatory bowel disease: results from the DEVELOP registry

Johanna Escher1, William Faubion2, Robert Baldassano3, Richard Colletti4, Salvatore Cucchiara5, Marla Dubinsky6, John Felt7, Benjamin Gold8, Anne Griffiths9, Jeffrey Hyams10, Sibylle Koletzko11, Subra Kugathasan12, James Markowitz13, Frank Ruemmele14, Gigi Veereman15, Harland Winter16, Yanli Wang17, Nicholas Masel18, Kezhan Tang19, Meena Thayu19

1 Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands
2 Mayo Clinic, Rochester, United States
3 The Children's Hospital of Philadelphia, Philadelphia, United States
4 University of Vermont Children's Hospital, Burlington, United States
5 Sapienza University of Rome/University Hospital, Rome, Italy
6 The Icahn School of Medicine at Mount Sinai, New York, United States
7 Chelsea and Westminster Hospital, London, United Kingdom
8 Children's Center for Digestive Health Care, LLC, Atlanta, United States
9 Hospital for Sick Children, Toronto, Canada
10 Connecticut Children's Medical Center, Hartford, United States
11 Ludwig Maximilians University of Munich, Munich, Germany
12 Emory University, Atlanta, United States
13 Cohen Children's Medical Center of New York, New York, United States
14 Necker Children's Hospital, Paris, France
15 University Hospital, Brussels, Belgium
16 Massgeneral Hospital for Children, Boston, United States
17 Advanced Technology Solutions, Inc, Oakhurst, United States
18 Docs, Durham, United States
19 Janssen Scientific Affairs, LLC, Horsham, United States

Objectives and study: Immunosuppressive therapy for pediatric inflammatory bowel disease (IBD) is associated with an increased risk of serious infections (SI), including serious opportunistic infections (SOI). The objectives of this study in pediatric IBD were: (1) to compare the incidence of SI and SOI in patients exposed to infliximab (IFX) vs. those unexposed to biologics, and (2) to identify risk factors for the development of SI.

Methods: DEVELOP is an ongoing global, multicenter prospective study of long-term clinical outcomes in pediatric IBD. Patients were categorized into three exposure cohorts: IFX (IFX as only biologic ± non-biologics), biologics (any biologic, including IFX, ± non-biologics), and non-biologics [non-biologics, including 5-aminosalicylates, corticosteroids (CS), and immunomodulators (IMM, thiopurines and methotrexate) in the absence of biologics]. Unadjusted incidence rates (IR) for all SI and SOI as well those within 91 days of biologic exposure were reported as events/100 pt-yrs (PY). Multivariate Cox proportional-hazards regression analyses evaluated risk factors for time to first SI by estimating hazard ratios (HR) with 95% confidence intervals (CI).

Results: Between 31 May 2007 and 30 June 2015, 5,402 patients [median age 13 y, IQ range 10-15 y; median follow-up (F/U) 3.9 y] have been enrolled. Unadjusted analyses (Table 1) showed a significantly increased cumulative incidence (events/100 PY; 95% CI) in the IFX cohort vs the non-biologics cohort of SI (4.06; 3.65,4.49) vs (2.25; 1.92,2.61) but not for SOI (0.35; 0.24,0.50) vs. (0.20; 0.11,0.32). Within 91 days of exposure to IFX, the following incidence rates were observed for SI: (4.65; 4.17, 5.18) and SOI: (0.48; 0.34, 0.67). In Crohn’s disease (CD) patients, monotherapy with either IFX or corticosteroids, combination therapy with IFX/IMM/CS, IFX/IMM, or IFX/CS, greater disease activity, younger age, non-white race, and hospitalization the year prior to enrollment (HR: 0.94-4.88; all, p < 0.05) were associated with an increased risk of time to first SI. In ulcerative colitis (UC) patients, CS monotherapy or CS/IFX or CS/IMM combination therapy, and hospitalization in the year prior to enrollment (HR: 3.49-3.99; all, p < 0.05) were associated with an increased risk of time to first SI.
Table 1 Unadjusted Rates of Serious Infections

<table>
<thead>
<tr>
<th>Cumulative Infections</th>
<th>All</th>
<th>Infliximab</th>
<th>Biologics</th>
<th>Non-biologics</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total PY</td>
<td>20369.5</td>
<td>9022.3</td>
<td>12755.3</td>
<td>7614.3</td>
</tr>
<tr>
<td>SI/100 PY [# of SI], 95% CI</td>
<td>4.10[836]</td>
<td>4.06[366]</td>
<td>5.21[665]</td>
<td>2.25[171]</td>
</tr>
<tr>
<td>SOI/100 PY [#SOI]</td>
<td>0.31[63]</td>
<td>0.35[32]</td>
<td>0.38[48]</td>
<td>0.2[15]</td>
</tr>
</tbody>
</table>

PY=patient years of follow-up, SI=Serious Infections, SOI=Serious Opportunistic Infections, CI=Confidence Interval

**Conclusion:** Unadjusted IR indicates that IFX exposure is associated with a greater risk of SI in pediatric IBD. Concomitant CS exposure increases the risk of time to first SI in CD patients exposed to IFX or IFX/IMM combination therapy and in UC patients exposed to IFX or IMM monotherapy.

Evolution of disease phenotype in paediatric-onset Crohn’s disease after more than 10 years follow up

Firas Rinawi1, Amit Assa2, Corina Hartman1, Yael Mozer-Glassberg1, Vered Nachmias Friedler1, Yoram Rosenbach1, Ari Silbermintz1, Noam Zevit3, Raanan Shamir1

1Schneider Children’s Medical Centre 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
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: Paediatric onset Crohn’s disease (CD) is a heterogeneous disorder which is subjected to progression and complications in a substantial proportion of patients. We aimed to assess the progression and changes in paediatric CD phenotype on long term follow up.

Methods: Using the Schneider Paediatric Inflammatory Bowel Disease (SPID) cohort, encompassing 482 paediatric onset CD patients seen between 1981 and 2013, we retrospectively evaluated the medical records of 215 patients with at least 10 years of follow-up. Disease phenotype was determined at diagnosis and during follow up at different time points. Phenotype was determined according to the Paris classification. The impact of possible predictors on phenotype progression including age at diagnosis, gender, clinical manifestations, disease location and behaviour was assessed as well as the association between different therapeutic regimens during disease course and phenotype progression.

Results: Progression of disease location, behaviour, and perianal involvement was observed in 28%, 38.2% and 20.4% of patients, respectively, after a median follow-up of 16.4 (± 4.4) years. Microscopic ileocolonic disease at diagnosis and treatment with immunomodulators during the first year following diagnosis were significant predictors for progression of disease extent. Treatment with anti tumour necrosis factor-ɑ agents and number of flares per years of follow-up were associated with progression of disease extent, behaviour and perianal involvement.

Conclusion: Disease’s extent, behaviour and prevalence of perianal disease change significantly over time in paediatric-onset CD. In our cohort, most clinical, laboratory and endoscopic parameters do not serve as predictors for long-term disease progression.
**Incidence of bowel surgery and associated risk factors in paediatric onset Crohn’s disease**

Firas Rinawi\(^1\), Amit Assa\(^1\), Corina Hartman\(^1\), Yael Mozer - Glassberg\(^1\), Vered Nachmias Friedler\(^1\), Yoram Rosenbach\(^1\), Ari Silbermintz\(^1\), Noam Zevit\(^2\), Raanan Shamir\(^2\)

\(^1\)Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach-Tikva, Israel

\(^2\)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

**Objectives and study:** Data describing the incidence and the risk factors for surgical interventions in paediatric Crohn’s disease (CD) is scarce and inconsistent. Our aim was to describe the rates of intestinal surgery and to identify associated risk factors in a large cohort of children with CD.

**Methods:** Medical charts of 482 children with CD from the Schneider Paediatric Inflammatory Bowel Disease (SPID) cohort who were diagnosed between 1981 to 2013 were carefully reviewed retrospectively.

**Results:** Median follow-up time was 8.6 years (range, 1-30.5 years). Of 482 patients 143 (29.7%) underwent intestinal surgery. Kaplan – Meier survival estimates of the cumulative probability of CD-related intestinal surgery were 14.2% % at 5 years and 24.5% at 10 years from diagnosis. Of these 14% needed more than one operation. Multivariate Cox models showed that isolated ileal disease (HR 2.39, \(P = 0.008\)), complicated behaviour (HR 2.44, \(P < 0.001\)) and higher severity indices at diagnosis including Harvey-Bradshaw (HR 1.06, \(P=0.009\)) and short paediatric Crohn’s disease activity index (PCDAI) (HR 1.02, \(P=0.001\)) were associated with increased risk for surgery. Age, gender, family history of CD, early introduction of immunomodulators or diagnosis prior to the year 2000 did not affect the risk of bowel surgery.

**Conclusions:** Ileal location, complicated behaviour, higher disease activity indices at diagnosis are independent risk factors for bowel surgery while early introduction of immunomodulators and diagnosis during the “biologic era” are not associated with diminished long-term surgical risk.
The prevalence of irritable bowel syndrome-type symptoms in pediatric inflammatory bowel disease and the relationship with biochemical markers of disease activity

Kay Diederen¹, Daniel Hoekman¹, Thalia Hummel², Tim de Meij³, Bart Koot¹, Merit Tabbers¹, Arine Vlieger⁴, Angelika Kindermann¹, Marc Benninga¹

¹Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Medisch Spectrum Twente, Department of Pediatrics, Enschede, Netherlands
³Vu University Medical Center, Paediatric Gastroenterology, Amsterdam, Netherlands
⁴St. Antonius Hospital, Department of Pediatrics, Nieuwegein, Netherlands

Objectives and study: A large proportion (25-46%) of adults with inflammatory bowel disease (IBD) in remission has symptoms of irritable bowel syndrome (IBS). These symptoms have been suggested to reflect ongoing inflammation. Data on pediatric IBD patients are lacking. Therefore, we aimed to investigate (i) the prevalence of IBS-type symptoms in pediatric IBD-patients in clinical remission and (ii) the relationship of IBS-type symptoms with biochemical markers of disease activity.

Methods: In this cross-sectional study, we included all patients (<18 years) with Crohn’s disease (CD), ulcerative colitis (UC) or IBD-unclassified attending the outpatient clinic of one of three Dutch hospitals between March 2014 and June 2015. Clinical disease activity was determined using the abbreviated Pediatric CD Activity Index or Pediatric UC Activity Index. Biochemical disease activity was assessed using fecal calprotectin (FC) and serum CRP. The physician-administered Rome III questionnaire was used to determine the presence of IBS. Differences between groups were analyzed using T-tests, Mann-Whitney U-tests or Fisher’s exact tests, where appropriate. 95%-CI was based on bootstrapping with 1000 iterations.

Results: In total, 186 patients (94 female; mean age: 14.4 years) were included (CD: 123, UC: 61). The prevalence of IBS-type symptoms in children with IBD in clinical remission without steroid use (n=113) was 6.2% (95%-CI: 1.9-11.1%; CD: 4.8%; UC: 10.3%). No difference in levels of FC or CRP was found between patients with or without IBS-type symptoms (FC: IBS+ median 88 µg/g, IBS- 146 µg/g, p=0.24; CRP: IBS+ median 1.1 mg/L, IBS- 1.0 mg/L, p=0.63). The majority of children with IBS-type symptoms had diarrhea-predominant IBS (IBS-D, 56.2%) or constipation-predominant IBS (IBS-C, 25.0%). Children with IBS-type symptoms had a shorter disease duration, compared to children without IBS-type symptoms (p=0.03). Other characteristics did not differ significantly between patients with and without IBS-type symptoms (table 1).
**Table:**

<table>
<thead>
<tr>
<th></th>
<th>IBS+ (n=24)</th>
<th>IBS- (n=162)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (mean, SD)</td>
<td>13.8 (3.3)</td>
<td>14.5 (2.4)</td>
<td>0.23</td>
</tr>
<tr>
<td>Females (n,%)</td>
<td>14 (58.3%)</td>
<td>80 (49.4%)</td>
<td>0.51</td>
</tr>
<tr>
<td>Crohn’s disease (n,%)</td>
<td>16 (66.7%)</td>
<td>107 (66.0%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Months since diagnosis of IBD (median, IQR)</td>
<td>11.7 (8.1-19.0)</td>
<td>26.3 (9.5-42.4)</td>
<td>0.03</td>
</tr>
<tr>
<td>Age at diagnosis (mean, SD)</td>
<td>11.9 (4.8)</td>
<td>11.8 (3.5)</td>
<td>0.86</td>
</tr>
<tr>
<td>Currently receiving medical therapy for IBD (n,%)</td>
<td>21 (87.5%)</td>
<td>154 (95.1%)</td>
<td>0.16</td>
</tr>
</tbody>
</table>

Table 1. Characteristics of patients with and without IBS-type symptoms.

**Conclusion:** The prevalence of IBS-type symptoms in children with IBD is much lower than previously reported in studies in adult IBD-patients. IBS-type symptoms appear to be unrelated to gastrointestinal inflammation.

**Disclosure of interest:** None Declared.
Variability of Human Anti-Transglutaminase Assay Across Mediterranean Countries

Andrea Smarrazzo¹, Carmela Arcidiaco¹, Dušanka Mičetić-Turk², Aydan Kansu³, Virtut Velmishi⁴, Camilla Panico⁵, Mongi Ben-Hariz⁶, Maria Legarda Tamara⁶, Eleftheria Roma⁷, Enzo Bravi⁸, Giuseppe Magazzù⁹, Renata Auricchio¹, Luigi Greco¹

¹University of Naples "Federico II", Dept. of Medical Translational Sciences and European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
²University Medical Centre, Paediatric Department, Maribor, Slovenia
³Ankara University Hospital, Paediatric Gastroenterology, Ankara, Turkey
⁴"Mother Teresa " Hospital, Service of Pediatric Gastroenterology, Tirana, Albania
⁵Mongi Slim’s Hospital, Pediatric Unit, Tunis, Tunisia
⁶Cruces University Hospital, Paediatric Gastroenterology Unit, Barakaldo, Spain
⁷University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
⁸Europital Spa, Trieste, Italy
⁹University of Messina, Celiac Regional Centre, Pediatric Gastroenterology and Cystic Fibrosis Unit, Messina, Italy

Objectives and study: The 'epidemic' of Coeliac Disease across Mediterranean countries stimulated the need to standardize the commonly used diagnostic tests. ESPGHAN made a significant effort to estimate the variability of the anti-transglutaminase test across Europe, but only few studies deal with specific measures of accuracy and precision. The aim of this study is to verify the precision and the accuracy of the anti-transglutaminase assay across Mediterranean countries.

Methods: This study involved 8 Referral Centres for Coeliac Disease in 7 Mediterranean countries. A central laboratory prepared 8 kits of 7 blinded and randomized serum samples, with a titrated amount of Human Anti Transglutaminase Antibodies (TGA) IgA, obtained by progressive dilution of pooled human samples. Each sample was analyzed three times in three different days and so, each centre ran 21 tests. The results were included in a blindly coded report form, which was sent to the coordinator centre. The coordinator estimated the Mean Coefficient of Variation (measure of precision, CoVar = σ/μ), the Mean Accuracy (Accur = Vobserved – Vreal) and the Mean Percent Variation (Var% = [(Vobserved – Vreal)/Vreal]*100).

Results: 70.83% of the mean variation fell between -25% and +25% of the expected value, with accuracy and precision progressively increasing with higher titres of anti-transglutaminase antibodies. From values 3 or more times the normal cut-off, the measurement results were highly reliable (at 3 times the normal cut-off: CoVar= 0,0715, Var% = -24,72%, Accur = -12,36; overall: CoVar= 0,1113, Var% = -38,33%, Accur = -10,64).

Conclusion: The anti-transglutaminase assay is a high quality diagnostic tool, given its accuracy and precision. This is ever more relevant in light of the forthcoming revision of coeliac disease diagnostic criteria by ESPGHAN; this study supports the hypothesis that anti-transglutaminase titres higher than 10 times the cut-off value could be adequate to establish a diagnosis without using invasive techniques.

Disclosure of interest: None Declared.
Assessment of ESPGHAN criteria for diagnosis of coeliac disease in New Zealand children

Jonathan Bishop¹, Peter Reed², Stephen Mouat¹, Simon Chin¹, Helen Evans¹

¹Starship Children’s Hospital, Department of Paediatric Gastroenterology, Auckland, New Zealand
²Auckland District Health Board, Adhb Research Office, Auckland, New Zealand

Objectives and study: The 2012 European Society of Pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) guidelines into the diagnosis of coeliac disease challenge the previously held paradigm that diagnosis relies on demonstrating typical histological findings on small intestinal biopsy. These guidelines recommend that, for symptomatic patients with strongly positive coeliac serology (tissue transglutaminase greater than ten times the upper limit of normal and positive endomysial antibodies) and consistent HLA typing, the diagnosis of coeliac disease may be confirmed without the need for biopsy. Although these guidelines are supported by robust scientific evidence, they have not been tested in our population.

Starship Children’s Hospital is the sole referral centre for Paediatric Gastroenterology in New Zealand’s North Island (population 3.5 million). The majority of referred cases undergo screening blood tests in one of two laboratories. Our primary aim was to evaluate accuracy of these guidelines in our population prior to introduction into clinical practice.

Methods: We prospectively recruited children referred to the paediatric gastroenterology service with a clinical concern of coeliac disease. Blood was drawn at the time of endoscopy. Serological testing and HLA serotyping as per ESPGHAN guidelines was performed by both the hospital and local community laboratories. Results were correlated with the small intestinal biopsy findings.

Results: A total of 104 children were recruited over an 18 month period. Of these, 93 had symptoms suggestive of coeliac disease and 11 were asymptomatic patients screened because of genetic risk. A total of 84 patients (80.8%) were diagnosed with coeliac disease, including all 11 asymptomatic at-risk patients.

a) Hospital laboratory
59 (57%) cases fulfilled criteria for diagnosing coeliac disease without biopsy. A total of 51 cases had diagnosis confirmed on initial biopsy, with a further two cases having diagnostic changes on a subsequent biopsy (total 53 of 59 (93%)).

b) Community laboratory
58 (56%) cases fulfilled criteria for diagnosing coeliac disease without biopsy. A total of 55 cases had diagnosis confirmed on initial biopsy and a single case on a second biopsy (total 56 of 58 (97%))

c) Inter-laboratory agreement
For reaching threshold for diagnosis of coeliac disease on serology, there was concordance between the two labs in 53 cases.

d) HLA typing
All 104 cases were found to have consistent HLA serotypes (DQ2.2, DQ2.5 and/or DQ8).

Conclusion: Although the ESPGHAN guidelines for diagnosis correlated with histology findings in the majority of cases, in up to 7% of cases, the biopsy failed to confirm the diagnosis. The accuracy of the serological testing differed between laboratories and is likely dependent on the testing platforms utilised. In our cohort, HLA subtyping does not seem to contribute to the diagnostic accuracy of serological testing for coeliac disease.

Disclosure of interest: None Declared.
In vitro hepatogenic differentiation of umbilical cord matrix stem cells enables Hepatitis B entry by modulating the expression of the Sodium Taurocholate Cotransporter Polypeptide

Camillo Sargiacomo 1, Hoda EL Kechedy 2, Kai Dallmeier 3, Juri de Kock 4, VERA Rogiers 4, Johan Neyts 5, Arturo Ortega 6, Mustapha Najimi 7, Etienne Sokal 8

1 Catholic University of Louvain, Irec; Pedi, Brussels, Belgium
2 ULB, Pedi, Brussels, Belgium
3 Kul, Louvain, Belgium
4 VUB, Brussels, Belgium
5 Cinvestav, Mexico City, Mexico
6 ULB, Brussels, Belgium

Objectives and study: HBV carriers worldwide are approximately 240 million people and around 780,000 people die every year of HBV infection. Hepatitis B virus (HBV) entry and uptake are functionally linked to the presence of the human sodium-taurocholate cotransporting peptide (hNTCP) receptor. Recently, our group demonstrated that human umbilical cord matrix stem cells (UCMSCs), after in vitro hepatogenic differentiation (D-UCMSCs) become susceptible to HBV virus, however, the presence of hNTCP was never investigated in D-UCMSC. In the present study, we examined D-UCMSCs susceptibility to HBV by characterising the modulation of hNTCP expression.

Methods: D-UCMSCs production was achieved by plating naive UCMSCs on collagen I coated flasks and by growing them up to 90% confluence. Serum free differentiation medium (IMDM) containing specific growth factors/cytokines was applied as a sequential three step modified protocol. After 21 days of differentiation, D-UCMSCs hepatogenic potential was tested by CYP3A4 functional activity using Lytic P450-Glo™ assay (Promega) following manufacturer indication. HBV infection of D-UCMSCs was obtained by incubating the virus for 24 h at 37 °C and monitoring viral replication every 24 hours for 4 days post-infection. Infection efficiency was established using high viral loads [multiplicities of infection (MOIs) 10 5 10 8] and tested on several UCMSCs donors. Infectious HBV relaxed circular (RC) DNA particles were extracted directly from the supernatant by PureLink® Viral RNA/DNA Mini Kit (Invitrogen). HBV production was performed by real time PCR using Absolute quantification method. Intracellularly, HBV pgRNA viral transcripts detection was obtained by total RNA extracts of infected D-UCMSCs and by ΔΔCt comparative analysis method using specific TaqMan assay. HBV cccDNA detection was conduct on infected D-UCMSCs total DNA extraction using specific TaqMan probes by digital droplet PCR and expressed as copy numbers/cells (RNaseP was used as house-keeping gene). D-UCMSCs total RNA extracts were used for hNTCP mRNA detection and analyzed by ΔΔCt comparative method. Naive UCMSCs and D-UCMSCs protein lysate samples were achieved by dissolving cell pellets in RIPA buffer, loaded on a 10% Tris-glycine SDS-PAGE gel for protein separation. hNTCP primary antibodies, kind gift from Prof Bruno Stieger were incubated overnight at 4 °C, (1:1000) and were detected by fluorescently labeled secondary antibody.

Results: We demonstrate that D-UCMSCs display several hepatogenic differentiation markers at the morphology, genotypic and functional levels as compared to naive UCMSCs. As for instance, CYP3A4 activity is 10 fold increased in differentiated D-UCMSCs. Subsequently, we confirmed, using molecular biology approaches, that HBV rapidly infects D-UCMSC, as supported by the formation of cccDNA, the production of HBV pre-genomic RNA transcripts, and by the secretion of relaxed circular DNA particles. Furthermore, we demonstrate that such infectability of D-UCMSCs is correlated to an up-regulation of the NTCP hepacocellular transporter at both mRNA and protein expression levels when compared to naive UCMSCs.

Conclusion: These data suggest that HBV infection of D-UCMSCs is mediated by NTCP which supports their use as an alternative in vitro tool to study early HBV infection stages and efficiency of NTCP antiviral drugs.

Disclosure of interest: None Declared.
The 3-dimensional structures of human and microbial transglutaminases complexed to gliadin are similar

Patricia Jeremias¹, Sandra Neidhöfer², Torsten Matthgias¹, Aaron Lerner³

¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Aesku.Diagnistics, Research, Wendelsheim, Germany
³Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel

Objectives and study: In the food industry, microbial transglutaminase (mTg) is used to modulate texture and improve the properties of food products. Due to their common enzymatic functions, the question has arisen whether complexes of mTg formed by transamidation reactions could be relevant for celiac patients. Linear and three dimensional structures of the complexes formed by tTg or mTg and gliadin (tTg neo-epitopes or mTg neo-epitopes, respectively) were compared.

Methods: mTg neo-epitopes and tTg neo-epitopes were formed, separated by asymmetric flow field-flow fractionation and confirmed by SDS-PAGE and multi-angle light scattering. For structural alignment and docking experiment the program YASARA was used. Structural alignment was performed with the primary structures of mTg and tTg by using the MUSTANG-algorithm.

Results: No alignment on the α-C atoms of the protein backbones and the 3D structure between mTg and tTg were observed. Glutamine or other positive residues are directed to the active centre due to a mainly negatively charged surface. After docking of the gliadin peptide to mTg and tTg, both enzymes show adjacent partial-positive charges. Moreover, both neo-epitope complexes show a superimposed epitope similarity, even though homology at the entrance to the active centre is still low.

Conclusion: Only after docking of gliadin peptides to mTg or tTg, similarities in charges and structure of the epitopes appear. If molecular mimicry leads from mTg neo-epitopes to tTg-neo-epitopes there must exist a similarity between these enzymes. If an antibody-paratope exists, an anti-mTg neo-epitope antibody might show cross-reactivity and binds to a tTg neo-epitope.

Disclosure of interest: None Declared
Fecal calprotectin concentration reflects disease severity but not disease extent in pediatric patients with new onset ulcerative colitis. The PROTECT Study

Thomas Walters¹, Lee Denson², Brendan Boyle³, David Mack⁴, Anne Griffiths¹, Anthony Otley⁵, David Keljo⁶, Neal Leleiko⁷, James Markowitz⁸, Joel Rosh⁹, Susan Baker¹⁰, Ashish Patel¹¹, Marian Pfefferkorn¹², Maria Oliva-Hemker¹³, Joshua Noe¹⁴, Subra Kugathasan¹⁵, Jeffrey Hyams¹⁶

¹The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada  
²Cincinnati Children’s Hospital Medical Center, Cincinnati, United States  
³Nationwide Children’s Hospital, Columbus, United States  
⁴Children’s Hospital of Eastern Ontario, DIV GI, Ontario, Canada  
⁵Iwk Health Centre, DIV GI, Halifax, Canada  
⁶Children’s Hospital of Pittsburgh, Pittsburgh, United States  
⁷Hasbro Children’s Hospital Rhode Island Hospital, Providence, United States  
⁸Cohen Children’s Medical Center, New York, United States  
⁹Goryeb Children’s Hospital/Atlantic Health, Morristown, United States  
¹⁰Women & Children's Hospital of Buffalo, Buffalo, United States  
¹¹Ut Southwestern, Dallas, United States  
¹²Riley Children's Hospital Indiana University School of Medicine, Indianapolis, United States  
¹³Johns Hopkins Children’s Center, Baltimore, United States  
¹⁴Medical College of Wisconsin, Milwaukee, United States  
¹⁵Emory University, Atlanta, United States  
¹⁶Connecticut Children’s Medical Center, Hartford, United States

Objectives and study: Therapeutic decisions for children presenting with new onset ulcerative colitis (UC) vary depending on both disease extent and severity. Ileocolonoscopy is the gold standard for determining disease extent, but is invasive and expensive. Calprotectin has an established role for discriminating inflammatory from non-inflammatory bowel disease. Its utility in distinguishing extensive disease from left-sided disease is unknown. We aimed to examine the relationship between a patient’s fecal calprotectin concentration ([fCal]), their disease extent, and their disease severity.

Methods: Baseline data were obtained from 314 children (4-17 years) at 29 centers in the on-going prospective PROTECT Study: Predicting Response to Standardized Pediatric Colitis Therapy (DK 095745-01). Diagnosis of UC extending above the rectum was made using standardized criteria including ileocolonoscopy. Phenotype assessments included disease extent by Paris criteria (E1-E4), endoscopic severity by Mayo sub-score, and disease activity scored by the Pediatric Ulcerative Colitis Activity Index (PUCAI) and Physician Global Assessment (PGA). Pre-therapy stool samples were collected on all participants. [fCal] was measured by enzyme-linked immunosorbant sandwich assay using a commercially available kit (Bühlmann Laboratories AG, Schönenbuch, Switzerland; sensitivity: 10 mcg/g, inter-assay variation: 10.6%). High titer samples were diluted as necessary. Non-parametric approaches were used to compare the distribution of [fCal] between different clinical and disease extent strata. Area under the curve (AUC) of the Receiver Operator Characteristics (ROC) Curve was utilized to demonstrate the discriminative capacity of [fCal].

Results: Of 314 children (50% female), 195 (67%) had pancolonic (E4) disease and 58 (20%) had left-sided disease (E1/2). The median PUCAI was 50 (IQR 35-65; 33% ‘Severe’); 30% were ‘Severe’ by PGA and 36% were Grade 3 on Endoscopy. [fCal] was >200 mcg/g in 301/314 patients; median 2202 mcg/g (IQR 1125-3897). As disease severity increased, median [fCal] also increased (see table). Notably, however, [fCal] did not vary with disease extent: Median [fCal] was 2201 and 2288 mcg/g for E1-2 and E3-4 respectively (p=0.8). ROC analysis demonstrates that although [fCal] is a modest discriminator of disease severity (AUC 0.58 to 0.63 for PUCAI, PGA and Endo) it does not discriminate disease extent (AUC 0.51 for E1-2 vs E3-4).
Table:

<table>
<thead>
<tr>
<th></th>
<th>Median [fCal]</th>
<th>p*</th>
<th>AUC (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PUCAI Mild</td>
<td>1433</td>
<td>Mod</td>
<td>Severe</td>
</tr>
<tr>
<td>PGA Mild-Mod vs</td>
<td>1672</td>
<td>1913</td>
<td>3376</td>
</tr>
<tr>
<td>Severe Endo Grade 1-2 vs 3</td>
<td>1388</td>
<td>2010</td>
<td>2943</td>
</tr>
</tbody>
</table>

**Conclusion:** Fecal calprotectin concentrations relate to both clinical and endoscopic measures of disease severity but do not predict the extent of colonic involvement.

**Disclosure of interest:** None Declared.
Reliability assessment of endoscopic disease severity using central video review of colonoscopies in paediatric patients with Crohn’s Disease: data from the Canadian Children IBD Network

Nicholas Carman¹, Peter Church¹, Hien Huynh², Thomas Walters¹

¹The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
²The University of Alberta, Ibd Department, Edmonton, Canada

Objectives and study: Reliable and consistent endoscopic assessment of mucosal disease severity is important in the evaluation of patients with inflammatory bowel disease (IBD), both in clinical practice and in the context of clinical trials. There are a number of scoring tools available for use in the endoscopic assessment of Crohn’s disease, however none have been formally evaluated in Pediatric patients. To reduce variability in the assessment of endoscopic severity, centralised review of video colonoscopies has been increasingly implemented in adult clinical trials, where excellent inter-rater reliability has been noted in the hands of IBD experts. To date, similar assessments have not been performed in Paediatric IBD. We undertook to assess inter-rater reliability for the Simple Endoscopic Score (SES-CD) and Crohn’s Disease Endoscopic index of Severity (CDEIS), using videos of colonoscopies performed in paediatric patients from the Canadian Children IBD Network, (a joint partnership of the CIHR and CH.I.L.D Foundation).

Methods: Video recordings of colonoscopies obtained from paediatric patients with Crohn’s Disease undergoing endoscopic assessment at Network sites were utilised for the analysis. 3 central readers reviewed the videos independently, and were blinded to clinical information. Colonoscopies were assessed using data encompassing the commonly employed scoring tools for Crohn’s disease (SES-CD and CDEIS), assessing the total score and individual items across each anatomical segment. A global assessment of endoscopic lesion severity (GELS) was also recorded using a visual analogue scale. Inter-rater agreement was measured using Intraclass correlation coefficients (ICCs) with 95% confidence intervals. Correlation between scoring tools was measured using Pearson’s test of correlation (r).

Results: The ICC for inter-rater reliability for SES-CD was 0.94 (95% CI: 0.84 – 0.98.), for CDEIS was 0.83 (95% CI: 0.58 – 0.93), and for GELS was 0.90 (95% CI: 0.74 – 0.96). There was very good correlation between the SES-CD score and CDEIS (r = 0.81, p <0.001). The correlation between GELS and each scoring tool was also very good, with SES-CD and CDEIS demonstrating r = 0.77 (p = <0.001) and r = 0.81 (p = <0.001) respectively. The most common sources of disagreement between readers were estimation of the degree of ulcerated surface and evaluation of the depth of ulceration. Disagreement was most notable in the transverse colon (ICC 0.48 and 0.46 for ulcer surface and ulcer depth respectively).

Conclusion: Centralised video review of colonoscopy is a feasible way to assess endoscopic severity in Paediatric Crohn's disease. Assessment of the existing scoring tools (SES-CD and CDEIS) using video recordings showed excellent inter-rater reliability in the hands of IBD physicians familiar with the tools. These scores also correlated well with GELS, demonstrating some measure of validity for these tools in Paediatric Crohn’s disease. Ongoing assessments are planned in order to explore the variability in scoring and relationship to GELS across different disease phenotypes.

Disclosure of interest: None Declared.
Constitutive alterations of the intracellular vesicular trafficking in CD (Celiac Disease) enterocytes and fibroblasts: relationship with stress/innate immune response to gliadin

Giuliana Lania¹, Merlin Nanayakkara¹, Mariantonia Maglio¹, Renata Auricchio¹, Salvatore Auricchio¹, Riccardo Troncone¹, Maria Vittoria Barone¹

¹University of Naples, Department of Translational Medical Science, Elfid, Naples, Italy

Objectives and study: CD is an autoimmune disease characterized by inflammation of the intestinal mucosa due to immune response to wheat gliadins.

Some gliadin peptides (e.g.: P57-68) induce an adaptive Th1 pro-inflammatory response, other gliadin peptides (e.g. P31-43) induce a stress/innate immune response involving interleukin-15 (IL-15). P31-43 shares sequence similarity with HRS (Hepatocyte growth factor Regulated tyrosine kinase Substrate) and delays HRS mediated maturation of early endosomes.

In CD cells constitutive alterations related to a “cellular stress” were present. Recently in the literature, several human diseases, characterized by inflammation and/or autoimmunity, have been attributed to alterations of the vesicular trafficking at various levels.

Our hypothesis is that endocytic maturation and stress/innate immune response could be constitutively altered in CD cells rendering the celiac cells more sensitive to the effect of P31-43 and IL15. We investigated whether delay of the endocytic maturation, by siHRS, could induce in controls similar alterations.

Methods: Intracellular trafficking was analyzed by immunoflorescence experiments in intestinal biopsies and skin fibroblasts. Total lysates from the same compartments were analyzed by Western blot with anti- IL15R-alpha, anti-MxA, anti- NFkB and anti-phosphorylated Stat5. Delay of the endocytic trafficking was induced by HRS silencing

Results: In CD fibroblasts and intestinal biopsies EGFR co-localized more with early compartment and less with the late. The early endocytic compartment was altered in CD cells. P31-43 treatment induced a sustained trafficking delay in CD cells and a transient one in controls. IL15R-alpha, MxA and inflammation marker, nuclear NFkB, are constitutively increased in CD fibroblasts. To investigate the functional effects of the increase of IL15R-alpha in CD fibroblasts, we evaluated the activation of the downstream effector, STAT5, in dose response curve to IL15 and p31-43 increasing concentration. Low concentrations of IL15 and p31-43 respectively (5ng/20ug) were sufficient to induce STAT5 phosphorylation in CD fibroblasts, but not in controls. HRS silencing and P31-43 treatment induced EGFR, IL15R-alpha, NFkB phosphorylation and nuclear NFkB increase in control fibroblasts.

Conclusion A constitutive alteration of the intracellular vesicular trafficking in fibroblasts and enterocytes in CD patients was present. In control cells the delay of the endocytic trafficking can reproduce the same alterations present in CD cells. These data demonstrated that a specific alteration of the endocitic trafficking, similar to that found in the celiac cells, was able “per se” to activate markers of innate immunity and inflammatory response, that could render the celiac cells more sensitive to gliadin effects.

Disclosure of interest: None Declared
GASTROENTEROLOGY: Coeliac disease

G-O-058

Short gluten challenge in the wide spectrum of genetic gluten intolerance.

Luigina De Leo¹, Stefania Picascia², Giorgio Cozzi¹, Fabiana Ziberna¹, Serena Vatta¹, Stefano Martelossi¹, Alessandro Ventura¹, Carmen Gianfrani², Tarcisio Not¹

¹Institute for Maternal and Child Health - Ircs “Burlo Garofolo”, Trieste, Italy
²Institute of Protein Biochemistry, Cnr, Naples, Italy

Objectives and study: It has been demonstrated that oral gluten challenge in celiac disease (CD) patients treated with gluten free diet (GFD) mobilizes gluten-sensitized T cells detectable by interferon (IFN)-γ enzyme-linked immunospot (ELISPOT) assay. We utilized the short gluten challenge test to measure the gluten-dependent immune response in the wide clinical spectrum of genetic gluten intolerance.

Methods: We enrolled 38 subjects who were in GFD for at least 1 year: 30 CD patients (group A) who were diagnosed by gastrointestinal symptoms, intestinal atrophy and pathological concentration of anti-tissue transglutaminase antibodies (anti-tTG); 6 CD patients (group B) who were diagnosed by gastrointestinal symptoms and the presence of intestinal anti-tTG deposits with normal both intestinal mucosa and serum anti-tTG concentration, 2 individuals (group C) with non-celiac gluten sensitivity (NCGS).

The subjects were invited to consume gluten-containing food for 3 days (20 grams of gluten/day). Immune reactivity to gluten was evaluated detecting, by ELISPOT, the IFN-γ before and after 6 days the gluten challenge. The ELISPOT assay was based on the peripheral blood mononuclear cells stimulated for 36-48 hours with deamidated or native gliadin fragments. The serum levels of endomysium antibodies (EMA) were tested before and after the gluten challenge.

Results: All the patients were tested negative for EMA.

Twenty-five out of thirty (83%) CD patients (group A) responded to the short gluten challenge with an increased IFN-γ-spot-forming cells (SFC) to deamidated and/or native gliadin fragments stimulation.

Five out of six (83%) CD patients (group B) showed an increased IFN-γ response to deamidated and/or native gliadin fragments.

The IFN-γ-SFC did not increase in the 2 NCGS patients (group C) neither in response to deamidated gliadin stimulation nor to the native one.

Conclusion: Our findings confirm that the short gluten challenge is a non-invasive method to detect gluten-related immune response in peripheral blood from CD patients with a diagnosis based on the European Society of Paediatric Gastroenterology and Nutrition (Espghan) criteria (positive serum anti-tTG and intestinal histological damage). Our data on symptomatic patients tested positive for intestinal anti-tTG deposits with normal both intestinal mucosa and serum anti-tTG concentration are preliminary but of interest. These data confirm, for the first time, the CD diagnosis in symptomatic patients with genetic gluten intolerance not fulfilling Espghan criteria.

Further efforts are necessary to increase the number of patients with genetic gluten intolerance and of NCGS individuals.

Disclosure of interest: None Declared
Clinico-epidemiologic Features and Genotypes of Rotavirus Acute Gastroenteritis in Egyptian Children: A Single Tertiary Care Center Study

Ahmed Megahed¹, Niveen Saudy², Walaa Othman², Mona Foad², Aly Mohamed³

¹Monsoura University Children’s Hospital, Mansoura University, Pediatrics; Pediatric Gastroenterology, Hepatology and Nutrition, Mansoura, Egypt
²Mansoura University, Faculty of Medicine, Clinical Pathology, Mansoura, Egypt
³Vacsera Institute, Virology Sector, Cairo, Egypt

Objectives and study: Rotavirus acute gastroenteritis (AGE) is a very common cause of severe childhood diarrhea worldwide. The clinico-epidemiologic features, risk factors as well as dominant circulating rotavirus genotypes may vary between and within different regions and from year to year. The present study aimed to determine the rotavirus genotypes among infants and children less than 3 years admitted to Mansoura University Children’s Hospital at Delta Egypt, their relation to clinico-epidemiologic characteristics and their possible impact on vaccination choice and its presumed efficacy.

Methods: A pilot study evaluating 92 infants and children, less than 3 years old, with AGE admitted at our hospital (one of the main referral hospitals for both urban and rural districts in the Nile Delta) was conducted during the period from September 2012 to February 2014 (17 months). Clinico-epidemiologic data in addition to fresh stool samples were collected. Rota virus dsRNA was extracted and subjected to G and P typing by multiplex reverse transcription–polymerase chain reaction (RT-PCR) with type-specific primers.

Results: Rotavirus was detected in stool of 45 (48.9%) children with acute diarrhea, 91.1% of positive cases of rotavirus gastroenteritis were under 2 years of age with highest prevalence in infants 7-12 months of age. Rotavirus-associated diarrhea peaked in autumn and winter. Regression analysis demonstrated that breast fed infants were at a lower risk of rotavirus diarrhea (OR 0.3, 95% CI 0.11–0.85, P=0.02) than none breastfed infants. Severe dehydration and vomiting (OR 1.4, 95% CI 0.06–2.6, P=0.03 and OR 1.66, 95%CI 0.74–3.7, P=0.021) were found to be significantly present in the Rota virus positive (RVP) patients. Genotypes G1P[8] (26.7%), G9P[8] (20%) and G3P[8] (15.6%) were the most prevalent strains accounting for 62.3% of rotavirus AGE cases. Patients infected with G9 strains showed statistical significant more prolonged gastroenteritis compared to G1 and G3 patients.

Conclusion Rotavirus gastroenteritis is common particularly in infants and there is a diversity of rotavirus strains admitted at our center. Lack of breast feeding is an important risk factor. The emergence of G9 necessitates wider survey studies and its consideration in rotavirus vaccines for use in Egypt.

Disclosure of interest: None of the authors has any conflict of interest to declare.
Prevalence and predisposing factors of functional constipation in adolescent Nigerians

Ekong Udoh¹, Shaman Rajindrajith², Niranga Devanarayana³, Martin Meremikwu⁴, Marc Benninga⁵

¹Institute, Paediatrics, Uyo, Nigeria  
²Institute, Department of Paediatrics, Ragama, Sri Lanka  
³Institute, Department of Physiology, Ragama, Sri Lanka  
⁴Institute, Paediatrics, Calabar, Nigeria  
⁵Academic Medical Center / Emma Children’s Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Functional constipation is of public health importance in some parts of Europe, the USA and Asia. The condition is associated with poor health-related quality of life in affected children. The burden and determinants of the condition have not been ascertained in African children due to lack of epidemiological data. This study was aimed at determining the prevalence and predisposing factors of functional constipation in adolescent Nigerians.

Methods: A cross sectional study was conducted in rural and urban areas of two states in southern part of Nigeria in June 2014. Adolescents aged 10 – 18 years were recruited from 11 secondary schools using a stratified random sampling technique. A validated self-administered questionnaire on Rome III criteria for diagnosing functional constipation and its predisposing factors was filled by the participants in a class room setting.

Results: A total of 874 participants filled the questionnaire. Of whom, 818 (93.4%) were included in the analysis, having filled the questionnaires properly. The mean age of participants was 14.6 ± 2.0 years with 409 (50.0%) being males. Functional constipation was present in 223 (27.3%) participants with no difference in prevalence based on sex and study setting. Constipation was significantly associated with lower social class (p= 0.01) and remarriage of a parent (p= 0.04).

Conclusion: Functional constipation is a significant health problem among adolescent Nigerians. Social class and parental remarriage are identified predisposing factors in adolescent Nigerians.

Disclosure of interest: None Declared.
FOXP3 epigenetic features in children with cow milk allergy

Lorella Paparo, RITA NOCERINO, Rosita Aitoro, Antonio Amoruso, Viviana Granata, Linda Cosenza, Germana Gioielli, Carmen Di Scala, Roberto Berni Canani

1University of Naples "Federico II", Translational Medical Science, Naples, Italy
2University of Naples "Federico II", Translational Medical Science-Elfid-Geinge Advanced Biotechnologies, Naples, Italy

Objectives and study. Epigenetic changes in DNA methylation have been recently demonstrated during cow milk allergy (CMA) disease course. The suppressive phenotype of regulatory T (Treg) cells, characterized by stable expression of transcription factor Forkhead box Protein 3 (FoxP3), is involved in oral tolerance acquisition. We aimed to assess whether tolerance acquisition in children with IgE-mediated CMA involves a different DNA methylation profile of FoxP3.

Methods: DNA methylation of CpGs in the promoter regions and respective mRNA levels of FoxP3 from peripheral blood mononuclear cells (PBMCs), were assessed in children with active IgE-mediated CMA (Group 1), CMA subjects who outgrew CMA with extensively hydrolyzed casein formula EHCF plus Lactobacillus GG (EXCF+LGG, Group 2), or with other formulas (Group 3) and in healthy controls (Group 4).

Results: 40 children (24 male, aged 3-18 months) were enrolled: 10 in Group 1, 10 in Group 2, 10 in Group 3 and 10 Group 4. DNA methylation profiles of FoxP3 clearly separated active CMA patients from healthy controls. Active IgE-mediated CMA patients showed significantly higher rate of DNA methylation in FoxP3 promoter region compared to healthy controls (52% vs 80%; p<0.0001). DNA methylation analysis of this transcription factor clearly separated CMA patients by disease-state: tolerant subjects presented an opposite DNA methylation profile compared with active CMA patients (42% vs 80%, p<0.0001), but with significant difference comparing children treated with EHCF+LGG or with other formulas. This profile was similar but not identical to that observed in healthy controls. A strong correlation between gene promoter DNA methylation rates and respective mRNA levels was also demonstrated (R² = 0.946; p<0.0001).

Conclusion: Tolerance acquisition in children with IgE-mediated CMA involves demethylation of promoter region of Foxp3 gene leading to an increased expression in Tregs. This feature could be a new epigenetic biomarker to follow the CMA disease course.

Disclosure of interest: None declared.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-O-062

STAT3 gain of function mutation causes IPEX-like autoimmune enteropathy due to excessive IL-17 production.

Sytze de Roock¹, Marielle van Gijn², Joris van Montfrans³, Nicolette Moes⁴

¹University Medical Center Utrecht, Laboratory of Translational Immunology, Utrecht, Netherlands
²University Medical Center Utrecht, Medical Genetics, Utrecht, Netherlands
³University Medical Center Utrecht, Paediatric Immunology, Utrecht, Netherlands
⁴University Medical Center Groningen, Pgn, Groningen, Netherlands

Objectives and study: The Immune Dysregulation Polyendocrinopathy X linked (IPEX) syndrome is a rare but severe form of autoimmune enteropathy. It is due to mutations in FOXP3 and regulatory T-cell (Treg) dysfunction. Recently, patients with IPEX-like poly-autoimmune symptoms and severe enteropathy with normal FOXP3 gene and Treg function were described, suggesting in these patients a different molecular basis of disease. We describe a novel Pro471Arg STAT3 mutation in a patient with IPEX-like autoimmune enteropathy, causing hyper activation of the IL-17 pathway.

Methods: A 17 year old female was followed in our clinic because multi-organ autoimmune disease that was present since early childhood. The main organs affected were her intestine and her liver, resulting in severe protein losing enteropathy (anti-enterocyte antibodies positive) requiring tacrolimus immunosuppressive treatment and autoimmune hepatitis requiring liver transplantation due to acute liver failure. Other autoimmune symptoms were alopecia, eczema and hypothyroidism. A screening of immunodeficiency genes was performed. Peripheral Blood Mononuclear Cells) PBMC and supernatant of patient and healthy controls were collected. STAT3 phosphorylation tests were performed. Cytokine levels were measured in plasma and culture supernatants by multiplex immunoassay. Treg Suppression assays were conducted. And cell stimulation tests were performed in the presence of Interleukin (IL)-6 and IL-10 and rhIL-21 and rh-IL17.

Results: We describe a novel Pro471Arg STAT3 mutation in a patient with a multi-organ autoimmune disease closely resembling IPEX-like autoimmune enteropathy. The molecular basis of disease lies in hyper activation of the IL-17 pathway. We show that IL-17 production by primary T cells was enhanced and could not be further increased by IL-6, while IL-10 could reduce T cell numbers. Moreover, specific STAT 3 activation resulted in diminished IL-17 production. We show that the Pro471Arg STAT3 mutation yields both increased levels of IgA and IgG, probably due to high IL-21 levels. When remission was reached through medical intervention, IL-17 levels normalized and clinical symptoms improved supporting the idea that STAT3 gain of function mutations can cause hyper activation of the IL-17 pathway and thereby contribute to the clinical symptomatology of IPEX-like autoimmune enteropathy.

Conclusion: These data show for the first time a STAT3 mutation with excessive production of IL-17 as cause of a patient clinically presenting as IPEX-like autoimmune enteropathy. We suggest that sequencing of STAT3 should be considered in these patients. Specified treatment options on the Thelper-17 pathway like tocilizumab should be further explored.

Disclosure of interest: None Declared.
Analysis of the early infantile gliadin antibody response by recombinant food allergen microarray and prospective evaluation of a protective role

Ilma Rita Korponay-Szabo¹, Bharani Srinivasan², Katharina Werkstetter³, Judit Gyimesi⁴, Sandra Pahr², Luisa Mearin⁵, Rudolf Valenta², Sibylle Koletzko on behalf of PREVENTCD Group³

¹University of Debrecen and Heim Pál Children’s Hospital, Debrecen, Hungary
²Medical University of Vienna, Dept of Pathophysiology and Allergy Research, Vienna, Austria
³Dr. von Hauner Children’s Hospital, Ludwig-Maximilian’s University, Munich, Germany
⁴Heim Pál Children’s Hospital, Budapest, Hungary
⁵Leiden University Medical Center, Leiden, Netherlands

Objectives and study: Antibodies against native (AGA) and deamidated gliadin peptides (DGP) are produced in coeliac disease (CD) in conjunction with transglutaminase 2(TG2)-directed autoantibodies. During the prospective PREVENTCD double-blind, randomized intervention study approx. 30% of healthy infants produced AGA and DGP without anti-TG2 antibodies shortly after gluten introduction (N Engl J Med 2014;371:1304-15). The aim of the present study was to search for the characteristic antigenic determinants and evaluate clinical outcome by prospective follow-up.

Methods: 944 newborns with a familiar risk of CD and HLA DQ2/8 alleles participating in the PREVENTCD study received either 100 mg/day gluten or placebo for 8 weeks from the age of completed 4 months and were prospectively followed clinically and by serology tests for AGA and TG2 antibodies at 6, 9, 12, 24 months of age and then annually. CD was diagnosed by small bowel biopsy performed in reason of clinical symptoms or persistent seropositivity. IgA and IgG serum antibodies were measured from serum samples of a subset of 133 children using 177 microarrayed recombinant food or inhalative antigens which included 25 wheat antigens, DGP and its non-deamidated homologues, 14 cow’s milk and 4 egg antigens.

Results: High levels of serum AGA and/or DGP (>2SD of normal) at 6 months conferred a measurable but decreasing protective effect in regard of CD development within the gluten group at 2, 3 and 6 years of age: CD 0.96% vs 1.92%, 4.8% vs 7.6% and 28.5% vs 33.6%, odds ratios 0.5; 0.61; 0.78 [95%CI 0.34-1.64] respectively). Antibodies against recombinant gamma gliadin GG1 showed the best correlation with gluten intake (81% accuracy for IgA and 88% accuracy for IgG antibodies in revealing whether the child got gluten or not). Children reacting to gluten also displayed antibody reactivity to amylase-trypsin inhibitors, proteins closely binding to gluten (accuracy for gluten intake 76% by IgA, 87% by IgG antibodies). Antibodies to globulin protein fractions of wheat only appeared when children started to consume gluten in foods, so the effect of the intervention product and other gluten-containing foods were clearly distinguishable. There were no significant differences in the proportion of children having antibodies reacting with cow’s milk (IgA 21.8% vs 31.6%, IgG 82% vs 66%) and egg proteins (IgA 7.0% vs 4.6%, IgG 39.2% vs 36.0%) between the groups with high and low gliadin antibodies.

Conclusion: Taking advantage of the uniform dosage and administration of gluten, the results obtained with gluten and non-gluten wheat antigens indicate that AGA and DGP production are part of the normal immune response to foreign alimentary antigens in young infants. High serum levels of these antibodies after early gluten introduction are associated with an effect delaying CD development. DGP or AGA antibodies not accompanied by anti-TG2 antibody positivity should not be regarded as diagnostic for CD in children below 2 years of age.

Disclosure of interest: None Declared
The Use of Concomitant Immunomodulators with Adalimumab Therapy in Pediatric Crohn’s Disease

Keith Benkov1, George Russell2, Charles Samson3, Steven Steiner4, Eileen C. King5, Jesse Pratt5, Samantha Eichner6, Richard Colletti7, Improve Care Now8

1Icahn School of Medicine at Mount Sinai, Division of Pediatric Gastroenterology Box 1656, New York, United States
2Boston Children’s Hospital, Boston, United States
3Washington University in St Louis School of Medicine, Gastroenterology, Hepatology and Nutrition; Department of Pediatrics, St. Louis, United States
4Riley Hospital for Children, Indianapolis, United States
5Cincinnati Children’s Hospital Medical Center, Division of Biostatistics and Epidemiology, Cincinnati, United States
6Abbvie Inc., North Chicago, United States
7University of Vermont Children’s Hospital, Burlington, United States
8ImproveCareNow, Cincinnati, United States

Objectives and study: Anti-tumor necrosis factor-α (ATNF) therapy is an effective treatment of Crohn’s disease (CD) in up to 85% of patients, but as many as 50% will experience a loss of response (LOR) at 12 months. LOR is likely multi-factorial but often is associated with the development of antibodies to ATNF. Studies have shown that concomitant use of an immunomodulator (IM), either thiopurine (TP) or methotrexate (MTX), significantly reduces the development of antibodies. We aimed to determine the use of adalimumab (ADA) and concomitant therapy over the last 5 years in a large pediatric CD population.

Methods: We identified all consented patients with CD aged <18 years in the ImproveCareNow registry who ever received ADA between June 2010 and June 2015, and determined the rates of treatment with ADA and concomitant therapy with TP or MTX, including variation by age, gender, geographical region and annual change in the last 5 years. We used Chi-square tests to compare percentages and the Cochran Armitage Trend Test to test percentages over time and across age groups.

Results: Of 7,271 patients, 1009 (14%) were treated with ADA. ADA treatment was more common with increasing age (16% in ages 15-17 years vs 5% in ages 0-5 years; p<0.001); in females than males (16% vs 13%; p<0.001); and in the West than the Northeast (17% vs 11%; p<0.001) of the US. From year 1 (2010-2011) to year 5 (2014-2015), the use of ADA increased from 7% to 13% of patients (p<0.001). Of the 1009 treated with ADA, 47% received concomitant therapy with either TP (19%) or MTX (28%). Concomitant therapy occurred in 63% of patients aged 0-5 years, 59% aged 6-10, 49% aged 11-14, and 43% aged 15-17 (overall p<0.01); and in 49% of males and 44% of females (p=0.17). Concomitant therapy occurred in 54% of patients in the West, 54% in the Midwest, 43% in the South and 38% in the Northeast of the US (overall p=<0.001). From year 1 to year 5, the use of concomitant therapy increased from 25% to 49% of patients treated with ADA (p<0.001) (Figure). Of patients taking concomitant therapy, use of TP vs MTX was 31% vs 69% in males, 56% vs 44% in females, and 40% vs 60% overall. Over the last 5 years, there was an increase in the use of MTX (14% in year 1, 30% in year 5; p<0.001) and of TP (11% in year 1 and 19% in year 5; p=0.01).
**Table:** Use of adalimumab and concomitant therapy with thiopurine or methotrexate over 5 year period

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>MTX</td>
<td>14%</td>
<td>14%</td>
<td>16%</td>
<td>21%</td>
<td>30%</td>
</tr>
<tr>
<td>Thiopurine</td>
<td>11%</td>
<td>13%</td>
<td>16%</td>
<td>15%</td>
<td>19%</td>
</tr>
<tr>
<td>Neither</td>
<td>75%</td>
<td>72%</td>
<td>63%</td>
<td>55%</td>
<td>51%</td>
</tr>
</tbody>
</table>

**Conclusion:** In pediatric CD there is increasing use of ADA, with 13% treated in the last year. Of these, about half receive concomitant therapy, and of this group, 40% receive TP and 60% MTX. Males are more likely to receive MTX. There are also regional differences in the use of ADA and IM. There is no consensus in the use of concomitant therapy with ADA and in the choice of IM. Further studies are needed to determine whether IM therapy is indicated with ADA treatment.

**Disclosure of interest:**
K Benkov, G Russell, C Samson, S Steiner, E King, J Pratt: none declared; S Eichner: Employee of AbbVie; Colletti, R. Consultancy: Consultant for AbbVie, University of Vermont receives research support for registry from Abbvie. Financial support for research: Study funded by AbbVie
Objectives and study: Ileo-colonoscopy (IC) may be complicated by the mobile nature of the colon especially in the sigmoid and transverse regions largely due to unpredictable looping during insertion. In the adult literature it has been suggested that 90% of loops are resolved with clockwise rotation of the scope and withdrawal. There is no parallel data in children. We hypothesize that the age of the child may be factors in the type of loop formation. Hence the aims of the study are: (1) to assess the frequency of loop formation and types of loops during IC; and (2) to identify if there are any differences with the types of loop formation dependent on age.

Methods: One hundred consecutive patients undergoing IC were studied using real-time, three-dimensional magnetic endoscopic imaging, performed by 5 experienced endoscopists. The imager view of each procedure was recorded prospectively as were the type of loop, the resolution manoeuvre required and the position of the child when the loop was formed and resolved.

Results: 100 IC procedures occurred (50 male), median age 11.2 years (range 2 - 17 years). Indications included: suspected IBD; suspected polyp; and reassessment of IBD. A variable stiffness 3-D imager compatible colonoscope was employed.

Loops occurred in 90% of cases: of these only 57 were Alpha loops (57%) being the most common loop followed by reversed alpha (18%), deep transverse (16%), gamma (10%) and lastly large N loops (3%). There was no significant difference in the sex related complexity of the loop formation or having multiple loops (multiple loops - i.e. sigmoid AND transverse colon) -occurred in 8 females and 6 males). 60 loops were formed while the patient in supine position and 45 loops were formed in the left lateral position.

Eight loops were managed by pressure alone (4 gamma loops and three deep transverse loop and one N loop) as it was felt that advancement can be achieve safely without ‘de-looping’.

All alpha loops were resolved successfully using the clockwise rotation and all reversed alpha loops were resolved using the anticlockwise rotation.

For large N loops, deep transverse and gamma loops, clockwise or anticlockwise were needed. Of note 50% of the deep transverse loops needed a combination of clockwise followed by anticlockwise to resolve the loops successfully.

In children younger than five years old, reversed alpha and gamma loops were formed more frequently seen compared to older children.
**Table:** Characteristic of loop formation in the paediatric sample

<table>
<thead>
<tr>
<th>Loop type</th>
<th>All paediatric ages (n=100)</th>
<th>5 years or less (n=15)</th>
<th>6 - 10 years (n=22)</th>
<th>10-17 years (n=63)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha</td>
<td>57 (57%)</td>
<td>5 (33%)</td>
<td>13 (59%)</td>
<td>39 (62%)</td>
</tr>
<tr>
<td>Reversed Alpha</td>
<td>18 (18%)</td>
<td>6 (40%)</td>
<td>2 (9%)</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>Large N</td>
<td>3 (3%)</td>
<td>1 (7%)</td>
<td>2 (9%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>Gamma</td>
<td>10 (10%)</td>
<td>4 (31%)</td>
<td>2 (9%)</td>
<td>4 (6%)</td>
</tr>
<tr>
<td>Deep transverse</td>
<td>16 (16%)</td>
<td>2 (13%)</td>
<td>4 (18%)</td>
<td>10 (16%)</td>
</tr>
<tr>
<td>No loops</td>
<td>10 (10%)</td>
<td>1 (7%)</td>
<td>3 (14%)</td>
<td>5 (8%)</td>
</tr>
<tr>
<td>Multiple loops</td>
<td>14 (14%)</td>
<td>4 (31%)</td>
<td>4 (18%)</td>
<td>5 (8%)</td>
</tr>
</tbody>
</table>

**Conclusion:** Only 10% of paediatric colonoscopies in this first paediatric series were loop free. Alpha loops were the most common loop formed in our patient cohort and clockwise rotation was the most common loop resolution manoeuvre. In the subgroup of children of five year old or less, different loops (alpha, reversed alpha and gamma loops) were equally predominant.

**References:**

**Disclosure of interest:**
None Declared.
Targeted next generation sequencing: a powerful and sensitive tool for molecular diagnosis in monogenic enteropathies

Fabienne Charbit-Henriot\textsuperscript{1}, Sylvain Hanein\textsuperscript{2}, Begue Bernadette\textsuperscript{3}, Olivier Alibe\textsuperscript{4}, Cecile Fourrange\textsuperscript{5}, Marina Alo\textsuperscript{6}, Jorge Amil Dias\textsuperscript{7}, Mara Cananzi\textsuperscript{7}, Clara Cremilleux\textsuperscript{8}, Odül Eğritas Gürkan\textsuperscript{9}, Fabre Alexandre\textsuperscript{10}, Marta German\textsuperscript{11}, Yago Gonzalez Lama\textsuperscript{12}, Frédéric Gottrand\textsuperscript{13}, Olivier Goulet\textsuperscript{14}, Matjaz Homan\textsuperscript{15}, Jean-Pierre Hugot\textsuperscript{16}, Paraskevi Karanika\textsuperscript{17}, Alain Lachaux\textsuperscript{18}, Peter Lewindon\textsuperscript{19}, Janos Major\textsuperscript{20}, Emmanuel Mas\textsuperscript{21}, Mattyus Istvan\textsuperscript{22}, Luisa Mearin\textsuperscript{23}, Anders Paerregaard\textsuperscript{24}, Bénédicte Pigneur\textsuperscript{14}, Isabel Pinto Pais\textsuperscript{25}, Claudio Romano\textsuperscript{26}, Nadia Siala\textsuperscript{27}, Caterina Strisciuglio\textsuperscript{28}, Patrick Tounian\textsuperscript{29}, Dan Turner\textsuperscript{30}, Vaidotas Urbonas\textsuperscript{31}, Frank Rueemmele\textsuperscript{14}, Nadine Cerf-Bensussan\textsuperscript{1}

\textsuperscript{1}Imagine Institute, Inserm Umr 1163 - Intestinal Immunity, and Genius Group, Paris, France
\textsuperscript{2}Imagine Institute for Genetic Diseases, Paris, France
\textsuperscript{3}Imagine Institute, Inserm Umr 1163 - Genomic Platform, Paris, France
\textsuperscript{4}Imagine Institute, Paris Descartes University Bioinformatics Platform, Paris, France
\textsuperscript{5}Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Department of Pediatrics, and Genius Group, Rome, Italy
\textsuperscript{6}Centro Hospitalar São João, Department of Pediatrics, and Genius Group, Porto, Portugal
\textsuperscript{7}Unit of Pediatric Hepatology, Dpt. of Woman and Child Health, University Hospital of Padova, and Genius Group, Padova, Italy
\textsuperscript{8}Centre Hospitalo-Universitaire de St-Etienne, Département de Pédiatrie, and Genius Group, St-Etienne, France
\textsuperscript{9}Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
\textsuperscript{10}Hôpital de la Timone Enfant, Service de Pédiatrie Multidisciplinaire, and Genius Group, Marseille, France
\textsuperscript{11}12 de Octubre” Hospital, Infant Nutrition Unit, Madrid, Spain
\textsuperscript{12}Hospital Universitario Puerta de Hierro., Ibd Unit, and Genius Group, Madrid, Spain
\textsuperscript{13}Jeanne de Flandre Children’s Hospital, Lille University Faculty of Medicine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, and Genius Group, Lille, France
\textsuperscript{14}Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, and Genius Group, Paris, France
\textsuperscript{15}University Children’s Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia
\textsuperscript{16}Robert-Debré Hospital, Assistance Publique-Hôpitaux de Paris, Departments of Pediatric Digestive and Respiratory Diseases, and Genius Group, Paris, France
\textsuperscript{17}Department of Paediatric Gastroenterology Papageorgiou Hospital, Thessaloniki, Greece
\textsuperscript{18}Hôpital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology; Reference Centre for Wilson Disease, Lyon, France
\textsuperscript{19}Children’s Health Queensland Hospital and Health Service | Queensland Government, Lady Cilento Children’s Hospital, and Genius Group, Brisbane, Australia
\textsuperscript{20}Mre Bethesda Gyermekkórház, Department of Pediatrics, and Genius Group, Budapest, Hungary
\textsuperscript{21}Centre Hospitalier Universitaire de Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, and Genius Group, Toulouse, France
\textsuperscript{22}Semmelweis University , Pediatrics, and Genius Group, Budapest, Hungary
\textsuperscript{23}Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
\textsuperscript{24}Hvidovre University Hospital, Department of Paediatrics, and Genius Group, Copenhagen, Denmark
\textsuperscript{25}Centro Hospitalar Gaia Espinho, Department of Pediatrics, and Genius Group, Vila Nova de Gaia, Portugal
\textsuperscript{26}University of Messina, Pediatrics Department, Messina, Italy
\textsuperscript{27}Hôpital Mongi Slim , Service de Pédiatrie, and Genius Group, La Marsa, Tunisia
\textsuperscript{28}Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy
\textsuperscript{29}Hôpital Trouseau, Aphp, Service de Nutrition et Gastroentérologie Pédiatriques, and Genius Group, Paris, France
Objectives: Mendelian mutations causing early-onset enteropathies are identified in an increasing number of genes expressed either in hematopoietic immune cells, in epithelial cells or in both. Prediction of the affected genes can be difficult due to broad clinical heterogeneity or overlapping clinical presentations. Sanger sequencing is time-consuming and not always informative. Herein our goal has been to design and to test a dedicated gene panel for targeted next generation sequencing in order to simultaneously screen multiple candidate genes in a large number of patients.

Methods: To screen patients by targeted gene panel sequencing (TGPS), approximately 1000 regions encompassing 69 ID genes mutated in early onset immune-mediated enteropathies (including FOXP3, IL-10R, XIAP, LRBA, CTLA4...) or congenital diarrhea (including MYO5B, EPCAM, TTC37, NEUROG3, SPINT2, SLC26A3...) were captured with the 120-pb cRNA baits designed with SureSelect SureDesign, Agilent Genomics’ next generation custom design software (H. sapiens, hg19, GRCh37, February 2009). After informed and signed consent, genomic DNA libraries were produced from patients’ DNA using SureSelectXT Target Enrichment Reagent Kit (Agilent). Targeted regions were sequenced on an Illumina HiSeq2500, and data were analyzed by Imagine Institute Bioinformatics core facilities. Genome variations were defined using the in-house software PolyDiag, which eliminates irrelevant and common polymorphisms (Bioinformatics Paris Descartes University). Consequences of mutations on protein function was predicted using 3 algorithms: Polyphen2 (http://genetics.bwh.harvard.edu/pph2/), Sift (Sorting Intolerant From Tolerant, J. Craig Venter Institute) and Mutation Taster (www.mutationtaster.org). Between August and December 2015, TGPS was applied in 14 patients with known molecular diagnoses for panel validation and in 84 patients with early-onset enteropathies of unknown mechanism. Characteristics of the cohort are summarized in the Table.

Results: Coverage of the targeted 69 genes was between 400 and 800 reads for each region of interest. Known causal mutations were detected in 14/14 patients tested for panel validation, including one large deletion and one duplication of IL10R2 exons not detected by Sanger sequencing. Novel causative mutations were identified in 8 patients in 5 genes (NEUROG3, SKIV2L, FOXP3, TTC7A, CYBB) (Table), providing a precise diagnosis useful to adapt therapy. In 3 of the latter patients, enteropathy was known for over 10 years but had remained without molecular diagnosis.

Table:

<table>
<thead>
<tr>
<th>Total patients</th>
<th>Age at onset (months)</th>
<th>Enteropathies</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Median</td>
</tr>
<tr>
<td>84</td>
<td>53</td>
<td>12</td>
</tr>
<tr>
<td>New molecular diagnosis</td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>

Conclusion: Targeted next generation sequencing provides a sensitive genetic screening method for rapid identification of known monogenic causes of early-onset enteropathies. This cost-effective tool can now be applied to screen cases of severe enteropathies of unknown origin in children but also in adults even in the absence of familial pedigree given mounting evidence of disease causing de novo heterozygous mutation, of incomplete penetrance and of very variable age at onset.
Disclosure of interest: None Declared.

GASTROENTEROLOGY: Coeliac disease

Coeliac Disease across Mediterranean Countries: a prospective study

Andrea Smarrazzo¹, Carmela Arcidiaco¹, Virtut Velmishi², Eleftheria Roma³, Aydan Kansu⁴, Dušanka Mičetić-Turk⁶, Stefano Costa⁶, Karim Bouziane-Nedjadi⁷, Maria Legarda Tamara⁸, Mongi Ben-Hariz⁹, Zrinjka Mišak¹⁰, Veselinka Đurišić Kraljačić¹¹, Thomas M Attard¹², Mona Abu-Zekry¹³, abkari mohamed¹⁴, Giuseppe Magazzù⁶, Renata Auricchio¹, Luigi Greco¹

¹University of Naples “Federico II”, Dept. of Medical Translational Sciences and European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
²“Mother Teresa” Hospital, Service of Pediatric Gastroenterology, Tirana, Albania
³University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
⁴Ankara University Hospital, Paediatric Gastroenterology, Ankara, Turkey
⁵University Medical Centre, Paediatric Department, Maribor, Slovenia
⁶University of Messina, Celiac Regional Centre, Pediatric Gastroenterology and Cystic Fibrosis Unit, Messina, Italy
⁷Faculté de Médecine D’orlan, Oran, Algeria
⁸Crucens University Hospital, Paediatric Gastroenterology Unit, Barakaldo, Spain
⁹Mongi Slim’s Hospital, Pediatric Unit, Tunis, Tunisia
¹⁰Children’s Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
¹¹Clinical Centre of Montenegro, Pogdorica, Montenegro
¹²University of Malta, Msida, Malta
¹³Cairo University Children Hospital, El Cairo, Egypt
¹⁴Hospital Abderrahim Elharouchi Chu Ibn Rochd, Gastroenterology Unit, Casablanca, Morocco

Objectives and study: After the last revision of the ESPGHAN guidelines on Coeliac Disease (CD), most prospective studies about the application of these guidelines were performed in tertiary centres of affluent countries in subjects with classical gastrointestinal symptoms. This is the first and the largest multicentric study across Mediterranean countries involving unselected new cases referred for suspected CD, including asymptomatic subjects with associated diseases or familiarity for CD. The main goal was to assess how the diagnosis of CD is made and, as secondary aim, how the new ESPGHAN guidelines can be applied in different Mediterranean countries. Moreover, factors that may influence the onset of CD in the Mediterranean basin were investigated.

Methods: This study involved 14 Referral Centres for Coeliac Disease (from 13 different countries), members of the Mediterranean Network for the Management of Food-Induced Diseases (MEDICEL). 1974 children, who were investigated and then classified as confirmed or unconfirmed CD (UCD) according to shared criteria, were enrolled. Following data were collected into a web-based database of MEDICEL (www.medicel.unina.it): pregnancy duration and outcome, birth weight, breastfeeding and its duration, age of gluten introduction, number of previous hospital admissions, familiarity, associated diseases, clinical symptoms, anti-transglutaminase antibodies (t-TG) as N x Upper Limit Normal, EMA, and histology result (Marsh-Oberhuber classification). HLA-DQ2/DQ8 and follow-up visits were performed to confirm uncertain cases. t-Test, Odds Ratio (OR) and Positive Predictive Value were estimated for each variable assuming histology as gold standard.

Results: CD was confirmed in 511 (25.9%) and was unconfirmed in 1391 (70.5%); 14 patients were diagnosed according to the new ESPGHAN guidelines (0.7%; 2.47% of the final amount of diagnosis of CD); 43 patients were classified as having potential CD (7.4% of the CD). Among reported symptoms for referral, many common and typical symptoms of CD were equally present in the UCD group (also diarrhoea and failure to thrive), abdominal pain and constipation were more common (near double) in the UCD group, while food refusal, globose abdomen and paleness were slightly more frequent in the CD group. Having a positive titre of t-TG confers an OR of 1883.5 of being coeliac and a risk to have an intestinal atrophy 79 times higher, irrespective of HLA or EMA results. Out of the 427 patients with tTG>10 x ULN, applying the new ESPGHAN criteria in 3 (3.41%) the diagnosis of
potential CD would have been missed in absence of the biopsy. No clinical relevance could be found for duration of pregnancy, birthweight, breastfeeding or timing of weaning.

**Conclusion:** Our study provides a wide picture of CD diagnosis feasibility in Mediterranean countries with different health resources and facilities. Symptoms are not able to assign a pre-test probability to serological tests. The observed findings support a more cost-saving and less invasive approach to diagnose coeliac disease, avoiding HLA and EMA, that do not add diagnostic accuracy to t-TG and endoscopy for patients with high titres of t-TG, even though the chance of a potential CD has to be kept into account and discussed with the families. This is a result of great value especially for countries with limited resources.

**Disclosure of interest:** None Declared.
**GASTROENTEROLOGY: Coeliac disease**

**G-O-068**

**Anti-neo-epitope tTg complexed to gliadin are more reliable than tTg for celiac disease diagnosis**

Torsten Matthias¹, Patricia Jerermias¹, Sandra Neidhöfer¹, Aaron Lerner²

¹Aesku.Kipp Institute, Reseasrch, Wendelsheim, Germany
²Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel

**Objectives and study:** The guidelines of ESPGHAN for the diagnosis of pediatric celiac disease (PCD) rely on anti-human tissue transglutaminase (tTg) as the prime and unique antibody for screening PCD population. None of the CD-associated antibodies has challenged tTg premiership. tTg complexed to gliadin presents neo-epitopes and antibodies against the complex are called tTg neo-epitope. Reliability of anti-tTg and tTg-neo antibodies in diagnosis of PCD was compared.

**Methods:** 95 pediatric CD patients (mean 8.3y), 99 normal children (NC) (8.5y) and 79 normal adults (NA) (28y) were tested using the following ELISAs detecting IgA, IgG or both IgA+IgG: AESKULISA® tTg (tTg; RUO) and AESKULISA® tTg New Generation (tTg neo-epitope). The results were compared to the degree of intestinal injury, using revised Marsh criteria.

**Results:** A significantly higher OD activity was detected for tTg neo-epitope IgA, IgG and IgA+IgG than for tTg (p<0.0001, p<0.0001, p<0.001, respectively). tTg neo-epitope IgA, IgG correlated better with intestinal damage than tTg (r²=0.968, 0.989 compared to 0.909, 0.488 (p<0.001), respectively).

**Conclusions:** The tTg neo-epitope IgA, IgG and IgA+IgG isotypes exhibited a higher OD activity and better reflected intestinal damage in PCD, compared to tTg isotypes. The tTg neo-epitope IgA+IgG ELISA kit had higher sensitivity and a comparable specificity for the diagnosis of childhood CD. tTg neo-epitope should be included in the ESPGHAN diagnostic flow chart.

**Disclosure of interest:** TM is the head of Aesku.Kipp Institute. PJ, SN are employed by Aesku.Kipp Institute.
AL, “none declared”.

Vol. 62, Supplement 1, May 2016
Once versus twice daily mesalazine to induce remission in pediatric ulcerative colitis: an investigator-initiated randomized controlled trial

Dan Turner1, Baruch Yerushalmi2, Michal Korin3, Efrat Broide4, Yael Mozer-Glassberg5, Ron Shaoul6, Kaja Leena Kolho7, Eyal Shteyer8, Hussein Shamali9, Oren Ledder10, Shlomi Cohen1, Sarit Peleg12, Avi On13, Arie Levine14

1Shaare Zedek Medical Center, Genius Group, Jerusalem, Israel
2Soroka Medical Center, Beer Sheba, Israel
3Kaplan Medical Center, Petach Tiqva, Israel
4Assaf Harofeh, Tel Aviv, Israel
5Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel
6Rambam Medical Center, Haifa, Israel
7Helsinki University, Helsinki, Finland
8Shaare Zedek Medical Center, Pediatric Gastroenterology Institute, Jerusalem, Israel
9St Vincent Hospital, Nazereth, Israel
10Shaare Zedek Medical Center, Pediatric Gastroenterology, Jerusalem, Israel
11“Dana-Dwek” Children's Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology Unit, Tel Aviv, Israel
12Haemek, Afula, Israel
13Poria, Teverious, Israel
14Wolfson Medical Center, Holon, Israel

Objectives and study: Trials in adults have suggested that once daily 5ASA may be as or more effective than twice daily dosing in UC. There are no similar studies in children. In this 9-week induction investigator-blinded randomized controlled trial we aimed to compare the effectiveness and safety of once vs. twice daily Pentasa in paediatric UC.

Methods: Children, 4-18 years with a PUCAI of 10-55 were eligible for enrollment if they were not treated with effective 5ASA dose, in 13 centers in Israel and Finland. Children were randomized into two arms: once (OD) and twice (BID) daily Pentasa using a weight-based dosing table (max 3gr/d) and computer generated randomization. Primary outcome was week 6 mean PUCAI score, which has a high concordance with sigmoidoscopy in children. Physicians who completed the PUCAI were blinded to the treatment allocation as was the persons analyzing the data. Six visits were schedules until week 9 when safety was assessed. Missing data were imputed using the LOCF method; analyses were performed using the modified ITT approach.

Results: 86 children were randomized and 3 were excluded (1 withdrew consent before receiving study drug, 1 Crohn’s and 1 C. Difficile). 83 were analyzed: 43 in the OD and 40 in the BID groups (mean age 14±2.7 years, range 7-18, 43 (52%) males, 51 (62%) extensive colitis). 31 (38%) dropped due to disease aggravation, 7 (8%) lost to follow-up, and 45 (54%) completed the primary visit. There was no difference in completion rates between the OD (28 (65%)) and BID (28 (70%)) arms; P>0.2. Mean PUCAI scores at weeks 2, 3, 6 and 9 were similar between the OD vs BID arms (24±17 vs 21±16, 19±17 vs 17±17, 23±20 vs 19±20, and 22±21 vs 20±20; all P>0.2). The proportion of children who responded (PUCAI≤20) was similar at both weeks 6 and 9 (25 (60%) vs 25 (63%); p=0.78, and 25 (60%) vs 22 (55%); P=0.68, respectively). The proportion of children in remission (PUCAI<10) at week 6 and 9 was similar between the OD and BID groups (13 (30%) vs 16 (40%); P=0.35 and 15 (35%) vs. 17 (43%); P=0.48). Mean reported compliance with treatment was 94% in the OD vs 89% in the BID arms; P=0.17. There were no differences in the mean values of CRP, albumin, hemoglobin, and ESR at week 6 (all P>0.1). Most adverse events were related to disease aggravation and the rate of serious adverse events was similar (P=0.2); there were 9 events possibly related to the study medication with similar occurrence (4 vs. 5).

Conclusion: There were no differences in effectiveness, safety and compliance when prescribing Pentasa once or twice daily for inducing remission in active UC.
Disclosure of interest: This investigator-initiated study has been partially supported by an educational grant from Ferring. Ferring were not involved in any aspect of the study design, conduct, analyses and writing. DT, AL declare receiving travel grants from Ferring.
Gastroenterology: Coeliac disease

G-O-070

Gliadin an alimentary protein, regulated the INF-alpha immune response in celiac small intestine and in an enterocytes cell line

Merlin Nanayakkara¹, Giuliana Lania¹, Mariantonia Maglio¹, Valentina Discepolo¹, Cristiana De Musis¹, Salvatore Auricchio¹, Riccardo Troncone¹, Maria Vittoria Barone¹

¹University of Naples, Department of Translational Medical Science, Efld, Naples, Italy

Objectives and study: Celiac Disease (CD) is an autoimmune disease that is caused by the loss of oral tolerance to gluten, a protein contained in wheat, barley and rye. Gliadin peptides, P31-43, due to a sequence similarity with HRS (Hepatocytes Regulated Substrate kinase), a key molecule needed for the vesicular trafficking regulation, can impair the endocytic traffic and activate innate immune response in CD. Type 1 interferons are deregulated in CD patients, and rotavirus infections are associated with increased incidence of CD. Genetic studies suggest that Toll-like receptor 7 (TLR7) play a pathogenic role in CD.

In this paper we investigated in small intestinal biopsies the effect of gliadin peptide P31-43, on the INF-alpha pathway in CD patients both on GCD and GFD. In CaCo2 cells comparing the effects of P31-43 peptide with those of loxoribine (Lox) a TLR7 viral ligand, we have investigated: 1) the innate immune and inflammatory pathways, 2) their cooperation to activate the downstream signaling, 3) the role of HRS silencing, on the activation of the MxA/INF-alpha and NFkB pathways in absence of ligands and gliadin.

Methods: Western blot analysis of intestinal biopsies from CD patients and CaCo2 cells treated with P31-43 allowed to investigate the INF-alpha pathway. Total lysates of CaCo2 cells treated with P31-43 and Lox were also immunoprecipitated with MyD88 to detect TLR7/MyD88 complex. We analyzed, by PCR, INF-alpha mRNA levels. Immunofluorescence experiments allowed to analyze localization and trafficking of TLR7 under different conditions.

Results: In small intestinal biopsies gliadin peptide P31-43, activated INF-alpha pathway in CD patients both on GCD and GFD. After 30 min and 3h Lox treatment of CaCo2 cells, the amount of TLR7 in complex with MyD88 increased. Similarly the gliadin peptide P31-43 was able to induce a comparable increment of TLR7 in complex with MyD88 at 30 min and 3h. Both Lox and P31-43 treatment of CaCo2 cells increased NFkB phosphorylation and an increase of MxA protein. P31-43 and Lox treatment delayed TLR7 trafficking in the early endocytic compartment. A delay of the endocytic trafficking maturation by silencing HRS, induced an increase of the MyD88/TLR7 complex, and of INF-alpha and MxA levels.

Conclusion: In this paper we demonstrated, in small intestinal biopsies, that gliadin peptide P31-43, originated in the intestine by digestion of gliadin, was able to activate, INF-alpha pathway in CD patients. The peptide P31-43 like the viral ligand Lox, was able to activate, in intestinal epithelial cells, the pathway of TLR7, with a consequent innate immune response mediated by IFN alpha and NFkB activation.

A delay of the endocytic trafficking maturation induced by silencing HRS, in absence of the viral ligand and the gliadin peptide ended in an increase of the MyD88/TLR7 complex, and of INF-alpha and MxA. All this suggested that the mechanism by which P31-43 activated the pathway of TLR7 could be the delay of the endocytic trafficking

Disclosure of interest: None Declared
Effect of calcium and vitamin D supplementation in celiac disease

Paola Sgaramella\(^1\), Martina Fomasi\(^1\), Patrizia Corsin\(^1\), Stefano Mora\(^2\), Graziano Barera\(^1\)

\(^1\)San Raffaele Scientific Institute, Department of Pediatrics, Milan, Italy
\(^2\)San Raffaele Scientific Institute, Pediatric Bone Densitometry Unit, Milan, Italy

Objectives and study: Children with celiac disease (CD) have low bone mineral content and density at diagnosis. After 12 months, the gluten-free diet (GFD) normalises bone metabolism and bone mass, but it is unclear whether supplementation with calcium and vitamin D can achieve the same results in less time.

Evaluation of the effect of oral supplementation of calcium and vitamin D on the recovery of bone mass and on normalization of bone metabolism in children with CD on GFD.

Methods: This randomized double-blind trial included 31 patients between 5 and 17 years at diagnosis. The patients were randomly assigned to two groups receiving, for 6 months, a supplementation of oral calcium and vitamin D or a placebo. Markers of bone turnover and metabolism (serum calcium, magnesium, phosphorus, Bone-specific alkaline phosphatase (BALP), C-terminal telopeptide of type I collagen (CTX), 25OH vitamin D (25OHD)), were estimated at baseline and after 2, 6 and 12 months. Bone Mineral Density and Bone Mineral Content were detected by DXA at baseline and after 6 and 12 months.

Results: 24 patients completed the trial, 10 in the placebo group and 14 in the supplemented one. The trial documented not changes in serum calcium, phosphorus and magnesium. BALP and CTX decreased and 25OHD increased in the group supplemented for 6 months. No difference in bone mass among all patients was found.

Conclusion: GFD and supplementation with calcium and vitamin D cause reduction in bone turnover, increase in levels of 25OHD and no significant change on bone mass.

Disclosure of interest: None Declared.
Epitopes of human and microbial transglutaminases are similarly recognized by celiac disease sera

Patricia Jeremias¹, Kai Prager², Sandra Neidhöfer², Aaron Lerner³, Torsten Matthias¹

¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Aesku.Diagnostics, Research, Wendelsheim, Germany
³Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel

Objectives and study: The use of microbial transglutaminase (mTg) in the food industry is expanding alongside its ingestion in Western diet. 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). These complexes were purified by asymmetric flow field-flow fractionation and confirmed by multi-angle light scattering and SDS-PAGE. Sera of 81 CD patients (mean age 30±17) and 81 healthy controls (mean age 29±21) 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 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 and 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 impact the food industry additive policy and regulation.

Disclosure of interest: T M is the head of the Aesku.Kipp Institute, and the owner of Aesku.Diagnostics. PJ is employed by Aesku.Kipp Institute. KP, S N, are employed by Aesku.Diagnostics. A L “none declared”.
Gastroenterology: Coeliac Disease

G-eP-003

Outside the normal limits: False positive/negative of anti TG2 autoantibodies

Aaron Lerner¹, Patricia Jeremias², Torsten Matthias²

¹Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel
²Aesku.Kipp Institute, Research, Wendelsheim, Germany

Objectives and study: Detection of IgA-transglutaminase2 (TG2) autoantibodies has become the test of choice for the diagnosis and monitoring of celiac disease (CD), and is recommended as the serological ‘gold standard’ by most of the CD societies. Despite its wide acceptance and reasonable performance, several aspects are problematic and disputed. The aim of the review is to summarizes the literature for clinical and laboratory circumstances for false positive and negative anti TG2 antibody titers.

Methods: A systematic review was performed to identify Studies referred to false positive/negative anti TG2 antibody levels, using Medline, Google, and Cochrane Library databases.

Results: The normal range levels between positivity and negativity are modified, manufacturers’ cut-off levels are extremely variable, far from matching in house determinations, insufficient standardization, inadequate reference protocols and no reliable quality assessment of the ELISA antibody (AB) kits for CD diagnosis and follow-up of dietary adherence. Numerous limitations exist in its detection, diagnosis, and follow-up capacities, resulting in frequent clinical circumstances when professionals encounter false positive and negative situations. True false positivity includes: other autoimmune diseases, association with IgM rheumatoid factor, in CD patients with negative EMA, in CP children, in transient positivity, during febrile infectious fever. False negative include: IgA deficiency, refractory CD, intestinal bacterial overgrowth, older age, in face of sub epithelial deposit and negative serum antibodies, on GFD, in primary care determinations, temporary fluctuations on GCD, influenced by age/genetic risk.

Conclusions: Multiple false positive and negative situations face the clinicians/laboratories in antiTg2 levels interpretation. The medical CD professionals are using routinely IgA-TG2 serology and face often the dilemma of its interpretation. Understanding the circumstances and the significance of the false positive/false negative anti-TG2 ABs will improve the clinical judgment of the CD associated health workers in face of a suspected CD patient.

Disclosure of interest: T M is the head of the Aesku.Kipp Institute, PJ is employed by Aesku.Kipp Institute. A L “none declared“.
GASTROENTEROLOGY: Coeliac disease

Epigenetic of Coeliac Disease: Expression in epithelial cells and cells of the lamina propria

Donatella Cielo1, Martina Galatola1, Daniela Furlan1, Marinita Morelli1, Tarcisio Not2, Renata Auricchio1, Luigi Greco1

1University of Naples "Federico II", Dept. of Medical Translational Sciences and European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
2Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Trieste, Italy

Objectives and study: In the context of celiac disease (CD), it was not identified a strong association with alterations in a single gene. The studies focused of the intestinal mucosa, analyzed the whole tissue, but this is composed of two compartments with very different characteristics: the epithelium and lamina propria. Nothing has been done so far to clarify the contribution of each of the two components as part of the CD. Given the "missing heritability" of CD, a post-genomic analytical approach could help to better understand the molecular pathogenesis, and finding a new diagnostic marker. The aim of the study is to analyze the change in the levels of expression, in some candidate genes and in two different cell types extracted from intestinal biopsies: epithelial and of the lamina propria cells. The ultimate goal will be to select a "top genes" of candidate genes to study the DNA methylation and other epigenetic mechanisms.

Methods: For this study we were analyzed both components (Epithelial and Lamina Propria) of the 20 subjects, 10 CD and 10 CTR, for a total of 40 analyzed samples. The experiments were performed with Real-Time PCR system using the TaqMan Gene Expression Assays. The relative expression of each gene was obtained using the ΔΔCt method.

Results: Firstly we evaluated the gene expression of the candidate genes in epithelial cells comparing CDs versus CTRs, 5 genes: REL, RGS1, TAGAP, SH2B3 and NFKB1 are significantly up-regulated and TNFRSF14 is down-regulated in CD patients. However, the other three genes (PTPRK, TJP1, and TNFAIP3) show a trend very obvious. Then, we analyzed gene expression also in lamina propria, three genes PTPRK, TJP1 and NFKB1 are significantly deregulated in CD and others genes (KIAA, TNFAIP3, TNFSF14 and SH2B3) show different expression levels. Finally, it was evaluated the expression of genes differential between the two compartments. The analysis was conducted in parallel in CTRs and in CDs. We have identified as "epithelial genes": LPP, TNFRSF14 PTPRK, and C1ORF10. Equally, we have classified with other genes, "lamina propria’s genes": REL, RGS1, SH2B3, TAGAP, TNFAIP3, TNFSF14 and ARGHAP. However, only five of these genes show the same trend in CD and CTRs, while REL and TNFAIP3 not show significant changes between the two cell populations in CD patients. Only one gene, TJP1 shows an imbalance of expression, most high in epithelium, only in CD. Using a discriminant analysis we had selected 4 genes (c-REL, NFKB1, TNFRSF14 and TNFSF14) for discriminating capacity. The same analysis was conducted in lamina propria cells, and 5 genes (PTPRK, TNFSF14, TJP1, LPP and NFKB1) were selected for their capacity of classification. For both the compartment, just control and none CD, was misclassified, with a final rate of 95% of correct classification.

Conclusion: Candidate genes, with the exception of NFKB1, have a very different expression profile between the two compartment cell, in at least one of the populations analyzed (CDs and CTRs). The different expression between celiac and control mainly occurs in the cellular compartment where the specific gene is more expressed. The characterization of the cell's district of intestine, where these genes are expressed, can help further clarify, in future, the pathogenic role of these candidate genes.

Disclosure of interest: None Declared.
Differential constitutive distribution of type 2 transglutaminase in skin derived-fibroblasts from celiac disease patients and from healthy subjects

Gaetana Paolella\textsuperscript{1}, Marilena Lepretti\textsuperscript{1}, Carla Esposito\textsuperscript{2}, Merlin Nanayakkara\textsuperscript{3}, Riccardo Tromcone\textsuperscript{3}, Salvatore Auricchio\textsuperscript{3}, Maria Vittoria Barone\textsuperscript{3}, Ivana Caputo\textsuperscript{2}

\textsuperscript{1}University of Salerno, Chemistry and Biology, Fisciano (Sa), Italy
\textsuperscript{2}University of Salerno, Chemistry and Biology, Elfid, Fisciano (Sa), Italy
\textsuperscript{3}University Federico II of Naples, Translational Medical Sciences, Elfid, Naples, Italy

Objectives and study: Celiac disease (CD) is a complex inflammatory disorder triggered by the consumption of cereals containing gliadins, or other prolamines, which cause a damage at the intestinal level in genetically predisposed individuals. Type 2 transglutaminase (TG2)-induced modifications of gliadin peptides are strongly implied in CD pathogenesis. Recently, an in vitro model of skin-derived fibroblasts has been developed to study constitutive differences between cells from healthy subjects and CD ones (Nanayakkara m. et al. Plos one 2013, 8 (11) e79763). With this study we aimed to investigate whether control and CD fibroblasts displayed constitutive differences regarding TG2 expression level, activity and subcellular distribution.

Methods: Fibroblasts were obtained from skin biopsies of four CD patients on a gluten-free diet (age range 17-43 years) and four HLA DQ2-negative healthy controls (age range 25-30 years) (protocol approved by the Ethical committee of the University Federico II of Naples, C.E. n. 230/05). To analyze TG2 levels in total cell lysates and in subcellular fractions obtained by ultracentrifugation, western blot analyses were performed by using the CUB7402 antibody. To monitor TG2 transamidating activity, a quantitative microplate assay was performed by using the substrate pentylamin-biotine. To visualize TG2 distribution into cells, confocal microscopic images were analyzed.

Results: We found that TG2 was expressed in all samples from cell lysates, however protein levels were variable in both groups of subjects. We also demonstrated that TG2 activity was inducible in all cell cultures tested and it well correlated with protein expression levels. By performing subcellular fractionating experiments, we observed that TG2 was always more abundant in membrane fractions, but in CD fibroblasts this phenomenon was greatly more evident. Finally, confocal images showed that TG2 differently distributed into vesicular compartment, in particular we found a higher association with the early endosome compartment in celiac fibroblasts with the respect to control ones.

Conclusion: These findings let us to affirm that in celiac fibroblasts TG2 preferentially associates to membranes and is more abundant in the early endosome compartment, thus contributing to determine a "CD cellular phenotype" which is independent from gliadin exposition and is also displayed far from the main site of inflammation.

Disclosure of interest: None Declared
The role of functional platelet indices in childhood coeliac disease

Nevzat Aykut Bayrak¹, Burcu Volkan², Serhat Samanci¹

¹Diyarbakir Children's Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
²Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey

Objectives and study: It's known that the inflammatory process in Coeliac disease (CD) is mediated by interleukin-3 and interleukin-6 (IL-6). Furthermore, IL-6 stimulates megakaryocytes to produce young platelets, which are more reactive and larger in size. A few adult studies demonstrated an association between mean platelet volume (MPV) and dietary adherence in CD. The aim of the study is determining the value of platelet count, MPV, plateletcrit (PCT) and platelet distribution width (PDW) on histologic disease stage and gluten free diet (GFD) adherence in pediatric CD.

Methods: Children diagnosed as CD and age and sex matched healthy subjects were recruited. CD patients were classified into two groups: newly diagnosed and on GFD at least over 1 year. CD patients on GFD were further divided into two groups according to their dietary adherence determined by anti-tissue transglutaminase IgA levels. Samples for complete blood count were obtained from all patients and studied within 2 hours. Patients with selective IgA deficiency, diabetes mellitus, acute infection and other accompanying systemic disease were excluded.

Results: A total of 236 CD patients (60 newly diagnosed, 83 with good GFD adherence and 93 with poor GFD adherence, mean age: 11±3.9 years, 59.3% female) and 92 healthy subjects (mean age: 10.7±3.8 years, 52.2% female) were studied. Mean thrombocyte, MPV, PCT and PDW values of CD and control groups are demonstrated in table 1. Thrombocytes, MPV, PCT and PDW values of new diagnosed CD cases and poor GFD adherence cases were statistically similar (p>0.05) while they were statistically higher than the control group and good GFD adherence cases (p<0.01). In ROC analysis, MPV had the highest area under the curve (0.758). The sensitivity and the specificity of MPV was 85.3% and 71.7% respectively for the cut off value of 8.65 fL. Only PCT was found correlated with modified Marsh stage in new diagnosed CD patients (r²:0.302, p<0.05).

Table:

<table>
<thead>
<tr>
<th>Group</th>
<th>Thrombocytes (10³/mL) (mean±SD)</th>
<th>MPV (fL) (mean±SD)</th>
<th>PCT (%) (mean±SD)</th>
<th>PDW (fL) (mean±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>286.13±82.8</td>
<td>8.29±1.09</td>
<td>0.23±0.06</td>
<td>16.39±0.5</td>
</tr>
<tr>
<td>New diagnosed CD</td>
<td>380.12±98.7</td>
<td>9.23±1.34</td>
<td>0.27±0.05</td>
<td>15.2±1.6</td>
</tr>
<tr>
<td>CD good GFD adherence</td>
<td>288.14±66.3</td>
<td>8.48±1.03</td>
<td>0.24±0.04</td>
<td>16±0.9</td>
</tr>
<tr>
<td>CD poor GFD adherence</td>
<td>324.95±92.6</td>
<td>9.28±1.11</td>
<td>0.29±0.07</td>
<td>15.4±1.1</td>
</tr>
</tbody>
</table>

Conclusion: This is the first report about platelet functions in children with CD. Functional platelet indices, especially MPV and PCT, would be a promising tool in CD patients for indirect determination of GFD adherence and stage of villous atrophy, respectively, at a low cost in comparison to other modalities.

Disclosure of interest: None Declared
Critical appraisal of the 2012 ESPGHAN diagnosis criteria. Spanish Working Group on Celiac Disease

Enriqueta Román Riechmann1, Mª Luz Cilleruelo Pascual1, Esther Donat2, Isabel Polanco1, José Ignacio García Burriel3, Francisco Javier Eizaguirre Arocena4, Beatriz Martín Sacristán-Martín5, José Carlos Salazar Quero6, Rosaura Leis Trabajo7, Felix Sanchez Valverde8, María José López Rodriguez9, Carolina Gutierrez Junquera1, Eva Martinez-Qinaga Nodal1, Salvador García Calatayud11, Honorio Armas Ramos12, Idoia Huade Tapia12, Javier Rubio Santiago14, Joseba Barrio Torres15, Luis Ortigosa del Castillo16, Ruth García Romero17, Pedro Urruzuno Tellería18, Cecilia Martínez Costa19, Gemma Castillejo20, Gonzalo Galicia Poblet21, Carmen Ribes Koninckx2

1Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
2La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
3La Paz University Hospital, Dept. of Pediatric Gastroenterology and Nutrition, Madrid, Spain
4Complejo Hospitalario Universitario de Vigo, Paediatric Gastroenterology Unit, Vigo, Spain
5Hospital de Donostia, Paediatric Gastroenterology Unit, Donostia-San Sebastian, Spain
6Hospital Virgen de la Salud, Pediatric Gastroenterology Unit, Toledo, Spain
7Hospital Universitario Infantil Virgen del Rocío, Pediatric Gastroenterology Unit, Sevilla, Spain
8Complejo Hospitalario Universitario Santiago, Pediatric Gastroenterology Unit, Santiago de Compostela, Spain
9Hospital Virgen del Camino, Pediatric Gastroenterology Unit, Pamplona, Spain
10Hospital San Pedro de Alcántara, Pediatric Gastroenterology Unit, Caceres, Spain
11Hospital Marqués de Valdecilla, Pediatric Gastroenterology Unit, Santander, Spain
12Hospital Universitario de Canarias, Pediatric Gastroenterology Unit, La Laguna (Tenerife), Spain
13Hospital Tzagorritxu, Pediatric Gastroenterology Unit, Vitoria, Spain
14Hospital S.A.S. de Jerez, Pediatric Gastroenterology Unit, Jerez de la Frontera, Cadiz, Spain
15Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
16Hospital Universitario Virgen de La Candelaria, Pediatric Gastroenterology Unit, Tenerife, Spain
17Hospital Universitario Miguel Server, Pediatric Gastroenterology Unit, Zaragoza, Spain
18Hospital Universitario 12 de Octubre, Paediatric Gastroenterology, Madrid, Spain
19Hospital Clínico Universitario, Pediatric Gastroenterology Unit, Valencia, Spain
20Hospital Universitario Sant Joan de Reus, Pediatric Gastroenterology Unit, Reus, Spain
21Hospital Universitario de Guadalajara, Pediatric Gastroenterology Unit, Guadalajara, Spain

Objectives and study: The new ESPGHAN criteria for Celiac Disease (CD) diagnosis allowing to skip the Small Bowel Biopsy (SBB) under well defined circumstances have not yet been sufficiently validated. The aim of the study was to assess the accuracy of the 2012 ESPGHAN criteria for CD diagnosis in children and adolescents.

Methods: Data were obtained from a nationwide prospective registry of new paediatric CD cases in Spain (REPAC).

Results: From 1/01/2011 till 31/10/2015 a total of 4470 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. In 2798 cases (62.6%) a SBB was performed. Out of these, 728 (26%) fulfilled the new ESPGHAN criteria to eventually avoid a SBB. A Marsh I lesion was found in 2.8% (21) out of 728 while 94% had Marsh III and 3.2% Marsh II. Thus, as only Marsh II and Marsh III lesions are considered to be diagnostic for CD, by applying the new criteria overdiagnosis risk would be 2.8%. Interestingly we observed that all 21 Marsh I cases pertained to only 8 PGUs. If we do not take HLA into consideration, 995 patients fulfilled the remaining criteria (symptoms plus transglutaminase antibodies ≥ 10x the upper level of normal and positive endomisial antibodies) but only 3 additional cases with Marsh I are found, thus amounting to 24 which corresponds to 2.4% (24 out of 995). Equally Marsh I was found in 4.7% (132/2798) of the whole population of reported patients with a SBB and in 5.38% of those who do not fulfil the criteria to avoid the SBB. Thus total risk of overdiagnosis among the total number of patients reported in the survey is 4.7%.
**Conclusion:** According to our study results if the new criteria are fulfilled diagnosis of CD without performing a SBB is a safe option with a risk of overdiagnosis lower than 3% which is even lower than the risk observed in the whole population reported in the survey. Moreover clustering of Marsh I cases in a very small number of PGUs questions the consistency of the histological evaluation and further supports the reliability of the new ESPGHAN guidelines for CD diagnosis. Considering HLA as a criteria to skip the SBB seems to have little impact on the risk of overdiagnosis.

**Disclosure of interest:** None Declared.
Tissue transglutaminase Antibody cut-off and diagnosis of celiac disease

Gloria Raimondi¹, Isabella Mezzina², Maria Elena Tripaldi³, Stefania Castellaneta⁴, Fernanda Cristofori⁵, Cinzia Ciullo⁶, ruggiero francavilla⁷

¹Policlinico DI Bari, Bari, Italy  
²Università DI Bari, Italy, Dipartimento Interdisciplinare DI Medicina, Sezione DI Pediatria., Bari, Italy  
³Dipartimento Interdisciplinare DI Medicina, Sezione DI Pediatria. Università DI Bari, Bari, Italy  
⁴San Paolo Hospital, Department of Pediatrics, Bari, Italy  
⁵Ss. Annunziata Hospital/ Pediatric Department, Taranto, Italy  
⁶Policlinico DI Bari-Giovanni XXIII Hospital, Bari, Italy  
⁷University of Bari Giovanni XXIII Hospital, Paediatrics, Bari, Italy

Objectives and study: It has been reported a correlation between tissue transglutaminase antibodies titers and degrees of duodenal biopsy, and based on this, ESPGHAN guidelines have proposed that duodenal biopsy can be omitted in some patients with high levels of tTg antibodies (N10 x upper normal limit).

Objectives: to evaluate the relationship between tTg antibody levels and histologic Marsh grading and to identify a lower value of tTG for which intestinal biopsy can be avoided.

Methods: a retrospective analysis of 524 celiac pediatric patients with positive tTG and small bowel biopsy were included. The positive predictive values (PPV) for different cut-off points of transglutaminase levels for the diagnosis of celiac disease was assessed.

Results: We studied 524 patients (322 women-61%) diagnosed in our Centre in the last ten years. The mean±SD age of the patients was 11,6 years (range 3,8 – 18 years). 515 out of 524 patients had villous atrophy (Marsh III). Abdominal pain, diarrhea and bloating were the first three common symptoms and anemia was the most common sign in this patients. Mean tTG titers was significantly higher in patients graded as Marsh III as compared to Marsh II and I (11,2 UNL vs. 5,1 UNL; p<0,001). Our results showed that tTG titer more than 6 folds higher then the kit's cut-off value have a specificity of 96% and a positive predictive value of 99,7% for Marsh III lesion.

Conclusion: There is a clear correlation between tTG titers and degrees of duodenal damage in patients with celiac disease. We propose that, in case of high clinical suspicion, when tTG level is more than 6 folds higher than the manufacture's recommended cut-off value, duodenal biopsy can be avoided.
Clinicopathological features of gastrointestinal and liver GVHD in children with allogeneic stem cell transplantation

Arzu Demir1, Zarife Kuloğlu1, Aytaç Yaman1, Hasan Fatih Çakmakli2, Talia İleri2, Elif İnce2, Mehmet Ertem2, Arzu Ensari3, Esra Erden3, Zümrüt Uysal2, Aydan Kansu1

1Ankara University Hospital, Paediatric Gastroenterology, Ankara, Turkey
2Ankara University Hospital, Paediatric Haematology, Ankara, Turkey
3Ankara University Hospital, Pathology, Ankara, Turkey

Objectives and study: Graft-versus-host disease (GVHD) is a major complication of hematopoietic stem cell transplantation (HSCT), and the digestive system is commonly affected. Our aim was to investigate the frequency and clinicopathological features of digestive system GVHD.

Methods: We retrospectively analyzed the medical records of 256 children who underwent allogeneic HSCT between 1996–2012 and extracted data from those who underwent endoscopy and/or liver biopsy for suspected GVHD. The histological diagnosis of GVHD was based on gland apoptosis for gastrointestinal (GI) GVHD; the lymphocytic infiltration in portal tract, ductitis, endothelitis and cholestasis for liver (L) GVHD. GI involvement was graded as grade (G)1; increased crypt apoptosis, G2; crypt apoptosis with abscess formation, G3; individual crypt necrosis and G4; denudation of areas of mucosa.

Results: Digestive system GVHD was suspected clinically in 26 patients. Upper GI endoscopy (UGIE) (n=14), colonoscopy (n=10), both UGIE and colonoscopy (n=6) and liver biopsy (n=15) were performed. The median endoscopy and liver biopsy time were 35 days (range 20–840 day) and 10 months (range 5–17 months) posttransplant, respectively. No complication was seen. GVHD was histologically diagnosed in %84.6 (22/26); all over, %8.5 of 256 transplant recipients. The median age was 12.30±4.26 years and %59.1 of patients were male. Underlying diseases were thalassemia major (n=6), acute myeloid leukemia (n=4), chronic myelogenous leukemia (n=4), myelodysplastic syndrome (n=4) and others (n=4). The sources of stem cells for transplantation were bone marrow in 4 patients, peripheral blood from related donors in 17 patients and both bone marrow and peripheral blood from related donors in 1 patients. Isolated GI, L and both GI and L GVHD were seen in %40.9, %22.7 and %36.3 of patients. The most frequently reported symptoms and findings in 22 patients were diarrhea (%63), nausea (%54), vomiting (%50), abdominal pain (%31), anorexia (%27), intestinal bleeding (%13.6), hypoalbuminemia (%81), abnormal liver enzymes (%59) and hyperbilirubinemia (%4). Seventeen patients had GI-GVHD. UGIE was abnormal in all subjects. Colonoscopy was abnormal except for one patient. Edema, erythema, ulcer, fragility, granularity and loss of vascularity were seen in endoscopy. Histologically, Grade I, II, III and IV GVHD were seen in 4, 1, 5 and 2 patients with upper GI-GVHD. Grade II, III and IV GVHD were seen in 3, 7 and 2 patients with lower GI-GVHD. L-GVHD was present in 13 patients. All patients with L-GVHD had abnormal liver enzymes. Liver biopsies showed ductitis (%76.9) endothelitis (%30.7), lymphocytic infiltration (%38.4), fibrosis (%23) and hemosiderosis (%53.8). All over mortality was %18.1 (4/22).

Conclusion: Digestive system GVHD was histologically diagnosed in %8.5 of all recipients. Non specific endoscopic findings like edema, erythema, ulcer and fragility were common in GI-GVHD patients. So histopathological evaluation is essential for definitive diagnosis of GI-GVHD. The most common histopathological finding in L-GVHD was bile duct injury. Abnormal liver tests is predictor for L-GVHD.

Disclosure of interest: None declared.
A single center experience with endoscopic and surgical gastrostomy in pediatric patients: A 10 year review

Jiyoung Kim¹, Seung Kim¹

¹Severance Children's Hospital, Seoul, Rep. of South Korea

Objectives and study: Objectives: Gastrostomy insertion is an effective and validated method of nutritional supplementation even in pediatric patients. The purpose of this study is to review the outcomes of gastrostomy insertion (endoscopy and surgery) in children and to suggest the algorithm for choosing the optimal method of gastrostomy.

Methods: Retrospective chart review of 236 patients who had their gastrostomy insertion done before the age of 18 years old at our institution from Oct. 2005 to March 2015. The most minimally invasive method for gastrostomy insertion was chosen for each patient, following an algorithm considering demographics, underlying disease, comorbidities, evaluation for gastric reflux, and ventriculoperitoneal shunt insertion status.

Results: Of the 236 patients included in our study, 120 patients underwent endoscopic gastrostomy, 101 patients had laparoscopic gastrostomy, 15 patients had open gastrostomy procedures. The time interval between disease onset and insertion of gastrostomy was variable from 1 day to more than 8 years. The mean length of follow-up was 45 months. All short term postoperative complications and long term gastrointestinal complications were monitored. Short term (1month) complication rates were 11.2% in surgical groups and 5.8% in endoscopy groups. Only one case of major complication was in each group. During the total follow up duration, the major complication rate for endoscopic gastrostomy insertion was 12.5%, and for surgical gastrostomy insertion 11.2 %. The minor complication rate was 39.1 % for endoscopic gastrostomy insertion and 50.8 % for surgical gastrostomy insertion. The most common major complication was GERD needing Nissen fundoplication (5.4%), and other complications included peritonitis (1.2%), hiatal hernia (1.2%), bowel perforation (0.8%), and dumping syndrome (0.4%). Gastrostomy removal was successful in 8.6%, and 5.0% of endoscopic gastrostomy insertion and surgical gastrostomy insertion patients respectively. After removal of gastrostomy 60% of patients who had gastrostomy removal after surgical gastrostomy insertion had gastrocutaneous fistula, needing a second operation. However, none of the patients who had endoscopic gastrostomy insertion had gastrocutaneous fistula, and the opening naturally healed in all cases.

Conclusion: The procedure of gastrostomy insertion is invasive and can have significant complications, therefore the most minimally invasive but safe and guaranteed method should be chosen for each patient. The algorithm we used seems to be appropriate which prioritized the endoscopic approach and used the laparoscopic approach in patients with severe anatomical abnormality in peritoneum, infants less than 10kg, patients needing fundoplication.

Disclosure of interest: The authors declare no conflict of interests.
Kinga Kowalska-Duplaga¹, Izabela Łazowska-Przeorek ², Katarzyna Karolewska-Bochenek ², Marek Woynarowski², Grażyna Czaja-Bulsa³, Andrzej Stawarski³, Stanisław Pieczarkowski⁴, Ewa Hapyn⁵, Jan Józefczuk⁶, Bartosz Korczowski⁵, Anna Szafiarska-Popławska ¹⁰, Aleksandra Banaszkiewicz²

¹Department of Pediatrics, Gastroenterology and Nutrition Jagiellonian University Kraków, Poland
²Medical University of Warsaw, Department of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
³Children’s Memorial Health Institute, Department of Gastroenterology Hepatology and Feeding Disorders, Warsaw, Poland
⁴The Pomeranian Medical University, Paediatric and Paediatric Nursery Unit of The Pomeranian Medical University in Szczecin, Poland
⁵Medical University of Wroclaw, Department of Pediatrics, Gastroenterology and Nutrition, Wroclaw, Poland
⁶Jagiellonian University Medical College, Department of Pediatric, Gastroenterology and Nutrition, Cracow, Poland
⁷Area Hospital in Torun, Department of Pediatrics and Gastroenterology, Torun, Poland
⁸Specialist Hospital of Holy Spirit, Pediatric Department With Children’s Cardiological Subunit, Sandomierz, Poland
⁹Medical College, University of Rzeszów, Pediatric Department, Rzeszów, Poland
¹⁰Collegium Medicum Nicolaus Copernicus University, Department of Pediatrics, Allergology and Gastroenterology, Bydgoszcz, Poland

Objectives and study: Solitary rectal ulcer syndrome (SRUS) is a rare disease occurring both in adults and children. Available data on SRUS in children are very limited and are based on case reports only. This study was undertaken with the objective of describing the clinical history, symptoms, diagnostic work-up and treatment of a large case series of pediatric patients with SRUS.

Methods: The study was multi-center and retrospective. All pediatric endoscopists in Poland were invited to participate. They received email invitations (three times in 2-month intervals) and were asked to look through their endoscopic databases to identify SRUS cases from last 10 years. The charts of identified patients were reviewed with regard to age at the diagnosis, sex, history and results of physical examination as well as laboratory and endoscopic and histological findings. Additionally, treatment methods and outcomes were assessed. Only patients under the age of 18 years at the time of diagnosis were included in the study. They could be diagnosed with SRUS and treated as such on inpatient or outpatient basis. Diagnosis of SRUS was based on characteristic endoscopic and histological findings. The histological criteria included splaying and hyperplasia of smooth muscle cells, fibrosis of the lamina propria leading to crypts and mucosal gland distortion and hyperplasia which could lead to polypoid appearance. Acute inflammation was assessed on the basis of presence of neutrophils in the lamina propria and glands, while chronic inflammation was characterized by lymphoplasmacytic infiltrate in the lamina propria.

Results: In total, 31 patients (18 males, mean age 13.5 years, ranged from 5.0 to 17.5 years) were included in the study. All patients reported rectal bleeding. Other common symptoms occurred with following frequency: abdominal pain (64.5%), perianal pain (54.8%), passage of mucus (51.6%). Constipation and diarrhea as well as straining at stool were present in 45% of patients, and sensation of incomplete defecation in 35% of them. Rectal digitation was recorded only in 19% patients and rectal prolapse in 16.% of them. The whole diagnostic work-up lasted 1 – 48 months (mean±standard deviation (SD): 9.98± 10.0 months). Colonoscopic findings revealed rectal ulceration in 96.8 % patients. The lesions, exclusively ulcers (32.2%), polyps (22.6%) or combination of those two, were located 7-13 cm from the anal verge. Therapeutic approaches included: high fiber diet (64.5%), laxatives (45.2%), topical corticosteroids (61.3%), sulfasalazine or mesalazine administered orally and topically (29% and 96.8%, respectively), sucralfate (10%) and biofeedback training (7%). Endoscopic
argon plasma coagulation was performed in 2 patients and surgical intervention was necessary in 4 of them. Treatment was unsuccessful in 36 % of patients.

**Conclusion:** Results of our study indicated that diagnosis of SRUS may be considerably delayed, and applied treatment is often ineffective.

**Disclosure of interest:** None Declared.
Esophageal Savary Dilation Is an Effective and Safe Treatment For Esophageal Narrowing Associated With Pediatric Eosinophilic Esophagitis

Abdulrahman Al-Hussaini

1King Fahad Medical City, Children's Specialized Hospital, Riyadh, Saudi Arabia

Objectives of the study: Data on management of esophageal narrowing associated with eosinophilic esophagitis (EoE) in children are scanty. We report the largest pediatric case series with the aim to assess the safety and effectiveness of esophageal dilation in pediatric EoE.

Methods: Children with EoE diagnosed during the period from 2004 to 2014, were reviewed for presence of esophageal narrowing. An esophageal narrowing limited to one portion of esophagus defined a short segment narrow caliber, a narrowing involving two or more portions defined a long segment narrow caliber, while a very short stenosis (< 1cm in length) defined esophageal stricture. The characteristics of the narrowed esophagus, therapeutic approach, clinical outcome, and complications were reviewed.

Results: Of the 50 EoE cases diagnosed during the study period, 11 cases (9 males; median age 9 years, range 4-12) were identified with esophageal narrowing (22%). Six had short segment narrow caliber esophagus and 5 had long segment narrow caliber esophagus (median length of the narrowing was 4 cm, range 3-20 cm). Three cases with narrow caliber esophagus also had esophageal stricture 2-3 cm below the upper esophageal sphincter. Nineteen dilation sessions were performed in 10 cases using Savary dilator. Esophageal size improved from median 7 mm to median 13.4 mm. Good response was obtained in all cases. Following the dilation procedure, longitudinal esophageal mucosal tear occurred in all cases without esophageal perforation or chest pain. One case with long narrow caliber esophagus responded dramatically to a 3-month course of swallowed inhaled fluticasone.

Table: Comparison of the clinical, endoscopic, and histological findings among children with EoE with and without esophageal narrowing.

<table>
<thead>
<tr>
<th>Variables</th>
<th>EoE without narrowing (n=39)</th>
<th>EoE with narrowing (n=11)</th>
<th>P -value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [Mean (SD) (year)]</td>
<td>8.1 ± 4.3</td>
<td>8.7 ± 2.2</td>
<td>0.67</td>
</tr>
<tr>
<td>Gender [(male (%)]</td>
<td>30 (77)</td>
<td>9 (82)</td>
<td>0.72</td>
</tr>
<tr>
<td>Consanguinity (%)</td>
<td>18 (46)</td>
<td>9 (82)</td>
<td>0.045*</td>
</tr>
<tr>
<td>Duration of symptoms [mean± SD (year)]</td>
<td>1.17 ± 1</td>
<td>4.1 ± 2.3</td>
<td>0.003‡</td>
</tr>
<tr>
<td></td>
<td>28 (84.8)</td>
<td>10 (100)</td>
<td>0.32*</td>
</tr>
<tr>
<td>Dysphagia (%)</td>
<td>9 (23)</td>
<td>1 (9)</td>
<td>0.66*</td>
</tr>
<tr>
<td>Vomiting (%)</td>
<td>4 (10)</td>
<td>0 (0)</td>
<td>0.57*</td>
</tr>
<tr>
<td>Heartburn (%)</td>
<td>6 (15.4)</td>
<td>6 (60)</td>
<td>0.011‡</td>
</tr>
<tr>
<td>Weight loss (%)</td>
<td>11 (33.3)</td>
<td>10 (91)</td>
<td>0.002‡</td>
</tr>
<tr>
<td>Meat impaction (%)</td>
<td>4 (10.2)</td>
<td>1 (9)</td>
<td>1.0*</td>
</tr>
<tr>
<td>Condition</td>
<td>Percentage</td>
<td>Reference</td>
<td>p-Value</td>
</tr>
<tr>
<td>---------------------------------</td>
<td>------------</td>
<td>------------</td>
<td>----------</td>
</tr>
<tr>
<td>Abdominal Pain (%)</td>
<td>17 (43.5)</td>
<td>7 (63.6)</td>
<td>0.29*</td>
</tr>
<tr>
<td>Asthma (%)</td>
<td>6 (15.4)</td>
<td>5 (45.5)</td>
<td>0.04‡</td>
</tr>
<tr>
<td>Eczema (%)</td>
<td>4 (10.2)</td>
<td>1 (9)</td>
<td>1.0*</td>
</tr>
<tr>
<td>Rhinitis (%)</td>
<td>24 (61.5)†</td>
<td>7 (63.6)Ω</td>
<td>1.0*</td>
</tr>
<tr>
<td>Food allergy (%)</td>
<td>34 (87.2)</td>
<td>10 (91)</td>
<td>1.0*</td>
</tr>
<tr>
<td>Family history of atopy (%)</td>
<td>17 (44.6)</td>
<td>8 (72.7)</td>
<td>0.08</td>
</tr>
<tr>
<td>Eosinophilia (%)</td>
<td>7 (18)</td>
<td>11 (100)</td>
<td>&lt;0.0001‡</td>
</tr>
<tr>
<td>Rings (%)</td>
<td>7 (18)</td>
<td>8 (72.7)</td>
<td>0.002‡</td>
</tr>
<tr>
<td>White exudate (%)</td>
<td>9 (23)</td>
<td>8 (72.7)</td>
<td>0.003‡</td>
</tr>
<tr>
<td>Eosinophilic abscess (%)</td>
<td>27 (81.8)</td>
<td>9 (90)</td>
<td>0.72</td>
</tr>
<tr>
<td>Eosinophilic degranulation (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Esophageal dilation using Savary dilator is safe and highly effective in the management of esophageal narrowing associated with EoE in children.

**Disclosure of interest:** None Declared
GASTROENTEROLOGY: Cystic fibrosis and pancreatic disorders

G-eP-013

Ursodeoxycholic Acid Treatment is associated with improvement of liver stiffness in cystic fibrosis patients

Hubert van der Doef1, van der Feen Cathelijne2, van der Ent Kors3, Houwen Roderick2

1University Medical Center Groningen, Groningen Transplant Center, Dept. Pediatrics, Netherlands
2University Medical Center Utrecht, Department of Pediatric Gastroenterology, Utrecht, Netherlands
3University Medical Center Utrecht, Department of Pediatric Pulmonology, Utrecht, Netherlands

Objectives and study: Cystic fibrosis (CF) is the most common life-limiting autosomal recessive disease in the Caucasian population. Although pulmonary complications are the usual cause of death, Cystic Fibrosis Related Liver Disease (CFRLD) is a serious complication too. Ursodeoxycholic acid (UDCA) might prevent progression of CFRLD, but objective parameters for its effect are lacking. Recent studies have shown that liver stiffness as measured by transient elastography (TE) has a good correlation with other parameters for liver fibrosis and cirrhosis in CF children and adults. The aim of this study is to investigate changes in liver stiffness over time, both in patients with and without UDCA.

Methods: In this prospective observational study patients were included if at least two measurements of liver stiffness by TE, at least one year apart, between January 1st 2009 and December 31st 2014 were performed. Difference between the first and last available measurement was expressed as Δ stiffness in kPa per year. Mann-Whitney U analysis was used to calculate differences between four subgroups: controls, ie patients without UDCA and normal liver ultrasound (n=73); patients with CFRLD according to the Colombo criteria (heterogeneous liver ultrasound in combination with either hepatomegaly and/or increased liver enzymes), but without cirrhosis; all were on UDCA during the observation period (CFRLD, n=15); patients who had UDCA, but no cirrhosis or CFRLD according to the Colombo criteria (mild liver disease, n=11); patients with cirrhosis, who all were on UDCA (cirrhosis, n=6).

Results: Paired measurements of liver stiffness, with a median interval of 40 months, were done in 105 patients. The initial liver stiffness (median with IQR) in the four groups (controls, mild liver disease, CFRLD, cirrhosis) was respectively 4.1 (3.7-4.7), 6.4 (5.0-11.1), 10.6 (8.1-15.8), 22.5 (14.4-32.1) kPa (p <0.001 for each of the 3 groups with liver disease vs controls).

The Δ stiffness in kPa per year (median with IQR) in the four subgroups (controls, mild liver disease, CFRLD, cirrhosis) was respectively 0.19 (-0.03 to 0.59), 0.23 (-0.20 to 0.51), -0.70 (-1.6 to 0.55), 4.6 (0.67 to12.4). Patients with CFRLD had a significant decrease in liver stiffness when compared to controls in (p=0.01); however in cirrhotic patients a significant increase was seen (controls vs cirrhosis p=0.006; CFRLD vs cirrhosis p=0.003).

Conclusion: These data suggest that UDCA might be able to reduce liver stiffness when used in cystic fibrosis patients with well defined mild liver disease, but not when cirrhosis has developed.

Disclosure of interest: Tramedico supported this study by an unrestricted educational grant.
Low sodium status is associated with decreased growth parameters in patients with cystic fibrosis

Peter Heinz-Erian¹, Helmut Ellemunter², Christiane Knepper¹, Johannes Eder², Katharina Niedermayr², Bettina Haerter³, Philipp Hofer⁴, Sabine Scholl-Buergi¹, Thomas Müller¹

¹Pediatrics I, Pediatrics and Adolescent Medicine, Innsbruck, Austria
²Pediatrics III, Pediatrics and Adolescent Medicine, Innsbruck, Austria
³Pediatric Surgery, Surgery, Innsbruck, Austria
⁴Medical Statistics and Informatics, Medical University of Innsbruck, Austria

Objectives and study: Sodium (Na) has been proposed as a possible growth factor. CF-patients are at risk for increased Na-losses via sweat and stool leading to chronic Na-depletion (NaD) which does not necessarily show as hyponatremia. This normonatremic Na+-depletion (NNaD) identified by fractional Na+-excretion (FE$\text{Na}$) values <0.5%, was recently linked to impaired growth in a small cohort of 10 CF infants. Our paper investigates the relationship between FE$\text{Na}$ and clinical parameters of growth in CF children >2 years.

Methods: FE$\text{Na}$ values were calculated in 35 CF- and 24 control children, and tested for correlations with z-scores for weight, height and BMI. An FE$\text{Na}$ < 0.5 % was considered to be pathologically decreased.

Results: All CF children and controls had normal plasma Na+-concentrations. 25/35 (71.4%) CF patients had decreased FE$\text{Na}$ values <0.5% (group I). FE$\text{Na}$ results of 10 CF patients (group II) and 23/24 controls (group III) were normal. In Na+-depleted CF-children, compared to normal controls, mean z-scores for weight (-0.18±0.87 vs +1.03±0.57, p=0.001), height (-0.06±0.89 vs +0.53±0.72, p=0.009) and BMI (-0.22±0.87 vs +1.00±1.06, p=0.001) were significantly reduced. Also, we found positive correlations between FE$\text{Na}$ values and z-scores for weight (r=0.521), height (r=0.292) and BMI (r=0.468), respectively.

Conclusion: Besides a variety of other important factors NNaD may contribute to poor growth in CF.

Disclosure of interest: None Declared.
RNA-based MAFA over-expression is sufficient to drive human pancreatic duct-derived cells toward a β-cell-like phenotype

Elisa Corritore¹, Erica Dugnani², Valentina Pasquale², Lorenzo Piemonti², Amedeo Vetere³, Susan Bonner-Weir⁴, Etienne Sokal¹, Philippe Lysy¹

¹Université Catholique de Louvain, Laboratory of Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium
²San Raffaele Scientific Institute, Milan, Italy
³Broad Institute, Cambridge, United States
⁴Joslin Diabetes Center, Boston, United States

Objectives and study: Pancreatic epithelial cells represent an attractive cell source for replacement therapy of type 1 diabetes. Previously, we designed a protocol for expansion of human pancreatic duct-derived cells (HDDCs) and showed their β-cell engineering potential. In this study, we reprogrammed HDDCs into β-cell-like lineage by over-expressing mRNAs of key pancreatic transcription factors (TFs).

Methods: Pancreatic duct cells (n=6) were purified and propagated into endothelial growth-promoting media. Synthetic modified (sm) RNAs were manufactured by unidirectional subcloning of PDX1, NGN3 and MAFA into a plasmid containing 5’ and 3’ UTR regions. The UTR-flanked inserts were excised and poly(A)-tailed. The final smRNAs were synthesized through in vitro transcription followed by phosphatase and DNase treatments, before being daily transfected in HDDCs.

Results: In all donors, transfection of PDX1, NGN3 and MAFA led to upregulation of endogenous target (ex: NGN3) and β-cell marker (ex: INS, synaptophysin, SLC2A2, GCK) genes with the highest expression levels being reached after MAFA transfection. Co-transfection protocols failed to show significant improvement of β-cell differentiation. Acceptable impact on innate immune response and cell viability was noticed after 7 consecutive daily smRNA transfections, based respectively on minimal IFNA and RIG-1 gene expression and on annexin-V/PI staining. After MAFA transfection, HDDCs stained positive for MAFA and insulin (19.3 ± 3.3 %) proteins, while ELISA assays showed detectable amounts of C-peptide content and release (21.45 ± 2.42 pg/mL/10⁶ cells) under basal conditions.

Conclusion: We showed that MAFA RNA over-expression is sufficient to efficiently reprogram HDDCs toward β-cell-like phenotype in a timely manner. Further research is mandatory to demonstrate a controlled insulin secretion capacity after differentiation and to assess the efficacy of these cells in treating immunosuppressed diabetic mice.

Disclosure of interest: None Declared
Lipid spectrum in paediatric patients with cystic fibrosis

Dorothea A. Schulkes¹, Cornelis K. van der Ent², Roderick H.J. Houwen³, Janna W. Woestenenk⁴
¹University Medical Centre Utrecht, Department of Paediatric Gastroenterology, Utrecht, Netherlands
²University Medical Centre Utrecht, Department of Paediatric Pulmonology and Cystic Fibrosis Centre Utrecht, Netherlands
³University Medical Centre Utrecht, Department of Paediatric Gastroenterology and Cystic Fibrosis Centre Utrecht, Netherlands
⁴University Medical Centre Utrecht, Internal Medicine and Dermatology, Dietetics and Cystic Fibrosis Centre Utrecht, Netherlands

Objectives and study: Current recommendation for dietary fat intake in children and adolescents with cystic fibrosis (CF) is as high as 35-40 energy percent (En%) to meet the advised 120% energy intake and thereby compensate for malabsorption and high resting energy expenditure. This will generally result in a high saturated fat intake, which was found to be well above the advised limit of 10 En% for healthy counterparts. This might cause abnormalities in serum lipids and therefore an increased risk on developing cardiovascular disease later in life. Whether the high (saturated) fat intake in children and adolescents with CF is indeed associated with an abnormal serum lipid spectrum is unknown. So we aimed to investigate this in a paediatric CF patient population and describe the lipid spectrum, expressed as total cholesterol, low-density lipoprotein cholesterol (LDL-cholesterol), high-density lipoprotein cholesterol (HDL-cholesterol) and triglycerides, and the triglycerides to HDL-cholesterol ratio (TG/HDL-ratio) as well as the correlation between the lipid spectrum and dietary fat intake and nutritional status.

Methods: Between March 1st 2013 and August 31st 2015 we randomly collected 112 fasting measurements of the lipid spectrum in paediatric patients with CF (aged 14.0±2.4 years, 55 girls). We obtained 73 corresponding completed 3-day dietary food records with calculated fat intake (En%) and saturated fat intake (En%). As a measure of nutritional status we included z-scores body mass index (BMI). Data of lipid spectrum were compared with those of healthy controls according to age and gender and were presented as percentage of the reference values (% ref val). Correlations between the lipid spectrum, dietary fat intake and nutritional status were studied by using the Spearman's rank correlation coefficient.

Results: In our study sample we found relative low levels of cholesterol, LDL-cholesterol and HDL-cholesterol and high levels of triglycerides compared to healthy controls (Table). In 21% of the patients, we found a TG/HDL-ratio ≥1.3, which is considered to be a risk factor for the development of cardiovascular disease. Furthermore we found a significant correlation between HDL-cholesterol and total fat intake (r 0.38, p<0.01) and HDL-cholesterol and saturated fat intake (r 0.25, p<0.04) as well as between TG/HDL-ratio and total fat intake (r -0.34, p<0.01). No other correlations between the lipid spectrum and dietary fat intake or nutritional status as such were found (p≥0.08).

Table: Lipid spectrum of 112 paediatric patients with CF (55 girls).

<table>
<thead>
<tr>
<th>Lipid spectrum</th>
<th>Median (range) expressed as % ref val</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total cholesterol</td>
<td>79 (68-91)</td>
</tr>
<tr>
<td>LDL-cholesterol</td>
<td>70 (57-78)</td>
</tr>
<tr>
<td>HDL-cholesterol</td>
<td>85 (72-101)</td>
</tr>
<tr>
<td>Triglycerides</td>
<td>125 (94-172)</td>
</tr>
</tbody>
</table>

Conclusion: We described low levels of total cholesterol, LDL-cholesterol and HDL-cholesterol and high levels of triglycerides in children and adolescents with CF, although we found no clear correlations between the lipid spectrum and dietary fat intake. Additionally we found an increased TG/HDL-ratio in 21% of our paediatric patients with CF. This might point to an increased risk of cardiovascular disease in patients with CF.

Disclosure of interest: None Declared.
Clinical Course of Chronic Pancreatitis in Children with CFTR Mutation.

Aleksandra Marach¹, Elwira Kołodziejczyk¹, Jarosław Kierkus¹, Jozef Ryzko¹, Grzegorz Oracz¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Chronic pancreatitis (CP) is a rare condition in children. It is a longlasting inflammatory disease of the pancreas leading to irreversible changes in pancreatic structure and it’s exocrine and endocrine function. Mutations in CFTR, PRSS1, SPINK1 genes are one of the most common causes of CP in children. The purpose of our study was to investigate the clinical course of chronic pancreatitis in children with CFTR mutation.

Methods: This is a single-center, retrospective review of 241 children with CP hospitalized in our Clinic from 1988 to 2014. Every patient underwent genetic testing to identify changes in CFTR gene. We analyzed data to illustrate clinical picture of CP in children with CFTR mutation.

Results: Mutations in CFTR gene were found in 43 patients (21 girls, 22 boys, median age 10.83 years). The rest of 198 patients analyzed in this study were children with CP of other etiology excluding patients with mutations in PRSS1 gene. There was no statistically significant difference in age of disease onset between patients with and without CFTR mutation (8.6 years vs. 9.0 years, respectively; NS). Also the severity of inflammatory changes estimated according to the Cambridge classification was comparable in both groups (1.69 vs. 1.57, NS). Statistically significant difference was observed in the number of disease exacerbations (4.74 vs. 3.94, p<0.05) and the number of performed endoscopic retrograde cholangiopancreatographies (ERCP) (2.6 vs. 2.0, p<0.05). No difference in pancreatic calcifications (27.9% vs. 36.9 %), endoscopic therapy (stent placement) (39.5% vs. 29.8%), diabetes mellitus (4.7% vs. 7.6%) and pancreatic insufficiency (14% vs. 13.6%) was observed between children with and without CFTR mutation.

Table:

<table>
<thead>
<tr>
<th>Analyzed data</th>
<th>Patients with CFTR mutation</th>
<th>Patients without CFTR mutation</th>
<th>Difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exacerbations</td>
<td>4.74</td>
<td>3.94</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>ERCP</td>
<td>2.6</td>
<td>2.0</td>
<td>p&lt;0.05</td>
</tr>
<tr>
<td>Disease onset</td>
<td>8.6 years</td>
<td>9.0 years</td>
<td>NS</td>
</tr>
<tr>
<td>Cambridge classification</td>
<td>1.69</td>
<td>1.57</td>
<td>NS</td>
</tr>
<tr>
<td>Calcifications</td>
<td>27.9%</td>
<td>36.9 %</td>
<td>NS</td>
</tr>
<tr>
<td>Stent placement</td>
<td>39.5%</td>
<td>29.8%</td>
<td>NS</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4.7%</td>
<td>7.6%</td>
<td>NS</td>
</tr>
<tr>
<td>Pancreatic insufficiency</td>
<td>14%</td>
<td>13.6%</td>
<td>NS</td>
</tr>
</tbody>
</table>

Conclusion: Clinical course of chronic pancreatitis in children with mutation in CFTR gene is more severe then CP of different etiology.
Disclosure of interest: The authors whose names are listed immediately below certify that they have NO affiliations with or involvement in any organization or entity with any financial or non-financial interest.

Marach: None Declared
Klodziejczyk: None Declared
Kierkus: None Declared
Ryzko: None Declared
Oracz: None Declared
Comparative effects of Clostridium difficile toxins on transepithelial chloride secretion and epithelial structure in in-vitro and ex-vivo human epithelium.

Vittoria Buccigrossi¹, Noemi Iannuzzi¹, Antonella Marano¹, Andrea Lo Vecchio¹, Alfredo Guarino¹

¹University of Naples Federico II, Dept. of Translational Medical Science, Section of Pediatrics, Naples, Italy

Objectives and study: Clostridium difficile (CD) releases toxins that induce diarrhea and colonic damage. Toxin A (TcdA) and B (TcdB) are thought to play a major role in inducing diarrhea. Binary toxin (CDT), produced by hypervirulent strains such as ribotype 027, is associated with severe CD infection (CDI).

The aim of this study is to comparatively investigate the direct role of CD toxins in inducing chloride secretion and epithelial damage in an in-vitro model of diarrhea in human epithelium.

Methods: The effects of CD toxins on chloride secretion (enterotoxic effect) were investigated in intestinal epithelial Caco-2 cells. Cell monolayers were exposed to TcdA, TcdB or CDT and the short circuit current (Isc) was measured in Ussing Chambers. The cytotoxic effect induced by CD toxins was evaluated by transepithelial resistence (TER). Intestinal epithelium was exposed to CD toxins added to mucosal, serosal or both sides. Colonic biopsies were obtained from children and used for organ culture experiments to validate the results observed in Caco-2 cells.

Results: Effect on chloride secretion:
TcdB, but not TcdA, induced a dose-dependent increase in Isc with a maximal effect at 100ng/ml (ΔIsc=+10.63±3.7 vs controls 1.7±2.9; p<.05) indicating a direct effect on chloride secretion. This effect was further increased when TcdB was preincubated with TcdA. CDT induced an increase in Isc both at mucosal and serosal side of Caco-2 cell monolayers (ΔIsc=+3.83±2.1 and 3.88±1.3, respectively). The ex-vivo results confirmed the effects of CD toxins seen in Caco-2 cells.

Effect on epithelial permeability:
TcdA did not affect the epithelial structure. On the contrary, TcdB induced a decrease in TER when added at serosal side after 48 hours (-81.2% serosal side vs -11.7% mucosal side; p<.05) but this toxin became able to reduce TER at mucosal side in presence of TcdA (-77.4% with TcdA vs -11.7% without TcdA; p<.05). Finally, CDT decreased TER at serosal side of Caco-2 cell monolayers after 4 days (-73.5% vs -13.2% of controls; p<.05).

Conclusion: CD toxins show a peculiar pattern of enterotoxic and cytotoxic effect in human intestinal mucosa. TcdB had the strongest effect on chloride secretion, particularly in combination with TcdA. The effect was polar being exerted on the luminal side. CDT induced chloride secretion on both side but with a minor potency. The cytotoxic damage was exerted by TcdB and CDT at serosal side but with a different timing. TcdA allow to TcdB to alter intestinal permeability acting on mucosal side.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: GI-infections

G-eP-019

The Accuracy of the Three Dehydration Scales in Children with Acute Gastroenteritis in a Developing Country of Kosovo.

Teuta Hoxha-Kamberi¹, Luan Xhelili², Mehm,edali Azemi¹, Muharrem Avdiu¹, Vlora Ismaili-Jaha¹

¹University Clinical Centre of Kosovo, Pediatrics, Pristina, Kosovo
²University Hospital Centre "Mother Theresa" in Tirana, Pediatrics, Tirane, Albania

Objectives and study: Although diarrhea is a preventable disease, it remains the second leading cause of death (after pneumonia) among children aged under five years worldwide. The World Health Organization (WHO) scale, the Gorelick scale, and the Clinical Dehydration Scale (CDS) were created to estimate dehydration status using clinical signs. The purpose of this study is to determine whether these clinical scales can accurately assess dehydration status of children in a developing country of Kosovo.

Methods: Children aged 1 month to 5 years with a history of acute diarrhea were enrolled in the study. After recording the data about the patients historical features the treating physician recorded the physical examination findings consistent with each clinical score. Receiver operating characteristic (ROC) curves were constructed to evaluate the performance of the three scales, compared to the gold standard, percent weight change with rehydration. Sensitivity, specificity and likelihood ratios were calculated using the best cut-off points of the ROC curves.

Results: We enrolled 230 children, and 200 children met eligibility criteria. The WHO scale for predicting significant dehydration (≥5 percent weight change) had an area under the curve (AUC) of 0.71 (95% : CI= 0.65-0.77). The Gorelick scales 4- and 10-point for predicting significant dehydration, had an area under the curve of 0.71 (95% : CI=0.63-0.78) and 0.74 (95% : CI= 0.68-0.81) respectively. Only the CDS for predicting the significant dehydration above ≥6% percent weight change, did not have an area under the curve statistically different from the reference line with an AUC of 0.54 (95% CI = 0.45 - 0.63).

Conclusion: The WHO dehydration scale and Gorelick scales were fair predictors of dehydration in children with diarrhea. Only the Clinical Dehydration Scale was found not to be a helpful predictor of dehydration in our study cohort.

Disclosure of interest: None Declared
**GASTROENTEROLOGY: GI-infections**

**G-eP-020**

**Differences in cytokines response during acute infection of bacterial and viral gastroenteritis.**

King Jun Koh¹, Shih-Chang Lin², Lung-Huang Lin³

¹Sijih Cathay General Hospital, Department of Pediatrics, New Taipei City, Taiwan
²Cathay General Hospital, Department of Allergy and Immunology, Taipei, Taiwan
³Cathay General Hospital, Department of Pediatrics, Taipei, Taiwan

**Objectives and study:** Acute gastroenteritis is a common pediatric disease worldwide. To further understand its pathophysiology, we try to quantify and compare the human cytokines response during acute bacterial and viral gastroenteritis.

**Methods:** This a prospective case-control research conducted in a tertiary health care institution from March 2012 until June 2013. Hospitalized pediatric patients below age of 14 year-old with the diagnosis of acute gastroenteritis were enrolled. The patients with positive stool culture or positive stool antigen response were tested for seven sera cytokines: interferon-gamma (IFN-γ), tumor necrotizing factor-alpha (TNF-α), interleukin-1beta (IL-1β), interleukin-2 (IL-2), interleukin-6 (IL-6), interleukin-10 (IL-10), and Interleukin-12 (IL-12). Control group was ten children without evidence of acute inflammatory process.

**Results:** A total of 190 patients were enrolled. Among them, 30 patients with rotavirus antigen positive, 26 patients with salmonella stool culture, four patients with pseudomonas aeruginosa culture and four patients with norovirus antigen positive, were analyzed. The patients in all four groups showed high IFN-γ, TNF-α, IL-6 and IL-10 responses during the acute phase of gastroenteritis, as compared to the control (Table, P<0.01). However, the cytokines level for IL-1β, IL-2 and IL-12 were not elevated. For the salmonella group, IFN-γ and IL-6 were significantly decreased at the convalescent phase, with the mean value 98.2 vs. 8 and 69.1 vs. 12.1 (pg/mL, P=0.01), respectively. Contrarily in the rotavirus group, TNF-α was significantly increased, with the mean value 10.5 vs. 31.6 (pg/mL, P=0.03), during the recovery stage.

**Table:** Comparisons of mean cytokines level during acute bacterial and viral gastroenteritis

<table>
<thead>
<tr>
<th>Cytokines (pg/ml)</th>
<th>Rotavirus (n=30)</th>
<th>Salmonella (n=26)</th>
<th>Pseudomonas (n=4)</th>
<th>Norovirus (n=4)</th>
<th>Control (n=10)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFN-γ</td>
<td>70.1(±106)</td>
<td>98.2(±123.8)</td>
<td>32.4(±18.8)</td>
<td>35.8(±71.6)</td>
<td>0.6(±1.8)</td>
<td>0.005*</td>
</tr>
<tr>
<td>TNF-α</td>
<td>10.5(±8.6)</td>
<td>19.9(±11.1)</td>
<td>11.2(±3.1)</td>
<td>9.2(±2.6)</td>
<td>0.9(±1.3)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IL-1β</td>
<td>1.2(±4.0)</td>
<td>4.5(±6.1)</td>
<td>0.0(±0.0)</td>
<td>0.0(±0.0)</td>
<td>1.1(±1.7)</td>
<td>0.055</td>
</tr>
<tr>
<td>IL-2</td>
<td>2.1(±11.5)</td>
<td>0.0(±0.0)</td>
<td>2.4(±3.3)</td>
<td>0.0(±0.0)</td>
<td>0.0(±0.0)</td>
<td>0.869</td>
</tr>
<tr>
<td>IL-6</td>
<td>31.3(±67.1)</td>
<td>69.1(±96.3)</td>
<td>23.9(±34.7)</td>
<td>19.4(±22.8)</td>
<td>0.0(±0.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IL-10</td>
<td>42.8(±36.3)</td>
<td>17.9(±24.3)</td>
<td>52.6(±45.9)</td>
<td>59.5(±67.4)</td>
<td>0.0(±0.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>IL-12</td>
<td>0.1(±0.2)</td>
<td>0.1(±0.2)</td>
<td>0.0(±0.0)</td>
<td>0.0(±0.0)</td>
<td>0.0(±0.0)</td>
<td>0.554</td>
</tr>
</tbody>
</table>
Conclusion: Our immune system modulates host cytokines response during the inflammatory process. The type and amplitude of cytokines released varied with different kinds of pathogen, and during different stages of infection. Understanding the in vivo cytokine changes help us to determine future strategies in shortening the disease course and minimizing its hazard to the host.

Disclosure of interest: None Declared
Congenital diarrhea with predominant protein losing enteropathy is associated with two different biallelic mutations in DGAT1, the enzyme that catalyze triglyceride synthesis

Yael Haberman1, Joshi Stephen2, Thierry Vilboux3, Ortal Barel Barel4, Ayelet Di Segni4, Eran Eyal4, Goni Hout-Siloni5, Avishay Lahad1 Avishay Lahad1, Tzipora Shalem1, Hadass Pri Chen2, Ben Pode-Shakked1, Dina Marek-Yager4, Gideon Rechavi14, May Christine V Malicdan2, William A. Gahl2, Yair Anikster1, Batia Weiss1

1Edmond and Lily Safra Children's Hospital, Sheba Medical Center, Tel-Hashomer, Israel
2National Institutes of Health, Bethesda, Maryland, United States
3Inova Translational Medicine Institute, Fairfax, Virginia, United States
4Sheba Medical Center, Tel-Hashomer, Israel

Objectives and study: Three affected children of consanguineous Arab-Muslim and of non-consanguineous Ashkenazi Jewish descent families were evaluated at the Sheba Medical Center due to congenital diarrhea with predominant protein losing enteropathy (PLE) and severe hypoalbuminemia. We therefore aimed to define the clinical course of these patients and determine the genetic background associated with this rare phenotype keeping in mind that a unique syndrome of congenital protein losing enteropathy was recently reported in a single family with mutation in DGAT1 (MIM #: 604900), an enzyme that catalyze triglyceride synthesis.

Methods: We used homozygosity mapping, exome sequencing, and expression studies at the transcript and protein levels to define the genetic background associated with this rare disease phenotype.

Results: In all patients, fecal alpha-1-antitrypsin was above 10 mg/g (normal, <2.6 mg/g), which is the hallmark of PLE. Duodenal and colonic biopsies showed no evidence of significant inflammation, microvillus inclusion disease, or tufting enteropathy, and neuroendocrine cells were present in intestinal biopsies. Congenital lymphangiectasia, a cause of protein-losing enteropathy, was excluded by endoscopy and histology. In the Arab-Muslim family, homozygosity mapping using SNP arrays revealed the DGAT1 gene as the best candidate gene for the proband. Sequencing of the gene identified a novel homozygous missense mutation, p.L295P (c.884T>C), in the highly conserved Membrane Bound O-acyl transferase (MBOAT) domain of DGAT1 protein. Expression studies verified reduced amounts of DGAT1 in patient's fibroblasts. In the Ashkenazi Jewish descent family, exome sequencing identified a previously reported splice site mutation in intron 8 (IVS8+2 T>C), which was associated with loss of DGAT1 protein.

Conclusion: We have identified a novel homozygous missense mutation, p.L295P (c.884T>C), in the highly conserved domain of DGAT1 protein, further establishing the connection between truncated DGAT1 and PLE phenotype. These cases of DGAT1 deficiency extend the molecular and phenotypic spectrum of PLE, which may be a more common cause of PLE than previously recognized.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Basic Science

G-eP-022

BAC treatment of the rectosigmoid in piglet: a reproducible model of partial aganglionnosis in a large animal

Alexis Arnaud¹, Juliette Hascoet¹, Francis Le Gouvec¹, Julien Georges¹, Gwenaelle Randuineau¹, Gaelle Boudry²

¹Ur Adnc Inra, St Gilles, France
²Inra Ur1341 Adnc, St Gilles, France

Objectives and study: Hirschsprung’s associated enterocolitis is a serious and somehow life-threatening complication of Hirschsprung’s disease. Its pathogenesis remains unclear. Many hypotheses have been proposed such as modifications of intestinal barrier function, innate immunity or microbiota. Our objective was to develop a porcine model of rectosigmoid aganglionnosis during the neonatal period that could be used to study these parameters in a model close to human physiology.

Methods: We implemented a surgical model inspired from published murine model with topical application of benzalkonium chloride (BAC) detergent on the rectosigmoid serosa. After ethical approval, piglets were operated on at day 5 of age under general anaesthesia. Through a midline laparotomy, application of either 0.5% BAC solution (BAC group) or saline solution (PHY group) around rectosigmoid and rectum was performed for one hour. Piglets from both groups were then breastfed till sacrifice 7 or 21 days later. Histology (Haematoxylin-Eosin stain), immunohistochemistry (Ab/PGP9.5) and Ussing chamber (short circuit current, conductance, permeability to Horse-radish peroxidase (HRP) and FITC-dextran 4 (FD-4)) were used to study the impact of BAC application and denervation on muscle layer thickness, crypt depth, and epithelial permeability. We used 2 way ANOVA comparing time to sacrifice (D7 vs D21) and type of treatment (BAC vs PHY) for statistical analysis. Data are given in mean±SEM..

Results: Twenty-three piglets were included in the study: 12 treated with BAC and 11 with saline solution. In the BAC group, aganglionnosis was noted in the myenteric plexus on 34 ± 4 % and 27 ± 5 % of rectum circumference at day 7 and day 21 respectively. External and internal layers thicknesses were significantly decreased in the BAC group at day 21 (p<0,001), but not D7, comparatively to the PHY group. Regarding crypts depth, there was no difference between the two groups at any ages. Similarly, treatment type or age did not influence ion permeability (p>0,1). Transcellular permeability, assessed through flux of HRP across the mucosa, did not change with age in the PHY group whereas it increased significantly within the BAC group between day 7 and day 21 (p=0.015), resulting in greater transcellular permeability at D21 in the BAC group compared to the PHY group (p=0.017). In contrast, paracellular permeability, assessed through FD-4 flux across the mucosa, decreased with age in the PHY group but not in the BAC one, resulting in greater paracellular permeability in the BAC group at day 21 (p=0.001).

Conclusion: Our study presents a promising large animal model of reproducible partial denervation of the rectosigmoid myenteric plexus. This partial aganglionnosis causes major changes of the intestinal barrier such as increase of the transcellular and paracellular permeability, external and internal muscle layer thickness decrease. These modifications could explain enterocolitis onset in Hirschsprung’s disease. This large animal model could be of interest in study on stem cell transplantation therapy for Hirschsprung’s disease.

Disclosure of interest: None Declared.
In vitro assessment of the influence of intestinal pH and enzyme/substrate ratio on fats digestion in Cystic Fibrosis patients

Joaquim Calvo Lerma¹, Ana Belén Heredia Gutiérrez², Carmen Ribes Koninckx³, Ana Maria Andrés Grau²

¹Instituto de Investigación Sanitaria La Fe, Valencia, Spain
²Universitat Politècnica de València, Instituto de Ingeniería de Alimentos Para el Desarrollo, Valencia, Spain
³La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

Objectives and study: More than 85% of patients with Cystic Fibrosis (CF) suffer from severe pancreatic insufficiency, leading to maldigestion of nutrients, especially fat. Pancreatic Enzyme Replacement Therapy (PERT) has to be carried out on an individual basis and this is nowadays a real challenge. Despite some factors have been identified to be determinant in the enzymatic activity, their influence in the gastrointestinal tract remains unknown, and so there is currently a lack of an evidence-based method for adjustment of the enzymatic supplements dose. In vitro digestion models offer an accurate approach to explore the mechanisms underlying enzymatic activity in the gastrointestinal tract. The aim of this study is to assess the influence of the intestinal pH value and the enzymes dose on the kinetics and the extension of lipolysis under simulated CF gastrointestinal conditions.

Methods: A static in vitro digestion model was specifically designed to address the simulation of the CF patients’ gastrointestinal environment on the basis of the Infogest’s internationally harmonized protocol for in vitro digestions (Minekus et al. 2014). Progress of lipolysis was measured during the intestinal phase by the pH-stat method, which allows for a continuous monitoring of the process. Digestion of a milk product was conducted under two intestinal pH values, 7 (healthy) and 6 (CF), and six different enzyme/substrate ratios were assessed. The enzyme substrate ratio (E/S) is the dose of enzymes (Lipase Units) / grams of fat in the food sample. Lipolysis was expressed as % of free fatty acids released from the initial fat content.

Results: We observed that kinetics of the reaction was divided into 3 phases: adsorption of the enzymes to the surface of the substrate, period of full activity of the enzymes or lineal rate hydrolysis period, and decreasing hydrolysis rate phase; the characterizing parameters that describe each phase were estimated and modeled. We found the pH value in the medium was the main determinant both in the kinetics and in the extension of the reaction: at pH 7 and at the highest E/S assayed, maximum extent of the lipolysis after 2 hours of intestinal digestion was found to be higher than 90% whilst it was around 60% with the same pH and the lowest E/S assayed. Additionally, it was found that the E/S, and not just the enzyme concentration, was another key variable for modulating and optimising the fats digestibility.

Conclusion: We were able to establish an experimental protocol to evaluate fats digestibility in a food product that allows for the study of kinetics and extension of lipolysis under simulated CF gastrointestinal conditions. Modeling the parameters of the lipolysis progress curves allows for obtaining equations that can be useful to estimate the optimal enzymes dose for different foods. Finally, further investigation of other factors that determine the behavior of enzymatic hydrolysis of fat by the enzymatic supplements are mandatory so as to lay the foundations of the knowledge for an accurate and evidence-based adjustment of the PERT.

Disclosure of interest: None Declared.
Primary eosinophilic gastrointestinal disorders after food oral immunotherapy

Sonia Fernández Fernández¹, Ana I. Rayo Fernández¹, Luis Echeverría Zudaire², Raquel Checa Rodríguez³, Belen Borrell Martínez¹, Ana Tabares González¹, Cristina Muñoz Archidona⁴, Loreto González Domínguez²

¹Hospital Universitario Severo Ochoa, Paediatric Gastroenterology Unit, Leganés, Madrid, Spain
²Hospital Universitario Severo Ochoa, Pediatric Allergy Unit, Leganés, Madrid, Spain
³Hospital Rey Juan Carlos, Pediatric Gastroenterology, Móstoles, Spain
⁴Hospital General de Villalba, Pediatric Allergy, Villalba, Spain

Objectives and study: Food oral immunotherapy (OIT) involves the administration of food causing allergy until the patient is desensitized to it. Primary eosinophilic gastrointestinal disorders (PEGDs) are defined as disorders that selectively affect the gastrointestinal tract with eosinophil-rich inflammation in the absence of known causes for eosinophilia. These disorders include eosinophilic esophagitis, eosinophilic gastroenteritis, and eosinophilic colitis. The onset of eosinophilic esophagitis have been described in patients undergoing OIT, but this relation remains controversial. No others PEGDs have been described after OIT. The aim of this study is to evaluate the presence of PEGDs in a group of children after OIT with milk and/or egg and to know the clinical features and evolution of these patients.

Methods: A prospective study enrolled consecutive patients from the Pediatric Allergy unit subjected to OIT with milk and/or egg between 2006 and 2014. When these children have persistent gastrointestinal symptoms, they are referred to the Pediatric Gastroenterology Unit and the presence of PEGDs was evaluated. Eosinophilic gastroenteritis (EoGE) is defined as an inflammatory disorder characterized by eosinophilic infiltration that may affect from the esophagus to the rectum, if only the esophagus is involved with eosinophilic inflammation counts ≥ 15 eos/hpf it's defined as eosinophilic esophagitis (EoE).

Results: One hundred and twenty eight cases of OIT was performed in our Pediatric Allergy Unit (97 cases with cow’s milk and 31 cases with egg). PEGDS were diagnosed in 8 of the 128 cases of OIT (6.25%). The most common initial symptom was abdominal pain, followed by vomiting and dysphagia. EoE was diagnosed in 6 children and EoGE in the other two cases. The time to development of PEGD was variable, 6 cases after OIT with a mean of 29 (15-48) months and the other 2 cases during OIT. Discontinuation of the food oral immunotherapy was not required in 5 of the 6 cases of EoE that resolved with medical treatment. OIT discontinuation was necessary in the patients with eosinophilic gastroenteritis.

Conclusion: We report the highest prevalence of PEGD in children after OIT, and the first cases of eosinophilic gastroenteritis after food OIT. The monitoring of new digestive signs and symptoms after OIT is very important for the diagnosis of these disorders, and prolonged follow-up is required. In our experience it’s not always necessary the OIT discontinuation. The management of these patients should be assessed on an individualized basis, according to the severity of the condition, evolution and response to different treatment alternatives. It will be important to consider the opinion of the family and patient for taking a decision about treatment.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Gastroenterology other

G-eP-026

Peculiarities of the abdominal and digestive system manifestations in Armenian children with familial mediterranean fever

Gayane Amaryan¹, Tamara Sarkisian², Tatevik Shahinyan³, Artashes Tadevosyan⁴

¹“Arabkir” Medical Centre-Institute of Child and Adolescent Health; Gastroenterology and Hepatology Service; National Pediatric Familial Mediterranean Fever Centre; Yerevan State Medical University, Yerevan, Armenia
²Centre of Medical Genetics and Primary Health Care; Yerevan State Medical University, Yerevan, Armenia
³Arabkir Medical Center, Institute of Child and Adolescent Health; Gastroenterology and Hepatology Service, Yerevan, Armenia
⁴Yerevan State Medical University, Yerevan, Armenia

Objectives and study: Familial Mediterranean fever (FMF) is an autosomal recessive disease characterized by recurrent febrile aseptic polyserosites (peritonitis, pleurisies, synovitis). FMF as an ethnic disorder is widespread in Armenia and it is more often diagnosed in children recently. Besides the acute abdominal attacks, different digestive system associations are observed in FMF. They make the differential diagnosis difficult and may result in late diagnosis of FMF and complicated course. More than 50% FMF patients are seen by gastroenterologists and undergo different abdominal examinations before the final diagnosis is made. Nowadays FMF is quite frequent in non Mediterranean basin countries due to active migration, increased number of mixed marriages, etc. Awareness on FMF manifestations in different countries is not well. Objectives: to investigate clinical and genetic characteristics of the abdominal and digestive system manifestations in Armenian children with FMF.

Methods: A group of 715 children with FMF was observed (438 boys and 277 girls, mean age 8.64±0.17). Diagnosis of FMF was confirmed according to Tel-Hashomer criteria and MEFV mutation analysis. Gastrointestinal involvements were diagnosed according to conventional endoscopic, radiologic and histological criteria.

Results: Besides the typical abdominal febrile attacks (92.4%) a number of other abdominal and digestive system manifestations of FMF were observed: splenomegaly (9.9%), hepatomegaly (17.7%), adhesive intestinal obstruction (AIO) (3.2%), concomitant ulcerative colitis (UC) (0.4%), as well as FMF - associated vacuities (4.2%) - protracted febrile myalgia (PFM) - 2.7%, Henoch-Shonlein purpura (HSP) - 1.5%. Among gastrointestinal (GI) features of these vasculitis are severe abdominal pains, bloody diarrhea, GI-bleeding, rarely – the ileoileal intussusceptions. The frequency of peritoneal attacks (p<0.05), AIO (χ²=1.94; р=0.75), splenomegaly (χ²=24.86; p<0.0001), UC, FMF - associated vacuities (χ² = 8.27; p <0.02) in FMF patients was associated mainly with M694V homozygous and compound-heterozygous genotypes, high disease severity (χ²=22.15; p<0.0001) and early onset. Some of them were more frequent than expected. Patients with UC had atypical onset of disease during the first year of life: recurrent febrile abdominal colics and/or episodes of diarrhea and/or abacterial haemocolitis. Later myalgia, recurrent arthritis, polyserosites, severe course of both diseases and resistance to conventional treatment of UC were observed.

Conclusion: Armenian children with FMF and M694V mutation, especially with homozygous genotype were at a high risk for some abdominal and digestive system manifestations (splenomegaly, AIO, UC, FMF-associated vasculitis), which might be considered as possible markers of severe course of disease. They might be the early, first and only manifestations of FMF. MEFV mutations screening is recommended for Armenian pediatric patients with above mentioned GI manifestations, especially in case of early disease onset, atypical presentations and resistance to treatment. Awareness on digestive system associations of FMF might improve earlier diagnosis, patient care, treatment and prevention of amyloidosis.


Disclosure of interest: “None Declared”
An International Individual Participant Data Meta-Analysis (IPDMA) to Assess if Lactobacillus reuteri DSM 17938 Effective for the Treatment of Infant Colic

Michael Cabana¹, Kim Chau², Frank D’Amico³, Gideon Koren², Francesco Savino⁴, Valerie Sung⁵, Hania Szajewska⁶, Daniel Tancredi⁷

¹University of California, San Francisco, Pediatrics, San Francisco, United States
²University of Toronto, Pharmacology & Toxicology, Toronto, Canada
³University of Pittsburgh, Mathematics, Pittsburgh, United States
⁴University of Turin, Pediatria 1 U Children Hospital Regina Margherita, Turin, Italy
⁵University of Melbourne, Pediatrics, Melbourne, Australia
⁶University of Warsaw, Pediatrics, Warsaw, Poland
⁷University of California, Pediatrics, Davis, United States

Objectives and study: There has been variation in the results of published studies evaluating the effectiveness of the probiotic Lactobacillus reuteri DSM 17938 for the treatment of colic, a common condition during infancy with few therapeutic options. Our objective was to conduct an individual participant data meta-analysis of randomized clinical trials to assess if treatment with the probiotic L reuteri DSM 17938 reduces crying time for infants with colic, compared to placebo.

Methods: We searched MEDLINE, EMBASE, CINAHL and registries for randomized controlled trials of L. reuteri DSM 17398 versus placebo, used for infants with colic (crying >3 hrs/day, >3 days/week, for at least 1 week). Successful reduction in crying time was defined as crying duration at day 21 post-intervention being less than or equal to 50% of crying duration at baseline. Between-study heterogeneity in unadjusted treatment effects (odds-ratios) at post-intervention day 21 was assessed using the Breslow-Day test. All follow-up measurements (at post-intervention days 7, 14 and 21) from individual participants was analyzed simultaneously in a mixed-effects Poisson regression model and used to estimate time point-specific summary adjusted risk ratio (ARR) and robust 95% CI for probiotic treatment vs. placebo, adjusted for the main fixed effects of study, delivery type, age at entry and family history of atopy. A pre-specified subgroup analysis restricted to participants who were predominantly breastfed was also conducted.

Results: We identified 4 published randomized controlled trials which enrolled a total of 292 patients. There were a total of 111 treatment successes observed in 148 probiotic patients (75%) and 62 successes observed in 144 placebo patients (43%). The pooled ARR (95% CI) at post-intervention day 21 was 1.7 (1.4, 2.1). When restricted to just mostly breastfed infants, 95 treatment successes in 113 probiotic patients (83%) was observed, compared to 46 of 113 placebo patients (41%), and between-study heterogeneity in unadjusted odds at day 21 was no longer statistically significant (p=0.06). In these infants, the pooled ARR (95% CI) is 2.0 (1.6, 2.6).

Conclusions: Based on published studies, L. reuteri DSM 17938 increases the odds of successful reduction in crying time duration, compared to placebo, particularly in breast-fed infants.

Disclosure of interest: HS has served as a speaker for BioGaia.
Long-term efficacy of proton pump inhibitor therapy in proton pump inhibitor-responsive Esophageal Eosinophilia

Sonia Fernández Fernández, Carolina Gutierrez Junquera, Mª Luz Cilleruelo Pascual, Ana I. Rayo Fernández, Luis Echeverría Zudaire, Carmen Gonzalez Lois, Enriqueta Román Riechmann

1Hospital Universitario Severo Ochoa, Paediatric Gastroenterology Unit, Leganés, Madrid, Spain
2Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
3Hospital Universitario Severo Ochoa, Pediatric Allergy Unit, Leganés, Madrid, Spain
4Hospital Universitario Puerta de Hierro-Majadahonda, Madrid, Spain

Objectives and study: Proton pump inhibitor responsive esophageal eosinophilia (PPI-REE) is frequently observed in children, in our own experience almost 70% of children with esophageal eosinophilia responded to PPI. Prospective studies of recurrence of symptoms and esophageal eosinophilia while on PPI maintenance therapy have not been addressed to date. The objective of this study is to evaluate the long-term efficacy of PPI therapy in PPI-REE patients.

Methods: This prospective study enrolled PPI-REE patients from two University Hospitals. All patients with histological response after treatment with esomeprazole (1mg/Kg/dose twice daily for 8 weeks) were included. Esomeprazol was continued at a maintenance dose of 1mg/kg/day for one year. Symptoms recurrence was monitored by regular visits to the hospital and follow up endoscopy was performed at 12 months or longer on PPI maintenance dose or before if symptoms reappeared. Histological relapse was defined as presence of ≥15 eos/hpf, complete response as <5 eos/hpf and partial response as ≥5 and <15 eos/hpf in esophageal biopsies. No patient had dietary restrictions or topical steroid therapy during follow-up.

Results: Twenty-five PPI-REE patients completed one year follow up and were initially enrolled (intention-to-treat population). Seven patients were excluded because follow-up endoscopy was not performed (4 lost follow-up, 2 treatment non-compliance and 1 parental refusal for endoscopy) Finally 18 patients (72.2% males) were included. Mean age 10.11 years (±3.61). Sixteen patients (89.4%) remained completely asymptomatic. The follow-up endoscopy was performed at a mean of 14.57 months (±3.80). Sustained histological remission on maintenance therapy was observed in 14 patients (77.7% per protocol, 56 % intention-to-treat), 11 had complete response and 3 partial response. Only 4 children (22.2%) displayed histological recurrence at follow-up, with eosinophilic infiltration in both the upper-mid and distal esophagus (mean peak eosinophil count 72.5 ± 27.7 and 56.2± 28.1 eos/hpf respectively). Among relapsing patients, 4 (100%) had personal history of atopy and 3 (75%) suffered rhinoconjunctivitis vs. 57.1% and 37.1% respectively in non-relapsing patients.

Conclusion: Most PPI-REE patients on lower dose maintenance treatment remain in remission at one-year follow-up. 89% of children were asymptomatic and persistent histological response was confirmed in 77.7%. Personal history of atopy and rhinoconjunctivitis was more frequent in relapsing children, but more patients are needed to confirm this result.

Disclosure of interest: None Declared.
The incidence of eosinophilic esophagitis and treatment efficacy in children with dyspeptic symptoms

Vlatka Konjik¹, Oleg Jadrešin², Zrinjka Mišak², Iva Hojsak², Sanja Kolaček²

¹Clinical Hospital Osijek, Pediatric Clinic, Department of Pulmology, Allergology, Immunology and Gastroenterology, Osijek, Croatia
²Children's Hospital Zagreb, Referral Center for Pediatric Gastroenterology and Nutrition, Zagreb, Croatia

Objectives and study: Eosinophilic esophagitis (EoE) is a chronic, immune, antigen-mediated disease characterized by esophageal dysfunction (dysphagia, retrosternal and/or epigastric pain, vomiting, food impaction). Histological criteria is ≥15 eosinophils per high-power field, and failure of pump inhibitors (PPI). Reported incidence of EoE in children is 2.1 - 4.9%, raising up to 63% in children with food impaction and to 83% if the food impaction is coupled with dysphagia. The aim of this study was to: a. evaluate the incidence of EoE in children who underwent upper endoscopy due to dyspeptic symptoms in the Children’s Hospital Zagreb; b. to assess treatment efficacy of elimination diet and topic corticosteroids.

Methods: This is a retrospective study which included all children who underwent upper endoscopy from May 2012 to May 2014 due to following reasons: dysphagia, dyspepsia, gastroesophageal reflux, epigastric pain, recurrent vomiting and esophagitis. Review of the patient charts included: age, gender, symptoms, endoscopical finding, histological findings of esophageal biopsies, and outcomes of the treatment. The first prerequisite for the diagnosis of EoE was the number eosinophils in esophageal biopsies (≥15 per high-power field), and the second one was failure to improve on 8 weeks treatment with the PPI. If there was no clinical improvement and/or histologically verified reduction in eosinophil count on control esophageal biopsy final diagnosis of EoE was established. Patients with diagnosed EoE were treated either with the elimination of specific foods that the child was sensitized to, or with the empiric elimination of the most common food allergens (cow’s milk, soy, gluten, fish, eggs, nuts and peanuts). In cases where children did not adequately respond to elimination diet, treatment with topic corticosteroids (swallowed fluticasone propionate) was initiated.

Results: During the study period 332 children were recruited. 29/332 (8.7%) children had esophageal eosinophilia. In 13/29 children (44%) there was clinical and histological improvement after treatment with PPI, and they were classified as having PPI-responsive esophageal eosinophilia. A similar number of children (15/29, 51%) were diagnosed with EoE (80% male, mean age 9.7 years). 10/15 (66%) children clinically responded to dietary treatment; elimination of 6 most common food allergens (4/10), more than one food allergen (3/10), cow’s milk (2/10); 6/10 (60%) children had complete histological remission to dietary treatment. 5/15 (33%) children required topical corticosteroids; a. because of incomplete clinical and/or histological response (3/5), b. because of non-compliance (2/5). In 3/5 (60%) there was histological remission to treatment with topical corticosteroids. 1 child was diagnosed Barrett esophagus.

Conclusion: In our tertiary Pediatric Gastroenterology Department, among all children with dyspeptic symptoms, the incidence of the EoE was 4.5%. 66% of children had a clinical resolution of symptoms and 60 % had a histological resolution to dietary treatment, while in 33% there was need for topical corticosteroids. In the corticosteroid group, 80% had clinical, and 60% had histological resolution.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Gastroenterology other

G-eP-030

Gastric lipase and other lipolytic enzymes activity in the preterm infant fed raw, pasteurized or pasteurized-homogenized human milk

Samira De Oliveira1, Yann Le Gouar1, Olivia Ménard1, Damien Faure-Bidégaray1, Amandine Bellanger1, Emelyne Dirson3, Patrick. Pladys2, Frédéric Carrière4, Didier Dupont1, Amélie Deglaire1, Claire Bourlieu5

1Inra - Agrocampus Ouest, Umr1253 Science et Technologie du Lait et de L'œuf, Rennes, France
2Chu Rennes, Service de Pédiatrie, Rennes, France
3Chu Rennes, Lactarium, Unité Nutrition et Diététique Infantile, Rennes, France
4Cnrs-Aix-Marseille University, Umr 7282 Eipl, Marseille, France
5Umr Stlo 1253 Inra-Agrocampus Ouest, Bioactivity and Nutrition, Rennes, France

Objectives and study: Hydrolysis of milk lipids is an essential step in their digestion, initiated in the digestive tract by human gastric lipase (HGL). Although limited, gastric lipolysis has been presented very early as a key phenomenon in efficient fat digestion for newborns. It compensates for the immaturity of exocrine pancreatic function and favours the subsequent action of other lipolytic enzymes such as pancreatic or bile salt dependant lipases (HPL and BSSL, respectively). Some values of HGL activity have been determined in gastric aspirates of infants in fasting state or postprandially. High variability was reported probably due to influence of the nature of the meal (infant formula versus human milk), the age of the infant or the analysis method. However, in these studies the HGL output has never been estimated after administration of various types of human milk, nor the potential contribution of non-gastric lipolytic enzymes. The objective of the present study is thus to determine HGL activity, output and the contribution of other lipolytic enzymes in gastric aspirates of preterm infants in fasting state or after administration of raw, pasteurized or pasteurized-homogenized human milk.

Methods: In vivo study was conducted at Rennes Hospital on preterm infants fed by nasogastric tube (NCT02112331). The infants were included in two independent groups determining the type of meals: A) raw and pasteurized human milk; B) pasteurized and pasteurized-homogenized human milk. After collection (twice a day, six-day sequence), aspirates were immediately blended with glycerol (50:50 v/v) and frozen. Fasted gastric contents were collected three hours after last meal (up to 12 times per patient to verify intra-individual variation) and postprandial digesta at 35, 60 or 90 min after administered meal. Gastric volume and pH decrease were monitored. Lipolytic activity was assessed by pH-stat at pH 6 (37°C) using tributyrin as substrate (as detailed by Gargouri et al., 1986), at least on triplicate. A subsequent determination at pH 8 allowed the estimation of non-gastric lipases contribution.

Results: Results evidenced high inter and intra-individual variability on estimated gastric lipolytic activities. In the group A (n=12), lipolytic activity measured at pH 6 ranged from 2 up to 100 U/mL of fasting gastric content. The determination at pH 8 revealed a contribution of non-gastric lipases activity ranging between 0 and 61%: as HGL is not active at such pH, a remaining activity will thus indicate the presence of BSSL or HPL. These contributions were higher in patients fed raw compared to pasteurized human milk in both fasted and postprandial states, probably indicating: i) active BSSL from residual raw human milk contributed to gastric activity even three hours after meal; ii) the presence of HPL (and hence intestinal content) in the stomach, which confirms the immaturity of motility function in preterms. In patients fed with pasteurized milk the lipolytic activity increased with postprandial time, indicating a HGL secretion induced by the meal. Lipolytic activities from group B are currently been analyzed and will be further detailed.

Conclusion: This study presents a unique set of data illustrating the specificity of preterm infants’ gastric digestive conditions. These data will be useful to develop relevant in vitro models of infant digestion and analyze the link between gastric lipolytic activity and lipid digestion.

Disclosure of interest: None declared.
Autoimmunity towards parietal cells in pediatric patients with Type 1 diabetes

Agata Chobot¹, Ewa Rusak², Janet Wenzlau³, Katarzyna Bak-Drabik⁴, Agnieszka Krzywicka¹, Anna Rotarska-Mizerá¹, Joanna Polanska⁵, Marian Rewers⁵

¹Clinical Hospital No1, Zabrze, Poland
²Upper Silesian Center of Child’s Health, Katowice, Poland
³University of Colorado Denver, Barbara Davis Center for Diabetes, Aurora, United States
⁴Medical University of Silesia, Katowice, Poland
⁵The Silesian University of Technology, Gliwice, Poland

Objectives and study: Autoantibodies (AuAbs) towards the 4A subunit of the parietal cells’ proton pump (ATP4A) are typically present in the sera of individuals with autoimmune atrophic body gastritis. This disease is associated among others with type 1 diabetes (T1DM). This study’s aim was to estimate ATP4A AuAbs prevalence in T1DM children with no other autoimmune diseases and assess if the presence of these AuAbs relates to complete blood count (CBC), iron metabolism parameters or glycemic control (HbA1c) values. Our earlier published results documented ATP4A AuAbs in 30% of the general pediatric T1DM population (no other autoimmune diseases excluded).

Methods: Serum, CBC and HbF samples were collected from 94 (55♀) T1DM children (aged 12.5±4.1yrs, T1DM duration 0-15.7yrs, mean HbA1c 7.34±1.53%) with no other autoimmune diseases. ATP4A AuAbs were measured using a novel radioimmunoprecipitation assay (RIA) developed at the Barbara Davis Center for Childhood Diabetes, UCD, USA. Sera of the patients were at the same time tested for various parameters related to iron metabolism (iron concentration (Fe), total iron binding capacity (TIBC), ferritin (F), transferring (T), hepcidin (H)). HbA1c was measured using HPLC.

Results: 16 (17%) children were ATP4A AuAbs positive. Results of CBC (red blood cell count (RBC), hemoglobin (Hb), hematocrit (Ht), mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), red blood cell distribution width (RDW)) and iron metabolism parameters are presented in the table below. Univariate analysis showed no significant (p>0.05) relation between ATP4A AuAbs presence and: gender, age, age at T1DM diagnosis, T1DM duration, HbA1c. Moreover ATP4A AuAbs presence did not impact (p>0.05) CBC values as well as the parameters of iron metabolism.

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>0.25</td>
<td>459</td>
<td>3.01</td>
<td>48.51</td>
<td>59.09</td>
<td>17.34</td>
</tr>
<tr>
<td>95%CI</td>
<td>0.19, 0.30</td>
<td>409, 509</td>
<td>2.34, 3.69</td>
<td>40.37, 56.64</td>
<td>57.14, 61.04</td>
<td>15.92, 18.76</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th></th>
<th>RBC [10⁶/ul]</th>
<th>Hb [g/dl]</th>
<th>Ht [%]</th>
<th>MCV [fl]</th>
<th>MCHC [g/dl]</th>
<th>RDW [%]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>4.72</td>
<td>13.79</td>
<td>40.8</td>
<td>86.5</td>
<td>33.8</td>
<td>13.5</td>
</tr>
<tr>
<td>95%CI</td>
<td>4.63, 4.81</td>
<td>13.54, 14.04</td>
<td>40.0, 41.5</td>
<td>85.6, 87.5</td>
<td>33.6, 34.0</td>
<td>13.3, 13.8</td>
</tr>
</tbody>
</table>

Table: Results of CBC and iron metabolism parameters of the studied patients.

Conclusion: ATP4A AuAbs are detectable using RIA in a significant percentage of T1DM children even when patients with other autoimmune diseases are excluded. Presence of these AuAbs does not appear to impact the CBC values, iron metabolism or to be related to glycemic control.
The study was partially financed by MNiSW grant IP2012 007672 and SUT grant BK/265/RAU1/2014/10. All the calculations were carried out using GeCONII infrastructure funded by project number POIG.02.03.01-24-099/13.

Disclosure of interest: None Declared.
Treatment of children with intestinal failure associated bone fractures with pamidronate

Esther Neelis¹, Annelies Brandsma², Jessie Hulst¹, Barbara de Koning¹

¹Erasmus MC - Sophia Children’s Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
²Erasmus MC - Sophia Children's Hospital, Paediatric Endocrinology, Rotterdam, Netherlands

Objectives and study: Children with intestinal failure (IF) are at risk for developing poor bone health. It is not well known how often these children develop bone fractures and if treatment with bisphosphonates is effective for these fractures. The objective of our study was to describe the children with IF and bone fractures in our center.

Methods: All children with IF who were attending the IF outpatient clinic in the Erasmus Medical Center – Sophia Children’s Hospital from 2003 to 2015 who had developed bone fractures were included. DXA scans were performed as part of routine monitoring. Bone mineral status was reported as bone mineral density (BMD) age- and sex-adjusted SD scores (SDS) of lumbar spine (LS) and total body (TB). We collected data from birth until November 23, 2015.

Results: Out of the total of 90 patients with IF, 4 children with bone fractures were identified Table 1 shows the characteristics of these children in relation to their age and duration of PN. Patient 1 received PN until the age of 10 years. Laboratory tests showed a secondary hyperparathyroidism, with normal calcium. One year after weaning of PN, she developed vertebral compression fractures and started with pamidronate. She did not develop any fractures after her last pamidronate infusion 8 years ago. Patient 2 started with pamidronate and wearing a brace after he developed vertebral compression fractures. Laboratory values showed a long-term increased alkaline phosphatase level. He is still receiving pamidronate and did not develop any new fractures. Patient 3 developed 2 fractures before and 5 after the start of pamidronate. Laboratory tests showed a vitamin D deficiency and a secondary hyperparathyroidism, with normal calcium. Vitamin D intake was increased. After the first treatment with pamidronate, he developed transient hypocalcaemia. He is currently still receiving pamidronate. Patient 4 did not receive pamidronate, because of good DXA results. Her laboratory values were normal.

All patients were fully PN-dependent at their first fracture. None of the patients used steroids.
<table>
<thead>
<tr>
<th>Gender</th>
<th>Underlying disease</th>
<th>Age at first fracture (years)</th>
<th>Duration of PN at first fracture (years)</th>
<th>Vertebral compression fractures</th>
<th>Other fractures</th>
<th>Age at start pamidronate (years)</th>
<th>DXA before pamidronate</th>
<th>BMD SDS</th>
<th>Age at November 23, 2015 (years)</th>
</tr>
</thead>
<tbody>
<tr>
<td>F</td>
<td>Villous atrophy of unknown origin</td>
<td>5.4</td>
<td>5.0</td>
<td>1: L3</td>
<td>1: Tibia</td>
<td>11.55</td>
<td>TB: -1.7</td>
<td>LS: not reliable</td>
<td>21.4</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2: L1-L2, Th10-Th12</td>
<td>2: Femur</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3: Humerus</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4: Radius</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>M</td>
<td>Jejunal atresia</td>
<td>7.7</td>
<td>7.7</td>
<td>1: Almost all thoracic vertebrae and L1-L4</td>
<td>-</td>
<td>7.93</td>
<td>TB: -2.5</td>
<td>LS: -3.3</td>
<td>8.9</td>
</tr>
<tr>
<td>M</td>
<td>Filamin A mutation with intestinal pseudo-obstruction</td>
<td>2.1</td>
<td>1.9</td>
<td>-</td>
<td>1: Radius</td>
<td>2.38</td>
<td>No SDS available</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2: Radius/ulna</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3: Femur</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>4: Radius</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>5: MT4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>6: Fibula</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>7: MT2-5</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>Microvillus inclusion disease</td>
<td>1.9</td>
<td>1.9</td>
<td>-</td>
<td>1: Femur</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>4.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>2: Femur</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>3: MT1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Table:** Table 1 Characteristics of the 4 children with IF and bone fractures

**Conclusion:** Four (4.5%) out of 90 children treated by our IF team since 2003 developed bone fractures. The young age of these children illustrates the severity of IF-associated bone disease. It is remarkable that all children were totally dependent on PN at the time of their first fracture. Treatment with pamidronate did not result in any serious adverse effects and seemed to decrease the incidence of fractures in two of the three children. Early detection, treatment and prevention of poor bone health is essential, including identifying patients at high risk, including patients fully dependent on PN.

**Disclosure of interest:** None Declared.
Bone health in children with intestinal failure measured by dual energy X-ray absorptiometry and hand radiography

Esther Neelis1, Noortje Rijnen1, Joanne Olieman2, Rene Wijnen3, Edmond Rings1, Barbara de Koning1, Jessie Hulst1

1Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
2Erasmus MC - Sophia Children's Hospital, Dietetics, Rotterdam, Netherlands
3Erasmus MC - Sophia Children's Hospital, Paediatric Surgery, Rotterdam, Netherlands

Objectives and study: Children with intestinal failure (IF) receiving parenteral nutrition (PN) are at risk for developing poor bone health, i.e. low bone mineral density (BMD). Current monitoring takes place with dual energy X-ray absorptiometry (DXA). The main disadvantage of DXA is the lack of reference data below the age of 4-5 years. A relatively new technique to measure BMD is to obtain a bone health index (BHI), using BoneXpert® software in hand radiographs. BHI is based on the cortical thickness of the three middle metacarpals. Besides the availability of normative data for infants, the advantage is that this technique adjusts for bone age. The aim of our study was: 1) to evaluate the prevalence of low BMD measured by DXA and hand radiography and 2) to compare these two methods in the assessment of low BMD in children with IF.

Methods: A retrospective study was performed in all children with IF treated from 2000 to 2015 by the IF-team of Sophia Children's Hospital Rotterdam, who had undergone a DXA scan or a hand radiograph. Standard deviation scores (SDS) of BMD total body (BMD_TB) and lumbar spine (BMD_LS) and BHI were collected. Low BMD is defined as < -2 SDS. Data were collected from birth until January 1, 2015. Statistics are reported as absolute values or median with interquartile range or mean with SD. Spearman correlation coefficient and Cohen’s kappa were used to assess the relationship between SDS of BMD_TB and BHI in the children who had a DXA scan and hand radiograph performed within a time period of ≤ 6 months.

Results: Forty-eight patients (22 boys) were identified. Diagnoses were short bowel syndrome (SBS) in 21 patients (44%), surgical IF-no SBS in 16 patients (33%) and functional IF in 11 patients (23%). Median PN duration at January 1, 2015 was 49 weeks (23-152 weeks). Thirty-eight patients had at least one DXA and 25 patients at least one hand radiograph. Five patients (13%) had a low BMD_TB and 6 patients (16%) had a low BMD_LS at the first DXA, at a median age of 6 years (3-16 years). At a median age of 5.1 years (2.3-16.3 years) the mean BHI SDS was -1.96 (±1.96). Twelve children (48%) had a BHI SDS below -2.
Sixteen of the 48 children (33%) had both DXA and hand radiograph performed within a time period of ≤ 6 months. Taking BMD_TB SDS as the standard, hand radiography had a sensitivity of 82% and specificity of 92% to detect a low BMD in these 16 children. The positive and negative predictive values were 90% and 86% respectively. Spearman correlation coefficient was 0.856 (p< 0.001) for BMD_TB SDS versus BHI SDS, whereas Cohen’s kappa for BHI SDS and BMD_TB SDS was 0.749 (substantial).

Conclusion: The prevalence of low BMD measured by DXA and hand radiography ranged between 14-48%, depending on the method used. Bone health status assessment by hand radiography and DXA showed good correlation. The agreement between DXA and hand radiography to detect low BMD in children with IF seems to be good. Hand radiography using the BoneXpert® software seems to be a feasible method for regular monitoring of bone health in these children.

Disclosure of interest: None Declared.
Diagnosis of non–coeliac gluten sensitivity: first double blind placebo controlled cross over trial in pediatrics.

Antonia Gentile1, Fernanda Cristofori2, Lucia Verzillo3, Francesca Arezzo1, Carlo Polloni3, Valentina Giorgio4, Silvia Marcanio4, Elvira Verducci5, Elisa D'Angelo5, Stefania Dell'Atte6, Ruggiero Francavilla1

1University of Bari Aldo Moro/Department of Interdisciplinary Medicine, Bari, Italy
2Ss. Annunziata Hospital/ Pediatric Department, Taranto, Italy
3S. Maria del Carmine Hospital/Pediatric Clinic, Rovereto (Tn), Italy
4Catholic University of Sacred Heart/Pediatric Department, 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 Mill, Corato (Ba), Italy

Objectives and study: Aim of the study is to evaluate the real prevalence of NCGS in children presenting with gluten related symptoms (after the exclusion of CD and WA) and to describe its clinical profile.

Methods: The present study includes 23 patients (aged 4–18 years; mean age 12.2 years). Per protocol patients who referred an improvement of symptoms of at least 30% after GFD underwent double-blind placebo-controlled cross over trial. While on GFD patients assumed either pure gluten (10 g/daily) and placebo for two week respectively, spaced out by a washout week. We evaluated symptoms with Daily Visual Analogue Scale, IBS-Severity Score, State-Trait Anxiety Inventory for Children, Bristol stool chart, extra-intestinal symptoms questionnaire.

Results: 15 children completed the challenge. Four (26%) patients presented symptoms only when eating gluten, eight (54%) patients eating placebo while three (20%) patients improved regardless the diet. Therefore the final diagnosis of NCGS was confirmed in 26% of patients with gluten related symptoms. Abdominal pain and bloating were the most prevalent symptoms (all patients) followed by diarrhea (three patients) and mouth ulcers (one patient). The extra-intestinal symptoms were asthenia (three patients), headache (three patients), arthromyalgia (one patient), foggy mind (one patient).

Conclusion: NCGS is a clinical condition that should be suspected also in children but the diagnosis requires a double-blind challenge.

Disclosure of interest: None Declared.
Filaggrin and Periostin in Children with Eosinophilic Esophagitis.

A. Angelakopoulou1, E. Politi2, D. Grapsa2, M. Zande3, K. Stefanaki4, I. Panagiotou1, E. Roma1, E. Syrigou3

1First Department of Paediatrics, University of Athens, School of Medicine, Athens, Greece
2Cytopathology Department, Areteion Hospital, University of Athens, School of Medicine, Athens, Greece
3Allergy Department, Sotiria General Hospital, Athens, Greece
4Histopathology Department, Aghia Sophia Children's Hospital, Athens, Greece

Objectives and study: Eosinophilic esophagitis (EoE) is a chronic inflammatory esophageal disease resulting from a complex interplay between environmental and genetic factors. Limited previous data suggest that the expression of filaggrin (FLG) and periostin (POSTN) proteins may be dysregulated in the inflamed esophageal mucosa of EoE patients, but the exact role of these candidate biomarkers remains poorly investigated.

Methods: A total of 61 prospectively collected paediatric cases, including 40 children with EoE and 21 children with Gastro-Esophageal Reflux (GERD), as well as, a control group of 14 gender and age-matched healthy children, were included in the study. The immunohistochemical expression of FLG and POSTN was evaluated in esophageal biopsies obtained from patients and archived esophageal tissue samples from controls. The immunohistochemistry results were correlated with EoE-related clinicopathological parameters, including severity of symptoms, maximum number of eosinophils (EOS)/high power microscopic field (HPF) and treatment data.

Results: Positive (+) FLG and negative (-) POSTN staining were observed in all esophageal biopsies from normal controls. In contrast, FLG and POSTN stained (-) and (+), respectively, in all pre-treatment biopsies obtained from patients with EoE, while FLG and POSTN stained (+) in 57.1% and 95.2% of GERD cases, respectively (p<0.001). A statistically significant decrease of the proportion of cases with (-) FLG and (+) POSTN staining was observed from the pre-treatment to the post-treatment biopsies in the subgroup of patients with EoE (p<0.001).

Table:

<table>
<thead>
<tr>
<th>Sample</th>
<th>1st BIOPSY</th>
<th>2nd BIOPSY</th>
<th>1st BIOPSY</th>
<th>2nd BIOPSY</th>
</tr>
</thead>
<tbody>
<tr>
<td>EoE</td>
<td>FLG-</td>
<td>34 (100)</td>
<td>7 (20.6)</td>
<td>0 (0)</td>
</tr>
<tr>
<td></td>
<td>FLG+</td>
<td>0 (0)</td>
<td>27 (79.4)</td>
<td>POSTN-</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>34 (100)</td>
</tr>
</tbody>
</table>

Table 1: Filaggrin and Periostin Immunostaining before and after treatment in EoE.

Conclusion: Our results suggest that FLG and POSTN expression may be down regulated and upregulated, respectively, in the esophageal mucosa of patients with active EoE, and these changes may be restored with treatment in a significant percentage of patients.

Disclosure of interest: None Declared
**GASTROENTEROLOGY: Gastroenterology other**

G-eP-036

**Cholesterol and bile acid synthesis in pediatric patients with short bowel syndrome**

Florian Gothe¹, Annika Mutanen², Laura Merras-Salmio², Sibylle Koletzko¹, Mikko Pakarinen²

¹Ludwig Maximilian’s University Munich Medical Center, Dr. von Hauner Children’s Hospital, Munich, Germany
²Children’s Hospital, Helsinki University, Pediatric Gastroenterology and Pediatric Gut and Liver Research Group, Helsinki, Finland

**Objectives and study:** Malabsorption of bile acids and cholesterol activates compensatory increases in their synthesis. We aimed to assess surrogate serum markers of bile acid and cholesterol synthesis in patients with pediatric onset short bowel syndrome (SBS).

**Methods:** We measured serum 7-alpha-hydroxy-4-cholesten-3-one (C4) and cholesterol precursors (cholestenol and lathosterol), respective surrogate markers of bile acid and cholesterol synthesis, in 23 SBS patients at median age of 5.1 (IQR 3.3-12) years in relation to mode of nutrition, extension and location of intestinal resection and liver histology. Fifteen patients had been weaned off parenteral nutrition (PN) for 3.9 (2.1-11) years after having received PN for 10 (3.7-24) months, while eight patients were still on PN after 60 (19-82) months. The remaining age-adjusted small bowel length was 30% (21-44%), five of the patients had enterostomy due to associated dysmotility disorder and in six patients the ileocecal region could have been preserved. Core needle liver biopsies were graded for inflammation, cholestasis, fibrosis and steatosis. Serum C4 and cholesterol precursor levels were compared to previously established normal values in 100 and 88 healthy controls, respectively.

**Results:** Serum C4 and cholesterol precursor levels were increased above the upper limit of normal (95th percentile of controls) in 19 (83%) patients (Table 1), the median increase being 7.9 times for C4 and 4.3 times for cholesterol precursors. Serum C4 correlated positively with cholesterol precursors cholestenol (r=0.468, P=0.024) and lathosterol (r=0.402, p=0.057), while all three were inversely associated with length of the remaining small intestine (r=-0.445- -0.535, P=0.033-0.009). Serum C4, but not cholesterol precursors, correlated negatively with histological liver cholestasis grade among all patients (r=-0.464, P=0.045) and in patients on PN (r=-0.757, P=0.049). After weaning off PN, serum C4 was positively associated with liver steatosis grade (r=0.656, P=0.021). Serum concentrations of C4, cholestenol and lathosterol were comparable between patients currently receiving PN and those off PN. Serum levels of all three synthesis markers were similar in patients with or without remaining distal 1/3 of the small intestine (ileum) and/or the ileocecal valve.

**Table:** Serum C4 (ng/ml) and cholesterol precursors (100x ug/mg cholesterol) in SBS patients and controls. (*Mann Whitney U test: P<0.001)

<table>
<thead>
<tr>
<th></th>
<th>Patients (n=23)</th>
<th>Controls (n=88-100)</th>
</tr>
</thead>
<tbody>
<tr>
<td>C4 n (% with value &gt; normal)</td>
<td>19 (83)</td>
<td>19 (7-54)</td>
</tr>
<tr>
<td>Median (5th-95th percentile)</td>
<td>150 (33-573)*</td>
<td>15 (6-27)</td>
</tr>
<tr>
<td>Cholestenol n (% with value &gt; normal)</td>
<td>19 (83)</td>
<td>15 (6-27)</td>
</tr>
<tr>
<td>Median (5th-95th percentile)</td>
<td>65 (20-207)*</td>
<td>15 (6-27)</td>
</tr>
<tr>
<td>Lathosterol n (% with value &gt; normal)</td>
<td>19 (83)</td>
<td>15 (6-27)</td>
</tr>
<tr>
<td>Median (5th-95th percentile)</td>
<td>356 (122-703)*</td>
<td>82 (40-151)</td>
</tr>
</tbody>
</table>

**Conclusion:** Both cholesterol and bile acid synthesis are markedly increased secondary to malabsorption in most individuals with pediatric onset SBS. Following surgical removal of the distal ileum, length of the remaining proximal small intestine may become increasingly important for conservation of bile acids and cholesterol. Cholestatic liver disease seems to inhibit the compensatory increase in hepatic bile acid synthesis during PN. After weaning from PN, patients with severe malabsorption indicated by higher C4 values have an increased risk for macro- and micronutrient deficiencies and consequently for fatty liver disease.

**Disclosure of interest:** None Declared.
Self-administered telemedicine empowers paediatric and adolescent patients with Inflammatory Bowel Disease

Katrine Carlsen\textsuperscript{1}, Christian Jakobsen\textsuperscript{1}, Lars Folmer Hansen\textsuperscript{1}, Anders Paerregaard\textsuperscript{1}, Thomas Kallemose\textsuperscript{2}, Gunnar Houen\textsuperscript{3}, Lene Buhl Riis\textsuperscript{4}, Pia Susanne Munkholm\textsuperscript{5}, Vibeke Wewer\textsuperscript{1}

\textsuperscript{1}Hvidovre Hospital, Department of Paediatrics, Hvidovre, Denmark
\textsuperscript{2}Hvidovre Hospital, Department of Orthopaedic Surgery and Clinical Research Centre, Hvidovre, Denmark
\textsuperscript{3}Statens Serum Institute, Department of Autoimmunology and Biomarkers, Copenhagen, Denmark
\textsuperscript{4}Herlev Hospital, Department of Pathology, Herlev, Denmark
\textsuperscript{5}North Zealand Hospital, Department of Gastroenterology, Frederikssund, Denmark

**Objectives and study:** Paediatric patients with Inflammatory Bowel Disease (IBD) face a life of repeated hospitalizations and frequent outpatient visits. Our aim was to optimize patient empowerment and care by allocating the patients’ time and hospitals resources to periods of active disease using a novel telemedicine application.

**Methods:** IBD patients 10-17 years were prospectively randomized to an open label case-control telemedicine intervention for 2 years with an inclusion period of 8 months. Patients in the telemedicine (web) group used the web-application young.constant-care.com. Disease burden was estimated by patient-reported symptom scores (monthly) and faecal calprotectin (FC) (every third month). The IBD-care team monitored the patients by weekly web-rounds and beside one annual pre-planned visit, further outpatient visits were only scheduled on demand in case of increased disease burden. The control group continued standard care by outpatient visit every third month including FC. Self-assessed Medication Adherence Report Scale (MARS) was measured every third month. The repeated measures were analysed by mixed effect model (MEM) ensuring correction of alterations during the observed period.

**Results:** 53 patients (32 ulcerative colitis (UC), 21 Crohns Disease (CD)) were included (27 web, 26 control); median duration of participations: web 86 weeks (IQR 36), control 92 weeks (IQR 20).

In total, 524 symptom scores (392 web, 132 control) and 247 FC (138 web, 109 control) were collected. The MEM analysis corrected by disease type (UC/CD) found no difference in disease activity between web and controls. Same model adjusted by age and disease type found no difference in FC levels. Mean baseline medical adherence (higher MARS score representing better adherence, range 5-25 point) were web: 23.7 (SEM 0.26 CI95% 23.2;24.3) control: 23 (SEM 0.5 CI95% 22.0;23.9). Medical adherence, adjusted by age and time from diagnosis, did not show any difference between the two groups.

8 (5 web, 3 control) gastroscopies and 8 (4 web, 4 control) colonoscopies were performed. Numbers of hospitalizations showed no significant difference; web 1 (in total 5 days), control 7 (in total 18 days distributed at 5 patients). Time to step-up in medical treatment and time to outpatient visit on demand did not differ between the two groups. Numbers of total outpatient visits were 74 (2.7 per patient) in the web and 172 (6.6 per patient) in the control group.

**Conclusion:** Telemedicine empowered paediatric and adolescent patients as self-administered monitoring was comparable to standard care despite fewer outpatient visits. An increased medical adherence was not obtained possibly because of the high baseline levels.

**Disclosure of interest:** None Declared.
Quality of life in paediatric inflammatory bowel disease patients in a self-administered telemedicine randomized clinical study

Katrine Carlsen¹, Christian Jakobsen¹, Lars Folmer Hansen¹, Anders Paerregaard¹, Thomas Kallemsø², Lene Buhl Riis³, Pia Susanne Munkholm⁴, Vibeke Wewer¹

¹Hvidovre Hospital, Department of Paediatrics, Hvidovre, Denmark
²Hvidovre Hospital, Department of Orthopaedic Surgery and Clinical Research Centre, Hvidovre, Denmark
³Herlev Hospital, Department of Pathology, Herlev, Denmark
⁴North Zealand Hospital, Department of Gastroenterology, Frederikssund, Denmark

Objectives and study: Health Related Quality of Life (HRQoL) has become an important patient-reported outcome. IMPACT III is an International validated measure of HRQoL in paediatric Inflammatory Bowel Disease (P-IBD). So far no validated Danish P-IBD HRQoL has been available. The aim of the study was evaluate the HRQoL by implementing the IMPACT III questionnaire in a self-administrated telemedicine randomized clinical trial.

Methods: In collaboration with the Paediatric IBD working group on QoL (Canada, United Kingdom, Netherlands) IMPACT III was translated to Danish using a Cross-Cultural Adaptation of Self-Report Measure method. The questionnaire was implemented in the telemedicine application www.young.constant-care.com. Participants in the telemedicine study were randomized to either a web or control group for a two year period and were asked to answer the IMPACT III questionnaire every third month. Beside one annual pre-planned visit, the web group only attended outpatient visits scheduled on the basis of monthly web-reported symptom score. In contrast, the control group continued their standard quarterly outpatient visits. The repeated measures of HRQoL were statistically analysed by a mixed effect model (MEM) ensuring correction of alterations during the observation period.

Results: 53 patients (32 ulcerative colitis (UC), 21 Crohn’s Disease (CD)) were included (27 web, 26 control); median duration of participations: web 86 weeks (IQR 36), control 92 weeks (IQR 20). Control patients had a total of 172 outpatient visits compared to 74 visits in the web group.

In total, 292 IMPACT III questionnaires were answered; web 146 (UC 102, CD 44), control 146 (UC 72, CD 74). Mean score at baseline showed no statistic significant difference; web 149 (SEM 2.8 CI 95% 144;155), control 145 (SEM 1.9 CI 95% 141;149). MEM adjusted for gender and age at inclusion, found no difference in total HRQoL score comparing web versus control group. Looking at sub-scores regarding six domains (Bowel symptoms, Systemic symptoms, Emotional functioning, Social functioning, Body Image and Treatment), only Emotional functioning scored significant lower HRQoL in the web group (P=0.01 Estimate -0.005 CI 95% -0.009-0.001).

Conclusion: The telemedicine intervention with less needed out-patient visits was equal to standard care regarding patient reported HRQoL outcome. IMPACT III is now available in Danish ensuring the possibility of patient reported outcome in future clinical trials.

Disclosure of interest: None Declared
GASTROENTEROLOGY: Inflammatory bowel disease

G-eP-039

Incidence and phenotype at diagnosis in very early compared to later-onset pediatric inflammatory bowel disease: a population-based study

Emeline Bequet¹, Sarter Hélène², Fumery Mathurin³, Armengol-Debeir Laura⁴, Pariente Benjamin⁵, Ley Delphine⁶, Spyckerelle Claire⁵, Coevoet Hugues⁶, Peyrin-Biroulet Laurent⁷, Savoye Guillaume⁴, Dominique Turck², Gower-Rousseau Corinne⁶

¹Chr Citadelle, Liège, Belgium
²Chru, Lille, France
³Chu, Amiens, France
⁴Chu, Rouen, France
⁵Groupe Hospitalier de L’institut Catholique, Lille, France
⁶Ch Les Bonettes, Arras, France
⁷Chu, Nancy, France

Objectives and study: More and more studies are published on very early-onset (<6 years) inflammatory bowel disease (VEO-IBD), but their phenotype is still poorly known. Age at diagnosis of inflammatory bowel disease in children has taken an important role. We aimed to compare the incidence and phenotype at diagnosis of VEO-IBD and IBD in older children (6-17 years) from a French population-based study over a 24-year period. Our goals were to answer two questions: (1) Is the incidence of VEO-IBD increasing? (2) Is there a different phenotype depending on age at diagnosis?

Methods: Data were obtained from a cohort of 1412 children (<17 years) with IBD enrolled in a prospective French population-based Registry from 1988 to 2011. Incidence, initial classification, clinical presentation and phenotype at diagnosis were compared according to age at diagnosis (<6 years and 6-16 years).

Results: 3% of the 1412 children enrolled started the disease before the age of 6 years. The incidence of overall IBD in children increased from 3 per 100.000 in 1988-199 to 6.3 per 100.000 in 2009-2011 (+110 %; p<10⁻³). The incidence of VEO-IBD remained stable (0.44 per 100.000 in 1988-199 and 0.36 per 100.000 in 2009-2011) while it increased from 4.43 per 100.000 in 1988 - 1990 to 9.54 per 100.000 in 2009-2011; +115%, p <10⁻³). Crohn’s Disease (CD) is the most common IBD, regardless of age, but the initial classification in Ulcerative Colitis (UC) and unclassified-IBD (IBD-U) is more common in children under 6 years than in 6-16 years (40% vs 26%). The diagnosis of IBD is most often done in hospital in < 6 years (69% vs 42%). Rectal bleeding and mucous stools are more common in children under 6 years; weight loss and abdominal pain are less than in 6-16 years group. Among the children with CD, isolated colonic disease is more common in <6 years group (39% vs 14%).

Conclusion: In this large population-based study, the incidence of VEO-IBD was low and remained stable from 1988 to 2011. Children diagnosed with VEO-IBD were more often diagnosed in hospital than those diagnosed after the age of 6. CD is most present in two age groups, but UC or IBD-U was more common among the VEO-IBD group. VEO-CD children presented more rectal symptoms, presumably in relation to a high prevalence of isolated colonic CD.

Disclosure of interest: None Declared.
Gastroenterology: Inflammatory bowel disease

G-eP-040

Mucosa-associated microbiome in paediatric patients with inflammatory bowel disease and the influence of treatment on its composition

Tina Kamhi Trop1, Bojana Bogovič Matijašić2, Blaž Stres3, Tanja Obermajer2, Irena Rogelj2, Rok Orel1

1 University Children's Hospital Ljubljana, Department of Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia
2 Biotechnical Faculty, University of Ljubljana, Institute of Dairy Science and Probiotics, Department of Animal Science, Rodica, Slovenia
3 Biotechnical Faculty, University of Ljubljana, Chair for Microbiology and Microbial Biotechnology, Department of Animal Science, Rodica, Slovenia

Objectives and study: Gut microbiota plays an important role in the development of inflammatory bowel disease (IBD). While faecal microbiota of paediatric IBD patients has been researched more frequently, the mucosa-associated microbiota and the influence of therapy on its composition has been less frequently investigated in children.

Objectives of our observational study were to examine the colonic and ileal mucosa's microbiota of children and adolescents with Crohn’s disease (CD) or ulcerative colitis (UC), and to investigate the effects of medical treatment and other factors on the mucosal microbiome.

Methods: Our study included 44 patients aged ≤18 years with active Crohn’s disease or ulcerative colitis, and 39 age-matched controls with functional gastrointestinal disease. Mucosal samples of terminal ileum and colon were collected during ileocolonoscopy in all subjects before initiation of treatment, and repeated in IBD patients approximately two months after the cessation of treatment. Microbiota composition of mucosal samples before treatment was analysed by plate counting on 83 subjects (CD, n=25; UC, n=19; Controls, n=39), and real-time PCR (qPCR) analysis of selected bacterial groups on 28 subjects (CD, n=7; UC, n=7; Controls, n=14). Illumina MiSeq sequencing of bacterial 16S rDNA amplicons (V4) of bioptic samples of 44 patients with IBD (CD (n=31) and UC (n=13)) subjected to treatment with enteral nutrition (CD patients only), steroids or biological drugs was performed before and after treatment initiation. Sequences were analyzed within 97% OTU assignment in Mothur using Human Microbiome standard approach.

Results: Plate counting revealed lower count (CFU/mg) of coliform bacteria in the ileum of CD patients and lower counts of bifidobacteria in the colon of CD patients compared to controls. The qPCR analysis didn’t show any significant differences among the groups. Next generation sequencing (NGS) resulted in 44,040,416 reads. Statistical analysis relating microbial community assembly to specific available patient parameters (diagnose, sex, age, geographical origin, sampling location (ileum or colon), time (pre- or post- treatment), or medical treatment) was conducted. The type of treatment, individual variation and mucosal location were found to be the most important parameters related to differences in microbial community structure. The largest part of variability in microbial community data was explained by the type of medical treatment suggesting that it had a higher impact on the microbiome than the other factors.

Conclusion: Despite very low amounts of mucosal samples (mean 3.2 mg) and corresponding bacterial DNA, we successfully quantified selected bacterial groups by plate counting, qPCR, as well as succeeded to analyse the microbiome composition by NGS. We found significant differences in coliform bacteria and bifidobacteria counts in CD patients compared to controls, whereas we were not able to show any significant differences in patients with UC. Using the NGS, we were able to show that the type of medical treatment of CD and UC patients had a significant impact on the mucosal microbiome analysed by NGS. Further and most importantly larger paediatric studies of the influence of different type of treatment on microbiome composition in IBD patients are needed to further elucidate these findings.

Disclosure of interest: None Declared.
Abdominal obesity in Paediatric Crohn’s disease is associated with adipokine dysregulation

Dhamyanthi Thangarajah¹, Karyn E. Chapell¹, Sundhiya Mandilia¹, Gary Frost², John M.E Fell³

¹Imperial College, Section of Academic Neonatal Medicine, London, United Kingdom
²Imperial College, Nutrition and Dietetic Research Group, Faculty of Medicine, London, United Kingdom
³Chelsea and Westminster Hospital NHS Foundation Trust, Department of Paediatric Gastroenterology, London, United Kingdom

Objectives and study: We have shown that paediatric Crohn’s disease (CD) is associated with a distinct obesity phenotype with both visceral and abdominal subcutaneous adipose tissue expansion, as defined by MRI [1]. Abdominal obesity is associated with metabolic syndrome, chronic inflammation and adipokine dysregulation. The aim of this study was to investigate disease specific determinants of abdominal obesity and define the metabolic and adipokine profile in our cohort of children with CD.

Methods: Children (7-18 years) with CD had visceral adipose tissue (VAT), subcutaneous adipose tissue (SCA) volumes (l) quantified from MRI as per our previous study [2]. All children had blood analysed for CRP, ESR, albumin, fasting insulin, fasting glucose, and lipid profile. Serum adipokines (adiponectin, leptin, visfatin and resistin) were measured using the Bio-Plex Pro Human Cytokine 27-plex Assay (Bio-Rad, Hemel Hempstead, U.K.) according to the manufacturer’s instructions. Analysis: Univariate and linear regression analysis was used to identify factors (disease duration, disease site, disease activity, active therapy, CRP, ESR, albumen, fasting insulin, fasting glucose, lipid profile and adipokines), associated with the dependent variable (VAT or SCA volume). All variables found to be significantly associated with dependent variable (p<0.2) were used to derive multivariable linear regression model, where significance level was p<0.05. All factors were adjusted for sex, weight z-score, time and whether children had received active therapy in the multivariable model.

Results: 25 children with CD (9 females) were recruited, with a median [IQR] PCDAI of 30 [15 to 42.5]. In CD VAT was found to be significantly positively associated with leptin levels p<0.05. No significant association was observed between VAT and PCDAI score, disease site, active therapy, lip profile, fasting glucose and insulin. VAT was positively associated with longer duration of disease in the univariate model only, p<0.05.

In CD SCA was found to be significantly positively associated with leptin levels, CRP, active disease (PCDAI score >11), visfatin, and steroid therapy p<0.05.

There was a predominance to VAT being higher on the left side in all participants regardless of disease site.

Conclusion: For the first time in children with CD we have shown that visceral obesity was not associated with current inflammation, but maybe associated with longer disease duration. On the other hand SCA is associated with markers of inflammation.

This pattern of expanded abdominal VAT and SCA is strongly associated with leptin and less so with adiponectin levels. These adipokines play a pertinent role in VAT and SCA deposition, insulin sensitivity and the inflammatory cascade.

References
1. Thangarajah, D., et al., Aberrant adipose tissue partitioning: abdominal obesity, defined by MRI is a hallmark of paediatric CD. ESPGHAN 2016 abstract submission no.314.

Disclosure of interest:
J.M.E Fell conflict with: served as consultant to Jansen.
No other conflict of interests declared.
Cyclosporin A efficacy in a paediatric ulcerative colitis - a retrospective single center study.

Marcin Osiecki, Maciej Dadalski, Grzegorz Oracz, Jaroslaw Kierkus

The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland

Objectives and study: According to ECCO/ESPGHAN consensus for managing acute severe ulcerative colitis in children, Cyclosporin A remains a rescue therapy in acute steroid-refractory ulcerative colitis. Our aim was to assess a therapeutic efficacy of CsA in such an indication.

Methods: It is a retrospective, single center study. We describe a clinical characteristic of 59 children (33F, 26M), mean age of 13.7 years, mean disease duration 32 months, who underwent CsA treatment in the course of UC in years 2005-2015. The primary endpoint was established as clinical remission (defined as PUCAI<10) or clinical response (defined as decrease in PUCAI scoring for at least 20 points) at Day 8. The secondary endpoints were clinical remission/response at month 6 and colectomy rate. The clinical outcome was related to clinical (PUCAI score), laboratory (CsA concentration), endoscopic (disease extension and severity) and demographic (age, age of onset, disease duration) data and previous anti-TNFalpha exposure.

Results: Short-term response/remission at Day 8 was achieved in 43 out of 59 (81%) and 31 out of 59 (58%) patients respectively. Long term remission evaluated in 6 month after therapy had been sustained in 19 out of 31 patients (63%). Colectomy rate was 25% (15/59). We observed no significant difference between groups with response/remission vs. no response remission at both analyzed timepoints in analyzed clinical, laboratory, endoscopic and demographic data. Previous anti-TNFalpha exposure did not affect clinical outcome.

Conclusion: CsA rescue therapy is effective in up to 80% of paediatric UC patients. 6 months remission is sustained in 32% patient. Colectomy rate is about 26%.

Disclosure of interest: conflict of interest- none declared
Tailored step-up approach results in beneficial long-term disease outcome in the prospective Belgian registry of paediatric Crohn’s disease (BELCRO)

Lucas Wauters1, Françoise Smets2, Elisabeth De Greef3, Patrick Bontems4, Ilse Hoffman5, Bruno Hauser6, Philippe Alliet6, Wim Arts7, Harald Peeters8, Stephanie Van Biervliet9, Isabelle Paquot10, Els Van de Vijver11, Martine De Vos12, Peter Bossuyt13, Jean-François Rahier14, Olivier Dewit15, Tom Moreels15, Denis Franchimont16, Vincianne Muls16, Fernand Fontaine17, Edouard Louis17, Jean-Charles Coche18, Filip Baert19, Séverine Vermeire1, Gigi Veereman3

1Ucl Leuven, Gastroenterology and Hepatology, Leuven, Belgium
2Ucl St Luc, Pediatric Gastroenterology, Brussels, Belgium
3Uz Brussel, Pediatric Gastroenterology, Brussels, Belgium
4Hudert, Pediatric Gastroenterology, Brussels, Belgium
5Uz Leuven, Pediatric Gastroenterology, Leuven, Belgium
6Jessy Ziekenhuis, Pediatric Gastroenterology, Hasselt, Belgium
7Zol Genk, Pediatric Gastroenterology, Genk, Belgium
8St Lucas, Gastroenterology, Ghent, Belgium
9Uz Gent, Pediatric Gastroenterology, Ghent, Belgium
10Chc Liège, Pediatric Gastroenterology, Liège, Belgium
11Uz Antwerpen, Pediatric Gastroenterology, Antwerp, Belgium
12Uz Gent, Gastroenterology, Ghent, Belgium
13Imelda Ziekenhuis, Gastroenterology, Bonheiden, Belgium
14Ucl Mont-Godinne, Gastroenterology, Mont-Godinne, Belgium
15Ucl St Luc, Gastroenterology, Brussels, Belgium
16Ulb Erasme, Gastroenterology, Brussels, Belgium
17Chu Liège, Gastroenterology, Liège, Belgium
18St Pierre, Gastroenterology, Ottignies, Belgium
19Heilig Hart Ziekenhuis, Gastroenterology, Roeselaere, Belgium

Objectives and study: The prolonged use of biologic agents with or without immunomodulators (IM) remains controversial in the management of paediatric Crohn’s disease (CD).

Methods: Five-year follow-up (FU) data from the BELCRO, an observational prospective cohort of children (< 18 years) diagnosed with CD in Belgium, were analysed. Disease severity was scored as inactive, mild or moderate-to-severe on a 3-point PCDAI scale and monitored yearly. Treatment and outcomes were recorded from diagnosis until 5 yrs FU. Remission was defined as inactive disease and sustained remission when achieved for ≥ 2 yrs FU. Univariate analyses were performed between patients with or without anti-TNF and Spearman’s correlation between treatment and outcomes.

Results: A total of 91 patients (median (IQR) age 12.7 (10.9 – 14.8) yrs, 53% male) were included. Disease location was 12% ileal, 23% colonic (L2), 64% ileocolonic, 76% upper GI and 30% perianal. Disease severity was 25% mild and 75% moderate-to-severe. Anti-TNF was started in 73% after median (IQR) 1.1 (0.6 – 2.2) yrs with duration of 3.9 (2.5 – 4.7) yrs of which 89% combination therapy with duration of 1.3 (0.6 – 2.0) yrs. Older age (13.1 (11.5 – 15.2) vs. 11.8 (8.7 – 13.8) yrs; p< .05) and location L2 (29% vs. 8%; p= .04) were associated with need to start anti-TNF. Despite shorter delay to corticosteroids (CS), total duration of CS treatment was similar and total duration of IM was shorter in the anti-TNF group. Time to first and sustained remission was longer with use of anti-TNF (Table 1). Mean disease severity (1.7 (1.4- 1.9) vs. 1.4 (1.3- 1.6); p< .01) during 5 yrs FU was higher in the anti-TNF group but rates of inactive disease (65% vs. 76%; p=.32) after 5 yrs FU were similar with less ongoing CS (41% vs. 72%; p= .008) with anti-TNF. Delay to IM treatment was positively correlated with mean disease severity (r=.26; p=.02) and duration of CS treatment negatively with duration of sustained remission (r= -.24; p=.03), though not significantly after correction for multiple testing. Rates of perianal flares, hospitalizations or surgery were similar and no serious infections, cancer or deaths were reported with anti-TNF.
Table: Univariate analyses of treatment and outcome variables between anti-TNF exposed and naïve CD patients.

<table>
<thead>
<tr>
<th>Treatment and outcome variables in years, median (IQR)</th>
<th>Anti-TNF exposed (n= 66)</th>
<th>Anti-TNF naïve (n= 25)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to corticosteroid treatment</td>
<td>0 (0 – 0.02)</td>
<td>0.02 (0 – 0.06)</td>
<td>.04</td>
</tr>
<tr>
<td>Time on corticosteroid treatment</td>
<td>0.4 (0.3 – 0.7)</td>
<td>0.6 (0.3 – 1.2)</td>
<td>.41</td>
</tr>
<tr>
<td>Time to immunomodulator treatment</td>
<td>0.08 (0.01 – 0.22)</td>
<td>0.07 (0 – 0.66)</td>
<td>.86</td>
</tr>
<tr>
<td>Time on immunomodulator treatment</td>
<td>2.5 (1.4 – 4.7)</td>
<td>4.7 (3.6 – 5.2)</td>
<td>.001</td>
</tr>
<tr>
<td>Time to first remission</td>
<td>1.1 (0.5 – 1.8)</td>
<td>0.6 (0.3 – 1.1)</td>
<td>.01</td>
</tr>
<tr>
<td>Time to sustained remission</td>
<td>2.9 (2.3 – 3.9)</td>
<td>2.3 (2.1 – 2.9)</td>
<td>.03</td>
</tr>
<tr>
<td>Duration of sustained remission</td>
<td>2.2 (1.3 – 4.2)</td>
<td>3.1 (1.5 – 4.1)</td>
<td>.44</td>
</tr>
</tbody>
</table>

Conclusion: Prospective data from the BELCRO demonstrate beneficial long-term outcomes using a step-up approach with anti-TNF in over 2/3 of patients, limiting IM treatment. The gain of top-down and early combination therapy remains to be determined in paediatric CD.

Disclosure of interest: None Declared.
**Type of treating physician is associated with long-term disease outcome in the prospective Belgian paediatric Crohn’s disease registry (BELCRO)**

Lucas Wauers1, Françoise Smets2, Elisabeth De Greef3, Patrick Bontems4, Ilse Hoffman5, Bruno Hauser6, Philippe Alliet7, Wim Arts7, Harald Peeters8, Stephanie Van Biervliet9, Isabelle Paquot10, Els Van de Vijver11, Martine De Vos12, Peter Bossuyt13, Jean-François Rahier14, Olivier Dewit15, Tom Moreels15, Denis Franchimont16, Vincianne Muls16, Fernand Fontaine17, Edouard Louis17, Jean-Charles Coche18, Jérôme Paul19, Filip Baert20, Séverine Vermeire1, Gigi Veereman3

1Ucl Leuven, Gastroenterology and Hepatology, Leuven, Belgium  
2UcSt Luc, Pediatric Gastroenterology, Brussels, Belgium  
3Uz Brussel, Pediatric Gastroenterology, Brussels, Belgium  
4Hudert, Pediatric Gastroenterology, Brussels, Belgium  
5Uz Leuven, Pediatric Gastroenterology, Leuven, Belgium  
6Jess A Ziekenhuis, Pediatric Gastroenterology, Hasselt, Belgium  
7Zol Genk, Pediatric Gastroenterology, Genk, Belgium  
8St Lucas, Gastroenterology, Ghent, Belgium  
9Uz Gent, Pediatric Gastroenterology, Ghent, Belgium  
10Chc Liège, Pediatric Gastroenterology, Liège, Belgium  
11Uz Antwerpen, Pediatric Gastroenterology, Antwerp, Belgium  
12Uz Gent, Gastroenterology, Ghent, Belgium  
13Imelda Ziekenhuis, Gastroenterology, Bonheiden, Belgium  
14Ucl Mont-Godinne, Gastroenterology, Mont-Godinne, Belgium  
15Ucl St Luc, Gastroenterology, Brussels, Belgium  
16Ulb Erasme, Gastroenterology, Brussels, Belgium  
17Chu Liège, Gastroenterology, Liège, Belgium  
18St Pierre, Gastroenterology, Ottignies, Belgium  
19Ondas, Statistics, Brussels, Belgium  
20Heilig Hart Ziekenhuis, Gastroenterology, Roeselaere, Belgium

**Objectives and study:** Treatment and outcomes in paediatric Crohn’s disease (CD) have not been compared between type of treating physician and centre of care.

**Methods:** Data from BELCRO, an observational prospective cohort of children (< 18 yrs) diagnosed with CD in Belgium, were analysed. Disease severity was scored as inactive, mild and moderate-to-severe using a 3-point scale and monitored yearly. Response was defined as a decrease of ≥ 1 point from baseline and remission as inactive disease, with sustained response and remission as score 2 and/or 1 for ≥ 2 yrs follow-up (FU). Univariate analyses were performed between paediatric or adult and secondary or tertiary level of care.

**Results:** A total of 91 children (median (IQR) age 12.7 (10.9 – 14.8) yrs, 53% male) were included. Disease location was 12% ileal, 23% colonic, 64% ileocolonic, 76% upper GI or 66% proximal (L4A) and 30% perianal. Disease severity at diagnosis was 25% mild and 75% moderate-to-severe. Level of care was 70% paediatric and 71% tertiary. Younger age (11.9 (9.8 – 13.4) yrs vs. 15.1 (13.8 – 16.7) yrs; p< 10^-3), and location L4A (77% vs. 41%; p=.02) were associated with paediatrics. Young age was associated with lower disease severity (11.4 (8.7 - 13.8) yrs for mild and 13.2 (11.6 – 15.3) yrs for moderate-to-severe disease; p=.02). Time to biological and combination treatment was longer and duration on biologicals was shorter in paediatrics (Table 1). Rates of both biological and combination treatment were similar but biological (60% vs. 26%; p=.008) and combination (65% vs. 26%; p=.005) treatment was initiated more often after first remission by paediatricians. Rates of sustained remission (95% vs. 67%; p< .001) and response (95% vs. 85%; p=.04) were higher for paediatric but similar for tertiary care. Time to first or sustained remission and response was shorter and duration of sustained remission was longer in paediatrics (Table 1). Mean disease severity during 5 yrs FU (1.5 (1.3 – 1.8) vs. 1.8 (1.6 – 2.0); p=.008) was lower in paediatrics. Rates of inactive disease after 5 yrs of FU (73%
vs. 56%; p= .09) were similar with more ongoing immunomodulator treatment (56% vs. 33%; p< .05)

<table>
<thead>
<tr>
<th>Treatment and outcome variables in years, median (IQR)</th>
<th>Follow-up by paediatrician (n= 64)</th>
<th>Follow-up by adult physician (n= 27)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time to biological treatment</td>
<td>1.5 (0.7 – 2.6)</td>
<td>0.6 (0.4 – 1.4)</td>
<td>.003</td>
</tr>
<tr>
<td>Time to combination therapy</td>
<td>18.5 (8 – 32.5)</td>
<td>7 (3 – 12)</td>
<td>.006</td>
</tr>
<tr>
<td>Time on biological treatment</td>
<td>3.6 (2.0 – 4.4)</td>
<td>4.6 (2.6 – 5.0)</td>
<td>.01</td>
</tr>
<tr>
<td>Time to first remission</td>
<td>0.7 (0.3 - 1.4)</td>
<td>1.2 (0.7 – 2.5)</td>
<td>.01</td>
</tr>
<tr>
<td>Time to first response</td>
<td>0.6 (0.3 – 0.9)</td>
<td>0.8 (0.4 – 1.2)</td>
<td>.02</td>
</tr>
<tr>
<td>Time to sustained remission</td>
<td>2.6 (2.1 – 3.2)</td>
<td>3.1 (2.5 – 3.9)</td>
<td>.05</td>
</tr>
<tr>
<td>Time to sustained response</td>
<td>2.2 (1.9 – 2.7)</td>
<td>2.6 (2.2 – 3.0)</td>
<td>.003</td>
</tr>
<tr>
<td>Duration of sustained remission</td>
<td>2.8 (1.6 – 4.2)</td>
<td>2.1 (1.3 – 3.5)</td>
<td>.004</td>
</tr>
</tbody>
</table>

compared to adult care.

**Table:** Univariate analyses of treatment and outcome variables between paediatric or adult follow-up.

**Conclusion:** Paediatric care was associated with longer delay to and shorter duration on biological or combination treatment with better disease control using a step-up approach. However, outcomes after 5 years were similar with adult care and use of top-down strategies for more severe disease course in older patients.

**Disclosure of interest:** None Declared.
GASTROENTEROLOGY: Inflammatory bowel disease

G-eP-045

Presence and severity of ulcerations in Crohn Disease does not contribute to response for induction therapy with infliximab in children

Maciej Dadalski1, Agnieszka Wegner2, Edyta Szymanska3, Jaroslaw Kierkus1

1The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
2Public Children's Clinical Hospital, Warszawa, Poland
3Children's Memorial Health Institute, Warsaw, Poland

Objectives and study: Induction therapy with infliximab is efficient in approximately 80% of children with Crohn disease (CD). It's documented that male sex, concurrent immunomodulators, non-smoking behavior and luminal disease are the predictors of good infliximab response. It is questionable if presence of colonic and ileal ulcerations can contribute response for biological therapy. The aim of the study was to explore the contribution of presence and severity of ulcerations to response for induction therapy with infliximab in children.

Methods: This is a subanalysis of CIMIT study (JPGN: May 2015 - Volume 60 - Issue 5 - p 580–585). 99 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 were involved to the study and received induction therapy with infliximab 5 mg/kg at weeks 0, 2, and 6. Clinical (PCDAI score) response (decrease of PCDAI≥15 AND PCDAI<30) and remission (PCDAI<10) were assessed at Week 10. Scorings of ulcer size and ulcerated surface were used as two independent variables in analysis of discrimination between: group with clinical response vs. no response and group with clinical remission vs. no remission.

Results: None of the analyzed variable had significant impact on discrimination between group with clinical response vs. no response – all partial Wilks’ Lambda > 0.99. The optimal model of discrimination had sensitivity 1.00 and specificity 0.00.

None of the analyzed variable had significant impact on discrimination between group with clinical remission vs. no remission – all partial Wilks’ Lambda > 0.99. The optimal model of discrimination had sensitivity 1.00 and specificity 0.00.

Conclusion: Presence and severity of colonic and ileal ulcerations in Crohn Disease does not contribute to response for induction therapy with infliximab in children.

Disclosure of interest: None Declared
Therapeutic drug monitoring in 45 children with IBD on maintenance infliximab treatment

Helena Rolandsdotter1, Per Marits2, Ulrika Fagerberg3, Ulf Sundin2, Michael Eberhardson4, Yigael Finkel1

1Karolinska Institute, Sachs’ Children and Youth Hospital, Gastroenterology and Nutrition, Stockholm, Sweden
2Karolinska Institute, Karolinska University Hospital, Dept of Clinical Immunology and Transfusion Medicine, Karolinska University Hospital, Stockholm, Sweden
3Vastmanland Hospital Vasteras, Center for Clinical, Department of Gastroenterology, Vasterås, Sweden
4Karolinska Institute, Karolinska University Hospital, Center for Digestive Diseases, Stockholm, Sweden

Objectives and study: The anti-TNF antibody infliximab (IFX) is frequently used as maintenance therapy in pediatric inflammatory bowel disease (IBD). However, the role of monitoring trough s-IFX and antibodies toward IFX (ATI) during maintenance treatment remains unclear in children. The aim of the present study was to investigate the trough levels of IFX and the presence of ATI in order to identify any correlation with inflammatory activity and clinical response in a pediatric IBD cohort.

Methods: We conducted a cross-sectional study of s-IFX in all IFX-treated children with IBD (n=45, Crohn’s disease, CD=32, ulcerative colitis, UC=13) in the two Swedish counties Stockholm and Vasteras. The children were on maintenance IFX treatment and had received 4-48 infusions. IFX trough levels and ATI were analysed 1-4 times in each patient using an in-house ELISA assay. ATI could only be analysed when IFX was undetectable. A total of 93 IFX trough level tests were collected. Demographics, concomitant immunosuppression, CRP, ESR, albumin, and the validated clinical activity indices Pediatric UC Activity Index (PUCAI) and Pediatric CD Activity Index (PCDAI) were recorded.

Results: The children received a mean IFX dose of 6.4±1.7 mg/kg with a mean interval of 44.8±11.2 days. The mean s-IFX trough level was 5.2 μg/mL (median 4.5 μg/mL). The trough s-IFX was significantly higher in the samples taken during remission (mean 8.0 μg/mL, median 6.5 μg/mL) as compared with s-IFX in active disease (mean 4.0 μg/mL, median 2.7 μg/mL, P<0.05). The trough IFX levels displayed a significant correlation with ESR, CRP, and albumin. When comparing the 45 children with an adult population of 79 IBD-patients treated with IFX and analysed with the same ELISA assay (previously published in Marits et al, JCC 2014 Aug;8(8):881), the mean s-IFX trough levels were significantly higher in the pediatric remission group (8.0 vs 4.1 μg/mL; P<0.05) as well as in the active disease group (4.0 vs 1.8 μg/mL, p<0.05). Compared to the adult IBD population on IFX treatment, who reached clinical remission at 53% of their visits, the percentage of children achieving clinical remission was lower (32% of the visits). A larger proportion of adults (35%) had at least one trough level analysis below detection level compared to 18% of the children. In these patients, all of the children and approximately 80% of the adults had ATI formation. Interestingly, in 25% of the visits the adults were in clinical remission despite undetectable s-IFX. In the children, all patients with s-IFX<0.02μg/mL and ATI had active disease at the time of the sampling.

Conclusion: S-IFX trough concentration correlated to the clinical response to infliximab in 45 children with IBD and IFX maintenance treatment. In comparison with an adult IBD population on maintenance IFX (previously reported), the pediatric cohort showed higher levels of trough s-IFX. There was also a stronger correlation between undetectable trough levels and disease activity in children compared to adults.

Disclosure of interest: None Declared
**Anti-TNF treatment in pediatric crohn´s disease... just a question of time?**

**Patricia Domínguez Sánchez**, Gemma Pujol, Sergio Pinillos Pison, Víctor Vila Miravet, Javier Martín de Carpi, Paula Mariel Soriano Villaverde

1Sant Joan de Déu, Barcelona, Spain
2Sant Joan De Deu Hospital, Gastroenterology and Nutrition, Barcelona, Spain
5Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain

**Introduction:** Previous studies have shown the efficacy of exclusive enteral nutrition (EEN) for induction of remission in pediatric Crohn’s disease (CD). The recent ECCO-ESPGHAN guidelines recommend the use of EEN (6-8 weeks) combined with early use of immunosuppressants as the optimal therapy in these patients at diagnosis. However, a high rate of relapse after EEN has been reported. Moreover, the potential effect of this strategy in postponing or avoiding the future need of biological treatment has not been evaluated. Our aim is to determine the proportion of our CD patients diagnosed in the last years in our center and treated with EEN and thiopurines at diagnosis have required escalation to anti-TNF treatment during their follow-up.

**Methods:** Data from our pediatric (age at onset <18 years of age) CD patients diagnosed in our Unit between 2007 and 2014 and who entered remission with EEN combined with thiopurines, were retrospectively collected. The percentage of patients that needed to escalate to anti-TNF therapy (infliximab or adalimumab) after failure of maintenance treatment during their follow-up in our Unit was analyzed. The follow-up period was considered until their last visit in our Unit at the time of preparing the abstract (October 2015) or up to the end of the transition program to an adult IBD Unit.

**Results:** 50 patients (33 boys; mean age at diagnosis 13.6 years) fulfilled the inclusion criteria. Mean follow-up was 3.2 years, median 2.8 years. During the follow-up in our Unit, 38 had a relapse; in 10 of them a new EEN treatment was initiated, being effective in 5. The other 5 patients and the other 28 received anti-TNF. In total, up to 66% of the patients required treatment escalation to anti-TNF treatment. 12 patients received Infliximab and 21 Adalimumab. Mean time to onset of biologics was 465.8 days, (median 290 days).

**Conclusion:** The use of EEN has proved to be effective for the remission of pediatric CD and may delay somewhat the use of biological treatment. However, in our study two thirds of the patients required escalation of therapy and initiation of anti-TNF treatment. Further studies showing the long-term follow-up of patients treated with standard therapy (EEN and immune-modulators) are needed to know the real effect of this combination in avoiding initiation of biological therapy.

**Disclosure of interest:** None Declared.
Enterocytes and dendritic cells both contribute to the intestinal inflammation in pediatric inflammatory bowel diseases

Caterina Strisciuglio1, Serena Vitale2, Laura Pisapia3, Erasmo Miele4, Pasquale Barba3, Alessandra Vitale1, Sabrina Cenni4, Giovanna Del Pozzo3, Riccardo Troncone3, Annamaria Staiano4, Carmen Gianfrani2

1Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy
2Institute of Protein Biochemistry, Cnr, Naples, Italy
3Institute of Genetics and Biophysics Adriano Buzzati Traverso, Cnr, Naples, Italy
4Federico II University, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy
5University Federico II, Department of Translational Medical Sciences, Naples, Italy

Objectives and study: The contribution of both adaptive and innate immune response to the development and maintenance of mucosal lesions in inflammatory bowel diseases (IBD) has been extensively dissected. Recent evidences have underlined the role of enterocytes as non-immune inflammatory cells in the pathogenesis of IBD. However, since very little is known we want to deepen the knowledge of cellular and cytokine inflammatory pathways occurring in very young subjects with IBD.

Methods: Through an ex-vivo analysis, we investigated the cytokine production profile and phenotype of enterocytes, dendritic cells, and T lymphocytes in uninflamed colonic biopsies of children with Crohn’s disease (CD), ulcerative colitis (UC), and non-IBD controls (HC). The different cell populations were monitored in freshly isolated intestinal cells by specific surface cell markers, as EpCam, CD11c, and CD3, respectively for enterocytes, dendritic cells and T lymphocytes, as well as for HLA-Class I and II molecule expression. The production of pro-inflammatory cytokines (IL-15, TNF-α, INF-γ), was evaluated in intestinal colonic mucosa in the steady state condition, or after a brief in vitro cell stimulation with mitogens, by multicolor flow cytometry and ELISA.

Results: In biopsies from pediatric IBD we observed a higher frequency of IL-15 producing cells. Furthermore, in IBD mucosal explants we found an enhanced densities of EpCam+ enterocytes expressing IL-15, and of CD11c+ dendritic cells producing TNF-α compared to healthy mucosa. Interestingly, increased densities of enterocytes were detected in biopsies from UC patients, whilst no differences were observed in CD11c+ dendritic cell or CD3+ lymphocyte infiltrates among IBD and healthy intestinal mucosa. Furthermore, in UC a more prominent infiltration of intestinal cells expressing HLA Class I molecules, and of CD11c+ DGs producing IFN-γ was detected. IFN-γ was found markedly secreted by IBD intestinal cells after a mitogen stimulation.

Conclusion: Our study demonstrates a pro-inflammatory phenotype of both epithelial and dendritic cells in the intestinal mucosa of pediatric subjects with IBD. A pathogenic function of IL-15 in addition to TNF-α is also reported, thus suggesting IL-15 as a potential therapeutic target in pediatric IBD.

Disclosure of interest: None Declared.
Bacterial richness and the ratio of Bacteroidetes to Gammaproteobacteria are decreased in the colonic mucosa of pediatric ulcerative colitis

Marko Kalliomäki\textsuperscript{1}, Jing Cheng\textsuperscript{2}, Kaisa Hiippala\textsuperscript{2}, Jarmo Ritari\textsuperscript{2}, Pirkko Mattila\textsuperscript{3}, Veera Kainulainen\textsuperscript{4}, Jarkko Salojärvi\textsuperscript{5}, Reetta Satokari\textsuperscript{2}

\textsuperscript{1}University of Turku, Pediatrics, Turku, Finland
\textsuperscript{2}University of Helsinki, Veterinary Biosciences, Helsinki, Finland
\textsuperscript{3}University of Helsinki, Institute of Molecular Medicine in Finland, Helsinki, Finland
\textsuperscript{4}University of Helsinki, Pharmacology, Helsinki, Finland
\textsuperscript{5}University of Helsinki, Biosciences, Helsinki, Finland

Objective and study: Crohn’s disease (CD) and ulcerative colitis (UC) are the two major forms of inflammatory bowel disease (IBD). So far genome-wide association studies have uncovered 163 risk loci for IBD highlighting a key role for epithelial barrier, immunological function and bacterial handling in the pathogenesis. Changes in epigenetic environmental factors including microbiome are thought to account for the growing incidence of IBD around the world. However, the exact role of dysbiosis, altered microbiota found both in fecal and mucosal biopsy samples of these patients, in the pathogenesis of IBD remains unsolved.

Methods: We used bacterial high-throughput 16S rDNA amplicon sequencing to comprehensively profile the microbiota in the colonic biopsies of UC (n=26), CD (n=14) and healthy control (HC) (n=27) children. In addition, effect of certain bacterial species on intestinal epithelial cell integrity and lipopolysaccharide (LPS)-induced interleukin 8 (IL-8) production was evaluated in human enterocyte cell line \textit{in vitro}.

Results: The overall composition of mucosal microbiota was comparable between UC, CD and HC, but the richness of microbiota was decreased in both UC (p=0.02) and CD (p=0.01) as compared to HC. The mucosal dysbiosis of UC children with active disease was characterized by a decreased ratio of Bacteroidetes to \(\gamma\)-Proteobacteria as compared to HC (p=0.03). Two bacterial species belonging to the Bacteroidetes phylum and found to be associated with HC bacterial taxa, namely \textit{Parabacteroides distasonis} and \textit{Bacteroides fragilis} were found to increase intestinal epithelial integrity and to attenuate LPS-induced pro-inflammatory IL-8 release from enterocytes \textit{in vitro} whereas a species of the \(\gamma\)-Proteobacteria, \textit{Escherichia coli}, had opposite effects.

Conclusion: Mucosal dysbiosis found in pediatric ulcerative colitis may impair intestinal epithelial integrity and promote local pro-inflammatory response.

Disclosure of interest: None declared.
Clinical outcomes in paediatric ulcerative colitis: a single-centre cohort study

Vivien Wong-Spracklen¹, Marco Gasparetto¹, Franco Torrente¹, Robert Heuschkel¹, Mary Brennan¹, Gabriele Noble-Jamieson¹, Matthias Zilbauer¹

¹Cambridge University Hospitals, Addenbrooke's, Paediatric Gastroenterology, Hepatology and Nutrition, Cambridge, United Kingdom

Objectives and study: The disease course of children with ulcerative colitis (UC) can vary substantially. Published data on clinical outcomes of large paediatric cohorts remains scarce. Here we describe the outcomes of children and adolescents with UC or unclassified inflammatory colitis (IBD-U) based on induction treatment and requirement for subsequent medical and surgical treatment interventions focussing on the first 18 months upon diagnosis.

Methods: We retrospectively identified all patients aged 2 to 18 years diagnosed with UC or IBD-U from the hospital's electronic patient record system. Patients diagnosed between September 2006 and February 2014, who had a minimum follow-up period of 18 months, were included. The initial diagnosis of UC and IBD-U colitis was based on standard criteria including macroscopic as well as histological findings. For all patients we recorded the type of induction treatment (i.e. steroids or 5-Aminosalicylic acid (5-ASA)) received within 3 months following diagnosis; maintenance therapy at 6, 12 and 18 months follow-up; commencement dates of second-line therapy such as Azathioprine (AZA), 6-mercaptopurine (6MP); and requirement for third-line therapy (i.e. biologics) and surgical intervention (i.e. colectomy). Patients were stratified into 3 different groups of disease course severity based on their requirements for escalation therapy over an 18-month period: mild disease course maintained on 5-ASA alone (Group 1), moderately severe disease course requiring escalation to AZA or 6-MP (Group 2), and severe disease course requiring biologics (IFX) and/or colectomy (Group 3). The requirement over time for the different medical and surgical treatments was determined by Kaplan-Meier survival analyses.

Results: 93 patients were included in our study with a mean follow-up duration of 59.2 months +/- SD 33.4 months (median= 49.7 months, range 18-195 months), 58/93 (62.3%) were diagnosed with UC and 35/93 (37.6%) with IBD-U colitis. The mean age at diagnosis was 11.7 years (+/- SD 3.12 years, range 2.2 - 17 years). 77/93 (82.8%) required induction of remission with steroid therapy, while only 16 patients (17.2%) were started on 5-ASA as induction treatment upon diagnosis. Taking the first 18 months following diagnosis into consideration 38/93 (40.9%) patients were stratified into Group 1, 38/93 (40.9%) into Group 2, and a minority of 17 patients (18.2%) into Group 3. Within Group 3, 15/17 (88.2%) patients progressed to IFX therapy, out of which 12/15 (80%) required IFX as part of their treatment for acute severe colitis (ASC) (80%). Only 3/15 (20%) received IFX as maintenance treatment for chronic active colitis (CAC). Interestingly, all 8 patients experiencing ASC were found to progress from IFX to colectomy.

Conclusion: Our study provides important insight into disease behaviour and outcome in children diagnosed with UC and UC-like IBD-U. The data indicates that only a relatively small proportion (18%) of patients with UC and IBDU colitis experience an aggressive phenotype, characterised by a rapid progression to treatment with IFX and/ or requirement for colectomy within 18 months from diagnosis. Importantly, in our cohort, all patients receiving IFX for ASC failed to respond to medical therapy and required colectomy. Future work has to focus on identifying reliable disease prognostic biomarkers, which allow early detection of at risk patients and potential preventative treatment strategies.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Inflammatory bowel disease

G-eP-051

Fecal microbiota transplantation for CMV infection in pediatric patients with IBD

Katarzyna Karolewska-Bochenek¹, Izabella Lazowska-Przeorek¹, Aleksandra Banaszkiewicz¹, Agnieszka Gawrońska¹, Maria Kotowska¹, Marcin Dziekiewicz¹, Piotr Albrecht¹, Andrzej Radzikowski¹, Paweł Grzesiowski²

¹The Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
²Institute of Infectious Disease Prevention, Warsaw, Poland

Objectives and study: Growing amount of scientific evidence suggests that cytomegalovirus (CMV) infection may have deleterious effect on the clinical course of inflammatory bowel disease (IBD) especially those being steroid-resistant. The treatment of CMV infection in IBD includes ganciclovir that could generate severe adverse events, and discontinuation of immunosuppressive agents that could result in IBD flare. The fecal microbiota could be a new, promising option of therapy.

Aim: The aim of the study was to investigate the effectiveness of fecal microbiota transplantation (FMT) in the treatment of CMV infection in pediatric patients with IBD.

Methods: 4 children (3 girls), 1-17 years old, with steroid refractory IBD and CMV-DNA detected by PCR in colonic biopsies were analyzed. All patients received 50 ml of FMT via gastroscopy on 5 consecutive days in first week and every other day in the second week (8 infusions in 14 days). Donors, not related to patients, were healthy and screened for HIV, HAV, HBV, HCV, HAV, EBV, Treponema pallidum, Clostridium difficile, ova & parasites. Study subjects were maintained on their pre-transplant medications and PPI was added during FMT treatment.

Results: All 4 patients, included 3 patients with UC (mean PUCAI -33 ) and 1 patients with CD (PCDAI- 35 ), had good clinical response and good tolerance to FMT. After the 2 week course of FMT therapy, we achieved negative control test (PCR) for CMV in colonic biopsies in all patients during control sigmoidoscopies. We registered no serious adverse effects. In one patient only mild abdominal pain was observed right after the infusion.

Conclusion: For the first time we report that FMT may play a significant role in the treatment of CMV infection in IBD patients, however further studies are needed to confirm our results.

Disclosure of interest: None Declared

Silvia Ghione¹, Giulia Fusi¹, Monica Paci¹, Pietro Garlatti¹, Sara Naldini¹, Anna Gissi¹, Paolo Lionetti¹

¹Meyer Children's Hospital, Gastroenterology and Nutrition, Florence, Italy

Objectives and study: Acute severe ulcerative colitis (ASC) is a medical emergency that occurs more frequently in children than in adults. We report a retrospective evaluation of ASC episodes over a period of 20 years in an Italian paediatric referral centre. The aim of this study was to evaluate trend of prevalence over time of ASC, response rate to first-line corticosteroid (CS) and second-line cyclosporine (CyA) or infliximab (IFX) treatments and rate of colectomy.

Methods: We retrospectively reviewed medical records of all children with ASC admitted to the Paediatric Gastroenterology Unit at Meyer children's Hospital-Florence from December 1995 to November 2015. Data collected included number of ASC/year, age at time of ulcerative colitis (UC) diagnosis and at time of ASC, clinical and laboratory assessment, response to treatments. CyA was used as second line therapy before 2010 whereas IFX was mainly used thereafter. Short and long-term efficacy was expressed in terms of avoiding urgent (first 15 days) or elective colectomy, respectively.

Results: Over the last 20 years, we have seen overall 193 patients with UC and, among them, 43 (22,3%) had at least one episode of ASC. We collected, altogether, 62 ASC episodes, with 29 children having only 1 episode and 14 having more than 1 (10 children 2; 3 children 3; 1 child 4). Children with more than 1 episode were significantly younger at UC diagnosis compared to children with only 1 episode (7,8±5 yr vs. 13,5±2,3 yr, p<0,0001). 25 ASC episodes occurred at UC onset (40%), whereas 37 were disease relapse (60%). During the 20 year-time interval there was a sharp linear increase in UC patients, going from 24 to 168 patients followed the 1st quinquennium and 4th quinquennium respectively (p=0,01). A concomitant increase of ASC from 6 to 21 episodes per quinquennium was observed. ASC prevalence (expressed as number of ASC episodes/number of UC patients) had a significant linear reduction over time, that was solely due to a reduction in ASC relapses (that halved from 0,13 to 0,06 ASC as relapse/UC patients), whereas number of ASC as disease onset remained stable over time. As regards efficacy, 34 episodes (54,8%) responded to CS, whereas 28 (45,2%) needed a second-line medical treatment and received CyA (14, 53,8%) or IFX (13, 42,3%). One patient received Tacrolimus. Response to CS was higher in ASC episodes that occurred at UC diagnosis, (17/25, 68%) when compared to ASC as disease relapse (17/37, 46%), although this difference was at the limit of significance (p=0,08). ASC relapses more frequently required urgent or elective colectomy compared to ASC episodes at diagnosis (11/37, 29,7% vs. 0/25, 0% p<0,05). CyA and IFX did not show significant difference as far as concern efficacy and numbers of urgent and elective colectomy (Cys 7/14, 50% vs. 3/13, 23% p=ns). Colectomy was required less often in responders compared to non-responders to CS (1/34, 3% vs. 11/27, 40,7% p<0,05).

Conclusion: ASC episode among children with UC is a frequent event as it involves almost one quarter of patients. In young UC patients, more than one episode often occurs in agreement to a more severe course of the disease. ASC episodes as disease relapse seem to have declined over time possibly because of a better early management and diagnosis of these patients although they have a worse prognosis and are at risk of colectomy. CyA and IFX showed a similar efficacy as second-line therapy in our cohort and response to CS had the better predictive outcome.

Disclosure of interest: None declared.
Quality of life in pediatric Crohn’s disease: Data from Imagekids study

Victor Manuel Navas López1, Javier Martín-de-Čarpi2, Amy Grant3, Thomas D Walters4, Franck Ruemmele5, David Mack6, Malgorzata Śladek7, Raanan Shamir8, Ron Shaoul9, Shehzad Saeed10, Richard K Russell11, Ruthi Cytter-Kuint12, Anne Griffiths4, Dan Turner12, Anthony Otley3

1Hospital Materno Infantil, Málaga, Spain
2Unit for the Comprehensive Care of Pediatric Inflammatory Bowel Disease, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Barcelona, Spain
3Iwk Health Centre, Halifax, Nova Scotia, Canada
4Hospital for Sick Children, Toronto, Ontario, Canada
5Hôpital Necker-Enfants Malades, Paris, France
6Children’s Hospital of Eastern Ontario, Ottawa, Ontario, Canada
7Jagiellonian University Medical College, Krakow, Poland
8Schneider Children’s Medical Center, Petach Tikvah, Israel
9Rambam Health Care Campus, Haifa, Israel
10Cincinnati Children's Hospital Medical Center, Cincinnati, United States
11Royal Hospital for Children, Glasgow, United Kingdom
12Institute of Pediatric Gastroenterology, Shaare Zedek Medical Center, The Hebrew University of Jerusalem, Israel

Objectives and study: The evaluation of health related quality of life (HRQOL), using the validated disease-specific IMPACT-III questionnaire, has a key role in ascertaining the impact of disease on patients with Crohn’s disease (CD). We sought to describe HRQOL variations across a large prospective cohort of pediatric CD patients with varying disease experience.

Methods: We used the prospectively collected data from the ImageKids study (multicentre, multinational study designed to develop the pMEDIC and PICMI scores for magnetic resonance enterography) on children diagnosed with CD. IMPACT-III (35-item self-administered scale) was used to assess HRQOL in this cohort.

Results: Data from 180 patients were analysed, 94 males (52.2%) with a mean age of 14.2 ± 2.2y and a median of 27 month (IQR 0.05-4.2) of follow-up. According to wPCDAI, 29.0% of patients were in clinical remission, while 39%, 13% and 19% had mild, moderate and severe disease respectively. IMPACT III total score had a poor but significant correlation with degree of mucosal inflammation judged by the SES-CD (r=0.285, p<0.0001). Correlation was strong with clinical activity judged by wPCDAI (r=0.550, p<0.0001). Patients with higher disease activity had lower total IMPACT-III score as did the 4 domains (wellbeing, emotional functioning, social functioning and body image, Table I). Differences across wPCDAI groups were higher for wellbeing and lower for body image domains.

| Table I. IMPACT III total and domain scores (mean (SD)) according to wPCDAI and SES-CD |
|-----------------|---------------|-----------------|-----------------|-----------------|-----------------|
| IMPACT III      | Total         | Well Being      | Emotional        | Social functioni | Body image      |
| Remission       | 77.0 (10.3)   | 80.1 (13.5)     | 64.9 (18.4)      | 85.2 (9.9)       | 71.8 (15.8)     |
| Mild            | 67.5 (12.4)   | 64.8 (17.5)     | 56.5 (20.2)      | 78.9 (13.5)      | 66.7 (17.9)     |
| Moderate        | 63.1 (14.2)   | 56.8 (20.5)     | 54.1 (20.7)      | 75.4 (11.7)      | 64.6 (18.6)     |
| Severe          | 55.0 (17.7)   | 48.3 (22.4)     | 46.0 (21.4)      | 66.8 (18.6)      | 59.2 (17.0)     |
| wPCDAI Remission| 71.6 (13.4)   | 69.7 (21.9)     | 62.5 (16.7)      | 81.7 (9.7)       | 70.6 (13.8)     |
| Mild            | 72.1 (15.3)   | 72.5 (19.0)     | 61.8 (21.7)      | 80.6 (13.4)      | 69.2 (23.2)     |
Patients with perianal disease had lower well being ($p=0.026$) and body image ($p=0.004$) domain scores. Steroid treatment was associated with lower emotional functioning score more than those on enteral nutrition ($p=0.028$).

**Conclusion:** In this ImageKids cohort, HRQOL was lower in patients with higher disease activity and in those with perianal disease. An awareness of which domains within IMPACT may be differentially affected by various therapies or disease characteristics, can help the clinician by focussing interventions (ie psychological) to address these areas of concern.

**Disclosure of interest:** Financial support for research: The ImageKids study is funded by a grant from Abbvie
Mucosal Healing in a cohort of IBD pediatric patients in clinical remission

Francesca Paola Giugliano¹, Caterina Strisciuglio², Massimo Martinelli¹, Marialuisa Andreozzi¹, Sabrina Cenni¹, Annamaria Staiano¹, Erasmo Miele¹

¹Federico II University, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
²Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy

Objectives and study: The Mucosal healing (MH) has now become an important endpoint to assess the therapeutic efficacy in patients affected by Inflammatory Bowel Diseases (IBD). MH is related to a long-term remission and a reduction of disease complications. The aim of our study was to compare histologic findings with endoscopic features and serological markers of inflammation in a cohort of pediatric IBD patients, both Crohn's Disease (CD) and Ulcerative Colitis (UC), whose achèd clinical remission after 1 year of immunosuppressive therapy with Azathioprine (AZA).

Methods: Between December 2012 and July 2015, we prospectively enrolled all IBD pediatric patients in clinical remission, defined as PCDAI/PUCAI ≤ 10, after at least one year of AZA therapy at 2-2.5 mg/Kg/die. Blood and fecal samples were collected in order to evaluate serological markers of inflammation and fecal calprotectin (FC). All enrolled patients underwent colonoscopy. In order to compare serological, endoscopic and histological findings before starting AZA, all data before AZA introduction were also collected. Macroscopic disease activity was assessed by SES-CD and Mayo endoscopic scores for CD and UC, respectively. For microscopic assessment, an average histology score (AHS) was obtained by dividing the sum of individual intestinal segmental scores by the total number of intestinal explored segments. An AHS reduction of at least 50% compared to the time of AZA introduction was considered statistical significant.

Results: Fifty consecutive children, 23 (46%) with CD and 27 (54%) with UC were enrolled in the study. The mean age was 15.5 years (range: 9-17) for CD and 15.4 years (range: 8-17) with a mean disease duration of 5 years for both groups. Endoscopic healing was detected in 14/23 CD patients (60.8%) and in 21/27 UC patients (77.7%) reaching a statistical significant difference compared to the time of AZA introduction (p<0.001 for UC and CD, respectively). Consistently with these findings, for both CD and UC, we found a significant reduction of the inflammation parameters such as erythrocyte sedimentation rate (p<0.001 for both UC and CD, respectively), C-reactive protein (p<0.001 respectively) and FC (p=0.001 and p<0.01 respectively). In CD patients there was also found a significant increase of albumin (p<0.001). Only 6 UC (22%) and 2 CD patients (8.6%) showed mean AHS values reduction of at least 50% compared to baseline (p=0.8 and p=0.5, respectively).

Conclusion: In our population of pediatric IBD, clinical remission after one year of AZA is associated with endoscopic but not with histologic MH. Endoscopic healing is also related to an improvement of serologic markers of inflammation.

Disclosure of interest: None Declared.
Comparison of Efficacy and Safety of Biosimilar Infliximab to Originator Infliximab in Children with Inflammatory Bowel Disease

Corinne Legeret¹, Theodoric Wong¹, Wolfram Haller¹, Susan Protheroe¹, Lisa Whyte¹, Ronald Bremner¹, Rafeeq Muhammed¹

¹Birmingham Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom

Objectives of study: CT-P13 is the biosimilar Infliximab approved for use in Europe and it is marketed in the UK in two brand names, Remsima (NAPP pharmaceuticals) and Inflectra (Hospira pharmaceuticals). European Medicines Authority (EMA) has approved CT-P13 for all the indications of originator Infliximab (Remicade, MSD Immunology). No clinical trials in paediatric inflammatory bowel disease (IBD) of biosimilar Infliximab are completed till date. We have compared the efficacy and safety of biosimilar Infliximab to the originator Infliximab in our clinical practice.

Methods: Clinical and laboratory data of patients receiving Infliximab from January 2015 to date was collected from patient records and electronic case records.

Results: We have used biosimilar Infliximab (Inflectra) for all new starters of Infliximab treatment in our unit since July 2015. Prior to that all patients on treatment with Infliximab were receiving originator Infliximab (Remicade). 24 patients (18 with Crohn’s disease (CD) and 6 with ulcerative colitis (UC)) were started on Inflectra this year. 17 patients (14 patients with Crohn’s disease and 3 with ulcerative colitis) were started on Remicade from January to July this year. A total of 72 Inflectra infusions were administered compared to 96 infusions of Remicade. Median number of infusions per patient was 3 and 6 respectively for Inflectra and Remicade. 1 patient receiving Inflectra had a major infusion reaction needing a switch of treatment to Adalimumab. This was comparable to the incidence of major infusion reaction in patients receiving Remicade (1/17). 5/18 (28%) patients with Crohn’s disease on treatment with Inflectra needed dose or frequency escalation of infusions. Clinical remission was achieved in 5/8 (63%) patients receiving Inflectra treatment. 10/14 (71%) children with Crohn’s disease on treatment with Remicade achieved clinical remission. Dose or frequency escalation was needed in 3/14 (21%) patients on Remicade. Co-immunosuppression was used in 15/18 (83%) patients with Crohn’s disease on Inflectra compared to 12/14 (86%) patients with Crohn’s disease on Remicade. 2/5 (40%) patients with UC achieved clinical remission using Inflectra. 2/3 (67%) patients with UC on Remicade achieved clinical remission. Cost of Inflectra is less than that of Remicade (100 mg vial of Inflectra costs approximately £210 and 100 mg vial of Remicade costs approximately £350). Results are summarised in Table 1.

Table 1: Comparison of patients with IBD on treatment with Remicade and Inflectra

<table>
<thead>
<tr>
<th></th>
<th>Patients on treatment with Remicade</th>
<th>Patients on treatment with Inflectra</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>17 (CD 14, UC 3)</td>
<td>24 (CD 18, UC 6)</td>
</tr>
<tr>
<td>Total number of infusions</td>
<td>96</td>
<td>72</td>
</tr>
<tr>
<td>Number of infusions per patient median (range)</td>
<td>6 (2-8)</td>
<td>3 (1-6)</td>
</tr>
<tr>
<td>Major infusion reaction</td>
<td>1/17 (6%)</td>
<td>1/24 (4%)</td>
</tr>
<tr>
<td>Patients with CD on Azathioprine</td>
<td>12/14 (86%)</td>
<td>15/18 (83%)</td>
</tr>
<tr>
<td></td>
<td>Patients with CD needing dose escalation</td>
<td>Patients with CD in remission</td>
</tr>
<tr>
<td>------------------------------------</td>
<td>----------------------------------------</td>
<td>------------------------------</td>
</tr>
<tr>
<td></td>
<td>3/14 (21%)</td>
<td>5/18 (28%)</td>
</tr>
<tr>
<td>Patients with CD in remission</td>
<td>10/14 (71%)</td>
<td>5/8 (63%)</td>
</tr>
<tr>
<td>Patients with UC in remission</td>
<td>2/3 (67%)</td>
<td>2/5 (40%)</td>
</tr>
<tr>
<td>Drug cost of 6 month's treatment</td>
<td>£3500</td>
<td>£2100</td>
</tr>
</tbody>
</table>

**Conclusion:** In our clinical practice, the efficacy and safety of biosimilar Infliximab (Inflectra) is comparable to the originator Infliximab with significant cost savings offered by the use of biosimilar Infliximab.

**Disclosure of interest:** Dr Rafeeq Muhammed 7th author has conflict with MSD Immunology, Abbvie, Dr Falk, Tillotts Pharma, Nestle, Takeda and Pfizer.
Efficacy of oral Tacrolimus-as a concomitant rescue therapy in children with biologic refractory IBD

Anne-Marie Grima¹, Tracee Reid¹, Dhamayanthi Thangarajah¹, Babu Vadmalayan¹

¹King's College Hospital, Paediatric Liver, Gi and Nutrition Centre, London, United Kingdom

Objectives and study: Tacrolimus is widely used in children after liver transplantation and also in autoimmune liver disease. It is shown to be effective in steroid / biologic refractory IBD in adults but its long-term efficacy is not clear. Evidence of tacrolimus to treat Pediatric IBD is limited. We report our tertiary center experience of tacrolimus treatment in refractory pediatric IBD patients as a rescue therapy with and with out liver disease.

Methods: All patients’ ≤18 years old with histologically proven IBD and on oral tacrolimus between January 2008 and November 2015 were identified from our database. We collected information regarding patient demographics, diagnosis, age of diagnosis, comorbidities, indication for starting tacrolimus (TAC), treatment used prior to tacrolimus, trough levels on initiation of treatment, remission and relapse, faecal calprotectin (FC), C-reactive protein (CRP), disease activity index according to disease (DAI), adverse events, and duration of follow up.

Results:

- Total of 10 children (6-16years of age,) with pancolitis were identified (Ulcerative colitis: 5 (M: 3), Crohn’s disease (2 males (M): 1), Indeterminate colitis (IBDU): 3 (M:2).
- 6 of this cohort had autoimmune liver disease (diagnosed prior to IBD - CD:2, IC:3, UC:3).
- Five children were already on lower dose of tacrolimus for liver disease. Three children had Post liver transplant colitis
- All Patiens were refractory to Standard IBD treatment prior to starting on tacrolimus. (steroid resistant, refractory to azathioprine, methotrexate and had lost response to biologic treatment (infliximab and adalimumab)
- 2 Patient were on tacrolimus and adalimumab together (refractory to infliximab)

All patients responded well to tacrolimus and clinical remission was documented at 1 and 3 month follow up. Mean follow up period was of 43 months (range from 5-70 months). Starting dose was 0.1mg/kg/day and aim to have level between 8-10 ug /L with in 2 weeks of treatment. Mean pooled tacrolimus trough level on remission was 6.57μg/L (range 3.9-12.9μg/L). Patients with concurrent autoimmune liver disease required tacrolimus at lower trough levels to achieve remission compared to patients with only IBD (6.08μg/L:12.9μg/L). Mean faecal calprotectin change on starting tacrolimus was 905.83. (1383.33: 462.5) One patient had reported persistent vomiting and developed hyponatraemia and tacrolimus was stopped. No mortality was recorded. None required surgery.

<table>
<thead>
<tr>
<th>Patient</th>
<th>DAI –pre TAC</th>
<th>DAI –Post TAC</th>
<th>Weight-pre TAC</th>
<th>Weight-Post TAC</th>
<th>FC – Pre TAC</th>
<th>FC-post TAC</th>
<th>CRP-Pre TAC</th>
<th>CRP-Post TAC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>45</td>
<td>20</td>
<td>45</td>
<td>49.2</td>
<td>&gt;4800</td>
<td>568</td>
<td>20.3</td>
<td>&lt;5</td>
</tr>
<tr>
<td>2</td>
<td>65</td>
<td>20</td>
<td>67.2</td>
<td>66.7</td>
<td>1032</td>
<td>6.4</td>
<td>&lt;2</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>70</td>
<td>10</td>
<td>17.24</td>
<td>18.3</td>
<td>3856</td>
<td>1000</td>
<td>5</td>
<td>&lt;2</td>
</tr>
<tr>
<td>4</td>
<td>75</td>
<td>20</td>
<td></td>
<td></td>
<td>134</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>70</td>
<td>30</td>
<td>44.4</td>
<td>44.78</td>
<td>&gt;4800</td>
<td>1432</td>
<td>10.9</td>
<td>&lt;2</td>
</tr>
<tr>
<td>6</td>
<td>30</td>
<td>20</td>
<td>48.6</td>
<td>206</td>
<td>114</td>
<td>23.4</td>
<td>&lt;2</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>55</td>
<td>15</td>
<td>33.2</td>
<td>38</td>
<td>1440</td>
<td>320</td>
<td>10.6</td>
<td>&lt;2</td>
</tr>
<tr>
<td>8</td>
<td>50</td>
<td>15</td>
<td></td>
<td></td>
<td>172</td>
<td>68</td>
<td>11.6</td>
<td>&lt;2</td>
</tr>
</tbody>
</table>
Conclusion: Tacrolimus is safe and effective in inducing and also maintaining remission in Paediatric patients with refractory IBD to biologic therapy. None of our cohort needed surgery and further long-term data is warranted to confirm the efficacy of tacrolimus.

Disclosure of interest:
"None Declared by all authors".
Assessment of disease activity with Magnetic Resonance Enterography in Paediatric Crohn’s Disease

Giovanna Zuin¹, Marta Vecchi¹, Cecilia Mantegazza¹, Francesca Penagini¹, Alice Munari², Giorgio Fava³, Milena Meroni³, Marcello Napolitano²

¹”V. Buzzi” Children’s Hospital, University of Milan, Department of Paediatrics, Milan, Italy
²”V. Buzzi” Children’s Hospital, Department of Radiology, Milan, Italy
³”V. Buzzi” Children’s Hospital, Department of Paediatric Surgery, Milan, Italy

Objectives and study: Magnetic Resonance Enterography (MRE) is considered the imaging test of choice in children affected by Crohn’s Disease (CD) in order to study the small bowel. Few studies have evaluated the role of MRE in assessment of disease activity in paediatric CD. The primary aim of our study was to determine whether MRE can be used to evaluate disease activity in a paediatric population affected by CD, studying the correlation between the activity index obtained by means of MRE and the standardized reference indices commonly used in clinical practice. We also compared MRE and endoscopy in their definition of disease localization.

Methods: We recruited 39 CD paediatric patients who underwent 79 MRE at the time of diagnosis or during follow-up. At the same time of MRE, serum C-reactive protein (CRP), fecal calprotectin and the clinical activity index for paediatric CD (PCDAI) were performed. To evaluate the correlation of these parameters with disease activity on MRE, we applied a Paediatric Magnetic Resonance Index of activity, called P-CDMRI, which includes 11 parameters, for a total score ranging from 0 (remission), to 25 (maximal disease activity). Forty-five MRE performed within two months from a full endoscopic examination were used to evaluate the concordance of disease location and activity as detected by the two methods. The Simplified Endoscopic Score for Crohn’s disease (SES-CD) was used to evaluate endoscopic activity. Spearman correlation coefficients were calculated between P-CDMRI, PCDAI, CRP and fecal calprotectin levels. We also considered the correlations between PCDAI and the two most important RME variables, using the Kruskal Wallis test. Statistical significance was considered for p values ≤0.05. Concordance in disease localization between MRE and endoscopy was evaluated with Cohen k statistics.

Results: The P-CDMRI significantly correlated with the clinical (PCDAI, r = 0.690, p<0.001), laboratory (CRP, r = 0.436 p<0.001; fecal calprotectin, r = 0.390 p=0.008) and endoscopic (SES-CD, r = 0.445 p=0.003) indexes of activity. We observed a good concordance in the localization of the involved gastrointestinal tracts between MRE and endoscopy (K= 0.630 p<0.001). However, some discrepancies were observed, probably due to a better ability of endoscopy in detection of superficial lesions and a more precise evaluation of transmural involvement by MRE.

Conclusion: Our study suggests that P-CDMRI is a good indicator of disease activity in CD paediatric patients, with significant correlations with the most commonly used clinical, laboratory and endoscopic parameters; it may thus be used to evaluate CD activity during response to therapy and during follow-up. However, studies with a larger population of patients should be warranted to confirm these results.

Disclosure of interest: None Declared
Irritable bowel syndrome (IBS) like symptoms in pediatric patients with Crohn’s disease: functional symptoms or organic disease?

Sara Isoldi¹, Paolo Rossi¹, Saverio Mallardo¹, Giulia Biscione¹, Franca Viola¹, Salvatore Oliva¹, Alessandra Lacopo¹, Anna Dilillo¹, Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy

Objectives and study: "IBS-like symptoms" are common in inflammatory bowel disease (IBD) patients in apparent remission and their real significance is still unclear. We aimed at evaluating: 1) prevalence of "IBS-like symptoms" in quiescent pediatric patients with Crohn’s disease (CD); 2) whether the presence and severity of IBS like symptoms correlate with duration and extent of disease; 3) quality of life and anxiety levels in patients with and without IBS like symptoms; 4) whether the presence and the severity of "IBS like symptoms" correlate with occult inflammation assessed by fecal calprotectin levels.

Methods: From January 2014 and February 2015, all patients with quiescent CD admitted to our Unit were consecutive enrolled. Remission was defined as: macroscopic normal mucosa on EGD and colonoscopy, including terminal ileum (SES-CD < 3); C Reactive Protein < 6 mg/L; Erythrocyte Sedimentation Rate < 20 mm/h; white cell count < 11 x 10⁹/L; platelets < 450 x 10¹²/L; no use of corticosteroids over the last 12 months; PCDAI < 10. All underwent abdominal and pelvic MRI: those having MRI features indicative of active CD were excluded. Patients with other coexisting diseases were also excluded. The Rome III criteria for IBS were used to define the IBS-like symptoms. Symptoms severity was evaluated using functional bowel disorder severity index (FBDSI) (Digestive Diseases and Sciences, Vol 40, No. 5 (May 1995), pp. 986-995), quality of life was assessed using Pediatric quality of life inventory (PedsQL) (J Behav Med 2002;25:175-93) and the State trait Anxiety inventory for children (STAIC) (Manual, revised version 2005, year of publication; 1973). Stool samples were collected from all patients enrolled for fecal calprotectin test.

Results: A total of 59 pediatric CD patients fulfilled the remission criteria, so were enrolled in the study. IBS-like symptoms were present in 38 patients (64%), according to Rome III criteria. Presence and severity of IBS like symptoms did not correlate with the duration and extent of disease. PedsQL scores were lower and STAIC scores higher in patients with IBS symptoms, compared to those without IBS-like symptoms. Fecal calprotectin levels were significantly higher in patients with IBS-like symptoms (225.6±34.3) than those who did not have IBS symptoms (45.23±25.1) (p<0.01), however IBS-like symptoms did not correlate with fecal calprotectin levels.

Conclusion: As reported in adults, IBS-like symptoms are not uncommonly reported among pediatric patients with CD in apparent remission, and seem to be independent from duration and extent of disease. In quiescent CD, high levels of fecal calprotectin suggest that in these patients persisting low-grade inflammation may be the underlying mechanism of IBS symptoms.

Disclosure of interest: None Declared.
Fecal Calprotectin and Haematochezia in Colicky Infants.

Angela De Marco¹, Simone Ceratto¹, Maria Garro¹, Silvia Nicoli¹, Francesco Savino²

¹Regina Margherita Children’s Hospital – Città Della Salute e Della Scienza, Turin, Italy
²University of Turin, Pediatria 1 U Chidren Hospital Regina Margherita, Turin, Italy

Objectives and study: Fecal calprotectin is a protein produced by neutrophils and has been recently reported as a marker of bowel inflammation, mainly in adult population. It could be useful in order to distinguish between organic and functional diseases, but studies in infantile colic are still limited. Infantile colic is defined as episodes of incontinable 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. We compared fecal calprotectin values between colicky and non-colicky infants. We also compared the presence of haematochezia between the two groups.

Methods: We enrolled 52 colicky (according to Wessel’s criteria) infants and 41 non-colicky ones. We collected a fecal sample for each enrolled subject and evaluated calprotectin values using the quantitative test BÜHLMANN Quantum Blue® Calprotectin High Range. We also noted which infants in each group showed haematochezia. Comparison between quantitative data was performed with Student’s T-Test or Mann-Whitney U-Test, while the comparison between qualitative data was performed using Fisher Exact Test. Tests were two-tailed and the statistical significance was set at p < 0.05.

Results: Results are reported in the Table. Data concerning subjects’ age are reported in the Table as mean and standard deviation. Data of fecal calprotectin values (μg/g) are reported in the Table as median and interquartile range.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Coliky Infants (n=52)</th>
<th>Non-colicky Infants (n=41)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (days)</td>
<td>43.8±19.1</td>
<td>51.1±18.5</td>
<td>0.067</td>
</tr>
<tr>
<td>Gender (male)</td>
<td>29 (56%)</td>
<td>21 (51%)</td>
<td>0.681</td>
</tr>
<tr>
<td>Delivery (vaginal)</td>
<td>28 (54%)</td>
<td>25 (61%)</td>
<td>0.532</td>
</tr>
<tr>
<td>Calprotectin (μg/g)</td>
<td>782.5 (932)</td>
<td>173 (235)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Haematochezia</td>
<td>11 (21%)</td>
<td>0 (0%)</td>
<td>0.002</td>
</tr>
</tbody>
</table>

Conclusion: According to our data, fecal calprotectin values are significantly higher in colicky infants than in non-colicky ones and haematochezia seems to be significantly more frequent in colicky subjects than in non-colicky ones. These observations suggest a possible inflammatory origin of infantile colic.

Disclosure of interest: Authors declare no conflict of interest.

References
- Savino et al. Fecal Calprotectin During Treatment of Severe Infantile Colic With Lactobacillus reuteri DSM 17938: A Randomized, Double-Blind, Placebo-Controlled Trial. Pediatrics 2015, Volume 135 / Supplement 1
Intestinal permeability is increased in children with history of Irritable Bowel Syndrome

Valentina Giorgio¹, Anna Galimberti¹, Arcangelo Schiattarella², Silvia Persichilli², Consuelo Russo², Valentina Tesori², Cristina Graziani², Franco Scaldaferri², 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: Irritable bowel syndrome (IBS) is a common chronic functional gastrointestinal disorder in pediatrics. We had previously demonstrated a significant prevalence of small intestinal bacterial overgrowth (SIBO) in a cohort of children with IBS, and that a short cycle of therapy with Rifaximin was effective and safe in SIBO treatment and IBS symptoms improvement. We aimed to assess long term symptoms recurrence after Rifaximin treatment and to study gut permeability of our IBS cohort.

Methods: Thirty-two SIBO positive IBS patients who completed treatment with Rifaximin were prospectively enrolled and followed-up by visuo-analogical scale (VAS score) for IBS items (bloating, flatulence and abdominal pain) at 5 years after their first attendance. We also measured urinary lactulose/mannitol ratio (LM ratio) in 16/32 children to study gut permeability. 14 healthy children also performed L/M ratio and constituted the control group.

Results: VAS scores for all IBS items were significantly reduced after 5 years follow up (p<0.05 for all items; abdominal pain VAS score: T0 6.12 +/- 1.02 vs T1 0.87 +/- 1.08; bloating VAS score: T0 5.97 +/- 0.95 vs T1 1.00 +/- 0.90; flatulence VAS score: T0 5.81 +/- 0.84 vs T1 0.96 +/- 0.76). LM ratios were found to be pathological in 15/16 patients and in none of the controls, and were significantly higher in patients than in controls (mean L/M in IBS 0.59 +/- 0.78 vs controls 0.02 +/- 0.01, p= 0.0001).

Conclusion: Rifaximin treatment appears to be related to long-term beneficial effects on IBS symptoms in children diagnosed with SIBO. However, the prevalence of pathological L/M ratio highlights the persistence of altered gut permeability in the studied population. Further studies are needed to clarify the pathophysiological basis of this condition.

Disclosure of interest: No conflict of interest to declare
**GASTROENTEROLOGY: Basic Science**

G-P-001

**Crosstalk between BMP and Notch signaling in intestinal epithelial cell fate decision after massive small bowel resection in a rat**

Dror Berkowitz, Yulia Pollak, Tatiana Dorfman, Nir Bitterman, Jacob Bejar, Igor Sukhotnik

1The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, Dept of Gastroenterology, Bnai Zion Medical Center, Haifa, Israel
2Technion-Israel Institute of Technology, Haifa, Israel
3The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, Laboratory of Intestinal Adaptation and Recovery, Haifa, Israel
4The Bruce Rappaport Faculty of Medicine, Technion-Israel Institute of Technology, Haifa, Israel, Dept of Pathology, Bnai Zion Medical Center, Haifa, Israel
5Technion - Inst. of Technology, Bnai Zion Medical Center, Haifa, Israel

**Objectives and study:** Various signaling cascades have been implicated in the control of intestinal stem cell activity. Bone morphogenetic proteins (BMPs) are a group of growth factors that are implicated in intestinal growth, morphogenesis, differentiation, and homeostasis. The Notch pathway is a master regulator of cell fate decisions and has been shown to stimulate cell differentiation in the normal intestine. The purpose of the present study was to evaluate the crosstalk between BMP and Notch signaling in the late stages of intestinal adaptation in a rat model of short bowel syndrome (SBS).

**Methods:** Male rats were divided into two groups: Sham rats underwent bowel transection and SBS rats underwent a 75% bowel resection. Illumina's Digital Gene Expression (DGE) analysis was used to determine BMP and Notch signaling gene expression profiling. 8 genes related to BMP signaling and five Notch-related gene and protein expression were determined using Real Time PCR, Western blotting and immunohistochemistry.

**Results:** From 8 genes related to BMP signaling, 5 genes were found to be up-regulated in jejunum (BMP1-10%, BMP2-2-fold increase, BMP3-10%, BMP2R-12% and STAT3-28%) and 4 genes to be up-regulated in ileum (BMP1-16%, BMP2-27%, BMP3-10%, and STAT3-20%) in SBS vs sham animals. Six genes (from seven) related to Notch signaling were upregulated in SBS rats. SBS rats also demonstrated a significant increase in BMP2 and STAT3 mRNA and protein levels (determined by Real Time PCR and Western blot) compared to control animals. Four genes related to Notch signaling (from five genes) and Notch protein levels were upregulated in resected rats.

**Conclusion:** Two weeks following massive bowel resection in rats, both BMP and Notch signaling pathways were activated. It appears that cell differentiation rather than proliferation is most important in the late stages of intestinal adaptation.

**Disclosure of interest:** None Declared.
Precocious gastrointestinal maturation can be induced in T-cell deficient athymic (nude) suckling rats

Ester Arevalo Sureda¹, Olena Prykhodko¹, Jian Zhou¹, Björn Weström¹

¹Lund University, Biology, Lund, Sweden

Objectives and study: The gastrointestinal tract (GIT) in neonatal rats is immature, adapted and optimized for digestion of the maternal milk diet. At weaning, the intestine matures, by replacement of the foetal-type epithelium by an adult-type, and the accessory organs adjust to digestion of a solid food diet. GIT maturation can be precociously induced by exposure to a lectin as shown in Sprague-Dawley suckling rats (Linderoth, 2006) and suckling pigs (Rådberg, 2001). Further studies indicated that this might be dependent on T-cells activation and was reduced by blocking with the immunosuppressant, cyclosporine A (Prykhodko, 2010). The aim of this study was to investigate if precocious GIT maturation can be induced in T-cell immunodeficient (nude) neonatal rats after provocation with lectin.

Methods: Suckling 14 days-old T-cell deficient rats (NIH nude) were gavaged a lectin, phytohaemagglutinin A (PHA) from red kidney beans (0.1 mg/ gb.wt, PHA group, n=11) or water (Control group, n=9). After 72 hours, intragastric feeding of a marker cocktail (bovine serum albumin, BSA, and IgG, BigG) 3 hours before they were euthanized and blood was collected was performed for in vivo permeability test. The small intestine was collected for morphological examination after H&E staining. Pancreatic homogenates were analyzed for protein content (Lowry method) and trypsin activity (BAPNA substrate).

Results: Provocation with PHA gavage resulted in increased small intestinal weight (29.8±3.0 mg/gbwt, p<0.001) compared to controls (39.1±5.6 mg/gbwt). Moreover, morphology of the distal small intestine changed with replacement of the immature vacuolated epithelium by the non-vacuolated adult-type. The intestinal barrier function was increased with almost complete cessation of permeability – gut closure – to both macromolecular markers (p<0.0001). The pancreatic function also matured with increased trypsin activity by 3.7 fold in PHA group compared to controls (p<0.001).

Conclusion: Provocation with PHA gavage of neonatal athymic rats resulted in precocious growth and maturation of the small intestine as well as the pancreatic function. Thus, despite our earlier results with partial inhibition of GIT maturation during immune suppression in wild-type rat pups, the results obtained with athymic T-cell deficient rats indicate that the mechanism of gut maturation is independent from thymus-derived T lymphocytes.

Disclosure of interest: None Declared
Information for Minors Participating in Research Projects: Current Practice and Evaluation of a New Format

Sabine Vriezinga1, Ronella Grootens2, Luisa Mearin1, Jos van den Broek2, Martine de Vries1

1Leiden University Medical Center, Pediatrics, Leiden, Netherlands
2Leiden University, Communication and Science, Leiden, Netherlands

Objectives and study: Informing minors participating in medical research is often not focused on their capacity of understanding. New information material in the form of a comic strip was previously developed in collaboration with children, parents, physicians and communication specialists. The aim of this study was to (1) identify pitfalls in current informed consent practice, (2) obtain feedback from end-users about previously developed new information material, and (3) share recommendations for improvement.

Methods: The previously developed new material and the standard material were evaluated by 12 research nurses in 8 Dutch medical centers and by 12 children 8-14 years old and their parents (n=11) participating in a clinical trial.

Results: All nurses expressed that current information is lengthy, complicated and hard to read. Identified pitfalls were timing and a gap in information for children 8-12 years old. All nurses found that the new material was intelligible to children and parents, and were eager to implement it. Children and parents demonstrated good understanding of the new material and were moderately enthusiastic: 12 preferred the new material, 7 preferred the standard, 4 had no preference. All participants recommended shortening and simplifying the material.

Conclusion: Current informed consent practice in minors is insufficient to achieve understanding. A shorter, simplified version, for example in the form of a comic as in our new material, should be implemented in order to improve the informed consent procedure for research with minors.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Coeliac disease

G-P-004

Gluten free diet may improve obstructive sleep apnea related symptoms in children with celiac disease

Anat Yerushalmy-Feler¹, Riva Tauman², Ari Derowe³, Eran Averbuch³, Shlomi Cohen⁴

¹“Dana-Dwek” Children’s Hospital, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Pediatric Gastroenterology Unit, Tel Aviv, Israel
²“Dana-Dwek” Children’s Hospital, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Pediatric Sleep Center, Tel Aviv, Israel
³“Dana-Dwek” Children’s Hospital, Tel Aviv Sourasky Medical Center and the Sackler Faculty of Medicine, Tel Aviv University, Pediatric Ent Unit, Tel Aviv, Israel
⁴“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology Unit, Tel Aviv, Israel

Objectives and study: Mesenteric lymphadenopathy is a potential part of the clinical course of celiac disease with resolution after institution of gluten-free diet. Obstructive sleep apnea (OSA) is a sleep disorder characterized by recurrent episodes of upper airway obstruction. Enlarged tonsils and adenoid are the major etiology for OSA in children. Since lymphatic hyperplasia is a common feature in both disorders, we aimed to investigate the effect of gluten free diet on OSA symptoms in children with celiac disease.

Methods: Children aged 2 to 18 years with celiac disease were prospectively recruited before initiation of gluten free diet. Children with negative celiac serology who underwent gastrointestinal endoscopies for other indications served as controls. All participants completed a validated OSA related symptoms questionnaire (PSQ) at baseline (PSQ1) and 6 months later (PSQ2) (prior to and 6 months after the initiation of gluten free diet for the celiac group).

Results: Thirty-four children with celiac (mean age 6.6±3.5 years) and 24 controls (mean age 7.3±4.6 years, p=0.5) were recruited. No significant differences in gender, body mass index or season at recruitment were found between the two groups. Mean anti-tissue transglutaminase antibodies levels in the celiac group decreased from 275±34 units/ml at baseline to 23±23 units/ml six months after the initiation of gluten free diet. PSQ scores were significantly higher in the control group compared with the celiac group at both baseline and 6 months follow-up (0.26±0.14 vs. 0.17±0.13, respectively, p=0.03 for PSQ1 and 0.2±0.11 vs. 0.07±0.06, respectively, p<0.001 for PSQ2). PSQ scores improved significantly in both groups at 6 months follow-up (p<0.001 for both groups). However, the degree of improvement was significantly higher in the celiac group compared to controls (0.1±0.09 vs.0.06±0.06, respectively, p=0.04).

Conclusion: Children with celiac disease were found to have less OSA related symptoms compared to controls. However, the degree of improvement following initiation of gluten free diet was significantly higher. Our findings suggest that gluten free diet may improve OSA related symptoms in children with celiac disease.
GASTROENTEROLOGY: Coeliac disease

G-P-005

Patients with mild enteropathy have apoptotic injury of enterocytes similar to that in advanced enteropathy in celiac disease: Implications on the treatment

Prasenjit Das1, Gaurav PS Gahlot1, Ritu Mehta1, Archita Makharia2, Anil Kumar Verma3, V Sreenivas4, Siddhartha DattaGupta1, Subrat K Panda1, Vineet Ahuja2, Govind K Makharia2

1All India Institute of Medical Sciences, Pathology, New Delhi, India
2All India Institute of Medical Sciences, Gastroenterology and Human Nutrition, New Delhi, India
3Universita Politechnica Delle Marche, Pediatrics, Ancona, Italy
4All India Institute of Medical Sciences, Biostatistics, New Delhi, India

Objectives and study: Severity of villous atrophy in celiac disease (CeD) is a trade-off between enterocyte loss and cell regeneration. A positive effect of gluten-free diet has recently been shown in patients with mild enteropathy. We explored the apoptotic enterocyte loss-cell regenerative activities in mild enteropathy CeD, versus those with advanced enteropathy and normal duodenal biopsies.

Methods: Duodenal biopsies from patients with positive anti-tissue transglutaminase antibody having mild enteropathy (Marsh grade 0&1)(n=26), advanced enteropathy (Marsh grade ≥2)(n=41) and 12 controls were subjected to immunohistochemical staining for end-apoptotic markers (M30, H2AX); markers of cell death (perforin, annexin V); and cell proliferation (Ki67). Composite H-score based on the intensity and distribution of markers was compared.

Results: End-apoptotic markers (M30 and H2AX) as well as the marker of cell death (perforin) were significantly up-regulated both in biopsies of mild and advanced enteropathies, compared to controls, with no significant difference between the two. Ki67 labeling index, was significantly up-regulated in mild enteropathy as compared to advanced enteropathy.

Conclusion: In patients with mild enteropathy the rate of apoptotic enterocyte loss was similar to that with advanced enteropathy. In mild enteropathy the maintenance of villous height is possibly related to increased crypt regeneration, with the same mechanism failed and resulting in atrophy in the advanced disease. This is the first objective evidence of early immunological insult at mucosal level, raising serious questions on the current practice of not treating patients with mild enteropathy with gluten free diet.

Disclosure of interest: Potential conflict of interests: There is none to declare.
I-FABP as an early marker of coeliac disease in the paediatric risk groups - preliminary study

Anna Rybak¹, Ewa Konopka², Marta Wysocka³, Małgorzata Wajda-Cuszlag³, Ilona Trojanowska², Bozena Cukrowska²

¹The Great Ormond Street Hospital, Neurogastroenterology and Motility Division, London, United Kingdom
²The Children’s Memorial Health Institute, Department of Pathology, Warsaw, Poland
³The Children’s Memorial Health Institute, Department of Diabetology, Warsaw, Poland

Objectives and study: Intestinal fatty acid binding protein (I-FABP) is a significant marker of enterocytes damage in small intestine and it is associated with villi damage in coeliac disease (CD). Aim of this study was to check whether I-FABP can act as an early marker of coeliac disease in paediatric CD risk groups.

Methods: 278 children with type 1 diabetes mellitus (DMT1) were recruited into the study and followed up for 3 years. Out of them, 29 had CD, but only 13 developed CD after at least 1 year observation. For the purposes of this study we included 12 children with DMT1 and CD with a 2 years of follow up, as well as 15 randomly selected children with DMT1 only. Newly diagnosed, tTG positive CD patients, without DMT1, comprised control. In all participants anti-tissue transglutaminase antibodies (IgG and IgA tTG) and deamidated gliadin peptide antibodies (DGP) were assessed, as well as plasma I-FABP was measured using immunoenzymatic assay (I-FABP Human ELISA Kit). Patients with DMT1 and positive coeliac screen were directed for the further diagnostic workup with accordance to the ESPGHAN guidelines. The remaining patients were re-screened and had I-FABP levels in serum repeated after 12 and 24 months months. Fisher’s exact test and Student t test for dependent and independent variables were used in the analysis.

Results: Overall 37 children (20 girls) with mean age of 9 years (11 months-16 years) were included into the study: 15 with DMT1, 12 with DMT1 and newly diagnosed CD and 10 with active CD only. Mean levels of I-FABP in DMT1 patients that developed CD were 857pg/ml before, and 1352 pg/ml after diagnosis of CD was established, however this difference was statistically not significant. In the group of patients with DMT1 only, the mean values of I-FABP levels in 0-1-2 years were 793 pg/ml, 714 pg/ml and 749 pg/ml, respectively. Mean I-FABP level in children with active (newly diagnosed) CD was 1538pg/ml. The mean I-FABP levels in children with DMT1 and CD were higher in comparison to patients with DMT1 only, however the numbers did not reached statistical significance.

Conclusion: In this preliminary study, the serum levels of I-FABP are almost doubled in patients with CD when compared to children with DMT1. An increase of I-FABP in patients with DMT1 who developed CD was observed, however from the baseline levels we could not predict which patients would be more susceptible to developing CD. Further prospective studies, including healthy controls, are needed to confirm the role of I-FABP in CD.

Disclosure of interest: None Declared
Specific antibodies for coeliac disease in patients with Crohn’s disease - preliminary report

Anna Szaflarska-Poplawska¹, Maria Klopocka², Ariel Liebert², Bozena Cukrowska³

¹Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Poland, Department of Pediatric Endoscopy and Gastrointestinal Function Testing, Bydgoszcz, Poland
²Collegium Medicum in Bydgoszcz, Nicolaus Copernicus University in Torun, Chair of Vascular Diseases and Internal Medicine, Bydgoszcz, Poland
³The Children’s Memorial Health Institute, Department of Pathology, Warsaw, Poland

Objectives and study: The previous studies assessing the prevalence of coeliac disease in patients with Crohn’s disease have produced conflicting results. Anti-tissue transglutaminase antibody (anti-TG2) is implemented in the diagnostic scheme of coeliac disease, but it is of limited value for the disease screening in patients with Crohn’s disease. Moreover, there is a lack of information which serum antibodies could be the most specific in this group of patients.

The aim of this study was to evaluate the occurrence of specific antibodies for coeliac disease in a prospective study including consecutive pediatric and adult patients from two tertiary referral units with Crohn’s disease diagnosed according to clinical, radiological, endoscopic and histopathological criteria.

Methods: In all patients anti-TG2 and anti-deaminated gliadin peptides antibodies (anti-DGP) measured by chemiluminescence assay (Thermo Fisher) and antiendomysium antibodies (EMA) measured by indirect immunofluorescence were assessed in both IgA and IgG classes. Anti-TG2 and anti-DGP concentrations > 10 units (AU/mL) and EMA titer > 1:5 were considered as positive.

Results: The study included 71 patients (42 male, 29 female, age range 8-64 years, mean age 26.2 years). Among the studied patients no patient had elevated anti-TG2, anti-DGP and EMA.

Conclusion: Coeliac disease is uncommon among Polish patients with Crohn’s disease to motivate screening for this condition in the regular workup of patients with Crohn’s disease.

Disclosure of interest: None Declared.
Characterizing Combined Esophageal Eosinophilia and Celiac Disease in Children

Anne Ari¹, Sara Morgenstern², Gabriel Chodik³, Manar Matar¹, Ari Silbermintz², Amit Assa¹, Corina Hartman⁴, Yael Mozer-Glassberg¹, Firas Rinawi², Vered Nachmias Friedler², Yoram Rosenbach², Raanan Shamir⁵, Noam Zevit⁵

¹Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition, and Liver Diseases, Petach Tikva, Israel
²Rabin Medical Center, Beilinson Hospital, Institute of Pathology, Affiliated With Sackler Faculty of Medicine, Tel Aviv University, Petach Tikva, Israel
³Sackler Faculty of Medicine; Tel Aviv University, Tel Aviv, Israel
⁴Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Hospital, 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, Petach-Tikva, Israel

Objectives and study: Studies have suggested an association between celiac disease (CD) and esophageal eosinophilia (EsEo) or eosinophilic esophagitis (EoE); however, these findings have been disputed. Patients with combined CD and EsEo (CD+EsEo) have not been adequately characterized. Our objectives were to characterize pediatric patients with CD+EsEo and to describe the incidence of EsEo in patients presenting with suspected CD.

Methods: In this retrospective cohort study, the medical records of children with CD+EsEo or isolated EoE diagnosed between 2000-2014 at Schneider Children’s Medical center of Israel were reviewed and compared to patients with isolated CD or epigastric abdominal pain who underwent upper endoscopy between June 2011 and November 2014. Demographic, clinical, laboratory, histopathology, and historical data were retrieved. EsEo was evaluated, as opposed to EoE, in patients with CD+EsEo because most patients did not undergo a PPI challenge, as required for a formal diagnosis of EoE.

Results: We identified 17 patients with combined CD+EsEo and 46 with isolated EoE. In addition, files of consecutive patients with isolated CD (n=302), or epigastric abdominal pain (n=247) were reviewed. CD+EsEo was diagnosed at an age similar to isolated CD but younger than EoE (5.4±3.7 yrs; 6.5±4.0 yrs; 9.23±5.6 yrs respectively, p<0.05). However, patients with CD+EsEo tended to be males (64.7%) as were EoE children (78%) but not CD (36%) (p<0.05). Personal or family history of atopic disease, eosinophilia and endoscopic findings of white papules in the esophagus were significantly more frequent in the CD+EsEo and EoE patients than in isolated CD (p<0.05). In contrast, anemia, autoimmune conditions and additional cases of CD in the family tended to be more common in the combined and CD group. CD+EsEo patients tended to present with symptoms typical of CD, and only rarely with classic EoE-associated symptoms. The extent of breast feeding did not differ between groups. Neither clinical history, nor laboratory values discriminated isolated CD patients from combined CD+EsEo adequately. EsEo was as frequent in patients with suspected CD (3.53%; 11/311) as it was in patients with epigastric pain (2.81%; 7/249) p=0.81.

Conclusion: Patients with combined CD+EsEo share the classical traits of each of the shared conditions except for presenting symptoms which were typically not characteristic of EoE. This may be due to the very early and usually incidental diagnosis of esophageal eosinophilia in CD patients. It is not known if the natural history of esophageal eosinophilia in isolated EoE is similar to that of CD+EsEo patients, and should be a focus of future longitudinal studies.

Disclosure of interest: None declared.
Raising the cut-off value for anti-tissue transglutaminase antibodies decreased the number of unnecessary biopsies in children with type 1 diabetes

Anouk Velthuis\textsuperscript{1}, Margreet Wessels\textsuperscript{1}, Ellen van Lochem\textsuperscript{2}, Eline Duijndam\textsuperscript{1}, Jos Meijer\textsuperscript{3}, Dick Mul\textsuperscript{4}, Janielle van Alfen-van der Velden\textsuperscript{5}, Petra van Setten\textsuperscript{1}

\textsuperscript{1}Rijnstate Hospital, Pediatrics, Arnhem, Netherlands
\textsuperscript{2}Rijnstate Hospital, Medical Microbiology and Immunology, Arnhem, Netherlands
\textsuperscript{3}Rijnstate Hospital, Pathology, Arnhem, Netherlands
\textsuperscript{4}Diabeter, Rotterdam, Netherlands
\textsuperscript{5}Radboudumc, Pediatrics, Nijmegen, Netherlands

Objectives and study: The aim of our study was to investigate whether the anti-tissue transglutaminase type 2 IgA antibody serum (TG2A) cut-off value for performing a biopsy to investigate celiac disease (CD) in children with type 1 diabetes mellitus (T1DM) can be raised. Reason for this was to overcome unnecessary biopsies, without losing too much sensitivity.

Methods: Children with T1DM who had both elevated TG2A titers during regular screening and duodenal biopsy during the course of their diabetes were included. The optimal TG2A cut-off value was determined using receiver operating characteristics (ROC) curve analysis; and compared with the cut-off value used in the ESPGHAN guidelines in terms of sensitivity, specificity, positive and negative predictive value and odds ratio. TG2A titers were expressed as the ratio between the value obtained and the upper limit of normal (ULN).

Results: A total of 63 children were included. The optimal cut-off value for performing a biopsy proved 11.5xULN. Raising the cut-off value from 3xULN to 11.5xULN changed the sensitivity from 96% to only 87%; increased the specificity from 36% to 73%, the positive predictive value from 88% to 94%, the negative predictive value from 67% to 53% and the odds ratio from 15 to 18. The number of unnecessary biopsies was reduced from 12% to 6%.

Conclusion: Raising the TG2A cut-off value for performing a biopsy in children with T1DM to 11.5xULN reduces the number of unnecessary biopsies. The subsequent slight loss in sensitivity is in our opinion acceptable.

Disclosure of interest: None Declared.
**GASTROENTEROLOGY: Coeliac disease**

**G-P-010**

**An Evaluation of Psychiatric Disorders such as Quality of Life, Anxiety and Depression in Celiac Patients**

Erkan Akkus¹, Aylin Yücel², Meltem Gumus³, Hasan Yaksekkaya²

¹Ne Univercity Meram Medical Faculty, Konya, Turkey
²Ne Univercity Meram Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Konya, Turkey
³Konya Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Konya, Turkey

**Objectives and study:** Celiac disease might affect the social life by creating concern for future and leading to depressive process. These psychological morbidities could be a consequence of dietary restrictions, compromised daily social relationships and concomitant chronic conditions (1). The studies in adult have not shown any relationship between the depression with socioeconomic variables (2). In our study aimed to evaluating the depression, anxiety and quality of life (QOL) in children with celiac disease (CD) and to showing whether there is a relationship between this psychological disorders, the adhering to gluten free diet (GFD) and socioeconomic factors.

**Methods:** 65 patients with CD and 65 healthy volunteers were included in the study. Sociodemographic data form, Trait/State Anxiety Inventory, Depression Scale for Children and Pediatric Quality of Life Inventory was applied.

**Results:** There was no significant difference in terms of depression, state anxiety level and QOL between patients with CD and the healthy control group. But, it was found that state anxiety levels of patients was higher than control group (p=0.023). There was no an effects of the parental educational status and income level on depression in patients with CD. But, we have found that this conditions had adverse effects on trait anxiety and QOL of patients (Table 1). The QOL of patients who have good compliance to diet and intentional noncompliance to diet was better than patients who have unintentional noncompliance (Table 2).

**Table 1:** The effects of the parental educational status and income level on depression, anxiety and QOL (*=p< 0.05). (CDI: children’s depression inventory; PedsQL: Pediatric Quality of Life Inventory, PHSS: Physical Health Summary Score, PsHSS: Psychosocial Health Summary Score, TSS: Total Scale Score)

<table>
<thead>
<tr>
<th>Income Level Detection</th>
<th>PedsQL PHSS</th>
<th>PedsQL PsHSS</th>
<th>PedsQL TSS</th>
<th>State Anxiety</th>
<th>Trait Anxiety</th>
<th>CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bad</td>
<td>76.97</td>
<td>74.63</td>
<td>75.44</td>
<td>33.56</td>
<td>35.30</td>
<td>10.70</td>
</tr>
<tr>
<td>Moderate</td>
<td>77.55</td>
<td>78.83</td>
<td>78.38</td>
<td>30.85</td>
<td>35.26</td>
<td>9.63</td>
</tr>
<tr>
<td>Good</td>
<td>94.20</td>
<td>91.19</td>
<td>92.24</td>
<td>27.00</td>
<td>29.43</td>
<td>5.86</td>
</tr>
<tr>
<td>p</td>
<td>0.008*</td>
<td>0.018*</td>
<td>0.004*</td>
<td>0.021*</td>
<td>0.067</td>
<td>0.073</td>
</tr>
<tr>
<td>Parental Educational Status</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Primary School</td>
<td>78.40</td>
<td>78.01</td>
<td>78.14</td>
<td>31.64</td>
<td>34.50</td>
<td>9.61</td>
</tr>
<tr>
<td>High School</td>
<td>75.62</td>
<td>76.67</td>
<td>76.30</td>
<td>34.20</td>
<td>40.20</td>
<td>12.80</td>
</tr>
<tr>
<td>University</td>
<td>100.00</td>
<td>95.00</td>
<td>96.74</td>
<td>28.00</td>
<td>26.67</td>
<td>5.00</td>
</tr>
<tr>
<td>p</td>
<td>0.037*</td>
<td>0.082</td>
<td>0.040*</td>
<td>0.437</td>
<td>0.020*</td>
<td>0.189</td>
</tr>
</tbody>
</table>

QOL (*=p< 0.05). (CDI: children’s depression inventory; PedsQL: Pediatric Quality of Life Inventory, PHSS: Physical Health Summary Score, PsHSS: Psychosocial Health Summary Score, TSS: Total Scale Score)

<table>
<thead>
<tr>
<th>Compliance Status</th>
<th>PedsQL-PHSS</th>
<th>PedsQL-PsHSS</th>
<th>PedsQL-TSS</th>
<th>State Anxiety</th>
<th>Trait Anxiety</th>
<th>CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good compliance</td>
<td>80.23</td>
<td>80.85</td>
<td>80.64</td>
<td>31.14</td>
<td>33.84</td>
<td>8.40</td>
</tr>
<tr>
<td>Unintentional noncompliance</td>
<td>75.33</td>
<td>70.79</td>
<td>72.37</td>
<td>32.58</td>
<td>35.58</td>
<td>10.58</td>
</tr>
<tr>
<td>Intentional noncompliance</td>
<td>85.94</td>
<td>90.83</td>
<td>89.13</td>
<td>36.00</td>
<td>45.00</td>
<td>26.50</td>
</tr>
</tbody>
</table>
Table 2: The effects of degree of adherence to diet according to results of Morisky scale on depression, anxiety and QOL (3) (*=p< 0.05).

<table>
<thead>
<tr>
<th></th>
<th>PedsQL-PHSS</th>
<th>PedsQL-PsHSS</th>
<th>PedsQL-TSS</th>
<th>State Anxiety</th>
<th>Trait Anxiety</th>
<th>CDI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good compliance</td>
<td>80.23</td>
<td>80.85</td>
<td>80.64</td>
<td>31.14</td>
<td>33.84</td>
<td>8.40</td>
</tr>
<tr>
<td>Unintentional noncompliance</td>
<td>75.33</td>
<td>70.79</td>
<td>72.37</td>
<td>32.58</td>
<td>35.58</td>
<td>10.58</td>
</tr>
<tr>
<td>p</td>
<td>0.213</td>
<td><strong>0.021</strong>*</td>
<td><strong>0.037</strong>*</td>
<td>0.390</td>
<td>0.108</td>
<td>0.023*</td>
</tr>
</tbody>
</table>

**Conclusion:** The results of the present data show that patients of adhering to the GFD have better QOL (3). Undoubtedly that, one of the most important factors affecting QOL in children with CD is adherence to a gluten free. But, it's difficult to buying the gluten-free products because of they are expensive and difficult to attain. Accordingly, it should not be forgotten that the parental educational status and income level had adverse effects on anxiety and QOL of patients. Gluten-free market should be increased. The financial support should be provided to patients with celiac in developing countries to prevent development of anxiety, depression and low QOL.

**Disclosure of interest:** None Declared
**Bone mineral density and vitamin K in children with celiac disease: Is there a link?**

Burcu Volkan¹, Ali Fettah², Ali İşlek³, Soner Sertan Kara⁴, Nezahat Kurt⁵, Atilla Çayır⁶

¹Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
²Erzurum Regional Training and Research Hospital, Department of Pediatrics, Erzurum, Turkey
³Ataturk University School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
⁴Erzurum Regional Training and Research Hospital, Department of Pediatric Infectious Diseases, Erzurum, Turkey
⁵Ataturk University School of Medicine, Department of Biochemistry, Erzurum, Turkey
⁶Erzurum Regional Training and Research Hospital, Department of Pediatric Endocrinology, Erzurum, Turkey

**Objectives and study:** A majority of children with celiac disease (CD) have been shown to have some degrees of impaired bone health. Several studies suggest beneficial role of vitamin K in bone mineral metabolism because of its impact on post-translational carboxylation of bone proteins. The aim of this study is to investigate bone mineral density (BMD) in children with CD and evaluate the association between vitamin K level and osteopenia.

**Methods:** CD patients and age and sex matched healthy subjects were studied. After anthropometric measurements, BMD of lumbar spine was measured in all subjects. CD patients were divided into three groups; newly diagnosed (ND), well adherence to gluten free diet (WFD) and poor adherence to gluten free diet (PFD) according to anti-tissue transglutaminase IgA levels. Serum ferritin, folate, vitamin B12, 25-hydroxy vitamin D, vitamin K₂, calcium, phosphate, magnesium, alkaline phosphatase (ALP), PTH, protein, albumin, iron levels, and iron-binding capacity were measured.

**Results:** Seventy two CD patients (mean age, 11.69±3 years; 59.7% female) and 30 healthy subjects (mean age, 12.27±2.1 years; 63.3% female) were included. Mean body mass index (BMI) Z-scores, serum levels of ferritin, phosphate, magnesium, ALP, PTH, protein, albumin, iron levels, and iron-binding capacity were measured.

<table>
<thead>
<tr>
<th>Group</th>
<th>ND (n=26)</th>
<th>WFD (n=21)</th>
<th>PFD (n=25)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height Z score</td>
<td>-2.34±1.15</td>
<td>-1.34±1.61</td>
<td>-1.49±1.32</td>
<td>0.02</td>
</tr>
<tr>
<td>Weight Z score</td>
<td>-2.55±1.22</td>
<td>1.6±1.57</td>
<td>-1.65±1.41</td>
<td>0.01</td>
</tr>
<tr>
<td>BMI</td>
<td>15.18±1.8</td>
<td>16.6±3.8</td>
<td>17.2±2.6</td>
<td>0.008</td>
</tr>
<tr>
<td>Ferritin*</td>
<td>7 (3-139)</td>
<td>26.2 (11-93)</td>
<td>21.2 (1-96)</td>
<td>0.001</td>
</tr>
<tr>
<td>Folate*</td>
<td>3.5 (1-16)</td>
<td>7.5 (4-13)</td>
<td>5.6 (2-52)</td>
<td>0.01</td>
</tr>
<tr>
<td>Vitamin B12*</td>
<td>254 (156-692)</td>
<td>414 (60-845)</td>
<td>389 (199-804)</td>
<td>0.001</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>17.88±9.19</td>
<td>19.76±10.67</td>
<td>19.86±8.8</td>
<td>0.7</td>
</tr>
<tr>
<td>Vitamin K</td>
<td>2.21±1.57</td>
<td>2.67±2.31</td>
<td>3.07±2.46</td>
<td>0.6</td>
</tr>
<tr>
<td>BMD Z score</td>
<td>-0.93±1.48</td>
<td>-0.96±1.25</td>
<td>-0.77±0.89</td>
<td>0.8</td>
</tr>
</tbody>
</table>

*median (range, minimum-maximum)
Conclusion: Celiac patients had lower BMD than control subjects. Vitamin D and K₉ levels were not different between two groups. Low levels of vitamin D in healthy children in this study can be concluded as a reflection of general population in our country. GFD improves BMD in celiac patients but does not normalize it in all patients even after recovery of intestinal mucosa. Other mechanisms of bone injury than calcium and vitamin D malabsorption are thought to be involved, such as proinflammatory cytokines, parathyroid abnormalities and misbalanced bone remodeling factors. A relationship between increased vitamin K₂ intake and enhanced osteocalcin carboxylation was demonstrated in recent studies in children and osteoporotic adults. So even though that there was no difference in the levels of vitamin K₂ between the two groups in present study, we believe that new studies should be done in celiac patients for evaluate the effect of vitamin K supplementation on the bone mineralization.

Disclosure of interest: None Declared
Pubertal development in children diagnosed with Celiac Disease

Burcu Volkan¹, Nevzat Aykut Bayrak², Belma Haliloğlu³, Soner Sertan Kara⁴, Atilla Çayır⁵

¹Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey
²Diyarbakir Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
³Diyarbakır Children’s Hospital, Department of Pediatric Endocrinology, Diyarbakir, Turkey
⁴Erzurum Regional Training and Research Hospital, Department of Pediatric Infectious Diseases, Erzurum, Turkey
⁵Erzurum Regional Training and Research Hospital, Department of Pediatric Endocrinology, Erzurum, Turkey

Objectives and study: Clinical manifestations of Celiac disease (CD) are primarily related to intestinal malabsorption. Its potential effects on growth and development also interfere reproductive health. Hypogonadism, delayed menarche, amenorrhea, infertility, recurrent abortions and early menopause are known manifestations of CD. Children and adolescents often present with constitutional delay of puberty. Aim of the study is to evaluate the association between pubertal disorders and CD.

Methods: In this multi-center, cross sectional study, age and sex matched CD patients and healthy individuals were studied. Demographic data such as height, weight, stage of puberty, age at menarche, menstrual cycle and diet compliance were obtained by physical examination and patient questionnaires. Blood samples for anti-tissue transglutaminase IgA, pituitary gonadotropins (LH and FSH), gonadal steroid hormones (estradiol and testosterone), prolactin, vitamin levels (ferri tin, folate, vitamin B12, and vitamin D), serum iron and iron-binding capacity (IBC) were assayed.

Results: Age and sex matched 129 celiac patient (mean age: 12.93±2.37 years, 69% female) and 81 non-celiac healthy individuals (mean age: 12.84±2.17 years, 64.2% female) were studied. Mean BMI z-scores were statistically indifferent between groups (-1.02±3 vs -0.39±1.17, p>0.05). Tanner stage was significantly higher in control group (CD vs control, boys and girls respectively: 1.95±1.08 vs 2.76±1.5, p<0.01 and 3.01±1.47 vs 3.6±1.41, p<0.02). The mean age at menarche was significantly younger in healthy individuals (12.2±1.01 vs. 13.1±0.99, OR: 2.46, %95 CI: 1.21-4.96, p<0.01). Menarche was present in girls with CD whose weight, weight z-score or BMI z-score are over 39 kg, -0.88, -0.65 respectively (Sensitivity 89.2%, specificity 81.8%). Menstrual cycle disorders was statistically indifferent among two groups (p>0.05). Estradiol and testosterone levels were similar in girls and boys of both groups, respectively. By multivariate analysis age, FSH, IBC and vitamin D status were found positively related with Tanner stage after adjustment (p<0.05). A correlation was found for Tanner stage and gluten free diet (GFD) compliance (r=0.2, p<0.05).

Conclusion: Delayed puberty has been recognized as one of the extra-intestinal presentations of CD in children which may be the only presenting sign. We demonstrated close association between CD and pubertal disorders. Our data shows that adequate weight gain, compliance to GFD, sufficient iron and vitamin D status are key factors for healthy puberty in CD patients. CD cases should be monitored closely during puberty and poor nutritional status must be corrected more efficiently by early diagnosis and higher compliance to GFD.

Disclosure of interest: None Declared
First Epidemiological Study on Celiac Disease in Children in Colombia. A Study on the Prevalence of Celiac Disease in Children with Type I Diabetes and Controls

Carlos Alberto Velasco-Benitez¹, Angeles Ruiz-Extremera², Miguel Saps³

¹Universidad del Valle, Cali, Colombia
²Universidad de Granada, Granada, Spain
³Nationwide Childrens Hospital, Columbus, United States

Objectives and study: The prevalence of celiac disease (CD) in the general population and patients with type I diabetes (T1D) is 0.5-1% and 2.6-10.4%, respectively. A systematic review and meta-regression analysis on the prevalence of CD in Latin America showed that Colombia has the lowest prevalence of CD and that CD is a rare condition in Colombians. This study did not include Colombian children and no studies have yet been conducted on the prevalence of CD in children in Colombia. We designed the first study on the prevalence of CD in children with and without T1D in Colombia. The objective is to determine the prevalence of CD on children with T1D and healthy controls. The study was conducted at 3 cities in Colombia.

Methods: 115 children (66 girls, 49 boys, mean age 11.0±3.6 years) with T1D from the Hospital Universitario del Valle “Evaristo García”, Cali and 302 healthy controls (172 girls, 130 boys, mean age 12.8±3.1 years from 3 cities in Colombia: La Unión (n=174), San Andrés de Sotavento (n=88) and Cali (n=40) had HbA1c and tissue transglutaminase (TTG)-IgA determination. Children with abnormal TTG/IgA results had HLA DQ2/DQ8 testing. HLA DQ2/DQ8 positive children whose parents consented underwent esophagogastroduodenal endoscopy (EGD).

Results: T1D: 12/115 (10.4%) and 4/302 (1.3%) controls had positive TTG/IgA. T1D: 4/12 children (33%) and 4/4 controls were HLA DQ2/DQ8 positive (100%). Relative Risk: TTG/IgA and HLA DQ2/DQ8 positive comparing T1D and controls = 7.88 (95% CI 2.60-23.93)(P = 0.0003). All children with T1D who had abnormal TTG/IgA and were DQ2/DQ8 positive had EGD with Marsh classification consistent with CD. Duration of T1D in CD children was 4.0±3.7 years. Parents of children in control group that qualified for EGD refused testing even after education on CD and their possible implications were given.

Conclusion: There is a higher prevalence of CD among T1D children in Colombia than controls. The results are consistent with the existing literature. Although all controls who were offered EGD refused testing, even if all controls with abnormal TTG/IgA who were DQ2/DQ8 positive would have been diagnosed with CD, the conclusions would have not changed due to their low number. We speculate that the parents refusal for further testing resulted from the lack of awareness of CD among the general population. There have been no campaigns on CD in Colombia and children and adults are rarely tested. The study underscores the need for screening for CD in all children with T1D in order to promptly recommend a gluten free diet in those diagnosed with CD and the importance of designing public health campaigns to inform the population of Colombia about the possible health consequences of untreated CD.

Disclosure of interest: None Declared
GASTROENTEROLOGY: Coeliac disease

G-P-014

Positive celiac serology at onset of diabetes and spontaneous normalization - Analysis of predictive factors

Claudia Banzato¹, Michela Andreatta¹, Francesca Bissolo¹, Anita Morandi¹, Claudio Maffeis¹

¹University of Verona, Pediatrics, Verona, Italy

Objectives and study: In children with type 1 Diabetes Mellitus, elevated levels of antitissue transglutaminase antibody (anti-TG) may spontaneously normalize despite continued consumption of gluten. We aimed to investigate the prevalence of spontaneous normalization of anti-TG levels and existence of predictive factors for this outcome.

Methods: 273 children had been diagnosed with type 1 diabetes mellitus between 2003 and 2014. All of them were screened for coeliac disease at diabetes onset and at specific intervals. We collected anamnestic and clinic data, as familiarity for autoimmune diseases, age at time of diagnosis of diabetes, period of symptomatology, height and weight at diagnosis and loss of weight during symptomatology. We also collected blood samples to check autoantibody titer of diabetes (anti-ZnT8, anti-GAD, anti-IA2 and anti-IAA antibodies), hemogasanalysis (pH, pCO₂, HCO₃⁻, BE), thyroid functionality (TSH, FT4, anti-TPO and anti-TG antibodies) and glycated hemoglobin.

Results: Of 273 children, 33 (12.1%) had a positive coeliac sierology at time of onset of diabetes: 14 (42.4%) of these developed coeliac disease, the same percentage (42.4%) became negative, 5 had persistent positive serology but not coeliac disease. The prevalence of coeliac disease in this population was about 9.5%. Children with positive coeliac serology at onset of diabetes that will not develop coeliac disease tend to have more loss of weight (until 30% of the entire body mass at onset of diabetes) and greater levels of glycated hemoglobin compared to the rest of the population (119 mmol/mol Hb vs 109 mmol/mol Hb). On the other side, children who will have diagnosis of coeliac disease, develop diabetes at younger age (medium age 6.6 years vs 8.6 years), have high levels of anti-TG at the time of diagnosis of diabetes and tend to have lower levels of anti-IA2 antibodies.

Conclusion: 12.1% of children had positive anti-TG at onset of diabetes. Serum anti-TG decreased spontaneously in 42% of children with type 1 Diabetes Mellitus, despite gluten consumption, in particular in children with higher glycated hemoglobin and higher loss of weight at onset of diabetes. This state of temporary positivity of coeliac serology in children with diabetes could be caused by an extended time of metabolic failure before diagnosis of diabetes, proved by greater loss of weight and higher levels of glycated hemoglobin in this population. According to these findings, the detection of high levels of anti-transglutaminase antibodies could be ascribed to a generalized transient autoimmune storm linked to the bad metabolic balance.

Disclosure of interest: None Declared conflict of interest.
GASTROENTEROLOGY: Coeliac disease

G-P-015

Iodine and autoimmune diseases. Urinary iodine concentration in children affected by coeliac disease or thyroiditis

Claudia Banzato1, Giacomo Tamanini1, Francesca Bissolo1, Paolo Cavarzere1, Franco Antoniazzi1, Gianluca Salvagno2, Rossella Gaudino1

1University of Verona, Pediatrics, Verona, Italy
2University of Verona, Department of Neurological, Biomedical and Movement Sciences, Verona, Italy

Objectives and study: Iodine is an essential micronutrient for thyroid function and its abundance is evaluated through urinary iodine concentration (UIC). Both deficiency and excess in iodine intake can initiate thyroid dysfunction and disease. In particular, autoimmune thyroid diseases seem to relate to an excessive iodine intake. However, any study describing the relationship between iodine intake and other autoimmune diseases is available. The objectives of this study were to investigate the correlation between the presence or absence of autoimmune disease (coeliac disease and thyroiditis) and UIC and to evaluate the iodine status in our population.

Methods: We included 107 children (4-18 years old) divided into 4 groups: 27 children with coeliac disease, 25 with autoimmune thyroiditis, 5 with both diseases, and 50 healthy children. We evaluated children's age at diagnosis, actual age, anthropometric parameters, biochemical parameters (TSH, fT4, Anti-TPO, Anti-Tg and Anti-tTG antibodies), family history of autoimmune diseases and we collected their urinary samples with informed consent. UIC was evaluated through titration after urinary purification. Iodine status was classified as deficitary when UIC was <9.9 μg/dl, adequate when UIC was between 10 and 19.9 μg/dl and more than adequate when UIC was >20 μg/dl.

Results: Mean UIC was 13.6 μg/dl among coeliac children, 13.4 μg/dl among children affected with autoimmune thyroiditis, 13.6 μg/dl among children affected with both diseases and 8.1 μg/dl in control group. A significant difference was observed in terms of UIC between coeliac and healthy children (p<0.01) and between subjects affected with autoimmune thyroiditis and control group (p<0.01). We didn't find a significant difference between UIC in children affected with coeliac disease and those affected with autoimmune thyroiditis. More in general we observed higher UIC values in children affected with autoimmune diseases than in healthy children (13.5 μg/dl vs 8.1 μg/dl, p<0.01). In addition, iodine deficiency was found in a higher percentage of patients from the control group (70%) compared to autoimmune diseases group (42.1%). Iodine deficiency (UIC<9.9 μg/dl) was found in about 56.1% of the children in our population.

Conclusion: This is the first study reporting higher UIC values in young patients affected with coeliac disease compared to healthy subjects and in patients affected with autoimmune diseases in general compared to healthy children. Other studies are useful to clarify the rule of iodine in the pathogenesis of autoimmune diseases.

Disclosure of interest: None Declared conflict of interest.
Severe rhabdomyolysis and celiac disease association

Claudia Mandato¹, Mariano Caldore¹, Marta Lamba¹, Alessandro Rossi², Andrea Apicella², Paolo Siani³, Pietro Vajro⁴

¹Aorn Santobono-Pausilipon, Pediatrics, Naples, Italy
²Second University of Naples, Pediatrics, Naples, Italy
³Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi, Italy

Objectives and study: Rhabdomyolysis is a rare, potentially life-threatening condition, caused by infections, trauma, extreme exertion, drugs, toxins, venoms, hyper/hypothermia, genetic/metabolic, endocrine and electrolyte disorders. The association with Celiac Disease (CD) has been rarely reported, and in these cases muscular damage was imputed to hypokalemia.

We describe a case of severe rhabdomyolysis in a child a with still clinically asymptomatic Celiac Disease, and previous reports.

Methods: Description of a case. A previously clinically well 3 y.o. boy was referred for brown urine, muscular pain/weakness, and no history of muscular trauma. At entry lab tests showed elevated levels of CK (x100vn) and AST (x10vn), ALT (x5vn); electrolytes were within normal range. 24 h after admission serum CPK peaked at 115,000 U/L and transaminases increased (x 30 vn). Hyperhydration treatment was started with renal function monitoring. Urine output decreased little, while serum creatinine and urea nitrogen remained in normal range. Potassium levels decreased down to 2.8 mEq/L at day 3 to day 6, in spite of supplementation. The patient completely recovered at day 16. Main causes of rhabdomyolysis were ruled out by appropriate tests. Because of the reported cases of CD/rhabdomyolysis, anti TGase antibodies were measured and found positive [IgA 34 U/ml]. HLA was DQA1 02 05, DQB1 02 03. Jejunal biopsy showed patchy villous atrophy, and gluten free diet was prescribed.

Review of literature: We reviewed the literature (search engines: PUB MED and GOOGLE SCHOLAR) from 1980 to 2015 by using the key words: Rhabdomyolysis AND celiac disease.

Results: Previous clinical reports on rhabdomyolysis and CD are summarized in Table.

Table

<table>
<thead>
<tr>
<th>Author</th>
<th>Age (y)</th>
<th>Clinical Presentation</th>
<th>CPK (U/L)</th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
<th>Na mEq/L</th>
<th>K mEq/L</th>
<th>Ca mg/dl</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nanji, 1982</td>
<td>75</td>
<td>Weakness</td>
<td>13000</td>
<td>105</td>
<td>na</td>
<td>138</td>
<td>2,1</td>
<td>6,9</td>
</tr>
<tr>
<td>Williams, 1995</td>
<td>60</td>
<td>Weakness</td>
<td>High*</td>
<td>na</td>
<td>na</td>
<td>Low*</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>Ertekin, 2003</td>
<td>12</td>
<td>Fatigue, failure to thrive, chronic diarrhea</td>
<td>6199</td>
<td>321</td>
<td>168</td>
<td>134</td>
<td>1,2</td>
<td>6,7</td>
</tr>
<tr>
<td>Selimoglu, 2004</td>
<td>12</td>
<td>Vomiting, chronic diarrhea, weakness</td>
<td>5598</td>
<td>412</td>
<td>270</td>
<td>na</td>
<td>1,7</td>
<td>na</td>
</tr>
<tr>
<td>Barta, 2005</td>
<td>22</td>
<td>Fatigue, chronic diarrhea, weakness, dermatitis herpetiformis</td>
<td>17000</td>
<td>na</td>
<td>na</td>
<td>2,1</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>Pena-Porta, 2008</td>
<td>38</td>
<td>Weight loss, diarrhea, fatigue, weakness</td>
<td>7489</td>
<td>190</td>
<td>na</td>
<td>146</td>
<td>1,83</td>
<td>7,6</td>
</tr>
<tr>
<td>San, 2012</td>
<td>31</td>
<td>Fatigue, diarrhea, weight loss</td>
<td>55000</td>
<td>850</td>
<td>na</td>
<td>131</td>
<td>1,8</td>
<td>6,2</td>
</tr>
<tr>
<td>Present case</td>
<td>3</td>
<td>Brown urine, muscular pain, weakness</td>
<td>115000</td>
<td>1539</td>
<td>554</td>
<td>131</td>
<td>2,9</td>
<td>8,2</td>
</tr>
</tbody>
</table>
Legend: CPK: creatine phosphokinase, AST: aspartate aminotransferase, ALT: alanine aminotransferase, na: not available, *not specified by authors

**Conclusion:** The 1st case of rhabdomyolysis/CD was reported in 1982; since then, only less than a dozen (mostly adult) cases followed. Our pediatric patient suggests to check CD in children with severe rhabdomyolysis, also in absence of classical GI symptoms. As severe rhabdomyolysis itself may elevate the serum [K], hypokalemia might go unrecognized as the cause of muscular damage, as happened initially in our patient. However, due to the absence of diarrhea and severe mucosal damage, we suggest that pathomechanisms other than hypokalemia might also be involved as well.

**Disclosure of interest:** None Declared.
Prevalence of eosinophilic esophagitis in children with celiac disease

Yasar Dogan1, Derya Altay1, Ugur Deveci1, Halil Kocamaz1, Kaan Demioren1, Ibrahim Hanifi Ozercan2

1Fırat University Faculty of Medicine, Pediatric Gastroenterology, Elazığ, Turkey
2Fırat University Faculty of Medicine, Pathology, Elazığ, Turkey

Objectives and study: The aim of this study was to evaluate the prevalence of eosinophilic esophagitis in children with celiac disease.

Methods: This study included celiac disease patients who attended our clinics from December 2005 to August 2015. We analysed their symptoms, laboratory evaluations, endoscopic and histopathological findings, treatment, and follow-up outcomes. We also retrospectively reviewed their medical files. Those diagnosed with eosinophilic esophagitis were invited for a control visit for clinical and endoscopic examinations.

Results: 183 pediatric patients with celiac disease were included in this study whose esophagus biopsy specimens were adequate for the evaluation. Of these patients, five (2.7%) were also diagnosed with eosinophilic esophagitis. Failure to thrive and short stature were observed in two of these five patients; two patients complained of abdominal pain, abdominal distention and diarrhea; and the remaining patient suffered from vomiting. An endoscopic examination revealed concentric ring formations in one patient, longitudinal linear furrows in two patients, and endoscopic findings in the other two cases were unremarkable. Two children had already undergone repeated endoscopic examinations. The esophageal biopsy of one case showed that previously detected eosinophilia regressed, while eosinophilic findings persisted in the other patient.

Conclusion: The prevalence of eosinophilic esophagitis in celiac disease patients is higher than that seen in the general population. A gluten-free diet therapy per se cannot be advocated as an effective treatment in eosinophilic esophagitis cases. Thus, future multi-location population-based studies are needed to identify the rationale behind the coexistence of eosinophilic esophagitis and celiac disease.

Disclosure of interest: None Declared
GASTROENTEROLOGY: Coeliac disease

G-P-018

Does type 1 diabetes mellitus increase the risk of gastritis in coeliac disease?

Elisabetta Manzali1, Olivier Goulet2, danielle canioni3, Gian Luigi de' Angelis1, Hélène Garnier-Lengliné2

1Aou Maggiore, Parma, Italy
2Hôpital Necker-Enfants Malades, Pediatric Gastroenterology, Hepatology and Nutrition, Paris, France
3Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Anatomopathologie, Paris, France

Objectives and study: Celiac disease (CD) and type 1 diabetes mellitus (T1DM) are autoimmune diseases that develop in genetically predisposed individuals. In T1DM, pancreatic beta-cells producing insulin are the target of autoimmune reaction, whereas in CD it is enterocytes from the proximal part of the small intestine. The prevalence of CD in patients with T1DM is around 8%. Different studies have described an impairment of gastric mucosa in CD. Our aim was to compare histological analysis of gastric biopsies in patients having CD alone or CD associated to T1DM to analyze if T1DM may influence the development of gastric lesions.

Methods: Between 2004 and 2014, in Necker Enfants-Malades Hospital, diagnosis of CD by upper endoscopy (including gastric biopsies) was performed in 76 patients. The first group was composed by 26 patients (9 boys, 17 girls) affected by CD and T1DM. The second group was composed by 50 patients affected only by CD (23 boys, 27 girls). Classification of gastritis was performed according to the update Sydney System and classification of duodenal lesions of CD by Marsh classification.

Results: In the first group, 13 patients (50%) had a family history of autoimmunity. Median age at diagnosis was 6.8 years (range 1 to 16) for T1DM, and 8.7 years for CD (range 2.5 to 17.5). In 14 patients (54%), diagnosis of CD was made after the onset of T1DM, after a mean interval of 2.7 years (range 1 to 6). Gastric biopsies, analysed according to the Update Sydney System, showed abnormal inflammation in 20 patients (77%): lymphocytic gastritis (LG) in 7 patients (27%), interstitial gastritis (IG) in 7 patients (27%), and chronic superficial gastritis (CSG) in 6 patients (23%). LG was found in older patients with a median age of 11.3 years (range 5-17.5 years). Helicobacter pylori was founded in 2 patients. No correlation between Marsh and gastritis was founded. Typical form of CD (abdominal pain, diarrhoea, bloating, failure to thrive) was found in 17 patients (65.4%) and gastritis was founded in 14 of them (82%). In the second cohort, median age at diagnosis of CD was 6.2 years (range 1 to 14), and familial history of autoimmune disease was found in 18 patients (36%). Gastric biopsies showed inflammation in 29 patients (56.8%): LG in 6 patients (13.8%), IG in 14 patients (27.5%) and CSG in 9 patients (15.7%). Symptomatic form of CD was found in 44 patients (88%): typical form in 40 of them and gastritis in 25 patients presenting typical form (62.5%). A significantly higher prevalence of chronic gastritis was found in patients affected by T1DM and CD compared to the group with CD alone (77% versus 56.8%, p< 0.001).

Conclusion: In our study we observed a higher prevalence of gastric inflammatory lesions in patients with T1DM and CD compared to patients affected only by CD. These data suggest that T1DM could play a role in the development of extra-duodenal lesions in CD. It could now be interesting to know if the presence of gastric lesions at diagnosis of CD could be a predictive factor for developing a T1DM later in life.

Disclosure of interest: None Declared
The Relationship between Vitamin D and Quality of Life in Children with Celiac Disease

Eylem Sevinç¹, Fatih Hilmi Çetin², Nergiz Sevinç³, Adem Arık⁴, Feyza Çetin⁵

¹Kayseri Training and Education Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Kayseri, Turkey
²Kayseri Training and Education Hospital, Child Adolescent Psychiatry, Kayseri, Turkey
³Erciyes University Public Health, Kayseri, Turkey
⁴Kayseri Training and Education Hospital, Pediatric, Kayseri, Turkey
⁵Kayseri Training and Education Hospital, Microbiology, Kayseri, Turkey

Objectives and study: Vitamin D deficiency is common in celiac disease (CD). Although some studies have found that quality of life is negatively affected by low levels of vitamin D, it was not investigated in children with CD. The aim of this study was to determine the relationship between vitamin D levels and Pediatric Quality of Life Inventory (PedsQL) scores in children with CD.

Methods: Fifty-two children with classic CD (aged 8-12) were compared to 40 healthy age and sex matched normal children as control. Serum 25-hydroxyvitamin D [25(OH)D] was measured and PedsQL was administered to children with CD and control group.

Results: The mean age of 52 celiac patients (31 female, 59%) and 40 controls (24 female, 60%) were 10.36 ± 0.36 and 10.35 ± 0.46 years respectively. Serum EMA levels were negative in fourteen (26%) of the celiac patients and was positive in thirty-eight of them (74%) while it was negative in all (100%) control patients. PedsQL scores were significantly lower in patients with CD compared with the control group (p <0.05). Vitamin D deficiency (< 20 ng/ml) was detected in 34% of CD (n=17) who had higher serum EMA levels. On the other hand there was not detected vitamin D deficiency in control group. PedsQL scores were significantly lower in celiac patients with low serum levels of [25(OH)D] compared to celiac patients with normal serum levels of [25(OH)D] (p<0.05). There was a positive correlation between serum [25(OH)D] and PedsQL mean scores in celiac group.

Conclusion: Our study demonstrated that low serum levels of vitamin D were associated with lower PedsQL scores in CD. Further studies are needed to explain possible effects of vitamin D in CD.

Key words: Vitamin D, Pediatric Quality of Life, Celiac disease.

Disclosure of interest: None Declared
Psychopathology, Quality of Life, and Associated Factors in children with Celiac Disease

Eylem Sevinç¹, Fatih Hilmi Çetin², Demet Banu Çoşkun³, Feyza Çetin⁴, Nergiz Sevinç⁵, Emre Baratali⁶, Yasemin Torun⁶

¹Kayseri Training and Education Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Kayseri, Turkey
²Kayseri Training and Education Hospital, Child Adolescent Psychiatry, Kayseri, Turkey
³Kayseri Training and Education Hospital, Gastroenterology, Kayseri, Turkey
⁴Kayseri Training and Education Hospital, Microbiology, Kayseri, Turkey
⁵Erciyes University Public Health, Kayseri, Turkey
⁶Kayseri Training and Education Hospital, Pediatrics, Kayseri, Turkey

Objectives and study: In this study, we aimed to survey the children with celiac disease (CD) for psychiatric disorders, determine the possible factors that predict psychopathology, and analyze health-related quality of life and possible factors that could affect the quality of life.

Methods: This study was conducted in Kayseri Education and Research Hospital, Emel-Mehmet Tarman Pediatric Diseases Clinic, Child and Adolescent Psychiatry and Pediatric Gastroenterology Departments between May and August 2015. All children completed Affective Disorders and Schizophrenia for School Age Children- Present and Lifetime Version- Turkish Version (K-SADS-PL-T) which is a semi-structured diagnostic scale, as well as Pediatric Quality of Life Inventory (PedsQL) 8-12 age group form, and sentence completion test. A face-to-face interview was made with the parents of the participants to inform them about the study.

Results: This study included 52 children between the ages of 8-12 years with CD, and age-matched 40 healthy children. The mean age of the study group was 10.36 ± 0.36 years, and 31 (%59) of them were females. The mean age of the control group was 10.35 ± 0.46 years and 24 (%60) of them were females. It was learned that 16 (%30) children obeyed well to gluten-free diet. The mean subscale scores of PedsQL were significantly lower in children with CD compared to the control group (p < 0.05). Among the sociodemographic variables (gender, disease duration, obeying diet, socioeconomic level, presence of a psychiatric diagnosis), only being female affected total physical health score and emotional functioning. There was at least one psychiatric disorder in 26 (50%) children with CD, and 10 (19%) of them had depression, 6 (12%) had anxiety disorder, 5 had (9%) adjustment disorder, 2 (4%) had simultaneous depression and anxiety disorder, and 3 (6%) had simultaneous adjustment and anxiety disorder. The sociodemographic or clinical variables did not affect presence of a psychiatric diagnosis.

Conclusion: This study has shown once more that CD is associated with some psychiatric signs/diagnoses, and it decreased quality of life. Further studies are needed to determine which factors resulted in a decrease in the psychiatric signs. It is apparent that those studies would contribute new approaches to improve diagnosis, treatment, and quality of life.

Key words: Celiac disease, quality of life, child, psychiatric diagnosis

Disclosure of interest: None declared
GASTROENTEROLOGY: Coeliac disease

G-P-021

Internalizing symptoms and parental mental health problems in untreated children with celiac disease

Daphne Margoni1, Giorgos Giannakopoulos1, George Chouliaras1, Magda Liakopoulou1, Ioanna Panayotou1, Christina Kanaka-Gantenbein1, George Chrousos1, Alexandra Papadopoulou2, Eleftheria Roma1

1University of Athens, Greece
2Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece

Objectives and study: Celiac disease (CD) has been frequently linked to an increased prevalence of mental disorders, although it is not clear whether this is due to a biological background or the chronic nature of the disease. As most of the chronic disorders of a pediatric population, it also affects the family of the patients. The aim of this study was to examine possible differences in emotional/behavioral problems and depressive symptoms between paediatric patients with coeliac disease and their parents to healthy controls.

Methods: The study comprised 50 patients with CD at the time of diagnosis and 38 healthy controls. Sociodemographic data were obtained for every participant. Children’s emotional and behavioral problems were evaluated using the Children’s Depression Inventory (CDI) and the Child’s Behavior Checklist (CBCL) questionnaires. In order to assess parental mental health, the Greek version of the Symptom-Checklist-90-Revised (SCL-90) questionnaire was used. Emotional and behavioral problems were compared between the patient and the control group.

Results: Fifty newly diagnosed patients with CD (aged 8.6±3.7 yrs, 64.0% females) and 38 controls (aged 7.7±3.8 yrs, 64.0 % females) were included in the analysis. Age and gender did not differ significantly between the two groups. Parental psychopathology values were significantly higher in CD untreated patients compared to controls (0.72±0.49 vs 0.54±0.58 respectively, p=0.0194, Mann-Whitney test). Child-reported depressive symptoms as well as depression risk classification for children aged above 7 years did not differ significantly between patients and controls (p=0.7 and p=0.3, respectively). In the CBCL for ages 6-18 years, CD children had significantly higher overall (51.6±8.7 vs 46.6±13.1 respectively, p=0.05, Mann-Whitney test) and internalizing symptoms T scores (55.8±9.3 vs 49.3±11.7 respectively, p=0.023, Mann-Whitney test), but significantly lower somatic symptoms score (0.0±0.0 vs 0.14±0.44 respectively, p=0.38, Mann-Whitney test). For the CBCL for ages 1.5-5 years, no statistically significant differences were recorded, probably due to the small number of observations (11 in CD and 10 in controls). In coeliacs, none of the assessed scales scores was related to BMI-zscore or type of symptomatology. In relation to age of symptom start, in patients aged above 5 years, there was a significant negative correlation to somatic symptoms (Spearman’s rho=-0.37, p=0.02), inattention (Spearman’s rho=-0.34, p=0.042), and externalizing symptoms (Spearman’s rho=-0.36, p=0.028) as well as child-reported depressive symptoms (Spearman’s rho=-0.50, p=0.008) for those aged above 7 years. In the age group above 5 years, disease duration at diagnosis was significantly and positively related to somatic symptoms (Spearman’s rho=0.45, p=0.005), and inattention (Spearman’s rho=0.38, p=0.02) as well as child-reported depressive symptoms (Spearman’s rho=0.42, p=0.032) for those aged above 7 years.

Conclusion: Paediatric coeliac disease seems to be associated with children’s internalizing symptoms (i.e. depression and anxiety) and parental mental health problems. Age of symptom onset and disease duration may be important correlates to specific aspects of children’s adjustment.

Disclosure of interest: No conflict to declare
Emotional/behavioral problems and frustration caused by gluten free diet compliance in treated patients with coeliac disease.

Giorgos Giannakopoulos1, Daphne Margoni1, Magda Liakopoulou1, Ioanna Panayotou1, Christina Kanaka-Gantenbein1, Alexandra Papadopoulou2, George Chrousos1, Eleftheria Roma1, George Chouliaras1

1University of Athens, Athens, Greece
2Gastroenterology, Hepatology and Nutrition Unit, First Department of Pediatrics, Athens, Greece

Objectives and study: Coeliac disease (CD), is a chronic disorder known to have an impact on the mental health of patients and their families. The only treatment for CD is a long-life gluten free diet (GFD). In this study we tried to identify possible emotional/behavioral problems and depression symptoms in treated coeliac patients and their parents compared to healthy controls.

Methods: The study comprises 59 coeliac patients on GFD for more than a year and 38 healthy controls. Frustration over complying with a GFD was registered for every patient. Children’s emotional and behavioral problems were evaluated using the Children’s Depression Inventory (CDI) and the Child’s Behavior Checklist (CBCL) questionnaires. In order to assess parental mental health, the Greek version of the Symptom-Checklist-90-Revised (SCL-90) questionnaire was used.

Results: Fifty-nine CD patients on GFD for > 1 year (aged 10.4±3.4 yrs, 65.8% females) and 38 controls (aged 7.7±3.8 yrs, 64.0% females) were included in the analysis. Coeliacs were older than controls (p<0.001, t-test), but gender did not differ significantly between the two groups. All aspects of psychological assessment were comparable between the two groups, with the exception of inattention which was significantly lower in the CD group aged above 5 years (0.0±0.0 vs 0.10±0.41, p=0.046). In details (CD vs controls): parental psychopathology (0.51±0.38 vs 0.54±0.58, p=0.5), internalizing (52.8±8.5 vs 49.3±11.7, p=0.1), externalizing (49.4±8.8 vs 48.4±11.3, p=0.5) and overall symptoms (49.3±8.4 vs 46.6±13.1, p=0.18) for those aged > 5 years, as well as internalizing (48.8±5.4 vs 44.1±23.3, p=0.1) externalizing (52.5±13.1 vs 49.4±19.4, p=0.7) and overall symptoms (47.8±9.0 vs 46.7±21.9, p=0.7) for those aged ≤ 5 years. In the CD group aged > 5 years there was a significant correlation of some psychological parameters to frustration caused by GFD: anxiety/depression symptoms were significantly higher in children showing mild/moderate frustration compared to those showing no frustration (0.42±0.69 vs 0.0±0.0, Kruskal-Wallis test, p=0.007, Mann-Whitney test p=0.002). Internalizing symptoms were, also, significantly higher in children showing mild/moderate frustration compared to those showing no frustration (56.8±8.9 vs 50.9±6.1, Kruskal-Wallis test, p=0.03, Mann-Whitney test p=0.02). Children whom their parents reported severe/extreme frustration had higher social problems compared to those who reported mild/moderate frustration (0.36±0.81 vs 0.0±0.0, Kruskal-Wallis test, p=0.01, Mann-Whitney test p=0.03). In addition, a trend for higher parental psychopathology across parent-reported frustration caused by GFD was observed, (Kruskal-Wallis test, p=0.035). Mild/moderate frustration group had higher scores of parental psychopathology compared to no frustration group (0.59±0.37 vs 0.34±0.24, Mann-Whitney test p=0.05). No correlation was found between GFD-related conflict between parents and children or GFD duration and the assessed psychological parameters.

Conclusion: The mental health of patients with treated CD seems to be comparable to that of healthy controls. Nevertheless, the obligation to follow a strict diet may cause higher internalizing (anxiety and depression) and social problems to some patients and increased psychopathological symptoms to their parents. Patients and their parents with elevated mental health symptoms may face more difficulties in complying with a GFD.
GASTROENTEROLOGY: Coeliac disease

G-P-023

Spectrum of autoimmunity at diagnosis of Celiac Disease

Mario Rocco d’Altilia1, Irene Rutigliano1, Maria Pastore1, Salvatore Cringoli2, Anna Pacilio2, Maria Pia Falcone2, Giuseppina d’Angelo2, Anthea Bottoni2, Luciana Romaniello2, Lazzarina Russo1, Carmela De Meco1, Massimo Pettoello Mantovani2, Michele Carmine Sacco1

1Paediatrics, Irccs “Casa Sollievo Della Sofferenza”, San Giovanni Rotondo, Italy
2Paediatrics, University of Foggia, Italy

Objectives and study: Celiac Disease (CD) is an autoimmune disorder strictly related to other autoimmune conditions. The aim of our study was to evaluate auto-antibodies positivity in CD patients at diagnosis.

Methods: We investigated the presence of: Anti-Smooth Muscle (ASMA), anti nuclear (ANA), anti thyroperoxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibodies in 258 children at diagnosis of CD, biopsy proven. Histological grading of CD was evaluated according to Marsh-Oberhuber classification. Patients were divided in four groups according to age-quartiles. Statistical analysis was performed with IBM SPSS v22.

Results: Mean age at diagnosis of CD in our population was 5±3.7 yrs, median age 5 yrs: 99 males (mean age 5.3±3.8 yrs) and 159 females (4.9±3.7 yrs). Autoimmunity screening revealed in 18/258 pts (6.9%) ASMA positivity, in 5/258 (1.9%) ANA positivity, in 39/258 (15.1%) anti-TPO positivity, 39/258 (15.1%) had anti-TG positivity, whose 33 pts with both anti-thyroid antibodies positivity. One patient had ANA e ASMA positivity (male, age 4.5 yrs), 2 patients ASMA positivity and anti TG positivity. No difference was recorded in autoimmunity distribution according to sex. There was no correlation between poliautoimmunity positivity and Marsh Oberhurer grading. Autoimmune positivity distribution into age-quartiles was statistically significant only for ANA positivity: 4 patients in the third quartile of age had ANA positivity screening (p=0.018).

Conclusion: An increased frequency of autoimmune diseases is well described in CD, but few studies have analysed this immunological phenomena at diagnosis: is autoimmunity positivity only an epiphenomenon at this stage? Follow up studies are needed.

Disclosure of interest: None Declared.
Prevalence of coeliac disease is not increased in hyperkinetic disorder in NE Slovenia

Jernej Dolinsek¹, Sanja Sobocan², Valerija Trojar², Ziva Klarer-Rebec², Dusanka Micetic-Turk², Hojka Gregoric-Kumperscak³

¹University Medical Centre Maribor, Paediatric Gastroenterology Unit, Maribor, Slovenia
²Medical Faculty, Maribor, Slovenia
³University Medical Centre Maribor, Department of Paediatric and Adolescent Psychiatry, Maribor, Slovenia

Objectives and study: Hyperkinetic Disorder or ADHD is one of the most widespread neuropsychiatric disorders in children and adolescents with prevalence of about 1-3%. Several studies in the past have tried to determine the prevalence of coeliac disease (CD) in ADHD in different regions and results varied dramatically (from 1% to as high as 15%). Some authors concluded that ADHD can be considered to be extra-intestinal sign of CD.

The aim of our study was to assess the prevalence of coeliac disease in children and teenagers with the diagnosis of hyperkinetic disorder in NE Slovenia.

Methods: 102 children and teenagers with the diagnosis of hyperkinetic disorder participated in the study (mean age 12.8 years, 84 boys and 18 girls). To establish a diagnosis of CD ESPHGAN diagnostic guidelines were used. The presence of IgA class antibodies against tissue transglutaminase was determined as an initial test. IgA deficiency was excluded in all participants. In 53 participants t-TG IgA antibodies were determined by ELISA test only using commercial kit Eu-TG™ IgA (Eurospital, Trieste, Italy) in 48 participants Biocard test (Ani Biotech, Vantaa, Finland) detecting antibodies against tissue transglutaminase IgA in capillary blood was used as well. Study was approved by Slovene Ethics Committee.

Results: Among 102 tested children and teenagers, we did not find anyone with elevated t-TG antibodies suspected of coeliac disease demanding further diagnostic work-up. One patient whose initial screening tests for coeliac disease indicated IgA deficiency, this deficiency was proven by standard total IgA determination. CD was later excluded by determining IgG antibodies.

Conclusion: Despite some studies in the past showed a higher prevalence of CD in patients with ADHD we were not able to prove this in our study. Harmful effects of gluten are well known in many diseases, however complex multifactorial neuropsychiatric disorders such as ADHD might not be influenced by gluten and patients therefore should not be unnecessarily exposed to a very demanding gluten free diet.

Disclosure of interest: None Declared.
Related factors to quality of life in celiac children

Josefa Barrio Torres¹, Mª Luz Cilleruelo Pascual², Enriqueta Román Riechmann², Luisa Mearín³, Cristina Fernandez⁴
¹Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
²Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
³Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
⁴Hospital Universitario Clínico San Carlos, Epidemiology, Madrid, Spain

Objectives and study: To evaluate related factors to Quality of life (HRQOL) in a group of Spanish coeliac patients aged 8-18 years assessed using both a generic and a specific questionnaire.

Methods: We previously performed a cross-sectional HRQOL study in Spanish coeliac patient on a gluten-free diet and their parents¹. In short, the Madrid Coeliac Association invited the members in the target age-category by e-mail to participate in the study. After an informed consent, 2 questionnaires were sent, one coeliac disease specific (CDDUX) and one generic (kidscreen). In addition we also assessed demographic and clinical variables possibly associated with HRQOL. Linear regression models were fitted to evaluate the association of the independent variables (demographic and clinical) with the dependent variable (scores of HRQOL). Models were built including those variables that obtained a statistical significance on univariate analysis (p <0.05). The project was approved by the Ethics Committee of the H.U. Fuenlabrada.

Results: The linear regression model showed that variables associated with a decrease in HRQOL assessed by CDDUX were the time since diagnosis < 4 years, the not classic clinical form and the economic or social difficulties with the diet. Variables associated with an increase in HRQOL were adherence to diet and age at diagnosis ≤ than 2 years. When assessed by Kidscreen, variables associated with decrease in HRQOL were age at diagnosis ≥ than 12 years, female gender, the economic or social difficulties to follow the diet and having symptoms after diet transgressions.

Table:

<table>
<thead>
<tr>
<th></th>
<th>CDDUX</th>
<th>KIDSCREEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Time since diagnosis &lt; 4</td>
<td>-4.69, 95% CI, -7.91; -1.48;</td>
<td>-1.93; IC 95%; -3. 8 -0.18;</td>
</tr>
<tr>
<td>years</td>
<td>p=0.004</td>
<td>p = 0.031</td>
</tr>
<tr>
<td>Non classic form vs others</td>
<td>- 3.71; 95% CI - 6.44; -0.98;</td>
<td>- 6.38, IC 95%, -10. 3 – 2. 49;</td>
</tr>
<tr>
<td></td>
<td>p = 0.008</td>
<td>p = 0. 002</td>
</tr>
<tr>
<td>Economic or social</td>
<td>- 6.69; 95% CI - 10, 59; -2.78;</td>
<td>- 6.38, IC 95%, -10. 3 – 2. 49;</td>
</tr>
<tr>
<td>difficulties with the diet</td>
<td>p = 0. 001</td>
<td>p = 0. 002</td>
</tr>
<tr>
<td>Adherence to the diet</td>
<td>6.03; 95% CI - 0.62; 12.69; p=</td>
<td>-3.19; 95% CI – 5. 59; - 0, 78; p =0.009</td>
</tr>
<tr>
<td>Symptoms after diet</td>
<td></td>
<td></td>
</tr>
<tr>
<td>transgressions</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis ≤2 years</td>
<td>3. 873; 95% CI 0.87; 6.97; p =0.</td>
<td>-6.27, IC 95% -9.02;-3.51; p&lt;0. 001</td>
</tr>
<tr>
<td></td>
<td>012</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis ≥12 years</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>- 2.87, IC95% - 4.75; - 1.10; p&gt;0.001</td>
<td></td>
</tr>
</tbody>
</table>
**Conclusion:** Social or economic difficulties to keep the gluten-free diet were the main factors related to decreased HRQOL assessed by both generic and specific questionnaire.

- That indicates the need to emphasize in these patients the importance to follow the diet, offering them more support both from health care professionals and from health policy makers.


**Disclosure of interest:** None Declared.
The effect of synbiotic use on the levels of anti-tissue transglutaminase IgA autoantibodies

Kaan Demirören

Yuzuncu Yil University, Pediatric Gastroenterology, VAN, Turkey

Objectives and study: Pre-, pro-, and synbiotics can prevent or alleviate intestinal pathologies influencing microbiota and modulating immune response. Anti-tissue transglutaminase (tTG) IgA autoantibody is a specific marker in diagnosis of celiac disease. To confirm the diagnosis in patients with elevated anti-tTG levels, endoscopic duodenal biopsy must be done. Present study aimed to investigate the effect of synbiotic use on the levels of anti-tTG IgA autoantibodies.

Methods: Patients having high anti-tTG levels, who were performed endoscopic duodenal biopsies but not diagnosed with Celiac disease, included in present study. All children were treated with a daily dose of a synbiotic (NBL Probiotic Gold® cachet, Nobel, Turkey including 2.5×10^9 cfu live bacteria including Enterococcus faecium, Lactobacillus acidophilus, Lactobacillus rhamnosus, Bifidobacterium bifidum, Bifidobacterium longum, and 625 mg fructooligosaccharide, and vitamins A, B1, B2, B6) for 20 days. Anti-tTG levels were re-measured 2-6 months after the end of treatment. The data were presented as the mean ± standard deviation (SD). The statistical analysis was performed using SPSS 12.00 statistical analysis package program (SPSS Inc, Software Chicago, IL, USA). The distributions of pre- and post treatment groups were checked for normality using the Kolmogorov–Smirnov test. Then, the comparisons of pre- and post treatment values were performed using Wilcoxon test, and a P value <0.05 was considered as statistically significant.

Results: Forty one patients were included in the study. Of the patients, the mean age was 6.9 ± 4.3 years (range: 1-15, median: 6 years), 51.2% were female. The mean level of pretreatment anti-tTG level was 55.6 ± 54.8, and post treatment one 27.4 ± 40. The difference was statistically significant (P < 0.001, Z -4.29).

Conclusion: In present study, anti-tTG levels significantly decreased after a synbiotic use. It may be speculated that synbiotic use can alleviate some intestinal pathologies or prevent triggered mechanisms for some diseases like celiac disease.

Disclosure of interest: None Declared.
Celiac disease and Down syndrome mortality: a nationwide case-control study

Jonas F Ludvigsson¹, Benjamin Lebwohl², Peter HR Green², Wendy K Chung³, Karl Mårild⁴

¹Karolinska Institutet, Department Medical Epidemiology and Biostatistics, Stockholm, Sweden
²Columbia University College of Physicians and Surgeons, Celiac Disease Center, Department of Medicine, New York, United States
³Columbia University Medical Center, Division of Molecular Genetics, Department of Pediatrics, New York, United States
⁴Norwegian Institute of Public Health, Division of Epidemiology, Oslo, Norway

Objectives and study: Individuals with Down syndrome (DS) have increased mortality and are also at increased risk of celiac disease (CD). It is unknown if CD influences mortality in DS.

Methods: In this nationwide population-based study, we identified individuals with DS through International Classification of Diseases codes (ICD) registered in the Swedish Patient Register (includes inpatients and hospital-based outpatients), the Medical Birth Register, and the Register of Congenital Malformations. Individuals with CD were identified through small intestinal biopsy report data showing villous atrophy (Marsh stage III) from Sweden’s 28 pathology departments and matched with up to five controls from the general population. Of 29,096 individuals with CD, 201 (0.7%) had DS compared to 124 of the 144,522 controls (0.09%). Data on mortality were obtained from the Swedish Cause of Death Registry. Hazard ratios (HRs) for death were calculated using Cox regression adjusting for age, sex, socioeconomic status, education, calendar year, country of birth, and type 1 diabetes.

Results: During follow-up, there were seven deaths among individuals with DS and CD (7/201, 3.5%) as compared with 14 deaths among DS individuals without CD (14/124, 11.3%). Adjusting for potential confounders, CD did not influence the risk of death in DS (HR=1.36; 95%CI=0.33-5.59). Cardiovascular death occurred in two individuals with CD and three individuals without CD, while death from malignancy occurred in one individual with CD and two individuals without CD.

Table. Causes of death among patients with Down syndrome.

<table>
<thead>
<tr>
<th>Cause</th>
<th>Celiac disease</th>
<th>Not Celiac disease</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total</strong></td>
<td>7</td>
<td>14</td>
</tr>
<tr>
<td>Chronic Leukemia</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Dementia</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Heart disease or atherosclerosis</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Liver cirrhosis</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Down syndrome*</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Neurodevelopmental disorder</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Brain tumor</td>
<td>1</td>
<td></td>
</tr>
</tbody>
</table>
*Diagnostic codes for underlying syndromes are often recorded as the underlying cause of death in the Swedish Cause of Death Register. In Sweden, however, the causes of death in individuals with DS has not been validated.

**Conclusion:** While both DS and CD have been linked to increased risk of death, this study found no excess mortality in DS patients with a concurrent diagnosis of CD. However, the study had limited statistical power.

**Disclosure of interest:** None Declared.
GASTROENTEROLOGY: Coeliac disease

G-P-028

Vitamin D status in cord blood and later risk of celiac disease

Ketil Stordal\(^1\), Lars C. Stene\(^1\), German Tapia\(^1\), Karl Mårild\(^1\)

\(^1\)Norwegian Institute of Public Health, Oslo, Norway

Objectives and study: Insufficient levels of vitamin D (25-OHD) have been associated with higher risk of autoimmune diseases such as multiple sclerosis. Increased risk of celiac disease for children born in spring/summer has been observed in some studies, and environmental factors changing with season such as infections or vitamin D status have been hypothesized to explain this. We aimed to study whether low cord blood levels of 25-hydroxyvitamin D are associated with celiac disease later in childhood.

Methods: In a case-control study nested in the Norwegian mother and child-study (MoBa), participants with celiac disease were identified from parental questionnaires and by linkage to the Norwegian Patient Register. We measured 25-OHD in cord blood from all 399 participants with celiac disease with available cord blood samples and 568 randomly selected controls. Analyses were performed with LC-MS/MS at the State Serum Institute, Copenhagen, Denmark. We analysed with 25-OHD as a continuous or categorical exposure (quartiles) for celiac disease, with unadjusted and adjusted risk estimates as described below. LR-test was used to assess the overall significance.

Results: Mean 25-OHD was 35.2 nmol/L (SD 19.0) for controls and 35.4 (SD 20.7) for those with later celiac disease. Children born during May-November had higher mean levels at birth (33.9-49.4 nmol/L) than those born during December-April (24.5-29.0 nmol/L).

The odds ratio for celiac disease for the lower quartile (<21.3 nmol/L) compared to the upper three quartiles was 1.17 (95% CI 0.88-1.56, \(p=0.29\)). After adjusting for maternal celiac disease, sex, attained age and month of birth the odds ratio for celiac disease in the lower quartile compared to the upper three was 1.35 (95%CI 0.97-1.89, \(p=0.08\)). The Table contains odds ratios for all quartiles.

Daily use of Vitamin D supplements at 6 months (OR 0.88, 95%CI 0.62-1.24) and 18 months (OR 1.14, 95%CI 0.76-1.72) was not independently associated to the later risk of celiac disease. The odds ratio for the cord blood 25-OHD remained non-significantly associated after adjustments for postnatal supplement use (\(p=0.19\)).

Table:

<table>
<thead>
<tr>
<th>Cord blood 25-OHD (nmol/L)</th>
<th>Controls n=568</th>
<th>Celiac disease n=399</th>
<th>Unadjusted OR (95% CI)</th>
<th>Adjusted OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quartile 1: &lt;21.3</td>
<td>142 (25.0)</td>
<td>112 (28.1)</td>
<td>1.05 (0.74-1.49)</td>
<td>1.18 (0.77-1.80)</td>
</tr>
<tr>
<td>Quartile 2: ≥21.3 and &lt;32.0</td>
<td>142 (25.0)</td>
<td>95 (23.8)</td>
<td>0.89 (0.62-1.27)</td>
<td>0.89 (0.59-1.33)</td>
</tr>
<tr>
<td>Quartile 3: ≥32.0 and &lt;46.1</td>
<td>142 (25.0)</td>
<td>85 (21.3)</td>
<td>0.79 (0.55-1.15)</td>
<td>0.76 (0.51-1.14)</td>
</tr>
<tr>
<td>Quartile 4: ≥46.1</td>
<td>142 (25.0)</td>
<td>107 (26.8)</td>
<td>1.00 (ref.)</td>
<td>1.00 (ref.)</td>
</tr>
</tbody>
</table>

Conclusion: In this first preliminary analysis, our data suggest that insufficient levels of vitamin D from birth are not associated with celiac disease later in childhood.

Disclosure of interest: None declared.
The value of a questionnaire based screening in identification of children at high risk for celiac disease

Laura Trandafir, Mihaela Moscalu, Chiriac Madalina Ionela, Alexandra Ana-Maria Tudose, Mihai Danciu

1 Sant Mary Clinical Emergency for Children Hospital, Pediatric Department, Iași, Romania
2 University of Medicine and Pharmacy “grigore T. Popa”, Preventive Medicine and Interdisciplinarity Department, Iasi, Romania
3 Clinical Pediatrics Emergency Hospital Cluj-Napoca, Pediatric Surgery, Cluj Napoca, Romania
4 “mavromati” Clinical Emergency Hospital, Neonatology, Botosani, Romania
5 Sant Spiridon Emergency Country Hospital, Pathology, Iasi, Romania

Objectives and study: Identifying the persons with high risk of celiac disease (CD) is a critical value for the diagnosis which has a high morbidity rate due to a lot of complications. The aim of the present study was to identify the children with a high risk of CD using a questionnaire.

Methods: The study started in November 2012 and included 1839 children between 3 and 18 years old, from Iasi, Romania. We applied the questionnaires contained the “Informed Consent” in 5 kindergartens, 2 primary and middle schools, 2 highschools. The questionnaire contained 15 relevant questions on CD signs and symptoms. The efficacy of this method was calculated to be over 85% for persons with a score higher than 24 points (Toftedal P, 2010). According to the answer, each question received 0 to 4 points. A total score of more than 24 points indicates a person at high risk for CD.

Results: Only 35.88% of the distributed questionnaires were included in the final analysis (891 persons - 48.45%, returned the questionnaire and 660 persons had correctly completed it). 12 children – 1.81%, achieved more than 24 points, presenting increased risk of BC. Clinical manifestations - suggestive for the celiac disease - were found predominantly in women (14% of subjects). Digestive symptoms (70%) were found predominantly in the age group 7-12 years, while extradigestive manifestations (77%) (such as asthenia, headache and arthralgia and behavioral disorders) were predominant in the age group 13-18 years.

The value of screening in identifying children at risk for celiac disease was evaluated based on the sensitivity and specificity of the questionnaire, the results showing a specific sensitivity of 91.24% and Se = Sp = specificity of 78.53%. In the same context, logistic regression results of increased risk of celiac disease indicated a risk of 3.56 (HR = 3.56, 95% CI: 1.81-5.09) in those with a score higher than 24 points. Most children identified to have a high risk for CD are between 15 and 17 years old. These children will be further investigated in order to certify the CD diagnosis.

Conclusion: The prevalence of CD may be higher than we actually know. Therefore, this questionnaire can be useful as a screening test in detecting persons with high risk for CD.

Disclosure of interest: no conflict of interests
Prevalence of increased liver values and their association with the clinical and histological features in children with celiac disease

Linnea Äärelä1, Samuli Nurminen1, Laura Kivelä1, Heini Huhtala2, Markku Mäki1, Katri Kaukinen3, Anna Viitasalo1, Timo Lakka4, Kalle Kurppa1

1University of Tampere and Tampere University Hospital, Centre for Child Health Research, Tampere, Finland
2University of Tampere, School of Health Sciences, Tampere, Finland
3University of Tampere, Finland, School of Medicine, Tampere, Finland
4University of Eastern Finland, Department of Physiology, Institute of Biomedicine, Kuopio, Finland

Objectives and study: Hypertransaminasemia is a well-known finding in celiac disease, but the true prevalence and factors associated with it in the era of modern diagnostic approach are poorly known. We investigated these issues in a well-defined cohort pediatric patients and controls.

Methods: Alanine aminotransferase (ALT) median values and percentages of increased values (>30 U/l) were studied in 150 children with untreated celiac disease and 161 disease controls (gastroesophageal reflux disease n=37, ulcerative colitis n=43, Crohn’s disease n=37, functional symptoms n= 45) and in 500 population-based controls. Furthermore, the association between ALT values and various clinical, laboratory and histological variables at diagnosis and the effect of a gluten-free diet were investigated in celiac disease patients.

Results: ALT was above reference range as follows: celiac disease 14.7%, ulcerative colitis 37.2%, Crohn’s disease 16.7%, reflux disease 16.2%, functional symptoms 8.9%, and controls 3.6%. Factors associated with increased ALT at celiac disease diagnosis were poor growth (P=0.048), weight loss (P=0.032) and presence of total villous atrophy (P=0.010), but not age, sex, body mass index, type or severity of the symptoms, and presence of concomitant associated disease. Furthermore, ALT had significant positive correlation to endomysial (r=0.334, P<0.001) and transglutaminase 2 (r=0.264, P=0.002) antibodies and negative correlation to ferritin (r= -0.225, P=0.03), but not to hemoglobin, alkaline phosphatase, total iron, transferrin receptor, albumin and thyroid hormones. On a gluten-free diet the median ALT decreased significantly (P=0.002); this was observed even in subjects having the value within normal range at diagnosis (P=0.006).

Conclusion: Increased ALT in children with celiac disease is rarer than previously thought. However, even these mostly normal values improved on a GFD, indicating incipient liver damage. Elevated ALT values are associated with more severe disease as regards to serology, histology and poor growth. The results indicate that an early diagnosis and dietary treatment of celiac disease can prevent future liver problems in children.

Disclosure of interest: None Declared
IL-15 gene polymorphism in celiac disease patient and their healthy siblings.

Makbule Eren¹, Yalcin Kara², Serap Arslan², Oguz Cilingir²

¹Eskisehir Osmangazi University, Pediatric Gastroenterology and Hepatology, Eskisehir, Turkey
²Eskisehir Osmangazi University, Eskisehir, Turkey

Objectives and study: Interleukin-15 (IL-15) is a potent proinflammatory cytokine that is considered a key component in the immune reaction triggered by gluten. In light of these findings we hypothesized that variations in the gene encoding IL-15, may influence the risk of celiac disease. The aim of this study was to evaluate the influence of IL-15 gene polymorphisms on celiac disease development, in celiac patients and their siblings.

Methods: The study was enrolled with celiac disease patient, diagnosed at Eskisehir Osmangazi University Faculty of Medicine Department of Pediatric Gastroenterology between August 2007 and July 2015, their healthy siblings and healthy controls. Demographic findings, the presence of celiac disease in their family and HLA types were recorded. Previously defined IL-15 gene polymorphisms rs2857261, rs10519613, rs1057972 were studied through PCR and analyzed.

Results: 90 celiac disease patient (49 female/41 male, median years of age: 11), their 38 healthy siblings (20 female/18 male, median years of age: 8) and 99 healthy controls (66 female/33 male, median years of age: 13) were eligible. There was a significantly higher frequency of GG genotype in rs2857972 polymorphisms and TT genotype in rs1057972 polymorphism in celiac patients compared to control groups [37 (41%) vs. 23 (23%), p=0.008, 19 (21%) vs. 11 (11%), p=0.04 respectively]. Comparing celiac patient and their healthy siblings in term of these polymorphisms revealed no difference [37 (41%) vs. 11 (28%), p=0.2 and 19 (21%), 14 (36%) p=0.1 respectively]. 75 (83%) of celiac disease patient and 23 (61%) of siblings were HLADQ2 positive. Of these, 23 (25%) of patients and 8 (21%) of siblings were homozygous (p=0.09). At homozygous state rs2857972 GG polymorphism was found to be prominent in celiac patients compared to their siblings [7 (30%) vs. 0 (0%), p=0.028]. Whereas this difference was not striking at heterozygous state [22 (42%) vs. 6 (40%), p=0.8, respectively]. Although rs1057972 TT genotype was more prominent in celiac siblings at heterozygote state [10 (19.2%) patient vs. 7 (46.7%) sibling, p 0.04] this difference was not observed in homozygous state [6 (26.1%) patient vs. 4 (50) sibling p=0.2].

Conclusion: IL-15 gene polymorphisms rs2857261, rs1057972 are more prominent in celiac families than healthy controls. However the impact of these polymorphisms on celiac disease development is dependent on HLADQ2 status.

Disclosure of interest: None declared.
Measuring diet compliance in coeliac children and adolescents: is there an easier way than the dietary interview?

Margreet Wessels¹, Marije te Lintelo¹, Rogier te Velde², Hein Putter³, Sabine Vriezinga¹, Erica Hopman⁴, Luisa Mearin¹

¹Leiden University Medical Center, Pediatrics, Leiden, Netherlands
²Leiden University Medical Center, Medical Statistics, Leiden, Netherlands
³Leiden University Medical Center, Statistics, Leiden, Netherlands
⁴Leiden University Medical Center, Dietetics and Nutrition, Leiden, Netherlands

Objectives and study: Compliance to the gluten free diet (GFD) in coeliac disease (CD) is preferably assessed by (time consuming) dietary interviews, together with CD specific antibodies. Short questionnaires for diet compliance have been developed, but as far as we know, they have never been validated in coeliac children.

Aims were to assess 1. The use of a standardized short questionnaire validated for coeliac adults (Biagi F, Br J Nutr 2012), in CD children, adolescents and young adults; 2. The correlation of the diet questionnaires and coeliac specific antibodies in serum in this population.

Methods: In 2013 and 2014, CD children and young adults (diagnosis > 1yr) who had their annual medical checks at the Leiden University Medical Center additionally completed the short questionnaire with a three-level score (1 indicating GFD not followed, 2 GFD with errors, 3 strict GFD). The score was compared with a written version of the dietary interview (hereafter called long questionnaire) with the same three-level score and with the presence of tissue transglutaminase antibodies in serum (TG2A). Where appropriate, Pearson’s Chi-square test for trend and unpaired t-test and one-way ANOVA were used. Cohen’s kappa was used to measure inter-rater agreement for the two questionnaires. A two-tailed probability of p < 0.05 was considered significant.

Results: 151 patients were studied, 66% were female. Mean age was 11.3yr (range 2-26, SD 5.4), mean age at CD diagnosis 4.9yr (range 1-23yr, SD 4.0). By means of the short and long questionnaire, dietary adherence problems were detected in 14% and 52% of the patients respectively. Correlation between the short and long questionnaire was poor (Cohen’s kappa 0.134). Especially errors in the diet were missed with the short questionnaire, with only 1 patient having score 2 when using the short questionnaire, whereas with the long questionnaire 40% of the patients had score 2. When using the short questionnaire, patients who did not strictly adhere to the diet were significantly more TG2A positive than patients who did adhere (p = 0.003). When using the long questionnaire, TG2A positivity was also seen more often in these patients, but the difference was not significant (p = 0.191). Age at CD onset and presence of more CD family members did not influence the compliance with the diet.

Conclusion: The short questionnaire for diet compliance correlates well with CD specific antibodies in coeliac children and adolescents, but should not be used as a substitute for the dietary interview in order to detect relevant errors with the GFD diet.

Disclosure of interest: None Declared.
Implementation of the 2012 ESPGHAN guideline and the diagnostic algorithm of Celiac Disease in children. Results of a retrospective study in the Netherlands.

Marijolijn Landman1, Theuns-valks SDM2, van Wering HM3, Tramper - Stranders GA4, van Ledden M5, Rietveld E6, vd Lely N7, Groeneweg-Doolhoven I8, Escher JC9, Groeneweg M10

1Maasstadhospital, Pediatrics, Rotterdam, Netherlands  
2Albert Schweitzer Ziekenhuis, Dordrecht, Netherlands  
3Amphia Hospital, Breda, Netherlands  
4Sint Francisus Hospital, Rotterdam, Netherlands  
5Van Weel Bethesda Ziekenhuis, Dirksland, Netherlands  
6Ijsselland Hospital, Capelle A/D Ijsse, Netherlands  
7Reinier de Graaf Hospital, Rotterdam, Netherlands  
8Ggz, Rotterdam, Netherlands  
9Erasmus University Hospital, Rotterdam, Netherlands  
10Maasstad Hospital, Rotterdam, Netherlands

Objectives and study: The implementation of the 2012 ESPGHAN guideline and the diagnostic algorithm of celiac disease in children was evaluated retrospectively, aimed at: the reduction of the number of endoscopies needed to diagnose celiac disease, and the use of diagnostic antibody tests and HLA measurement.

Methods: In the South-Western part of the Netherlands, N=253 were tested for suggestive celiac disease, based on symptoms (n=229). Data were collected retrospectively in one University Hospital (Erasmus Medical Center Rotterdam) and 7 General Hospitals from January 1, 2012 until July 1, 2013.

Demographic data: age, gender, first degree family member(s) with CD, presence of associated disorder(s) (not in this abstract), symptoms of CD, measurement of TG2, EMA, total IgA and HLA typing (HLA DQ 2.2, DQ 2.5 and DQ 8), duodenal biopsies and histological grade (MARSH)(2) were documented.

Results: Implementing the ESPGHAN guideline significantly reduces the number of endoscopies needed to diagnose celiac disease by 53 %. Celiac disease was diagnosed in 184 patients (73 %). Adherence to the ESPGHAN guideline was 50 % in children with TG2 > 10 times ULN, 85 % in children with TG2 between 10 and 100 IU/ml, and 60 % in children with TG2 , 10 IU/ml. In the total group of children with symptoms suggestive of CD, EMA was not measured in 35 % (80/229) and HLA was not measured in 22 % (51/229). Positive predictive value (PPV) of EMA and TG2 was calculated. EMA: PPV = 0.84 (sensitivity 0.70; specificity 0.87); TG2 PPV = 1.0 (sensitivity 0.32; specificity 1.0). This is indicates, that TG2 is the best predictor for the diagnosis celiac disease.
Conclusion: The implementation of the 2012 EPSGHAN guideline shows a significant reduction in the number of endoscopies needed to diagnose celiac disease. In a considerable number of patients, EMA measurement and HLA typing has no role in the diagnostic work-up of children with suspected celiac disease. Our results indicate that the 2012 ESPGHAN guideline needs revision based on prospective follow-up data.

Disclosure of interest:
None Declared
Administration of *Bifidobacterium breve* decreases the production of TNF-α and faecal fermentation index in children with coeliac disease

Martina Klemenak¹, Jernej Dolinšek¹, Tomaž Langerholc², Dušanka Mičetić-Turk³

¹University Clinical Center Maribor, Department of Paediatrics, Maribor, Slovenia
²Faculty of Agriculture and Life Sciences, University of Maribor, Department of Microbiology, Biochemistry, Molecular Biology and Biotechnology, Hoce, Slovenia
³Faculty of Medicine, University of Maribor, Maribor, Slovenia

**Objectives and study:** Many coeliac disease (CD) patients have problems with full compliance to gluten-free diet (GFD) and in approximately 40-50 % of them inflammation persists. Several studies suggest that gut microbiota imbalance (an increased number of *Bacteroides* and a reduced number of *Bifidobacterium* species) plays an important role in the pathogenesis of CD. These differences in microbiota are only partially restored after long-term treatment with GFD. *In vitro* studies showed that some strains of bifidobacteria can suppress pro-inflammatory milieu triggered by the large intestinal microbiota of CD patients. Faecal short chain fatty acids (SCFAs), the main end products of fermentation of dietary fibers by anaerobic gut microbiota, can be used as a marker of gut microflora function.

The aim of our study was to investigate the effect of two probiotic strains *Bifidobacterium breve* BR03 and B632 on serum production of pro-inflammatory cytokine tumor necrosis factor alpha (TNF-α), anti-inflammatory cytokine interleukin 10 (IL-10) and on faecal SCFAs pattern (acetic, propionic and n-butyric acid) in children with CD.

**Methods:** The study was a double-blind, placebo-controlled trial that included 49 children with CD (on GFD more than 6 months) randomized into two groups and 18 healthy children in the control group. Children were recruited at a Department of Paediatrics, University Clinical Center Maribor in a period from October 2013 to June 2014. The first group (24 children with CD on GFD) daily received *B. breve* BR03 and B632 (2×10⁹ colony-forming units) and the second group (25 children with CD on GFD) received placebo for 3 months. Faecal samples were analyzed with high performance liquid chromatography. Fermentation index (acetic acid – (propionic acid + n-butyric acid)) / [total SCFAs]) was used to illustrate the inflammatory properties of faecal SCFAs. A solid-phase enzyme-labeled chemiluminescent immunometric assay was used for TNF-α and IL-10 measurement. Data are presented as median [minimum- maximum]. The protocol was approved by the National Medical Ethics committee, Republic of Slovenia.

**Results:** Children with CD on GFD had significantly (p = 0.039) higher levels of propionic acid (8.91 [0.00- 35.12]) at baseline compared to healthy children (5.17 [0.00- 16.53]). Faecal fermentation index (0.32 [0.01- 1.00]) was significantly (p = 0.013) decreased in the first group after receiving probiotics for three months (0.21 [0.09- 0.44]). TNF-α levels (11.9 [6.8- 33.8]) were significantly (p = 0.020) decreased in the first group after receiving probiotics for three months (11.0 [7.4- 21.1]). IL-10 levels were below detection level in all groups of patients during the study.

**Conclusion:** Administration of *B. breve* strains has shown a positive effect on decreasing the production of pro-inflammatory cytokine TNF-α and faecal fermentation index in children with CD on GFD.

**Disclosure of interest:** None Declared.
The evaluation of muscle power in children patients with celiac disease and the effects of gluten free diet and exercise program on to muscle power

Havva Turac Cingöz 1, Meltem Gumus2, Aylin Yücel3, Ali Salli1, Hasan Ali Yüksekkaya3

1Ne University Meram Medical Faculty, Physical Medicine and Rehabilitation, Konya, Turkey
2Konya Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Konya, Turkey
3Ne University Meram Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Konya, Turkey

Objectives and study: We aimed to compare the muscle strength of the children with Celiac Disease and healthy children which are balanced with age and gender and to evaluate the efficacy of diet and exercise therapies in patients with Celiac Disease.

Methods: This study was designed as a randomized, controlled, prospective trial. We included 34 Celiac patients that diagnosed by Pediatric Gastroenterology Clinic and 17 healthy kids which are balanced with age and gender of Celiac patients. The study has been carried out in two stages. In the first stage 34 Celiac Patients (CP) has been compared with weight, height, weight-height weight Standard Deviation Score (SDS), upper extremity, hand grasp, knee extensor and flexor muscle group’s peak torque measurements. Hand grasp power evaluates the upper extremity power globally and can be measured with a dynamometer. We measured the hand grasp power with a dynamometer. Knee muscle power was evaluated with an isokinetic exercise system device in 60°/sec, 120°/sec and 180°/sec angular velocity which is more sensitive and objective to evaluate the muscle power. In the second stage of the study Celiac Patients were divided into two groups randomly. Both of the group’s gluten free diet programs have been arranged by Pediatric Gastroenterology and Feeding Expert. Patient’s diet persistency has been evaluated with tissue transglutaminase and EMA levels of blood serum at the 6th month of the therapy. One of the groups; under the supervision of a medical doctor, isokinetic bicycle exercise program has been applied for 30 minute a day, 3 days in a week during 8 weeks. Celiac Patient groups dominant hand grasping power, bilateral knee extensor and flexor muscle group peak torque measures have been compared in 0th, 24th and 36th weeks.

Results: Celiac Patients and healthy kids had compared with height, weight, height-weight SDS and Celiac Patients parameters were significantly lower than the healthy group (p<0.05). Diet and exercise subgroups of Celiac Patients group had compared and the increment of muscle power has been observed in both groups by the time but the increase of power were more prominent in the exercise subgroup (p<0.001 and p<0.05).

Conclusion: In this study muscle power deficiency has been determined in Celiac Patient kids when compared with healthy control kids. Muscle power increment has been observed in both diet and exercise subgroups of Celiac Patients but this increment was prominent in exercise subgroup. Exercise therapy as a necessity for life quality must be added in to treatment plan of children with Celiac Disease regardless to their muscle power improvement.

Disclosure of interest: None Declared
Vitamin-D receptor gene polymorphism in celiac disease

Esra Araç¹, Meltem Gumus², Aylin Yücel³, Selman Yıldırım⁴, Hasan Ali Yüksekkaya³

¹Aksaray Hospital, Pediatrics, Aksaray, Turkey
²Konya Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Konya, Turkey
³Ne Univercity Meram Medical Faculty, Pediatric Gastroenterology, Hepatology and Nutrition, Konya, Turkey
⁴Ne Univercity Medical Faculty, Genetics, Konya, Turkey

Objectives and study: Vitamin-D receptor (VDR) is suggested to be associated with gene alleles, cardiovascular diseases, obesity, Alzheimer’s, diabetes mellitus, many types of cancers, Hashimoto’s thyroiditis and other autoimmune disorders. The pathogenesis of celiac disease still remains unknown, and the role of genetics can only be described as genetic predisposition. Out of HLA alleles, genetic investigations should be performed.

Methods: Followed up due to celiac disease, 105 children and 100 healthy controls were included into the study. Bsm-I and Fok-I genotypes in both groups, and vitamin-D levels, bone-mineral density, Z scores, stages of celiac disease and association of Bsm-1/Fok-1 and alleles in patients’ group were analyzed in cases to be measured during the diagnosis.

- **Results:** Features related to age and gender in patients and controls were similar.
  - In patient and control groups, distributions of Bsm-I and Fok-I genotypes were found to be similar (p=0.43 p=0.97, respectively).
  - Mean Z score of bone mineral density in patients during diagnosis was -1.5±0.88 SD, and in 61% of patients, the rate was at osteopenic ve osteoporotic levels.
  - Mean vitamin D level was 19.5±12.4 ng/ml and found to be significantly lower in 24% of patients (<10ng/dl).
  - Between those with normal and low levels of vitamin D, Bsm-I/Fok-I alleles showed a similar distribution (p>0.05).
  - In cases with and without osteopenia (accordig to Z score), Bsm-I/Fok-I alleles showed a similar distribution (p>0.05).
  - Additionally, between patients at stages 3 and 4 of celiac disease, no difference was observed as to Bsm-I/Fok-I alleles (p>0.05).

- **Conclusion:** In children with celiac disease, genotypical distribution of vitamin-D receptor genes (Bsm-I/Fok-I) were found to be similar to those in healthy children.
  - Vitamin-D receptor genes seems to have no role in the development of celiac disease.
  - Additionally, between vitamin-D gene alleles, and stages of celiac disease, severity of osteoporosis and vitamin-D levels, no direct association was observed.

Disclosure of interest:
“None Declared.”
Examination of the Presence of Dental Enamel Defects and Oral Manifestation in Children with Celiac Disease

Damla Aksit¹, Nafiye Urganci², Serap Akyuz¹, Merve Usta², Nuray Uslu Kızılkın³, Burcin Alev⁴, Aysen Yarat⁴

¹Marmara University, Faculty of Dentistry, Department of Pediatric Dentistry, Istanbul, Turkey
²Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
³Koc University, Faculty of Medicine, Pediatric Gastroenterology, Istanbul, Turkey
⁴Marmara University, Basic Medical Sciences, Department of Biochemistry, Istanbul, Turkey

Objectives and study: The presence of dental enamel defects, recurrent aphthous stomatitis, xerostomia and caries among children with celiac disease and compare the results obtained with those of none diagnosed as celiac disease.

Methods: Thirty children with celiac disease aged between 6-16 and 30 children with gastrointestinal complaints but not proven as celiac disease with the same age and sex were included in the study. In oral examination; dental enamel defects were recorded according to Aine’s scale. Demographic data and oral findings were recorded. Saliva samples were collected from children to measure salivary flow rate, buffer capacity and pH values. In statistical analysis, Graph Pad programme was used, t test and chi square test were applied.

Results: Dental enamel defects were observed 66.7% of children with celiac disease while none of the subjects in the non-celiac children had dental enamel defects. According to the Aine’s scale 46.7% of patients had Grade I and 20% had grade II dental enamel defects. Dental enamel defects were observed in incisors 56.7% among celiac children and also salivary flow rate, sugar intake, recurrent aphthous stomatitis and DMFT numbers were found lower, salivary pH and delayed eruption were found higher than non-celiac children.

Conclusion: No association was found between recurrent aphthous stomatitis and celiac disease. The higher prevalence of specific dental enamel defects mainly in incisors and delayed eruption in celiac children shows that the diagnosis of these oral manifestations might be helpful for diagnosis of celiac disease.

Disclosure of interest: None Declared.
HLA Genotypes in Czech Children with Coeliac Disease

Milena Vrana¹, Peter Szitanyi², Eva Ratajova¹

¹Institute of Hematology and Blood Transfusion, Hla Department, Prague, Czech Republic
²First Faculty of Medicine and General Teaching Hospital, Charles University, Department of Paediatrics and Adolescent, Prague, Czech Republic

Objectives and study: Since 2012 due to ESPGHAN guidelines there is a possibility to implement new diagnostic non-biopsy approach in the diagnosis of Celiac disease (CD). HLA genotyping is an integral part of this approach. The correct and exact identification of the predisposing HLA genotypes is essential for its successful implementation. Our goal is to identify clearly all predisposing HLA genotypes in Czech CD patients.

Methods: Genotype of loci HLA-DQA1 and DQB1 on high/medium resolution level was analyzed in the cohort of patients with confirmed CD. The results were divided into three groups regarding to the CD predisposition: “confirmed predisposing genotypes” (DQA1*05+DQB1*02 or DQA1*03+DQB1*03:02), “rarely reported predisposing genotype” (DQA1*02+DQB1*02) and “genotypes without a predisposition to CD” (any other).

Results: The cohort consisted of 46 Czech pediatric patients from the Department of Paediatrics and Adolescent with confirmed diagnosis of CD (29 biopsy and 17 non-biopsy approach). 43 patients (93.5 %) carried at least one of “confirmed predisposing genotypes”. DQA1*05+DQB1*02 was present solely in 36 of them (78 %), DQA1*03+DQB1*03:02 solely was present only in two patients (4 %), combination of both genotypes was found in five patients (11 %). None patient of this cohort carried genotype without a predisposition to CD. Three CD patients (two biopsy and one non-biopsy diagnosed) carried only “rarely reported predisposing genotype” DQA1*02+DQB1*02 without any other predisposing allele. This represents 6.5 % of the tested cohort.

Conclusion: “Rarely reported predisposing genotype” (DQA1*02+DQB1*02) without any other predisposing allele is present in Czech pediatric CD patients. It seems to be even more frequent than one of the “confirmed predisposing genotypes” DQA1*03+DQB1*03:02. DQA1*02+DQB1*02 genotype is not mentioned in the guidelines (ESPGHAN Guidelines for the Diagnosis of Coeliac Disease; J Pediatr Gastroenterol Nutr. 2012 Jan; 54 (1):136-160). Nevertheless our results are in correlation with some reported studies (e.g. Mubarak at al.: Human leukocyte antigen DQ2.2 and celiac disease; J Pediatr Gastroenterol Nutr. 2013 Apr; 56(4):428-30). Due to these results we propose that the genotype DQA1*02+DQB1*02 should be considered as a predisposing HLA genotype to coeliac disease.

Disclosure of interest: None Declared.
Prevalence of Helicobacter pylori infection in pediatric patients with celiac disease

Zeynep Civelek¹, Nafiye Urganci², Merve Usta², Banu Ozguven³

¹Sisli Hamidiye Etfal Training and Research Hospital, Pediatrics, Istanbul, Turkey
²Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
³Sisli Hamidiye Etfal Training and Research Hospital, Pathology, Istanbul, Turkey

Objectives and study: The aim of the study was to determine the prevalence of H.pylori infection in children with celiac disease (CD).

Methods: Two hundred and two patients with CD aged from 6 months to 17 years (mean 7.12±4.64), and 209 age- and sex-matched children without CD were screened for H.pylori infection.

Results: Significant difference was observed in endoscopic appearance between patients with CD and the controls both in the antrum and the corpus (P<0.001). The patients with CD had more superficial gastritis than the control group. Panmucosal gastritis was more frequent in H.pylori-positive patients with CD than H.pylori-negative ones. Significant difference was obtained in terms of lymphoid aggregates between H.pylori-positive and H.pylori-negative patients with CD (P<0.001).

Conclusion: No significant difference was observed in prevalence of H.pylori infection between pediatric patients with CD and without CD.

Disclosure of interest: None Declared.
Prevalence of Asthma and Allergic Rhinitis in Children with Celiac Disease

Sebnem Ozdogan¹, Nafiye Urganci², Merve Usta², Nuray Uslu Kızılkan³

¹Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Thoracic Medicine, Istanbul, Turkey
²Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
³Koc University, Faculty of Medicine, Pediatric Gastroenterology, Istanbul, Turkey

Objectives and study: Celiac disease is an autoimmune disease characterized by damage to the small intestinal mucosa following the intake of gluten-containing foods in genetically predisposed individuals. Studies suggest that celiac disease is associated with asthma and allergic rhinitis. The aim of this study was to examine the prevalence of asthma and allergic rhinitis in children with celiac disease and compared to those healthy controls.

Methods: This study was conducted on 53 Celiac children and 80 healthy controls aged 6-19 years. Subjects completed the ISAAC questionnaire, and a pulmonary function test (spirometry) was performed on each subject.

Results: The prevalence of asthma symptoms and physician-diagnosed asthma were similar in both patients with celiac disease and healthy controls (30% and 19% in celiac group and 17.5% and 22.5% in control group) (p>0.05). Six (11%) patients with celiac disease and seven (9%) patients in control group showed obstructive changes on the pulmonary function test. The prevalence of allergic rhinitis symptoms and physician-diagnosed allergic rhinitis were similar in both celiac group and healthy controls (36% and 9% in celiac group and 34% and 9% in control group) (p>0.05).

Conclusion: The prevalence rates of asthma and allergic rhinitis in patients with celiac disease were not significantly higher when compared to healthy controls.

Disclosure of interest: None Declared.
Infrequent out-patient visits have deleterious effects on growth and nutritional status of children with Coeliac disease.

Nevzat Aykut Bayrak¹, Burcu Volkan², Serhat Samanci¹

¹Diyarbakir Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Diyarbakir, Turkey
²Erzurum Regional Training and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Erzurum, Turkey

Objectives and study: In children with Coeliac disease (CD), routine outpatient visits are important to monitor growth and development, compliance to gluten-free diet (GFD) and micronutrients deficiencies, as well as preventing complications and dietary counselling. It has been reported that CD patients who are lost to follow-up have serious problems in adherence to GFD. Aim of this study is to compare children with CD according to their regularity on attending outpatient visits, in means of growth, micronutrients status and adherence to GFD as well as determining risk factors for poor attendance.

Methods: In this multicenter, cross sectional study, biopsy proven CD patients under GFD at least for 1 year were recruited. Demographic data, height, weight, parent-reported GFD compliance were recorded. Blood samples were obtained for hemoglobin, ferritin, folate acid, vitamin B12 and D. Dietary adherence was evaluated by anti-tissue transglutaminase IgA (TTG) levels. Regular follow-up (RFU) patients had at least three outpatient visits in the last year and data obtained in the last visit was used in the study. Infrequent follow-up (IFU) patients had only one visit during last year. Patients with selective IgA deficiency, diabetes mellitus and other accompanying systemic disease were excluded.

Results: From a total of 691 outpatient visits, 213 CD cases (median age:11.9 years, 63.8% girls, 58.6% RFU patient) were eligible. Demographic characteristics and biochemical results of RFU and IFU groups are shown in Table 1. Parent reported GFD adherence for RFU and IFU patients was 63.4% vs 46.6%, respectively. When TTG levels were taken into account, only 58.4% of RFU patients and 29.6% of IFU patients were on strict GFD ($\chi^2$:17.2, OR:3.34 95% CI:1.87-5.97, p<0.001). A positive relationship was found between IFU and older age, lower socioeconomic status, lower BMI z-scores, lower ferritin and vitamin D status and higher TTG after regression analysis.

Table:

<table>
<thead>
<tr>
<th></th>
<th>RFU (n=125)</th>
<th>IFU (n=88)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (female %)</td>
<td>61.6</td>
<td>67</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Age (mean±SD years)</td>
<td>11.1±3.6</td>
<td>12.2±3.3</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>BMI z-scores (mean±SD)</td>
<td>-0.38±3.6</td>
<td>-1.5±1.18</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Hemoglobin (mean±SD g/dL)</td>
<td>13.1±1.3</td>
<td>12.6±1.5</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Vitamin B12 (mean±SD pg/mL)</td>
<td>339.6±168.6</td>
<td>305±156.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Folic acid (mean±SD ng/mL)</td>
<td>9.65±3.86</td>
<td>8.66±3.9</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Ferritin (mean±SD ng/mL)</td>
<td>20.8±16.2</td>
<td>13.6±14.2</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Vitamin D (mean±SD ng/mL)</td>
<td>20.1±9</td>
<td>17.3±6.9</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>TTG (mean±SD U/mL)</td>
<td>58.1±91.2</td>
<td>146.1±129.2</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Conclusion: Our cohort shows that IFU is associated with poor adherence to GFD and poor growth in children with CD. Besides, iron and vitamin D deficiency is more common. We found that older age and lower socioeconomic status were the major risk factors for IFU.

Disclosure of interest: None Declared

Vol. 62, Supplement 1, May 2016
206
Assessment of Liver Injuries Among Children With Celiac Disease

Oana Belei¹, Ioan Simedrea¹, Laura Olariu¹, Tamara Marcovici¹, Otilia Marginean¹

¹University of Medicine and Pharmacy Victor Babes, First Pediatric Clinic, Timisoara, Romania

Objectives and study: The aim of this study was to assess the prevalence of cryptogenic persistent hypertransaminasemia (CPHT) and autoimmune hepatitis (AIH) among children with CD and to evaluate the response to treatment.

Methods: We performed a retrospective study analyzing the medical files of all children diagnosed with CD over a period of 10 years (2005-2015) in a reference Center from Western part of Romania.

Results: From 258 CD patients, 72 cases (28%) presented elevated transaminases levels. We excluded from analyse children with CD and hypertransaminasemia due to viral or drug induces hepatitis. From 72 cases with high TGP and TGO levels, 65 cases had CPHT due to gluten-dependent nonspecific mild hepatitis and 7 cases had AIH. For AIH diagnosis, liver examinations, specific antibodies and liver biopsy were performed. CPHT normalized on gluten-free diet (GFD) in all patients. Clinical and biochemical parameters improve on immunosuppressive treatment and GFD in all 7 AIH patients (mean follow-up period: 5 years). After treatment withdrawal, 5 AIH cases relapsed only on GFD.

Conclusion: CD is associated with elevated transaminases levels in about one-third of cases. The prevalence of CPHT among CD children was 24%. The prevalence of AIH among CD children was 2.7%. CPHT resolved after 2-3 month of GFD in all cases. In CD children with AIH, GFD and immunosuppression determined a high remission rate. The impact of GFD alone on the outcome of AIH is ineffective in the treatment of children with comorbidity CD/AIH.

Disclosure of interest: None Declared.
Maternal and postnatal exposure to antibiotics and the risk of developing celiac disease

Olof Sandström¹, Fredinah Namatovu², Marie Lindkvist², Anna Myléus³, Anneli Ivarsson²

¹Umeå University, Clinical Sciences, Paediatrics, Umeå, Sweden
²Umeå University, Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå, Sweden
³Umeå, Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå, Sweden

Objectives and study Celiac disease is increasing worldwide indicating a role of modern life style in disease etiology. Dysbiosis has been suggested to play a role in the development of the disease and the microbiota is affected by antibiotic treatments. During normal delivery the mothers’ microbiota is transferred to the offspring. In this register based study we investigated the role of antibiotic treatment during pregnancy and the first year of life on the child’s risk of developing celiac disease.

Methods We included 521,045 children born 2005-2009 of which 741 developed celiac disease during the study period. Celiac disease data was obtained through the Swedish National Childhood Celiac Disease Incidence Register, birth data from the Medical Birth Register and data on antibiotic prescription from the National Prescribed Drug Register. We used Cox proportional hazards regression for estimating hazard ratios (HR) for developing celiac disease.

Results: Maternal prescription of antibiotics during 12 months preceding delivery was associated with reduced risk of celiac disease in the offspring (HR 0.67 [95% confidence interval 0.55-0.81]). Prescription of antibiotics to the child during the first 12 months of life did not affect the celiac disease risk (HR 1.11 [95% confidence interval 0.94-1.30]). Number of courses prescribed did not change the results.

Conclusion To our surprise we found a protective effect on offspring celiac disease by antibiotic prescription to the pregnant mother. This could be a by chance finding but could suggest that antibiotics promote a microbiota protective against celiac disease when transferred to the offspring. Antibiotics prescribed to the child were not associated to celiac disease risk and results from previous studies are conflicting.

Disclosure of interest: Conflict of interest for all authors: None Declared.
Treatment of HCT116 cells with gliadin, transglutaminases and complexes thereof imitating celiac disease

Tanja Barth¹, Patricia Jeremias¹, Torsten Matthias¹, Sandra Neidhöfer¹, Aaron Lerner²

¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel

Objectives and study: Tissue transglutaminase (tTg) is the autoantigen of celiac disease (CD) and the food additive, microbial transglutaminase (mTg) was recently emerged as a potential inducer of CD. Both enzymes transamidate gliadin, resulting in tTg-/mTg-gliadin complexes (neo-epitopes). Their effects on a human intestinal cell-line was never studied.

Aims: To explore gliadin, tTg, mTg and their cross-linked neo-epitopes (neo-tTg, neo-mTg) effects on HCT116 cells.

Methods: HCT116 at densities of 1000 cells/cm² were grown for 6 days in DMEM/F-12 medium, incubated with gliadin, tTg, mTg, neo-tTg and neo-mTg and corresponding vehicles for different concentration and time points. Proliferation was measured by MTT assay, necrosis by LDH release and apoptosis by Caspase 3/7 activities and DAPI.

Results: Gliadin decreases viability of HCT116 cells to 50%, while neo-mTg and neo-tTg decrease viability to 15% (p<0.05, 0.01, 0.05, respectively), at highest concentration. After 4h incubation, neo-mTg suppressed viability compared to mTg alone (p<0.02), no effect of uncomplexed mTg and tTg on cell viability was observed. Only gliadin induced LDH release over time (p < 0.01). Apoptosis was induced only by gliadin or neo-tTg complex. However, using DAPI staining for apoptosis detection, only gliadin induced apoptosis.

Conclusions: Gliadin decreases cell viability most probably due to necrosis and apoptosis. A moderate, but statistically significant decrease in viability was observed applying the neo-epitopes at high concentrations and after 4 hours. It seems that by complexing to the enzymes the cells are protected against the toxic and apoptotic effects of gliadin. Those in-vitro effects may simulate real life in vivo.

Disclosure of interest: All authors "none declared".
GASTROENTEROLOGY: Coeliac disease

G-P-045

Longitudinal study in celiacs relatives patients typing HLA DQ related to celiac disease

Raquel Furnes¹, Maria Laura Daruich¹, Eliana Polomino¹, Maria Eva Re Gea¹, Teresita Alvarellos¹, Isidoro Joaquin Kohn¹

¹Hospital Privado Universitario de Córdoba, Argentina

Objectives and study: Celiac disease (CD) is a disorder of multifactorial etiology that occurs with chronic gluten intolerance. It is greater incidence in first-degree relatives of patients diagnosed with CD. Objectives: Evaluate the diagnosis of CD in patients studied from the index case. Relate the CD diagnostic in patients with the corresponding first- and second-degree relatives. Use as a complementary tool typing HLA antigens DQ2 and DQ8.

Methods: Simple descriptive correlational longitudinal study a total of 98 relatives of celiac patients, treated at Pediatric Gastroenterology Private University Hospital in Córdoba, since April 2009 followed up of 6 months to 6 years. The relatives were dosed HLA-DQ typing and those (+) were annually clinical evaluated + Deaminated Gliadin Peptide Antibodies IgA-IgG class (anti-DGP) + Tissue transglutaminase antibody (tTGA), IgA class. Biopsy was done when antibodies were positives.

Results: The population was 98 relatives of celiac patients, 41.8% males. Age range of 1 to 42 years; 12.2% were over 18. From them 66.3% had HLA DQ2 and / or DQ8 positive related to EC. Of these, 27.6 % were diagnosed with CD. In 24.6% the diagnosis was made in the first controls (AC + Biopsy Marsh II-III). Only 9/16 (56%) were symptomatic. In 2 brothers of celiac children, after 4 years of follow up, they began with symptoms and antibodies (+) and ID biopsies confirmed the diagnosis of CD. The remaining population who had one or both of the DQ2 / DQ8 alleles, remain in control at the potential of developing CD.

Conclusion: first-degree relatives of celiac patients are at risk, they should be studied, even those asymptomatic (ESPGHAN 2012). It is useful typing of HLA-DQ2 / 8 alleles as a tool to select people with potential EC, and define controls and monitoring over time.

Disclosure of interest: None declared.
GASTROENTEROLOGY: Coeliac disease

G-P-046

Extraintestinal symptoms in celiac disease: prevalence and impact to the disease presentation

Samuli Nurminen¹, Laura Kivelä¹, Heini Huhtala², Markku Mäki¹, Katri Kaukinen³, Kalle Kurppa¹

¹University of Tampere and Tampere University Hospital, Centre for Child Health Research, Tampere, Finland
²University of Tampere, School of Health Sciences, Tampere, Finland
³University of Tampere, Finland, School of Medicine, Tampere, Finland

Objectives and study: Celiac disease (CD) may manifest with various extraintestinal symptoms, but their actual prevalence and association with the other clinical, histological and serological features of the disease is poorly known. We aimed to investigate these issues in large cohorts of children with CD and controls with inflammatory bowel disease (IBD).

Methods: 511 children with CD and 80 with IBD (Crohn’s disease n=36, ulcerative colitis (UC) n=43) underwent analyses of the presence of various extraintestinal symptoms described in the literature. In addition, CD patients were divided to three subgroups on basis of the main clinical presentation at diagnosis (gastrointestinal n=249, extraintestinal n=116 and screen-detected n=146), and the groups were compared in terms of histology, serology and adherence and response to gluten-free diet.

Results: Up to 60% of children with CD and even more of those with Crohn’s disease (72%) and UC (84%) had at least one extraintestinal symptom. Poor growth and anemia were the most common extraintestinal symptom in both CD (23% and 16%, respectively) and IBD (Crohn’s disease 36% and 47%, UC 48% and 39%). Other frequent symptoms were fatigue (CD 9%, Crohn’s disease 8% and UC 9%), recurrent aphthous ulcers (2%, 8% and 2%), arthrosis/arthralgia (6%, 0% and 7%) and neurological symptoms (8%, 6% and 5%). Skin symptoms were present in 13% of children with CD but none of those with IBD. In subgroup analysis, children with extraintestinal symptoms as the main presentation of CD had more severe histological damage (p=0.023) and those being screen-detected higher hemoglobin (p=0.032) and transglutaminase 2 antibody (p=0.030) values compared with the other subgroups. There were no differences between the groups in the other laboratory parameters, demographic data, growth and adherence and response to gluten-free diet. Although not being the main clinical presentation, extraintestinal symptoms were present in 55% of children with gastrointestinal presentation and 37% of those being screen-detected.

Conclusion: Almost two-third of the children with CD had at least one extraintestinal symptom, the most frequent being anemia, poor growth and skin symptoms. Having an extraintestinal symptom as the main presentation of the disease may be a sign of a more severe histological damage.

Disclosure of interest: None Declared.
Comparison of the reliability of celiac disease serology to reflect intestinal damage

Torsten Matthias¹, Patricia Jeremias¹, Sandra Neidhöfer¹, Aaron Lerner²

¹Aesku.Kipp Institute, Research, Wendelsheim, Germany
²Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel

Objectives and study: In view of the increasing importance of the serological biomarkers for the screening and diagnosis of celiac disease (CD), their differential performance, and the lack of head to head comparison, the reliability of those isolated or combined antibodies to reflect the intestinal damage in children with CD was evaluated.

Methods: 95 pediatric CD patients (mean age 8.3), 45 nonspecific abdominal pain children (AP) (mean age 7.3), 99 normal children (NC) (mean age 8.5) and 79 normal adults (NA) (mean age 28) were tested by the following ELISAs, detecting IgA, IgG or both, IgA and IgG: AESKULISA® Gliadin (AGA), AESKULISA® tTg (tTG; RUO), AESKULISA® DGP (DGP) and AESKULISA® tTg New Generation (Neo-epitope tTg complexed to gliadin=tTg-neo). The results were compared to the degree of intestinal injury, using revised Marsh criteria. Scatter diagrams and regression analysis comparing the 12 antibodies’ optical density (OD) activities to the degree of the intestinal damage were correlated.

Results: Most of the assays were able to differentiate 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 (r²=0.968, p<0.0025) and tTg-neo/DGP IgGs (r²=0.989, p<0.0001/ r²0.985, p<0.0001, respectively) stood out, significantly, as the best indicators of the intestinal damage in CD.

The highest OD values (medium 2.94±1.2, p<0.0001) were achieved by using the tTg-neo IgA ELISA in patients with Marsh 3c.

Conclusion: It is suggested that tTg-neo IgA/IgG antibodies should be preferably used to reflect intestinal damage during screening, diagnosing and monitoring compliance in childhood CD.

Disclosure of interest: T M is the head of the Aesku.Kipp Institute, PJ, S N, are employed by Aesku.Kipp institute.
A L “non declared”
Bone mineral density in children with screening-detected celiac disease: a case-control study

Sara Björck¹, Charlotte Brundin², Magnus Karlsson³, Daniel Agardh¹

¹Skåne University Hospital, Department of Pediatrics, Malmö, Sweden
²Diabetes and Celiac Disease Unit, Department of Clinical Sciences, Lund University, Malmö, Sweden
³Clinical and Molecular Osteoporosis Research Unit, Department of Clinical Sciences, Lund University, Malmö, Sweden

Objectives and study: To examine if children with screening-detected celiac disease have affected bone mineral density (BMD) and/or levels of 25(OH) vitamin D3 and parathyroid hormone (PTH) or signs of systemic inflammation reflected as elevated plasma cytokine levels.

Methods: BMD (g/cm²) of total body and spine was investigated by Dual X-ray absorptiometry (DXA) and serum levels of 25(OH) vitamin D3 (nmol/L) and PTH (pmol/L) were measured in 71 children aged 10.0±0.7 (mean±SD) at diagnosis of screening-detected celiac disease and in 142 controls matched for gender, HLA-DQ, and birth year. In addition, plasma levels of cytokines IL-1β, IL-2, IL-4, IL-5, IL-6, IL-8, IL-10, IL12p70, IL-13, IL-15, IFNγ, and TNFα were determined using a multiplex electrochemiluminiscence immunoassay. The same measurements were made in 30 children aged 10.5±0.8 years diagnosed at an earlier age with screening-detected celiac disease and on a gluten-free diet for 6.9±1.1 years and in another 60 controls matched in the same way. Data is presented as mean with 95% CI.

Results: Children with screening-detected celiac disease had, at diagnosis, compared to controls, lower BMD (g/cm²) of total body [0.84 (0.82 to 0.86) versus (vs.) 0.87 (0.86 to 0.88); p=0.009] and lower BMD of spine [0.76 (0.74 to 0.77) vs. 0.79 (0.78 to 0.80); p=0.005], lower levels of 25(OH) vitamin D3 (nmol/L) [65.7 (60.9 to 70.4)] vs. 77.1 (73.8 to 80.3); p<0.001] and higher PTH levels (pmol/L) [4.2 (3.9 to 4.5)] vs. 3.2 (3.0 to 3.4); p<0.001]. Both Th1 cytokines (IL-1β, IL-2, IL-8, IL-12p70, TNFα, and IFNγ) and Th2 cytokines (IL-4, IL-6, IL-10, and IL-13) were significantly increased in children with screening-detected celiac disease compared to controls. There was no difference in BMD, 25(OH) vitamin D3, PTH or systemic cytokine levels between children on a gluten-free diet and controls.

Conclusion: Children diagnosed with screening-detected celiac disease have lower BMD, lower vitamin D3, higher PTH, and show signs of systemic inflammation compared with matched controls. These differences are not found in children on a gluten-free diet, diagnosed at an earlier age with screening-detected celiac disease, when compared with matched controls. This suggests that children with screening-detected celiac disease could benefit from early identification and treatment.

Disclosure of interest: None Declared.
Evaluation of the correlation between tTG-IgA titer and duodenal biopsy findings in children with suspected celiac disease

Seyed Mohsen Dehghani¹, Mitra Aldaghi², Mahmood Haghighat¹

¹Shiraz University of Medical Sciences, Pediatrics, Gastroenterohepatology Research Center, Shiraz, Iran
²Sabzewar University of Medicine Sciences, Pediatrics, Sabzewar, Iran

Objectives and study: In this study, we aimed to evaluate the predictive value of tissue transglutaminase (tTG) antibodies for the diagnosis of celiac disease in a pediatric population in order to determine if duodenal biopsy can be avoided.

Methods: The subjects were selected among individuals with probable celiac disease, referring to a gastrointestinal clinic. After physical examinations and performing tissue transglutaminase-immunoglobulin A (tTG-IgA) tests, upper endoscopy was performed if serological titer was higher than 18 IU/ml. Therapy started according to pathologic results.

Results: The sample size was calculated to be 121 subjects (69 female and 52 male subjects); the average age of subjects was 8.4 years. A significant association was found between serological titer and pathologic results; in other words, subjects with high serological titer had more positive pathologic results for celiac disease, compared to others (P<0.001). Maximum sensitivity (65%) and specificity (65.4%) were achieved at a serological titer of 81.95 IU/ml; the calculated accuracy was lower in comparison with other studies. As the results indicated, lower antibody titer was observed in patients with failure to gain weight and higher antibody titer was reported in diabetic patients.

Conclusion: In our study, considering the lower sensitivity and specificity of serological titer and lower success in avoiding intestinal biopsy, in contrast with other studies, the utility of one serological test for the accurate diagnosis of celiac disease is not sufficient and further analysis is required. To obtain the best serological algorithm, future studies need to evaluate as many tests and test combinations as possible. Furthermore, a diversity of patient populations needs to be evaluated by taking different relevant aspects (e.g., disease prevalence and the magnitude of intestinal mucosal damage) into consideration.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Coeliac disease

G-P-050

Barriers to implementing the revised ESPGHAN guidelines for coeliac disease in children – a national cross-sectional survey across the paediatric units in England

Siba Paul¹, Sophie Harries², Dharamveer Basude¹

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

Objectives and study: In 2012, ESPGHAN guidelines¹ for diagnosing coeliac disease (CD) were modified. In symptomatic children a diagnosis of CD can be made serologically if the child has anti-tissue transglutaminase antibody (tTG) titre over ten times the upper limit of normal (10xULN), and has positive HLA-DQ2/8 haplotype. In selective group of children serological diagnosis without biopsy is advantageous as it is reliable, less invasive and economically favourable. However, there are several tTG assays available suggesting different threshold values, thus fostering potential interpretation error and diagnostic inconsistencies. The aim of this study is to explore how tTG is reported by all pathology laboratories in England in order to ascertain current practice and facilitate better implementation of the ESPGHAN guidelines.

Methods: A cross-sectional study was conducted in the form of a telephone survey involving all 139 acute hospitals in England providing paediatric services. The respondents were asked what tTG test assays were available in their laboratory, threshold value for normal, availability of anti-endomysial antibody testing, and whether they routinely report the total IgA-levels.

Results: 135/139 (96.4%) of laboratories responded. 83 (62.6%) of hospitals do their tTG testing in-house and 81.4% (n=) of these also do the IgA-EMA themselves. A range of different tTG assays and 10 different threshold values for normal are being used across England (ranging between 4 – 30 IU/ml [see figure]). Multiple values are being used in each geographical region covered by one or two specialist paediatric gastroenterology centres receiving referrals for diagnosis of CD. 96.3% of laboratories quantitatively reports tTGs. Automatic reporting of total IgA levels occurs in 29.6% of laboratories.
Conclusion: Despite calls to standardise, there is still much heterogeneity in tTG reporting in England. Tertiary paediatric gastroenterology centres need to be aware about different tTG threshold values to decide which child can be diagnosed with CD serologically or if biopsies are needed. Standardisation of tTG titres and routine reporting of IgA levels will be beneficial. There is plan to share the findings with all the paediatric gastroenterology units in England with a view to streamlining the diagnostic pathway.

Disclosure of interest: None to declare
Validation of the Diagnosis of Coeliac Disease by Linkage of National Patient and Pathology Registers, and Presence of Antibodies

Stine Dydenschborg Sander¹, Ketil Stordal², Søren Thue Lillevang³, Tine Plato Hansen⁴, Anne Marie Nybo Andersen⁵, Anne Vinkel Hansen⁵, Steffen Husby⁷

¹Odense University Hospital, Hans Christian Andersen Children’s Hospital, Odense, Denmark
²Norwegian Institute of Public Health, Oslo, Norway
³Odense University Hospital, Clinical Immunology, Odense, Denmark
⁴Hvidovre Hospital, Department of Pathology, Copenhagen, Denmark
⁵University of Copenhagen, Department of Public Health, Copenhagen, Denmark

Objectives and study: The objective was to validate registration of coeliac disease (CD) in the Danish National Patient Register (DNPR) by registration of histological analysis of biopsies in the Danish Database of Pathology (DDP) combined with data on CD specific antibodies, and HLA haplotypes registered in medical records at a national level.

Methods: Patients born 1 January 1995 to 31 December 2012 with ≥ 1 registrations of CD (ICD-10 K90.0) in DNPR by 1 May 2015 were included and identified as in- or outpatients at one of 30 different hospital departments in Denmark, primarily (87%) 11 paediatric departments. All biopsies from duodenum or small bowel registered with codes for inflammation, atrophy, or CD in DDP were included. Medical records were searched for CD specific antibodies (tissue transglutaminase (anti-TG2) IgA, anti-TG2 IgG, endomysium antibodies IgA (EMA), deamidated gliadin antibodies IgG (DGP)), and HLA haplotypes. All information was linked at an individual level using the unique 10-digit personal identification number assigned to all persons living in Denmark.

Results: Overall we identified 2263 patients registered in DNPR, and included 1214 (54%) of these patients based on the registered hospital department. The median number of registrations (hospital contacts) was 7 (IQR 3, 14). For 90 patients (7%) only an observational diagnosis was recorded.

A biopsy compatible with CD (corresponding to Marsh class 2-3) was registered in DDP for 485 patients (40%) additionally 24 patients (2%) had a biopsy with intraepithelial lymphocytosis (IEL), but no evidence of villous atrophy.

We found ≥ 1 registration of anti-TG2 IgA for 1134 patients (93%). The median number of registrations was 4 (IQR 2, 6). A positive anti-TG2 IgA was registered for 799 of the patients (70%), and 531 (47%) had ≥ 1 registrations of anti-TG2 IgA ≥ 10 times normal. EMA was registered for 252 patients (21%). Positive EMA was registered in 152 (60%) of these patients. Anti-TG2 IgG was registered for 156 patients (13%), and 51 of these patients (33%) had ≥ 1 registrations of positive anti-TG2 IgG. DGP was registered for 619 patients (51%), and 152 of these patients (25%) had ≥ 1 registrations of positive DGP. Registrations of total IgA was found for 785 patients (65%), 34 of these patients (4%) had IgA deficiency. HLA haplotype was registered for 191 patients (16%), and 173 of these patients (91%) were positive for DQ2 or DQ8.

Overall, we were able to identify ≥ 1 registration of CD specific antibody test (anti-TG2 IgA, anti-TG2 IgG, EMA, or DGP) for 1139 patients (94%), and 840 of these patients (74%) had ≥ 1 positive test. A biopsy compatible with CD and ≥ 1 positive CD specific antibody test was registered for 392 patients (32%).

We confirmed the diagnosis CD in 807 patients (66%) based on registration of positive EMA, anti-TG2 ≥ 10 times normal, or a biopsy compatible with CD registered in DDP. Of these confirmed cases 11 patients (1%) had only observational CD diagnoses registered in DNPR, and 767 patients (95%) had ≥ 2 registrations of CD in DNPR.
Conclusion: The CD diagnosis registered in DNPR could be confirmed in 66% of the patients by review of biopsies registered in DDP and CD specific antibodies registered in medical records. Even though these are minimum numbers, the study illustrates the limitations of registry-based observations.

Disclosure of interest: None declared.
Anaemia in children with celiac disease: association with the clinical, serological and histological findings and response to the gluten-free diet

Teemu Rajalahti¹, Marleena Repo¹, Laura Kivelä¹, Heini Huhtala², Markku Mäki¹, Katri Kaukinen³, Katri Lindfors³, Kalle Kurppa¹

¹University of Tampere and Tampere University Hospital, Centre for Child Health Research, Tampere, Finland
²University of Tampere, School of Health Sciences, Tampere, Finland
³University of Tampere, Finland, School of Medicine, Tampere, Finland

Objectives and study: Anemia is a very common and well-known finding in untreated celiac disease. However, at present the association between the presence of anemia and clinico-histopathological presentation of the disease in children remains obscure. We aimed to compare a variety of clinical and histological features between children with anemia and those without anemia at celiac disease diagnosis.

Methods: Altogether 455 pediatric (age <18 years) celiac disease patients were divided into anemic and non-anemic study groups. Next, the groups underwent comparisons of different clinical, serological and laboratory parameters and severity of the small-bowel mucosal damage. Furthermore, dietary adherence and clinical and serological response to the gluten-free diet were compared.

Results: Anemia was detected in 18.0% of the celiac patients. Children with anemia had higher values of transglutaminase 2 antibodies (120.0 U/l vs. 88.0 U/l, p<0.001) and, by definition, lower values of blood hemoglobin (10.5 g/dl vs. 12.8 g/dl, p<0.001) and different iron parameters. Anemic patients were also less often screen-detected (13.4% vs 34.6%), had more severe histological damage at diagnosis (p=0.048) and lower adherence to the gluten-free diet (78.3% vs 87.5%, p=0.035) than those without anemia. Anemia recovered in 92% of the children after a median of one year on a gluten-free diet, but the median hemoglobin value remained significantly lower compared with the non-anemic group (12.5 g/dl vs. 13.2 g/dl, p=0.045). There was no difference between the study groups in the clinical and serological response to the dietary treatment (p=0.318).

Conclusion: Anemia at celiac disease diagnosis is associated to more severe histological and serological presentation. Further, the low hemoglobin may not fully recover even after a median of one year on a strict gluten-free diet.

Disclosure of interest: None Declared.
HoxD12 is a potential disease biomarker in pediatric celiac disease

Paraskevi Stathakopoulou, Angeliki Balasopoulou, Biljana Stanković, Gordana Nikčević, Apostolos Stratopoulos, Maria Kanariou, Nikki Constantinidou, Maro Krini, Kleopatra Spanou, George Chrousos, Sonja Pavlovic, Eleftheria Roma, Branka Zukić, George Patrinos, Theodora Katsila

1University of Patras, Department of Pharmacy, Patras, Greece
2Institute of Molecular Genetics and Genetic Engineering, University of Belgrade, Laboratory for Molecular Biomedicine, Belgrade, Serbia
3“aghia Sophia” Children’s Hospital, Department of Immunology and Histocompatibility, Athens, Greece
4University of Athens Medical School, First Department of Pediatrics, Athens, Greece

Objectives and study: Celiac disease is a complex chronic immune-mediated disorder of the small intestine. Today, the pathobiology of the disease is unclear, perplexing differential diagnosis, patient stratification and decision-making in the clinic. In this context, the impact of precision medicine becomes of utmost importance. Indeed, genetics has been reported to play a key role. Notwithstanding, HLA-DQ2 and/or HLA-DQ8 expression is necessary, but not sufficient for disease development. Herein, whole genome sequencing analysis of a Greek trio revealed HoxD12 as a novel gene candidate for celiac disease. For this, HoxD12 was validated in pediatric celiac disease patients of Serbian (n=73) and Hellenic origin (n=109) and their ethnically matched counterparts (n=32 and n=111, respectively).

Methods: HoxD12 validation was performed by allele-specific PCR and Sanger sequencing. Amplification was carried out according to the KAPA2G Fast HotStart protocol (KAPABIOSYSTEMS, MA, USA). Sanger sequencing was also employed to ensure allele-specific PCR method verification. Hardy-Weinberg equilibrium was determined using the Chi-Square Goodness of Fit test and principal component analysis. 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: Findings report no deviation from Hardy-Weinberg equilibrium. Genotype and allele frequencies were similar between populations (Table 1). A statistically significant association for HoxD12 and disease phenotype was evident in the Serbian population (p=0.0068). Data failed to reach statistical significance in the Hellenic population (p=0.248), possibly due to small sample size.

Table 1

<table>
<thead>
<tr>
<th>Allele Frequencies (%)</th>
<th>Hellenic</th>
<th>Serbian</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NR</td>
<td>Vt</td>
</tr>
<tr>
<td>Healthy Individuals</td>
<td>100</td>
<td>0</td>
</tr>
<tr>
<td>Patients</td>
<td>99</td>
<td>1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Genotype Frequencies (%)</th>
<th>Hellenic</th>
<th>Serbian</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>NR/NR</td>
<td>Vt/Vt</td>
</tr>
<tr>
<td>Healthy Individuals</td>
<td>0</td>
<td>100</td>
</tr>
<tr>
<td>Patients</td>
<td>0</td>
<td>98</td>
</tr>
</tbody>
</table>

Conclusion: HoxD12 serves as a potential disease biomarker. Future cross-population and functional studies are expected to further delineate disease mechanisms towards tailored-made therapeutics.

Disclosure of interest: None Declared
Microvillous inclusion disease (MVID): a regional centre experience

Anjum Grewal\textsuperscript{1}, Marta Cohen\textsuperscript{2}, Michael Thomson\textsuperscript{1}, Prithviraj Rao\textsuperscript{1}, Sally Connolly\textsuperscript{1}, Priya Narula\textsuperscript{1}, David Campbell\textsuperscript{3}, Arun Urs\textsuperscript{3}

\textsuperscript{1}Sheffield Children's Hospital, Paediatric Gastroenterology, Sheffield, United Kingdom
\textsuperscript{2}Sheffield Children's Hospital, Histopathology, Sheffield, United Kingdom
\textsuperscript{3}Sheffield Children's Hospital NHS Foundation Trust, Sheffield, United Kingdom

Objectives and study: Microvillous inclusion disease is a rare congenital enteropathy of the intestinal epithelial cells characterized by severe intractable diarrhoea typically beginning in the first hours to days of life (early-onset form). Rarely, the diarrhoea starts later around 6 to 8 weeks of life (late-onset form). It is characterised by a mutation in the MYO5B gene and is inherited in an autosomal recessive pattern with incidence at 1 in 200,000 in children from United Kingdom.

Methods: We describe clinico-pathological features and management of 4 patients diagnosed with MVID at our unit over the past 10 years.

Results: Two children (Patient2 & 3) were siblings and parents had two other healthy boys. Both of them showed metabolic decompensation, repeated episodes of dehydration, with significant infectious and liver complications. In patient 1 due to significant co-morbidities palliative care was accepted. All the patients demonstrated intestinal failure secondary to diarrhoea. Electron microscopy revealed an increased number of secretory granules in the apical cytoplasm of the enterocytes, vacuolation of the surface enterocytes with apical inclusions containing microvilli, and absence of the brush border. All patients received parenteral nutrition and 3 of 4 were referred for bowel transplant. Two patients died whilst on waiting list for transplant.

Table:

<table>
<thead>
<tr>
<th>Pt no</th>
<th>Sex</th>
<th>Age at diagnosis</th>
<th>Parental consangui nity</th>
<th>Genetics (MYO5B Mutation)</th>
<th>Clinical features at presentation</th>
<th>Clinical course</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>&lt; 1 week</td>
<td>Yes</td>
<td>Negative</td>
<td>Antenatal scans -dilated fluid filled bowel loops, watery stools, abdominal distension, weight loss, metabolic acidosis.</td>
<td>Cerebral cortical atrophy, schizencephaly, Hyperglycaemia, seizures, DIC, left leg thrombus</td>
<td>Died at 5 weeks</td>
</tr>
<tr>
<td>2</td>
<td>F</td>
<td>&lt; 1 week</td>
<td>No</td>
<td>Positive</td>
<td>Antenatal scans- dilated bowel loops. Loose watery stools</td>
<td>Recurrent hypoglycaemia, GORD, IFALD, Line sepsis, renal calculi, hypocalaemia, Haemangioma right lobe of liver. Hypercholesterolemia, hypertriglyceridaemia.</td>
<td>Transplant at 17 months</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td>---</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>3 weeks</td>
<td>No</td>
<td>Positive</td>
<td>Severe watery diarrhoea since birth, lethargy, worsening acidosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Recurrent hypoglycaemia, metabolic acidosis, IFALD, Low IgG, hearing impairment, VUR- recurrent UTI, recurrent line sepsis, Vocal cord paralysis, Atrial septal defect</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Died at 11 months</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F</td>
<td>11 months</td>
<td>Yes</td>
<td>Not Tested</td>
<td>Antenatal scans - polyhydramnios. Abdominal distension, chronic diarrhoea, failure to thrive, HLH at 4 months - unrelated cord blood transplant</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Conjugated jaundice, delayed development, hepatosplenomegaly, coagulopathy, Vitamin D deficiency, Proximal tubular nephropathy</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Died at 13 months</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** MVID is a very rare disorder with generally poor long-term outcome despite diagnosis at specialist centre, early institution of parenteral nutrition and early referral for small bowel transplants. The partial or variant form can be missed till much later in infancy. Early small bowel transplant offers new horizon for disease management and outcome.

**Disclosure of interest:** None Declared.
Highly diverse digestive presentation of stat3 gain-of-function mutation in four affected members of the same family

Fabienne Charbit-Henrion¹, Begue Bernadette¹, Meresse Bertrand², Guegan Nicolas², Pierre Quartier³, Nicole Brousse³, Olivier Goulet⁵, Frank RUEMMELE⁵, Alexandre Aubourg⁶, Olivier Hermine¹, Christophe Cellier⁸, Georgia Malamut⁸, Nadine Cerf-Bensussan¹

¹Imagine Institute, Inserm Umr 1163 - Intestinal Immunity, and Genius Group, Paris, France
²Imagine Institute, Inserm Umr 1163 - Intestinal Immunity, Paris, France
³Hôpital Necker-Enfants Malades, Aphp, Unité D’immunologie, Hématologie et Rhumatologie Pediatrique, Paris, France
⁴Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Anatomopathologie , Paris, France
⁵Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, and Genius Group, Paris, France
⁶Chru Tours, Service D’hépatogastroentérologie, Tours, France
⁷Hôpital Necker-Enfants Malades, Aphp, Department of Hematology, Paris, France
⁸Hôpital Européen Georges-Pompidou, Aphp, Department of Gastroenterology and Digestive Endoscopy, Paris, France

Objectives: To delineate the molecular defect underlying severe but highly diverse digestive symptoms in one family with a pedigree suggestive of autosomal dominant transmission.

Methods:

Patients

Patient A first developed villous atrophy (VA) refractory to gluten-free diet (GFD) but responsive to corticoids at the age of 20. She was referred to our center when 45 year-old because of life-threatening protein losing enteropathy and malnutrition (BMI 11). She was successfully treated with pulse steroids therapy and anti-TNFα.

Patient B (patient A’s brother) developed rheumatoid arthritis, psoriasis and vitiligo at the age of 25 and, after one year, VA atrophy with severe malnutrition, which was initially improved by parenteral nutrition and GFD. After 10 years, enteropathy worsened and IgG deficiency developed. He died at the age of 48 from suicide.

Patient C (patient A’s first daughter) developed at 3 years autoimmune acute hepatitis and severe juvenile rheumatoid arthritis and, at 5 years, VA and scleroderma with cardiac insufficiency. She remained unresponsive to all immunosuppressive treatments including high doses corticoids, azathioprine, methotrexate, cyclophosphamide, IL-1 receptor antagonist and autologous stem cell transplantation. She died when 11 year-old.

Patient D (patient A’s second daughter) was diagnosed at the age of 18 with common variable immunodeficiency based on low serum IgG, frequent upper tract infections and bronchiectasis. She now receives immunoglobulin replacement therapy.

Laboratory testing

Anti-transglutaminase and anti-harmonin (enterocyte) antibodies, HLA DQ2/DQ8 screening, histology and immunohistochemistry, TCR rearrangements, flow cytometry phenotyping of peripheral and intestinal lymphocytes were performed as described. Whole Exome Sequencing (WES) was performed on DNA extracted from PBMC and analyzed with in-house POLYWEB Software. STAT3

Vol. 62, Supplement 1, May 2016 223
phosphorylation was analyzed by flow cytometry, and SOCS3 transcription (Suppressor of cytokine signaling 3) by quantitative RT-PCR in PBMC or EBV cell lines.

**Results:** In patients A, B and C, histology showed partial to severe VA with lymphocytic infiltration. High counts of polyclonal CD3^+^CD8^+^ Granzyme B^+^ intraepithelial lymphocytes were noted in patients A and B. Lack of at risk HLA and anti-TG2 antibodies however eliminated celiac disease and there was no detectable anti-enterocyte antibody. WES identified one heterozygous missense Stat3 variation c.1082A>G, that was common to patients A, B, and C. This variant, non described yet, predicts a glutamine to arginine substitution in position 361 (p.Q361R), a highly-conserved amino-acid located in STAT3 DNA-binding site. Substitution was predicted to be damaging by Polyphen2 and MutationTaster algorithms. STAT3 protein expression and IL-21-induced phosphorylation were normal but IL-21 induced transcription of SOCS3, a major transcriptional target of STAT3 was significantly higher in the EBV cell line from patient A compared to control EBV cell lines and was comparable to that observed in the EBV line from a patient with the known gain of function c.2147C>T; p.T716M STAT3 mutation. Analysis of patient D, who has only recently accepted testing, is in progress.

**Conclusion:** Our results emphasize the need to screen patients with very severe immune-mediated intestinal diseases for STAT3 mutations and illustrate the high heterogeneity of clinical phenotypes in this genetic disease.

**Disclosure of interest:** None Declared.
Unnecessary Abdominal Exploration in Neonates with Congenital Chloride Losing Diarrhea

Haifa Al Awadhi¹, Ali Almehaidib¹, Khaled Al Saleem¹, Mohammed Banemai¹, Wajeeh Mohammad N Al Dekhail³

¹King Faisal Specialist Hospital & Research Center, Pediatrics, Riyadh, Saudi Arabia

Objectives and study: Congenital chloride losing diarrhea (CCLD) is a disorder caused by a mutation in SLC26A3 gene leading to secretory watery diarrhea.

Methods: We describe 4 neonates who were missed and treated as intestinal obstruction. Clinical, radiological and laboratory data were reviewed.

Results: Four neonates underwent exploratory laparotomy for suspected intestinal obstruction. All patients were born vaginally at 32-36 weeks of gestation and had polyhydramnios. Antenatal ultrasound showed dilated bowel loops in all. Three patients underwent colostomy and colonic biopsies for Hirschsprung’s disease, which turned to be normal. One patient was closed based on finding no obstruction. Subsequent, re-evaluation of these patients revealed a clinical presentation compatible with CCLD. This diagnosis was confirmed by gene study.

Conclusion: A high index of suspicion is needed to diagnose these patients and avoid unnecessary surgical interventions. Intestinal obstruction like symptoms may be a misleading presentation.

Disclosure of interest: None Declared
Non-syndromic congenital tufting enteropathy results from cell contractility defects

Julie Salomon1, Florence Campeotto1, Jeremy Magescas2, danielle canioni3, Nicole Brousse3, Benoit Ladoux2, delphine delacour2, Olivier Goulet4

1Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
2Institut Jacques Monod, Cnrs Umr 7592 Laboratoire Cam, Paris, France
3Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Anatomopathologie, Paris, France
4Hôpital Necker Enfants Malades, Université Descartes Paris V, Paris Cité, Gastroentérologie Hépatologie et Nutrition Pédiatriques, and Genius Group, Paris, France

Objectives and study: Congenital Tufting Enteropathy (CTE) is a rare and incurable disease characterized by specific epithelial “Tufts”, and responsible for chronic intestinal insufficiency as well as diarrhoea persisting at fasting. EpCAM, which gene’s loss-of-function mutations are responsible for most of non-syndromic CTE cases, is a well-known tumour marker but its pathophysiological functions are poorly known. Our study aimed at characterizing precisely CTE defects when mutations of EpCAM are involved.

Methods: We finely studied intestinal biopsies of patients (n=15) and a cellular model of human enterocytes stably inactivated for EpCAM in 2-D and 3-D culture systems, and compared it to control biopsies (n=8) and control culture cells respectively. We performed analyses of cell differentiation and polarization protein markers using confocal microscopy, as well as ultrastructural analyses, using transmission electron microscopy.

Results: We found out that the absence of EpCAM in enterocytes results in an aberrant brush border translocation towards lateral tricellular contacts as well as an alteration of the cell contractility apparatus. These defects explain well the CTE criteria i.e. epithelial tufts, intestinal insufficiency and permanent diarrhoea. Inhibitors of cell contractility restored the luminal positioning of the brush border and the correct monolayer organisation of the epithelium

Conclusion: While progressing in the understanding of the pathophysiology of CTE enterocytes defects, we show that EpCAM is an active component of the apico-basal organization, ensuring the functional differentiation of individual cells and maintaining the collective organisation of epithelial cells in a functional monolayer, which could be of major interest in cancer researches. Moreover, our study reveals molecules able to restore a normal phenotype of EpCAM inactivated cultured enterocytes opening hopeful therapeutic perspective for CTE patients.

Disclosure of interest: “None Declared”.
Prevalence of cows' milk allergy (CMA) in infants could be influenced by socioeconomic factors: report of a Chilean cohort experience

Maria Eugenia Arancibia1, Isabel Miquei2, Francisco Alliende2, Gloria Rios2, Lorena Rodriguez2, Yalda Lucero2, Pamela Marchant2, Andres Maturana3

1Clinica Alemana de Stgo, Pediatric, Santiago, Chile
2Clinica Alemana de Stgo, Santiago, Chile
3Universidad del Desarrollo, Santiago, Chile

Objectives and study: The purpose of this study was to compare the prevalence of CMA of two infants cohorts from different socioeconomic status, in Santiago, Chile.

Methods: A prospective cohort of newborns in 2 centres in Santiago of very different socio-economic characteristics was followed until 1 year of age. Centre 1 (Hospital Padre Hurtado) is a public hospital located in one of the most underserved populations in Santiago. Centre 2 (Clinica Alemana) is a private hospital serving the medium and upper class population in Santiago. Patients were enrolled after consent during the first 3 days of life and followed using a structured questionnaire by phone to screen for signs or symptoms suggesting CMA by two trained nurses. All patients that screened positive with ≥ 2 signs or symptoms were evaluated by a paediatric gastroenterologist. Patients with a clinical diagnosis suggesting CMA were started on elimination diet for 4 weeks and an open food challenge using formula containing CMP. The food challenge was considered positive if symptoms reappeared.

Results: A total of 411 patients were enrolled (centre 1:211, centre 2: 200) with 382 (92.9) followed until 1 year of age. The only significant difference was more maternal smoking in centre 1. The incidence of CMA with positive food challenge was 3 (1.5%) and 17 (8.5%) for centres 1 and 2 respectively

Table:

<table>
<thead>
<tr>
<th>Variable</th>
<th>Centre 1 (n=211)</th>
<th>Centre 2(n=200)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)(SD)</td>
<td>3396 (414)</td>
<td>3332 (415)</td>
<td>NS</td>
</tr>
<tr>
<td>Male (%)</td>
<td>50.7</td>
<td>51</td>
<td>NS</td>
</tr>
<tr>
<td>APGAR(Median,p25-75)</td>
<td>10 (9-10)</td>
<td>10 (9-10)</td>
<td>NS</td>
</tr>
<tr>
<td>C-section (%)</td>
<td>22.3</td>
<td>31.5</td>
<td>NS</td>
</tr>
<tr>
<td>Maternal Allergies (%)</td>
<td>21.8</td>
<td>27.6</td>
<td>NS</td>
</tr>
<tr>
<td>Paternal Allergies (%)</td>
<td>14.5</td>
<td>14.1</td>
<td>NS</td>
</tr>
<tr>
<td>Maternal Smoking (%)</td>
<td>39.3</td>
<td>28.2</td>
<td>0.02</td>
</tr>
</tbody>
</table>

Conclusion: The prevalence of CMA was more than fivefold higher in the private centre compared to the public centre. Because participation was voluntary these prevalence could be biased and overrepresented in both centres. No predisposing variables were clearly different between centres. We could speculate that socio-economic factors could influence the incidence of CMA in Chilean population but further studies are needed to confirm this hypothesis

Disclosure of interest: This study was partially funded by Danone. The authors did not receive payments from the Company for doing this research. Danone did not participate in the study nor have access to the data nor participate in the analysis
Clinical Presentation and Food Allergens Associated with Food Protein-Induced Enterocolitis Syndrome - a Frequently Misdiagnosed Rare Form of Gastrointestinal Food Hypersensitivity

Roslyn Tarrant¹, Aideen Byrne²

¹Our Lady's Children's Hospital, Dept. of Clinical Nutrition and Dietetics, Dublin 12, Ireland
²Our Lady's Children's Hospital, Department of Allergy, Dublin 12, Ireland

Objectives and study: To profile patients with a diagnosis of Food Protein-Induced Enterocolitis Syndrome (FPIES) attending a single paediatric tertiary centre, and collect data related to their presenting symptoms and age at diagnosis, food allergens involved, atopic history and initial suspected diagnoses.

Methods: The medical and dietetic charts of all patients diagnosed with FPIES (Jan 2013-Dec 2015) at Our Lady's Children's Hospital, Dublin, were retrospectively reviewed. Data were recorded on the history of patients' diagnosis including any initial misdiagnosis, presenting symptoms, medical and feeding history, FPIES food allergens (amount of food eaten pre-reaction/timing of onset) and relevant specific IgE test results. SPSS® was used to analyse the data.

Results: From 13 patients identified as having FPIES (n = 8 males), the majority were white Caucasian (n = 11) and had other atopic symptoms (n = 9) including atopic dermatitis (n = 8) and IgE-mediated food allergy (n = 3). In eight patients, the first FPIES reaction occurred during the first 2 months of life; four patients in the total sample had FPIES reactions to more than one food. In eight cases, the food allergen was initially well tolerated by the infant, between 3-9 times. The first FPIES reaction occurred at a median of 120 minutes following ingestion of the food allergen (5-90g/ml). Cow's milk protein was identified as the most common allergen (n = 7), as well as fish (n = 3), chicken (n = 2), turkey (n = 1), avocado (n = 1), baby rice (n = 2), potato (n =1) and egg (n = 1); specific IgE results to these allergens, where available (n = 8/13), were all within normal limits. The most frequently documented symptoms at diagnosis included profuse vomiting (n = 12), listlessness (n = 10) and lethargy/dehydration (n = 9); less common symptoms included blood in stools (n = 2), early (n = 5) and delayed (n = 3) diarrhoea, severe reflux/colic type symptoms (back arching: n =2), feeding difficulties (n = 1) and eczema flare-up (n = 1). An initial incorrect diagnosis was made in 12 of the 13 cases. Gastro-infection was queried 14 times in 8 patients, as well as an immature digestion (n = 2), sepsis (n = 1), severe reflux (n = 2) and bowel obstruction (n = 1). Five patients required hospitalisation for intravenous fluids.

Conclusion: This study highlights that FPIES is a complex presentation of non-IgE-mediated gastrointestinal food allergy, and is difficult to recognise and correctly diagnose at the initial presentation. While cow's milk protein was identified as the most common food allergen associated with FPIES, other food proteins traditionally considered of low allergenicity (e.g. baby rice, potato, avocado) also have the potential to cause FPIES. Early recognition of FPIES and removal of the offending food/s are imperative to prevent misdiagnosis and mismanagement of symptoms that may mimic other causes.

Disclosure of interest: None declared.
Half cow’s milk-induced food protein induced enterocolitis syndrome (FPIES) require amino acid feeding

Sibylle Blanc¹, Delphine De Boissieu², Nicolas Kalach³, Soulaines Pascale², Campeotto Florence², Malka Clara², Marie-Pierre Cordier³, Montaudié-Dumas Isabelle¹, Piccini-Bailly Carole¹, Giovannini-Chami Lisa¹, Bourrier Thierry¹, Christophe Dupont²

¹Hôpitaux Pédiatiques de Nice Chu-Lenval, Service de Pneumologie et Allergologie Pédiatriques, Nice, France
²Necker Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition Department, Paris, France
³St Vincent de Paul Hospital, , Lille, France

Objectives and study: FPIES, a non-IgE mediated food allergy (FA) which seems to expand, is mainly related to cow’s milk and manifests as a chronic digestive disease or in its acute form with potentially life-threatening vomiting/diarrhea/dehydration. The objective of this study is to characterize the clinical features of cow’s milk-induced FPIES in children.

Methods: A cohort of patients with FPIES was constituted in French Children’s Hospitals (Necker, Paris – Lenval, Nice). Children were recruited from a cohort registered within the French Ministry of Health (DC-2009-955). Data were collected from medical records including all patients referred for an acute episode of FPIES, and divided into 2 groups according to their tolerance of extensively hydrolysed formula (eHF) or their need to be fed an amino-acid formula (AAF).

Results: 49 children were enrolled, 30 male and 19 female. Infants had been breastfed in 32 cases (67%), for a median duration of 91.5 days, with FPIES during breastfeeding in 4. Chronic symptoms (diarrhea, reflux, crying, failure to thrive, and/or blood in stool) had occurred in 36 (73%), after a median period of 10 days following introduction of milk-based formula. In the whole group, the acute episode occurred at a median age of 4 months, after a median delay from ingestion of milk of 2 hours. Median age at diagnosis was 12 months for FPIES and 3 months for FA. Clinical features of acute form were vomiting 45 (92%), hypotonia 24/37 (65%), diarrhea 27 (55%), pallor 19 (39%), lethargy 8 (16%). Emergency treatment consisted of intravenous rehydration in 16/26 (62%), corticosteroids in 5/26 (19%), epinephrine in 4/26 (15%), antibiotics in 2/26 (8%). Allergy testing was rarely positive: patch test 21 (51%), skin prick tests 3 (8%), specific IgE 13 (30%). Recovery was observed in 19 (40%) at a median age of 31 months. The eHF group comprised 24 (49%) infants and the AAF one 25 (51%). They exhibited the following significant or trend towards significance differences : number of hospitalizations before diagnosis per patient 0.9 vs 2.7 (p=0.02), age of food allergy 4.5 months vs 2.8 (p=0.04), food tolerance acquisition 54% vs 24% (p=0.02), associated FA 4% vs 48% (p=0.0002).

Conclusion: Half infants with milk-induced FPIES do not tolerate eHF, and need to be fed with an AAF, a condition associated with a delayed diagnosis.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-P-061

Our cases with sucrase isomaltase deficiency

Miray Karakoyun¹, Sirmen KIZILCAN², Yasemin OZDEMIR SAHAN³, Masallah BARAN⁴, Fatih UNAL⁴, Sema AYDOGDU⁵

¹Ege University Medicine Faculty İzmİr, Turkey; Ege University Department of Pediatrics, Pediatric Gastroenterology, Hepatology and Nutrition, İzmİr, Turkey
²Ege University Medicine Faculty, İzmİr, Turkey; Ege University Department of Pediatrics, İzmİr, Turkey
³Ege University Medicine Faculty, İzmİr, Turkey; Ege University Department of Pediatrics, Pediatric Cardiology Division, İzmİr, Turkey
⁴Tepecik Training Hospital, Pediatric Gastroenterology, Hepatology and Nutrition Division, İzmİr, Turkey
⁵Ege University Medicine Faculty, İzmİr, Turkey; Pediatric Gastroenterology, Hepatology and Nutrition Division, İzmİr, Turkey

INTRODUCTION
Sucrase isomaltase deficiency is a small bowel disease characterized by OR transitive, rare, osmotic diarrhea, meteorism and weight loss. Due to differences in specified different mutations, residual enzyme activity carbohydrate intake, gastric emptying and small intestine transit time, this disease may occur at different ages and in different clinical manifestations. Prevalence ranges from 0.05% to 3%. What are important in diagnosis are patient complaints, clinical presentation, age-related changes observed and the amount of carbohydrates received, and the gold standard is the measurement of disaccharidases enzyme activity in small intestinal biopsy tissue. However, as measuring enzyme activity is also not possible in Turkey, in the event of clinical suspicion, by loading sucrose-isomaltose, diagnosis is provided by the emergence of symptoms within hours. Sucrase-isomaltase enzyme extract is used in therapy.

CASE REPORT
5 patients including 3 boys, 2 girls were diagnosed as sucrase isomaltase deficiency between the years 2008-2014 in Pediatric Gastroenterology Hepatology and Nutrition branch of Ege University.

The ages of the patients applied were between 5 months and 9 years, the age of onset of complaints ranged from 15th day to 6 months. Reference symptoms were growth retardation, decreased weight gain, plenty of watery diarrhea, vomiting. 5 patients had previously applied to in health care organizations several times and they were followed by GERD, celiac, psödobartt, the lactose intolerance, and food allergy diagnosis but they did not respond to treatments. 5 patients also underwent upper gastrointestinal endoscopy. Esophagitis and gastritis were present in one patient, another biopsy results were normal. One of the cases had B12 and iron deficiency and in one of them, hypocalcemia was found. Routine biochemistry, hemogramme, sweat test, the CF mutation, IgA, IxS, SPT, stool examination of cases were normal. When the cases were examined in conjunction with beginning of complaints, diarrhea histories, and diet anamnesis, it was found to be a significant relationship between the intake of foods containing sucrose and isomaltose and complaints. Thereupon, in cases began to be fed with the sucrose-free foods, dramatically decreased complaints and the weight gain was observed. Thereupon, treatment began by bringing sakrosidaz enzyme extract from abroad; it was observed that after carbohydrate restriction is removed, there was no recurrence of symptoms.

RESULT
Congenital sucrase isomaltase deficiency is a disease of which true prevalence is unknown with the diagnostic challenge in the entire world. We presented these cases as this is the first case series diagnosed and treated with enzyme in Turkey and in order to contribute to the literature. The diagnosis of sucrase isomaltase deficiency is put first by knowing disease and clinically suspecting. In cases presenting with chronic diarrhoea symptoms, detailed content of the diet should be queried, in the event of clinical symptoms, the diet should primarily be regulated and in responsive patients, enzyme replacement therapy should be applied.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Enteropathy (other than Coeliac Disease)

G-P-062

An Italian study assessing the population prevalence of self-reported gluten sensitivity

Valentina Gasparre1, Giulia Paterno1, Claudio Cafagno1, Francesca Arezzo1, Giorgia Borrelli1, Flavia A Indrio1, Michele Abbaticchio2, Rosa Calò3, Schools Bitonto4, Fernanda Cristofori5, Ruggiero Francavilla1

1Giovanni XXIII Pediatric Hospital, Interdisciplinary Department of Medicine, Section of Pediatrics, University of Bari, Bari, Italy
2Town Hall Bitonto, Mayor, Bitonto, Italy
3Town Hall Bitonto, Deputy Mayor, Bitonto, Italy
5Santissima Annunziata Pediatric Hospital, Taranto, Italy

Objectives and study: Reports suggest that gluten sensitivity exists in the absence of coeliac disease (CD). This clinical entity has been termed non-coeliac gluten sensitivity (NCGS). No data are available in children. The aim of the study is to determine the population prevalence of self-reported NCGS in children.

Methods: A population-based questionnaire screened for NCGS and related symptoms was administered to all the pediatric population aged 3-18 years living in an area North of Bari (Italy). The questionnaire was self-administered and blinded.

Results: 8914 of a total of 9300 children (96%) were reached through the school networks and 4833 were recovered and considered valid. Overall, 643 children (7,4%; F:60%; mean age: 12,5 years) referred a gluten related symptoms (mainly GI related) with a rapid onset after meals (60% of cases within six hours) and lasting from minutes to hours after gluten ingestion. Foods considered most offending were: bread/past (47%), sweets (29%), cereals (13%) and pizza (11%). 25% consulted a specialist, while the majority ask an opinion to the general doctor. 60% had already excluded CD and 57% WA, 10% underwent endoscopy. 31 children followed a gluten free diet (GFD): 18% referred a complete, 30% partial, and 27% no improvement.

Conclusion: Self-reported NCGS is commonly reported in children mainly in female adolescents, with symptoms suggesting irritable bowel syndrome. GFD is often initiated without specialist consultation. This data stress the need to define a well defined informative campaign and diagnostic protocol to counsel children and their families.

Disclosure of interest: None Declared.
An Atypical presentation of Systemic Lupus Erythematosus

Viswanathan Sivaramakrishnan1, Muthukumaran R1

1Apollo Children's Hospital, Paediatric Gastroenterology & Hepatology, Chennai, India

Objectives and study: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory process with varied presentations involving any organ system and follows a relapsing-remitting course. It uncommonly manifests with gastrointestinal symptoms as initial presentation. We discuss one such case here.

Methods: A 16yr old boy weighing 37kg, presented with complaints of loose stools for 4 weeks associated with intermittent abdominal pain & weight loss of 6 kg over 6 months. On clinical examination he was undernourished and noted to have mild diffuse tenderness of abdomen. Initial investigations revealed mild anaemia (Hb 9.8 gm/dl) and elevated ESR (66mm/hr), ultrasound abdomen revealed long segment (10cm) jejunal wall thickening. Upper GI/Lower GI endoscopy with histopathology showed mild nonspecific sub-acute inflammation negative for crypt distortion or granuloma. Ileal biopsy for TB testing, including MTB gene xpert and AFB stain was negative as were subsequent AFB cultures. Barium meal follow through showed jejunal loops to be oedematous & thickened, ileal loops featureless & oedematous with mucosa showing granularity and slow transit of barium; all suggestive of systemic disease related pathology. In view of nonspecific arthralgia & intermittent fever, blood for ANA screening was sent, result of which was positive (speckled, 1:40). On clinical review he was found to have malar rash and a history of photosensitivity elicited.

Results: On further workup for connective tissue disorder he was tested positive for antibodies including anti ds DNA (1:160) and extractable nuclear antigens, Sm and Sm/Rnp. Anti-cardiolipin/anti-phospholipid antibodies were unremarkable. Direct globulin test was positive. With SLE very likely, he underwent renal evaluations including urine protein/creatinine ratio (high - 1.25), complements (low C3 & C4) and renal biopsy, which confirmed Lupus Nephritis of class V + III based on ISN/RPS classification. Echocardiogram showed moderate hypertrophy of left ventricle with mild dysfunction and small pericardial effusion. An ophthalmic examination was normal. He satisfied the systemic lupus international collaborative clinics (SLICC) diagnostic criteria for SLE. His initial presentation was suggestive of lupus enteritis. Paediatric Rheumatologist and Nephrologist was involved in management. He was commenced on corticosteroid therapy (high dose I.V. methylprednisone followed by oral prednisolone), hydroxychloroquine and mycophenolate mofetil along with symptomatic management and advised to have frequent follow up. On follow up to 6 months his disease was under control.

This case highlights the atypical presentation of SLE. SLE can present as abdominal emergency in up to 30% of cases and lupus enteritis is the common cause of it. Other notable GI presentations include oral ulcers, GERD, mesenteric inflammatory veno-occlusive disease, chronic pseudointestinal obstruction, protein losing enteropathy and elevated liver enzymes.

Conclusion: SLE can atypically present just with gastrointestinal manifestation to the paediatrician. SLE responds well to corticosteroids and immunosuppressive agents with timely intervention. Hence a thorough history, high index of suspicion with the constellation of clinical symptoms supported by appropriate investigations is essential to arrive at correct diagnosis promptly.

Disclosure of interest: Conflict of interest: For all authors - “None Declared”. 
The preliminary investigation of fecal microbiota transplantation for pediatric recurrent chronic bowel disease and literary review

Youhong Fang¹, Jie Chen¹, Jindan Yu¹, Youyou Luo¹, JINGAN LOU¹
¹Children's Hospital of Zhejiang University, Hangzhou, China

Objectives and study: Fecal microbiota transplantation (FMT) is a potential therapeutic method to treat intestinal diseases with fecal dysbiosis. FMT has demonstrated effective for recurrent clostridium difficile infection (CDI). And FMT also showed potential therapeutic effect for some inflammatory bowel disease (IBD). However the effect of FMT with treating intestinal disease is still exploring the way. This clinical research is a prospective study mainly to confirm the preliminary safety and potential efficacy of FMT in pediatric recurrent chronic bowel disease including Crohn's disease, Ulcerative colitis, and pseudomembranous colitis which are failed by regular medical treatment.

Methods: Five patients, aged 1Y6M to 11 years, among them two were under two years old, were diagnosed very early onset Crohn’s disease (VEOCD), Ulcerative colitis and pseudomembranous colitis respectively underwent seven times of FMT therapies by nasal jejunal tube and colonoscopy, and they were followed up every 2 to 4 weeks.

Results: Two patients achieved partial remission after FMT, around 6-8 weeks both of the patients’ symptoms relapsed. They received second time FMT. Three patients failed after FMT therapy, including two VEOCH patients and one Ulcer colitis patient with high score of disease active index. Four of five patients had fever after FMT, one patient had mild fever and it was self-limiting. Three patients had persistent fever and treated with antibiotics intravenously. Other adverse events such as abdominal pain, abdominal uncomfortable were mild and they were self-limiting.

Table: Adverse effect of patients and treatment

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age</th>
<th>Diagnosis</th>
<th>Adverse effect</th>
<th>Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>11 years</td>
<td>pseudomembranous colitis</td>
<td>Abdominal distension</td>
<td>Self-limited</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>2-year-1-month</td>
<td>Crohn’s disease</td>
<td>Consistent fever, elevate of WBC and CRP, infection</td>
<td>Antibiotic intravenously and steroid</td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>1-year-6-month</td>
<td>Crohn’s disease</td>
<td>Consistent fever, elevate of WBC and CRP, infection</td>
<td>Antibiotic intravenously</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>7 years</td>
<td>Ulcerative colitis</td>
<td>Transient fever, transient elevate of CRP, abdominal pain</td>
<td>Self-limited</td>
</tr>
<tr>
<td>5</td>
<td>F</td>
<td>10-year-9-month</td>
<td>Ulcerative colitis</td>
<td>Consistent of fever and elevate of WBC and CRP, abdominal pain</td>
<td>Antibiotic intravenously and IVIG</td>
</tr>
</tbody>
</table>
Conclusion: FMT had limited effect for Crohn’s disease and Ulcerative colitis in our preliminary clinical experience. The incidence of adverse effects of FMT was higher than reported. It should be more cautious to apply FMT with young age patients and patients with high score of disease active index.

Disclosure of interest: None Declared.
MicroRNA expression in the colonic mucosa of pediatric patients with eosinophilic colitis

Zoltán Kiss¹, Nóra Judit Béres¹, Erna Sziksz¹, Ádám Vannay¹, András Arató¹, Katalin Eszter Müller¹, Áron Cseh¹, Attila J. Szabó¹, Gábor Veres¹

¹Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary

Objectives and study: Allergic/eosinophilic colitis (EC) is a common cause of haematochezia in infants and young children. According to the current hypothesis it is a non-IgE type hypersensitivity reaction against unknown food allergens, but the pathomechanism is not well understood. Non-invasive tests are not available, and the diagnosis can be difficult in severe cases having overlapping features with Crohn’s disease (CD). The primary aim of the present study was to test whether a set of microRNAs (miRs) detected in pediatric CD patients (miR-17, -18a, -20a, -21, -99b, -125a, -126, -142, -150, -221, -223) is dysregulated also in EC, in order to find potential biomarkers. The miR set has been derived from our unpublished data and the relevant literature on the topic. The secondary aim was to analyze the expression of different miRs suggested to be important in pediatric eosinophilic esophagitis (EoE) in publicly available data (miR-20a, -21, -126, -142, -221, -223) to assess the similarities in the epigenetic factors of these two eosinophil-associated gastrointestinal diseases (EGID).

Methods: Real-time reverse transcription PCR was carried out on fresh-frozen biopsy specimen from young children with EC (EC, n=14) and control patients (C, n=10). In silico analysis was used to compare the results with publicly available miR profile data of pediatric CD and EoE patients and to retrieve potential miR-target interactions.

Results: Expression of miR-17, -18a, -20a, -21, -99b, -184, -216a, -221, and -223 was elevated in the colonic mucosa of children with EC compared to controls. However the expression of miR-150 and -559 showed decreased expression in the EC group compared to controls. Comparing the above miR expression profile to that of CD we found that the expression changes of miR-20a, -125a, -126, -142 and -150 were the opposite in EC than measured in CD. Amongst the previously reported miRs in EoE miR-20a, -21, -223, -221 expression changes were similar in EC, whereas miR-126 and -142 showed an opposite change in EC patients compared to EoE. Bioinformatics analysis of EC-related miR-target interactions revealed functional groups connected to inflammation, leukocyte activation, leukocyte trafficking and the regulation of apoptosis.

Conclusion: Our results show a characteristic difference between the miR expression of EC and CD. Differentially dysregulated miRs in EC and CD may serve as early potential biomarkers in severe form of EC. Several miRs reported to be relevant in EoE were dysregulated also in EC patients, suggesting similar epigenetic elements in the pathomechanism of these two EGID-s. The results of bioinformatics analysis suggests that amongst the targets of differentially dysregulated miRs disease specific elements can be found, therefore they may hold an important role in the pathomechanism of the disease.

This work was supported by grants OTKA-K105530, -K108688, -PD105361, LP008/2015

Disclosure of interest: None Declared
**GASTROENTEROLOGY: Cystic fibrosis and pancreatic disorders**

G-P-066

**Isolated Polycystic Pancreatic Disease In An Adolescent Of 14 Years Old**

**Case Report And Review Of Literature**

**Abdul-Monem Badran**, Fotiadou Anatoli, Kayemba Kay's Simon

1Dreux Hospital, Department of Pediatrics, Dreux, France

**Objectives and study:** Pancreatic cysts are an uncommon finding in paediatric medicine and most usually associated with inherited polycystic disease of kidney, liver, and spleen (dysontogenetic cysts). To the best of our knowledge, isolated pancreatic polycystic disease has not been reported in children. We describe here-in a case of isolated pancreatic polycystosis in an adolescent with discussion of the available literature.

**Methods:** A 14 year old female Caucasian adolescent, referred to the pediatric GI OPD of Dreux hospital (France) after the discovery of two cystic images (15 and 10 mm) on an abdomen US done for isolated upper abdominal pain persisting for ten days. Her physical examination was normal. No history of consanguinity or familial history of pancreatic, renal, hepatic, or cystic disease. Biochemical examination showed normal hepatic, renal function, ionic and CBC values. Plasmatic Lipase and Amylase were normal. The serology of Echinococcus Granulosus was negative. MRI showed a high number of pancreatic cysts of variable sizes scattered in the parenchyma, with the biggest one measuring 20 mm of diameter. No evidence of haemorrhage or inflammation was detected. No other parenchymal or ductal abnormality was seen. There were no cysts seen in the liver, spleen or kidneys. Faecal Elastase, Insuline and C peptide values were normal. Sweat Test as well as oral glucose tolerance test were negative. Genetic testing for chronic hereditary pancreatitis ou susceptibility genes did not detect any abnormality in CFTR (29 mutations), PRSS1, SPINK 1, or CTRC genes. The diagnosis of isolated polycystic pancreatic disease was retained, and periodic follow-up was started-up.

**Results:** Pancreatic cysts are broadly classified as congenital-developmental, retentional, duplication cysts, pseudo-cysts, neoplastic, and parasitic cysts. Localization in the head of the pancreas was reported in 32% of cases. In our patient, the cysts involved the entire pancreas. Congenital pancreatic cysts are generally asymptomatic, although abdominal distention, vomiting, jaundice, or pancreatitis can be observed. Most cases of congenital pancreatic cysts are associated with inherited polycystic disease of the kidney, liver, and spleen. Multiple pancreatic cysts have been described also in patients with cystic fibrosis. Multiple cysts and microcystic (serous) cystadenomas of the pancreas have also been reported occasionally in patients afflicted with von Hippel-Lindau syndrome, an autosomally dominant inherited cancer-prone disorder. MRI showed a significant interest in demonstrating the number of cysts with results comparable with those obtained by ultrasound. Also it provided an excellent tissue characterization and definition of anatomical details. Pancreatic cysts are generally asymptomatic so they require no treatment or only a symptomatic one. Indications for surgical treatment of pancreatic cysts are rare. Several modalities can be proposed like a coelioscopic fenestration in the case of macro-cystic forms.

**Conclusion:** Isolated pancreatic polycystic disease is extremely rare in children. Literature lacks information concerning the long term outcome and the modality of follow-up and treatment.

**Disclosure of interest:** None Declared
**Objective and study:** Despite the rising incidence of pediatric pancreatitis (PP) in the last decade, there are 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: 35 acute (AP), 8 recurrent acute (RAP) and 14 chronic pancreatitis (CP) cases were enrolled yet. Before genetic testing etiological factors were unidentified (idiopathic pancreatitis was found) in 20/35 (57.1%) children with AP, in 7/8 (87.5%) with RAP and in 12/14 with CP. Genetic tests have been completed for 15/35 from AP, 8/8 from RAP and 12/14. In 35 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 6 cases (3
RAP and 3 CP), in CFTR in 1 case (CP) and in CTRC in 18 cases (5 AP, 6 RAP and 7 CP). In 5 CP patients mutations in two genes were observed (3 SPINK1-CTRC, 1 PRSS1-SPINK, 1 CFTR-CTRC

APPLE-P: Just 3 patients from the 7 enrolled were met the data quality criteria. More data are required for analyses.

Conclusion: The APPLE trial is the first multicentre, prospective clinical trial on the field of PP. Genetic testing is essential to identify the etiological factors in children with pancreatitis.

Disclosure of interest: None Declared
Observational Clinical Trial About Pain IN EARly phase of Pediatric Pancreatitis (PINEAPPLE)

Dóra Mosztbacher1, Andrea Párniczky2, Fanni Zsoldos2, Anna Tóth3, Ilá Veronika4, István Tokodi5, Maisam Abu-El-Hajja6, Flora Szabo6, Boglárka Fehér1, Károly Bakó1, Gergely Tóth1, Natália Lásztity7, Zsolt Bognár2, Csaba Berczki3, Dániel Szűcs3, Noémi Vass3, Tamás Decsi8, Andrea Szentesi9, Péter Hegyi10

1Balassa János County Hospital Tolna, Department of Pediatrics, Szekszárd, Hungary
2Heim Pál Children's Hospital, Budapest, Hungary
3University of Szeged, Faculty of Medicine, Department of Pediatrics and Pediatric Health Center, Szeged, Hungary
4Dr. Kenessy 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
7University of Debrecen, Faculty of Medicine, Department of Pediatrics, Debrecen, Hungary
8University of Pécs, Faculty of Medicine, Department of Pediatrics, Pécs, Hungary
9University of Szeged, Faculty of Medicine, First Department of Internal Medicine, Szeged, Hungary
10University of Pécs, Mta-Szte Tgrrg & University of Szeged, Pécs, Szeged, Hungary

Objectives and study: The documented incidence of pediatric pancreatitis (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. Moreover, there is a large differences between the countries: the incidence decreases from the USA and Western Europe to Eastern Europe. The aim of the PINEAPPLE study is to understand the current practice of diagnosis of PP, to demonstrate the difference of the incidence of PP between the various countries based on the pancreatic enzyme measurement (PEM) and the abdominal imaging. Further to develop EBM guidelines that helps to evaluate (in a reliable and cost efficient way) the necessity of PEM and abdominal ultrasonography when a child has abdominal pain.

Methods: PINEAPPLE is a registered(ISRCTN35618458), observational, multinational clinical trial and the prestudy protocol already published (http://www.ncbi.nlm.nih.gov/pubmed/26641250). The PINEAPPLE-R subtrial is a retrospective review on children 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 occur. Until now 23644 patients records/PINEAPPLE-R and 162 patients/PINEAPPLE-P were enrolled from eight pediatric centres.

Results: PINEAPPLE-R: 8.3% (1970/23644) of the patients appearing at ER unit had abdominal pain. Only 9.7% (192/1970) of them had PEM, whereas 30% (592/1970) had transabdominal ultrasonography. Pancreatitis was diagnosed in five cases only. In case where 21.6% (157/728) PEM were performed, the incidence of pancreatitis (4/728) was six times higher, than in case where just 2.8 % (35/1242) PEM were performed (1/1242). PINEAPPLE-P: 2 pancreatitis of 162 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 could be the reason of low incidences of PP. More patients are crucially needed for PINEAPPLE-P in order to develop EBM guidelines.

Disclosure of interest: None Declared
Alpha1-antitrypsin deficiency and pancreatitis in children.

Elwira Kolodziejczyk¹, Karolina Wejnarska¹, Jaroslaw Kierkus¹, Jozef Ryzko¹, Grzegorz Oracz¹

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland

Objectives and study: Alpha1-antitrypsin (AAT) is one of the most important serum inhibitors of proteolytic enzymes such as trypsin, chymotrypsin and pancreatic elastase. There is a hypothesis that increased levels of pancreatic proteinases or a decrease in pancreatic antiproteinases can lead to pancreatitis.

The aim of our study was to evaluate the significance of alpha1-antitrypsin deficiency in children with chronic, acute recurrent and acute pancreatitis.

Methods: 83 children with chronic pancreatitis (CP), acute recurrent pancreatitis (ARP) and acute pancreatitis (AP) were enrolled into the study. Genotyping for E264V (PiS) and E342K (PiZ) variants of AAT was done. In 65% of patients (54/83) simultaneously with genetic testing, AAT serum level was measured. In view of the results as shown below it was not necessary to use statistical analysis.

Results: Only in 1 of 83 patients AAT deficiency was recognized. It was almost 13-years old, obese girl with CP, in which E342K mutation in one allele (PiZ heterozygote) and decreased alpha1-antitrypsin serum concentration were found. The first and only episode of severe AP occurred at the age of 12.6 years. The performed imaging studies (ultrasound, CT), beyond enlargement of the organ and heterogeneously hypoechoic parenchyma, revealed multiple pancreatic cysts. During ERCP biliary stones were revealed, there were no signs of CP. Due to the lack of capacity to perform endoscopic cystogastrostomy and the ineffectiveness of conservative treatment the girl was qualified for surgery - subtotal resection of the pancreas with Roux-y loop and cholecystectomy. Histopathological examination shown picture of CP- increased fibrosis, resorption, with foci of necrosis and non-specific inflammatory infiltration with abscess formation. After surgery there were no further episodes of pancreatitis, the girl requires pancreatic enzymes supplementation.

In addition to severe AP episode, elevated levels of serum transaminases and hepatic steatosis in CT imaging and liver biopsy was observed.

Conclusion: In the present study, genetic analysis of the two most common alpha1-antitrypsin deficiency alleles PiS and PiZ revealed no association between alpha1-antitrypsin genotypes and development of CP, ARP or AP, which remains in line with the results of most previous studies. In conclusion, it seems that alpha1-antitrypsin is not involved in the pathogenesis of pancreatitis in children.

Disclosure of interest: None Declared
**Microbial Colonization of Pancreatic Stents – Accidental Discovery or Reason for Concern?**

Elwira Kolodziejczyk¹, Anna Wojcieszek², Katarzyna Dzierzanowska-Fangrat², Karolina Wejnarska¹, Grzegorz Oracz²

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
²The Children's Memorial Health Institute, Department of Clinical Microbiology and Immunology, Warsaw, Poland

**Objectives and study:** Pancreatic stenting is a well-established therapeutic method in chronic pancreatitis (CP). Pancreatic duct system is considered to be sterile, because the sphincter of Oddi muscle acts as anatomic barrier between the pancreatic duct system and the duodenum, which prevents ascending of bacteria from the duodenum into the pancreatic ducts. Moreover, the pancreatic juice has an antibacterial activity. The insertion of stent into the pancreatic duct can lead to bacterial colonization of the duct. This prospective hospital-based study was designed to analyze the microbial colonization rate of pancreatic stents as well as spectrum and number of microorganisms in children with chronic pancreatitis.

**Methods:** Twenty two children with CP (13 females and 9 males; age range 6-17 years; median 12.3 years), who underwent endoscopic retrograde cholangiopancreatography (ERCP) between November 2013 and August 2015, were included into the study. Thirty seven pancreatic stents were collected and subjects to microbiological testing. During twelve ERCPs simultaneously with stents, pancreatic juice was obtained. In 2 patients without prior endoscopic intervention pancreatic juice was collected. Indwelling time ranged from 37 to 200 days, mean 136.9 days. In 25/39 (64.1%) patients antibiotic prophylaxis with carbapenem or cefoperazone with sulbactam was applied. The specimens were cultured on liquid and solid media, and incubated in both aerobic and anaerobic conditions. Isolation, identification and detection of mechanisms of antimicrobial resistance were performed by standard microbiological methods (API, NE, VITEK 2, Disc Diffusion Method according to EUCAST guidelines).

**Results:** Almost all investigated samples (50/51, 98%) both pancreatic juice and pancreatic stents showed polymicrobial growth with high microbial load 10³-10⁵ CFU/mL. The predominant microorganisms were *Escherichia coli* (55%; 28/51), *Enterococcus faecalis* (43%; 22/51), *Enterobacter cloacae* (39%; 20/51), *Streptococcus salivarius* (33%; 17/51) and *Klebsiella pneumoniae* (29%; 15/51). The distribution of isolated microorganisms in patients with pancreatic juice and pancreatic stents collected simultaneously were comparable between both investigated materials – only in 1/12 patient with polymicrobial growth from pancreatic stent, pancreatic juice occurred to be sterile. In 2 patients without previous endoscopic intervention pancreatic juice also showed a significant growth of the bacteria.

**Conclusion:** Bacteriological analysis of both pancreatic duct stents and pancreatic juice collected from children with CP revealed highly colonization rate with diverse spectrum of microorganisms. However our findings requires further investigations on large number of patients to determine the frequency of colonization and whether this fact has any clinical significance.

**Disclosure of interest:** None Declared
New ultrasonographic protocol for early diagnosis of Cystic fibrosis liver disease

Eyal Shteyer¹, Louise Stewart², Deirdre Kelly², Or Steg³, Eitan Kerem³, Moti Menachem³, Natasha Simanovski³, Michael Wilschanski³

¹Shaare Zedek Medical Center, Pediatric Gastroenterology Institute, Jerusalem, Israel
²Liver Unit, Birmingham, United Kingdom
³Hadassah-Hebrew University Medical Center, Jerusalem, Israel

Objectives and study: Cystic Fibrosis (CF) is the most common fatal genetic multisystem disorder. With increased life expectancy CF liver disease (CFLD) is now recognized as a major cause of morbidity and mortality. Sensitivity of current diagnostic tests (clinical examination and biochemistry) is insufficient to allow early detection of CFLD. The increasing use of Fibroscan detects advanced fibrosis rather than early disease. Inclusion of detailed early abdominal ultrasound (US) may facilitate earlier detection and prospective evaluation of CFLD. The aim of this study is to assess the ability of a novel US protocol (Stuart Ultrasound Scoring System (SUSS)) for early diagnosis of CFLD.

Methods: The SUSS protocol includes evaluation of liver edge and texture, size of spleen, portal tracts and hepatic vein waveform. These parameters were scored either as normal (1) or abnormal (2). In addition, the liver was categorized according to the general appearance as normal (A), bright or echogenic (B) and granular (C). A normal score is A5, and any other score is abnormal. Furthermore, portal vein and hepatic artery and vein diameter were measured. SUSS was correlated to blood tests, Aspartate transaminase to platelets ratio index (APRI score) and logistic regression was conducted.

Results: The protocol was studied in two centers. The initial study was performed on 241 CF patients (group A) and validation of the protocol on 79 patients (group B). Seventy percent of group A and 41% of group B had elevated liver enzymes. In both cohorts the SUSS score in patients with no CFLD was pathological in higher rates than expected (64% group A and 36% group B). When comparing the patients with the normal US scores and the abnormal US scores ALT, AST and GGTP was significantly higher in the abnormal score group, but only slightly higher than normal (medians of 32 vs 38 p=0.002, 20 vs 29 p=0.02, 16 vs 28, p=0.001, accordingly). There was significant association between APRI score and SUSS score.

Conclusion: This study verified the use of a novel US scoring system for CFLD. SUSS score is able to detect a patient with structural liver abnormalities which may be due to early CFLD. These patients had normal liver enzymes and were not regarded as having CFLD. Furthermore, our study underscores the problem of screening for CFLD by blood test only and implies that early detailed US should be performed in all CF patients. Early detection may lead to improved treatment and prognosis. Further evaluation of this scoring system and long term follow-up is warranted.

Disclosure of interest: None Declared
Genetic testing, MRT and Pancreatic function tests are essential in the investigation of Chronic and Recurrent Pancreatitis in Children

Fredrik Lindgren¹, Nikos Kartalis², Raphaella Pozzi-Mucelli², Thomas Mårtensson³, Matthias Löhr⁴, Thomas Casswall⁵

¹Karolinska University Hospital, Huddinge, Pediatric Gastroenterology, Hepatology & Nutrition, Astrid Lindgren’s Children’s Hospital and Department of Clinical Science, Intervention and Technology at Karolinska Institute, Stockholm, Sweden
²Karolinska University Hospital, Huddinge, Department of Radiology, Stockholm, Sweden
³Södertälje Hospital, Department of Women’s and Children’s Health, Södertälje, Sweden
⁴Karolinska University Hospital, Huddinge, Gastrocentrum, Stockholm, Sweden
⁵Karolinska University Hospital, Huddinge, Pediatric Gastroenterology, Hepatology & Nutrition, Astrid Lindgren’s Children’s Hospital, Stockholm, Sweden

Objectives and study: Few studies worldwide have been published regarding chronic (CP) and acute recurrent pancreatitis (ARP) in children and etiologies have been difficult to establish (1, 2). Recently, an international consortium, The INSPIRE (International Study group of Pediatric Pancreatitis: In search for a cure), has standardized definitions and developed a diagnostic algorithm (3). Thus, we wanted to:

a) Define our pediatric pancreatic patient cohort, by using the INSPIRE algorithm, b) classify patients into either CP or ARP, and c) identify the most likely etiologies.

Methods: Retrospective chart and radiology review of children with ARP or CP at Karolinska University Hospital, Stockholm Huddinge during 2004-2013. The diagnostic tools were: imaging (CT, MRCP, EUS, and ERCP), genetic testing (PRSS1, SPINK1, CFTR, CTRC), and pancreatic function tests; f-Elastase, Lundh’s test, MRT (magnetic resonance tomography) with secretin stimulation, f-B-glucose, and HbA1c. Two experienced radiologists, (NK and RP), re-evaluated the MRT and CT scans for signs of CP according to Mannheim and Cambridge-classification. Patients with a single episode of acute pancreatitis were excluded.

Results: Seventy patients (36 boys), with CP, were diagnosed at 0.9 - 20 years of age. Mean age 11.3 years (SD 4.9). The mean duration of follow up was 5.75 years (SD 3.3). The Mortality was 8.6 %. Etiologies were found in 89 %. The most common were genetic (20%) and biliary disease (19%), followed by typical imaging signs of AIP (13%) in a cohort of IBD-patients. There were no statistically significant age differences between genetic causes vs. other etiologies, or ARP vs. CP. Of all patients 41% had signs of exocrine -, and 16% of endocrine insufficiency. 71% were evaluated in a multidisciplinary conference. MRT was used in 94%, whereas CT in 66%, and genetic testing in 59%.

Conclusion: Genetic mutations and biliary tract diseases were the most common etiologies found. Signs of exocrine-, as well as endocrine dysfunction, was common in our cohort. Without imaging studies, it is difficult to distinguish between entities and etiologies. Earlier studies (1, 2) did not use MRT and genetic testing, and thus had a high idiopathic etiology in 75-96%. In our cohort of ARP and CP-patients, 11% were idiopathic. The complexity of the investigation and treatment of children with CP and ARP and the risk of complications requires multi-disciplinary experience. All pediatric patients with ARP and CP should be investigated with MRT, genetic testing and pancreatic function tests.


Disclosure of interest: None Declared.
Clinical experience of management of Acute Pancreatitis in children: needs to revise diagnostic criteria?

Gerarda Cappuccio¹, Valentina Fattorusso¹, Clara Coppola¹, Simona Errichiello², Luigi Martemucci²

¹Federico II University, Naples, Italy
²Santobono-Pausilipon Children’s Hospital, Naples, Italy

Objectives and study: The etiology of acute pancreatitis (AP) in children is often drugs, infection, trauma, or anatomic anomalies and presence of genetic risk factor (mutations in PRSS1, SPINK1 and CFTR gene). The diagnosis of pediatric AP requires the presence of at least two of the three following criteria: abdominal pain with or without other aspecific gastrointestinal symptoms (nausea and/or vomiting), elevated serum amylase or lipase (a threshold concentration 3 times the upper limit) and radiologic signs of pancreatitis (edema, necrosis, peripancreatic inflammation, hemorrhagia, abscessus, pseudocystis). We aim at estimating the epidemiological parameters and discussing causes and current management in a cohort of patients with AP. Another purpose is to verify the suitability of diagnostic criteria at the time of admission among pediatric population with AP.

Methods: We have retrospectively revised and collected data from 36 out 55 pediatric patients, females 19, males 17, with an average age 86 months (range 21-161 months) referred to Gastroenterology Department of Santobono Hospital, Naples for management of onset of acute pancreatitis (from 2013 to 2015). Each patient underwent anamnestic and clinical assessment, biochemical and imaging evaluation. Some patients performed genetic tests.

Results: About clinical clues 81% of patients presented with acute abdominal pain, 53% with vomiting while both signs were present in 39% of patients. Fever was detected in 25% of patients. Average values of lipase, amilase and pancreatic amilase were respectively 1260 U/L, 544 U/L, 539 U/L (normal values for lipase 13-60 U/L, amilase 10-100 U/L, pancreatic-amilase 2-39 U/L). PCR was high in 10 patients with an average value of 26 mg/L (highest value 177 mg/L). Blood glucose was within normal value but 1 case (average 91 mg/dl, from 45-216 mg/L). Genetic tests were performed in 21 patients and causative mutations were found in 24 patients. Abdomen ultrasound was performed in all patients and in at least 33% an anomaly was found (enlarged, hyperechoic pancreas, heterogeneous echotexture, dysmorphic gallbladder, peripancreatic fluid). TC of the abdomen and MRI were performed in 5 and 17 patients respectively. The mean length of hospitalization was of 12 days. 28 patients showed at admission diagnostic criteria of AP, in the other ones, criteria were fulfilled subsequently. 27 patients were treated with proton-pump inhibitors, 20 with antibiotics. Ursodeoxycholic Acid was used in 20 patients, while gabexate mesylate in 11 ones. Octreatide was never used. About the diet all patients was initially treated with avoidance of oral nutrition; 17 started with total parenteral nutrition while for none enteral feeding was used.

Conclusion: Abdominal pain, although aspecific, should recall AP in children. We confirm lipase as the biochemical hallmark for AP in pediatric patients. 8 patients did not fulfill diagnostic criteria of AP at hospital admission; these patients showed no clinical signs or mildly elevation of amilase and lipase. Despite clinical recommendation enteral feeding is not currently used in the early nutritional management of AP in children.
Combined Liver Pancreas transplant in an adolescent patient with Cystic Fibrosis - first Australasian experience

Jonathan Bishop¹, Stephen Munn², Adam Bartlett², Helen Pillmore³, Catherine Byrnes⁴, Simon Chin¹, Stephen Mouat¹, Helen Evans¹

¹Starship Children’s Hospital, Department of Paediatric Gastroenterology, Auckland, New Zealand
²Auckland City Hospital, New Zealand Liver Transplant Unit, Auckland, New Zealand
³Auckland City Hospital, Department of Nephrology, Auckland, New Zealand
⁴Auckland University, Department of Paediatrics: Child and Youth Health, Auckland, New Zealand

Objectives and study: Improvements in the care of cystic fibrosis (CF) have led to improved life expectancy related to lung disease and a coincident increase in clinically significant extrapulmonary disease manifestations. Cystic fibrosis liver disease (CFLD) encompasses a spectrum of disease, with approximately 5-10% of individuals developing biliary cirrhosis in the first decade of life. Not infrequently this results in clinically significant portal hypertension, though liver failure is a late event which rarely occurs within the paediatric age range. Liver transplant is an established therapeutic option for individuals with end stage liver disease and well maintained respiratory function. 85% of CF patients have pancreatic exocrine insufficiency and up to 34% of patients will develop CF-related diabetes (CFRD) requiring insulin, with a higher prevalence reported in individuals with coexistent CFLD. The option of combined liver-pancreas transplantation for these patients has great potential benefit, but clinical experience of combined transplantation remains limited.

Starship Children’s Hospital is the sole referral centre for Paediatric Hepatology in New Zealand (population 4.5 million). We present the first ever Australasian case of an adolescent patient with CFLD and CFRD undergoing a combined liver-pancreas transplant.

Methods: An 11 year old boy presented with lethargy, abdominal distension and bruising with minimal trauma. Clubbing and hepatosplenomegaly were noted. Investigation revealed CF (ΔF508 homozygous) and he remained under paediatric follow-up. Over the next 5 years, he developed worsening portal hypertension and hypersplenism, though without variceal bleeding. Despite aggressive nutritional support, he had longstanding growth and pubertal delay. At age 14 he developed CFRD and was commenced on insulin. He subsequently developed waning synthetic liver function, a rising bilirubin and a vitamin K resistant coagulopathy. His respiratory function remained well maintained (FEV1 86% and FVC 92% predicted).

In view of the end stage liver disease and early CFRD, he was assessed and listed for a combined liver-pancreas transplant.

Results: At 16 years and 10 months, the patient underwent a sequential liver and pancreas transplant (deceased donor whole liver graft with Roux-en-Y hepaticojejunostomy). Immunosuppression comprised basiliximab, steroids and tacrolimus.

The post-transplant course was uneventful. The patient experienced no vascular or duct issues and no episodes of liver or pancreas rejection. Strict glycaemic control was maintained in the immediate post-transplant period with a short acting insulin infusion. The insulin was discontinued on Day 5 and normoglycaemia was maintained. On day 4, a faecal elastase was normal, indicating satisfactory exocrine function.

At 1 year post-transplant, the patient remains off insulin and pancreatic enzyme supplements. He has normal liver function and his respiratory function is stable (FEV1 77% and FVC 86% predicted). He reports a markedly improved quality of life.

Conclusion: Combined liver-pancreas transplant is a viable option for individuals with CFLD and associated CFRD who require a liver transplant. The life-saving benefits of liver transplant are accompanied by significant improvements in quality of life and potential to minimise long-term complications associated with pancreatic exocrine and endocrine insufficiency.

Disclosure of interest: None Declared.
Analysis of causes and clinical course of chronic pancreatitis in children with the early-onset of the disease.

Karolina Wejnarska¹, Elwira Kołodziejczyk¹, Agnieszka Magdalena Rygieł², Katarzyna Wertheim-Tysarowska², Maciej Dadalski¹, Agnieszka Sobczynska-Tomaszewská³, Jarosław Kierkus¹, Jerzy Bai³, Grzegorz Oracz¹

¹The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
²Institute of Mother and Child, Warsaw, Poland
³Medgen, Warsaw, Poland

Objectives and study: The etiological factors of chronic pancreatitis (CP) in children vary to those described in adults. Our study was aiming to investigate the causes of CP in the youngest group of children with the disease onset before age of 5 years and evaluate the clinical presentation of the disease in these patients.

Methods: A group of 276 children with CP, hospitalized from 1988 to 2015, were enrolled in the study. Medical records of those patients were reviewed for data on presentation, diagnostic findings and treatment. All children were screened for mutations in major pancreatitis-associated genes, i.e. PRSS1, SPINK1 and CFTR.

Results: The disease onset before age of 5 years occurred in 51 patients (group 1), the later onset in 226 patients (group 2). We found no statistically significant discrepancies of etiological factors between compared groups. Children with early onset of CP turned out to have lower BMI (mean 15.79 vs. 18.11, p<0.05), however the difference was not confirmed by Cole’s ratio (mean 99.20% vs. 100.07%;NS). Patients from group 1 had more episodes of pancreatitis during follow up (mean 7.33 vs. 3.67;p<0.05) and underwent surgical procedures more frequently (25.49% vs. 8.85%;p<0.05).

Conclusion: The early- and late-onset pancreatitis turned out to have similar distribution of etiological factors, with predominance of gene mutations. The leading cause in both groups was SPINK1 p.N34S/ mutation. The clinical presentation differs in number of pancreatitis episodes and frequency of surgical intervention.

Disclosure of interest: None Declared
The clinical presentation of chronic pancreatitis in children with SPINK1 gene mutations

Karolina Wejnarska¹, Elwira Kołodziejczyk¹, Maciej Dadalski¹, Jarosław Kierkus¹, Grzegorz Oracz¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Etiological factors of chronic pancreatitis (CP) in children are diverse and include gene mutations. Although the list of genes associated with CP is constantly extending, the SPINK1 mutations remains to be one of the most frequently described genetic risk factor of CP in the Caucasian population. Our study was aiming to investigate the clinical course of the SPINK1 gene related CP in comparison with idiopathic chronic pancreatitis (ICP). Additionally we compared the clinical presentation of CP between patients heterozygous and homozygous for SPINK1 gene mutations.

Methods: A group of 277 children with CP, hospitalized from 1988 to 2015, were enrolled in the study. Medical records of those patients 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: Mutations in the SPINK1 gene were found in 66 patients (23.8%). 96 (34.7%) children had ICP. There were no relevant differences in clinical course assessed on the basis of age of the disease onset, nutritional status, number of exacerbations, calcifications on imaging or long-term complications of CP. Concerning treatment, patients with SPINK1 mutations underwent pancreatic duct stenting more often (45.5% vs. 21.9%; p<0.05), there was no significant difference in surgical procedures frequency. Among children with SPINK1 mutation, 52 (78.8%) patients were heterozygous and 14 (21.2%) were homozygous. Clinical presentation of CP was similar, the only significant discrepancy concerned the frequency of pancreatic duct stenting (38.5 % vs. 71.4%; p<0.05).

Conclusion: Children with SPINK1 mutation turned out to have similar clinical presentation of CP comparing to patients with ICP. The only difference of statistical significance concerned the frequency of pancreatic duct stenting – procedure was conducted more often in children with investigated gene alteration. Likewise, the frequency of pancreatic duct stenting was the only discrepancy of clinical course between patients homo- and heterozygous for SPINK1 mutations.

Disclosure of interest: None Declared.
Objectives and study: Cystic Fibrosis (CF) is usually related to malnutrition. However obesity has recently become a concern among children with CF. To evaluate the prevalence of obesity among children with CF and its relationship with age, sex, pancreatic insufficiency, pseudomonas colonization, lung function and genotype.

Methods: 56 children/adolescents (30 male) were evaluated. Body mass index (BMI), BMI z-score and nutritional status was assessed and classified according to the WHO BMI criteria. Lung function was assessed with Forced Expiratory Volume in 1 sec (FEV$_1$) % predicted and Lung Clearance Index (LCI). Pancreatic insufficiency (PI), pseudomonas colonization and genotype were also recorded.

Results: 56 patients with CF (mean age 9.5±4.6 years) were evaluated. 33 (58.9%) patients had normal nutritional status according to BMI z-score, 10 (17.9%) were underweight and 13 (23.2%) were overweight/obese. FEV$_1$ % was higher among overweight/obese patients but without statistical significance (112.6±13.5 vs. 100.73±22.7 in normal individuals and 96%±16.5 in malnourished children, p=0.07). LCI was significantly different across the weight categories (7.5±1.3 in overweight/obese individuals vs. 10.3±3.1 in normal weight patients and 10.86±2.7 in malnourished patients p=0.02). Nutritional status was significantly associated with PI, pseudomonas colonization and genotype (p<0.05). 7/13(52.8%) of the overweight/obese patients were pancreatic insufficient, 1/13(7.7%) was ΔF508 homozygote, 7/13(53.8%) were ΔF508 heterozygote. None of them was colonized with Pseudomonas Aeruginosa.

Conclusion: The prevalence of overweight and obesity in our CF center is high, although a significant number of the patients were pancreatic insufficient. Overweight and obesity were associated with better lung function. However, the benefit of increased lung function among this patient group needs to be balanced against the known health risks of obesity.

Disclosure of interest: None declared.
Association of TNF-α Gene Variants With Clinical Manifestation of Cystic Fibrosis Patients of Iranian Azeri Turkish Ethnicity

Mandana Rafeey1, Aziz Khorrami2, Mortaza Bonyadi2

1Tabriz University of Medical Sciences/Liver & Gastrointestinal Research Center/Children Hospital, Pediatric Gastroenterology & Hepatology, Tabriz, Iran
2Faculty of Natural Science, University of Tabriz, Iran

Objectives and study: Cystic fibrosis (CF), a life-limiting autosomal recessive disorder, is considered a monogenic disease that is caused by mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene. According to several studies, mutation analysis of the cystic fibrosis transmembrane conductance regulator (CFTR) gene alone is insufficient to predict the phenotypic manifestations observed in cystic fibrosis (CF) patients. In addition, some patients with a milder CF phenotype do not carry any pathogenic mutation. Tumor Necrosis Factor-alpha (TNF-α) contributes to the pathophysiology of CF by causing cachexia. There is a reverse association between TNF-α concentration in patient’s sputum and their pulmonary function. To assess the effect of non-CFTR genes on the clinical phenotype of CF, two polymorphic sites (-1031T/C and -308G/A) of the TNF-α gene, as a modifier, were studied.

Methods: Focusing on the lung and gastrointestinal involvement as well as the poor growth, we first investigated the role of TNF-α gene in the clinical manifestation of CF. Furthermore, based on the hypothesis that the cumulative effect of specific alleles of multiple CF modifier genes, such as TNF-α, may create the final phenotype, we also investigated the potential role of TNF-α in non-classic CF patients without a known pathogenic mutation. In all, 80 CF patients and 157 healthy control subjects of Azeri Turkish ethnicity were studied by the PCR-RFLP method. The chi-square test with Yates’ correction and Fisher’s exact test were used for statistical analysis.

Results: The allele and genotype distribution of the investigated polymorphisms, and their associated haplotypes were similar in all groups.

Table:

<table>
<thead>
<tr>
<th>SNP</th>
<th>Allele Frequency and Clinical Features of Patients with 4Fos Mutation in Homozygous Status 10</th>
<th>P Value</th>
<th>Allele Gastrointestinal Involvement</th>
<th>P Value</th>
<th>Allele Poor Growth</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>-1031T/C</td>
<td>G</td>
<td>0.99</td>
<td>G</td>
<td>1</td>
<td>G</td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>A</td>
<td></td>
<td>A</td>
<td></td>
<td>A</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2G(96.6)</td>
<td></td>
<td>10(33.7)</td>
<td>1(63)</td>
<td>15(53.9)</td>
<td>3(62.5)</td>
</tr>
<tr>
<td>Mild</td>
<td>2A(33.4)</td>
<td></td>
<td>2(63.3)</td>
<td></td>
<td>2(46.2)</td>
<td></td>
</tr>
<tr>
<td>308G/A</td>
<td>T</td>
<td></td>
<td>T</td>
<td></td>
<td>T</td>
<td></td>
</tr>
<tr>
<td></td>
<td>C</td>
<td></td>
<td>C</td>
<td></td>
<td>C</td>
<td></td>
</tr>
<tr>
<td>Severe</td>
<td>2T(76.5)</td>
<td></td>
<td>10(33.3)</td>
<td>1(63)</td>
<td>13(43.8)</td>
<td>2(46.2)</td>
</tr>
<tr>
<td>Mild</td>
<td>2C(23.5)</td>
<td></td>
<td>2(63.3)</td>
<td></td>
<td>2(46.2)</td>
<td></td>
</tr>
</tbody>
</table>

a Single nucleotide polymorphisms, T and C are two alleles of 1031T/C polymorphism and G and A are two alleles of 308G/A. T and C are wild type alleles, whereas G and A are mutant alleles (M).
Conclusion: There was no evidence that supported the association of TNF-α gene polymorphisms with non-classic CF disease or the clinical presentation of classic CF

Disclosure of interest: None Declared
Gender gap in clinical presentation of cystic fibrosis patients in Azeri Turkish populations

Mandana Rafeey, Lila Vahdi
1Tabriz University of Medical Sciences/Liver & Gastrointestinal Research Center/Children Hospital, Pediatric Gastroenterology & Hepatology, Tabriz, Iran
2Liver & Gastrointestinal Research Center, Tabriz University of Medical Sciences, Gastroenterology, Tabriz, Iran

Objectives and study: We aimed to investigate, gender gap in clinical presentations of cystic fibrosis patients in Iranian Azeri Turkish populations.

Methods: Data of cystic fibrosis patients who admitted at Educational and Treatment referral Children's hospital and Medical Genetic Laboratory in Tabriz, Iran for Azeri Turkish population from 2001 to 2014 was obtained. Parameters of age, genotype, clinical presentations at time onset, clinical presentations at time diagnosis, and clinical presentations at lifespan, were calculated for males and females by descriptive analysis. The association of gender with these variables was studied using a logistic regression, Chi-square or Fishers Exact test, and Independent-Samples T test by SPSS .18. Odds ratio with a confidence interval 95% and a p-value less than 0.05 were considered significant.

Results: Data were collected for 331 patients, who were 191(57.7%) males and 140 (42.3%) females with a significant difference (P=0.001). Age duration differed between genders while males and females had focused further, under 9 years and 4 years, respectively. Females were 0.51 times at risk for occurrence of ∆F508 mutation. There was a significant difference between gastrointestinal and nutritional features with sex at lifespan, females were 0.47 times more likely to develop gastrointestinal and nutritional abnormalities (P = 0.04). The risk of infertility in males was approximately two times more than females (p= 0.02). In contrast, females were confronted 53 % with the risk of intestinal problems (p = 0.04).

Table1: Demographic characteristics of the CF-patients.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Male</th>
<th>Female</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Numbers (%)</td>
<td>191(57.7)</td>
<td>140(42.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age &quot; mean&quot;</td>
<td>7.11</td>
<td>6.24</td>
<td>0.3</td>
</tr>
<tr>
<td>Age &quot; median (IQR)&quot;</td>
<td>5.06 (0.42-43 )</td>
<td>4.40(0.62-31 )</td>
<td></td>
</tr>
<tr>
<td>Positive for genetic testing</td>
<td>111(56.3)</td>
<td>86(43.7)</td>
<td>0.2</td>
</tr>
<tr>
<td>Positive for ∆F508</td>
<td>12(29.3)</td>
<td>29(70.7)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

- All age has been shown based on year. Data are " mean," median (IQR), or number (%). Age For CF-patients alive and rest ages for alive and dead CF-patients have been considered.

Conclusion: We found gender gap in clinical parameters in our CF population. This comparison indicates that prevalence of this disease is higher in males in our region and males showed clinical manifestations with a delayed time than females. Median age in males was higher than females. Gastrointestinal symptoms were predominant in females than males and respiratory symptoms had a higher prevalence in males than females at the time diagnosis. At lifespan, the prevalence of infertility and intestinal symptoms were higher in males and females, respectively than other sex. These findings indicating a gender gap in our region and Future studies need to establish the additional differences and reasons for gender gap.

Disclosure of interest: “None Declared”.
Clinical practice in acute pancreatitis in a prospectively collected pediatric cohort.

Natalia Lasztity¹, Andrea Párniczky², Dóra Mosztbacher², Anna Tóth³, Anna Demcsák⁴, Balázs Németh⁵, Andrea Szentesi³, Gergő Tóth⁶, Dániel Szűcs⁴, Nóémi Vass⁴, Csaba Berczki⁴, Veronika Illich Czelecz⁸, Judit Czelecz⁸, Csilla Andorka⁹, Gábor Veres⁹, István Tokodi¹⁰, László Gárdos¹¹, Erika Tomsits¹², András Tárnok¹³, Ildikó Gathy¹⁴, Péter Hegyi¹⁵

¹Heim Pál Children's Hospital, Gastroenterology, Budapest, Hungary
²Heim Pál Children's Hospital, Budapest, Hungary
³János Balassa County Hospital, Department of Pediatrics, Szekszárd, Hungary
⁴University of Szeged, Department of Pediatrics and Pediatric Health Center, Szeged, Hungary
⁵University of Szeged, First Department of Internal Medicine, Szeged, Hungary
⁶János Balassa County Hospital, Department of Pediatrics, Szekszárd, Hungary
⁷Dr. Konessey Albert Hospital, Department of Pediatrics, Balassagyarmat, Hungary
⁸Bethesda Children's Hospital, Budapest, Hungary
⁹Semmelweis University, First Department of Pediatrics and Pediatric Health Center, Budapest, Hungary
¹⁰Fejér County Hospitals, Department of Pediatrics, Székesfehérvár, Hungary
¹¹Zala County Hospitals, Department of Pediatrics, Zalaegerszeg, Hungary
¹²Semmelweis University, Second Department of Pediatrics and Pediatric Health Center, Budapest, Hungary
¹³University of Pécs, Department of Pediatrics and Pediatric Health Center, Pécs, Hungary
¹⁴Szabolcs-Szatmár-Bereg County Hospitals, Jósa András University Teaching Hospital, Nyíregyháza, Hungary
¹⁵University of Szeged; University of Pécs; Mta-Szte Translational Gastroenterology Research Group, First Department of Internal Medicine; Institute for Translational Medicine & 1st Department of Medicine Pécs, Szeged, Pécs, Hungary

Objectives and study: Acute pancreatitis is an emerging problem in childhood. Despite of the increasing incidence, data regarding the optimal management and clinical practice are still lacking. We have developed one of the first EBM guidelines in pediatric pancreatitis, however most of the treatments suggestions were based on adult literature data. Our aim was to prospectively collect uniform clinical data from children suffering from acute pancreatitis (AP).

Methods: In the National Registry of Hungarian Pancreatic Study Group 39 children suffering from acute pancreatitis were enrolled from 12 centres between 2012-2015. Based on the modified Atlanta criteria 85% of the AP patients had mild and 15% moderate episodes, no severe AP or death was observed. The mean age was 12.68 (range 3-18) years, 23 girls and 16 boys were enrolled. Please copy and paste the corresponding text here.

Results: The average hospitalization was 12.76±1.83 days in mild and 28.53±11.84 days in moderate AP. As suggested by the guidelines all of the children received intravenous fluid (IVF) in the first 24-48 hours of the treatment. Aggressive fluid replacement therapy on admission was given in 4/39 cases. Wide diversity was seen in the type of the administered IVF (normal saline, saline with lactate or dextrose 5%). Children were nil per os (starving) not longer than 48 hours and enteral nutrition, independently from the severity, was started in 16/39 (41%) cases. Nasogastric feeding were introduced in 1/39 cases. Total parenteral nutrition were administered in 1/39 cases. All patients with moderate AP (6/39 children) received antibiotic therapy (ciprofloxacin, cefuroxim, ceftriaxon). Minor analgetics were introduced in 15/39 cases, and in 7/39 cases PPI were given.

Conclusion: Pediatric AP seems to be less severe than adults AP. The large diversity in the management of the disease confirms both the lack and need of EBM guidelines in children. International, multicentre, prospective clinical trials are crucially needed to move forward in pediatric AP.

Disclosure of interest: None Declared.
Pancreaticobiliary maljunction in children presenting with severe abdominal pain and icterus

Sinan Sarı¹, Bulent Odemis², Onur Ozen³, Neslihan Gürcan Kaya ⁴, Aydin Dalgıç⁵, Buket Dalgıç¹

¹Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
²Türkiye Yüksek İhtisas Training and Research Hospital, Gastroenterology and Hepatology, Ankara, Turkey
³Gazi University, Pediatric Surgery, Ankara, Turkey
⁴Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
⁵Gazi University, Department of General Surgery, Ankara, Turkey

Objectives and study: Pancreaticobiliary maljunction (PBM) is a congenital malformation in which the pancreatic and bile ducts join anatomically outside the duodenal wall. Early diagnosis and timely treatment is important. We aim to describe the clinical and laboratory characteristics of patients with PBM.

Methods: We conducted retrospective analysis of children who were diagnosed with PBM at our institution between October 2012 and December 2015 based on clinical, laboratory, endoscopic and radiological features. Diagnostic criteria for PBM was accepted as an abnormally long common channel (≥ 6mm) and/or an abnormal union between the pancreatic and bile ducts on cholangiography (ERCP or MRCP). Choledochal cysts were classified according to the Todani classification.

Results: Seven patients (5 male, 2 female) diagnosed with PBM. The median age of the patients was 8.5 years old (range 4.5 – 15). All of the patients had pancreatitis and six of them presented with cholangitis. The laboratory findings showed at table 1. ERCP and MRCP were performed to all patients. Concomitant gallstone were observed three of them and choledochal cysts 6 of them. Sphincterotomy was applied to all patients and protein plug were drained during ERCP. Pancreatitis episodes were decreased after ERCP. Hepaticojejunostomy with Roux-en-Y anastomosis was performed to two patients because of recurrent pancreatitis and cholangitis episodes and the risk of developing cholangiocarcinoma.

Table:

<table>
<thead>
<tr>
<th>Patient No</th>
<th>Age, year</th>
<th>Sex</th>
<th>AST, IU/L</th>
<th>ALT, IU/L</th>
<th>GGT, IU/L</th>
<th>Total bilirubin, mg/dl</th>
<th>Direct bilirubin, mg/dl</th>
<th>Amylase, IU/L</th>
<th>Lipase, IU/L</th>
<th>Choledochal cyst type</th>
<th>Common channel length, mm</th>
<th>Surgical therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>6</td>
<td>M</td>
<td>789</td>
<td>771</td>
<td>618</td>
<td>5.4</td>
<td>3.4</td>
<td>1173</td>
<td>2151</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>5.5</td>
<td>M</td>
<td>558</td>
<td>306</td>
<td>210</td>
<td>4.0</td>
<td>3.4</td>
<td>1022</td>
<td>-</td>
<td>1</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>8.5</td>
<td>M</td>
<td>200</td>
<td>170</td>
<td>322</td>
<td>5.8</td>
<td>3.6</td>
<td>1625</td>
<td>4196</td>
<td>-</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>4</td>
<td>15.5</td>
<td>F</td>
<td>75</td>
<td>212</td>
<td>751</td>
<td>5.2</td>
<td>4.3</td>
<td>474</td>
<td>258</td>
<td>1</td>
<td>21</td>
<td>+</td>
</tr>
<tr>
<td>5</td>
<td>4.5</td>
<td>M</td>
<td>380</td>
<td>311</td>
<td>407</td>
<td>7.0</td>
<td>4.4</td>
<td>233</td>
<td>1732</td>
<td>1</td>
<td>12</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>12</td>
<td>F</td>
<td>82</td>
<td>271</td>
<td>271</td>
<td>5.0</td>
<td>3.9</td>
<td>423</td>
<td>512</td>
<td>4</td>
<td>9</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>11.5</td>
<td>M</td>
<td>26</td>
<td>9</td>
<td>42</td>
<td>0.4</td>
<td>0.1</td>
<td>1751</td>
<td>843</td>
<td>1</td>
<td>23</td>
<td>+</td>
</tr>
</tbody>
</table>

M, male; F, female
Conclusion: PBM is an important cause of recurrent pancreatitis and cholangitis in childhood. Early detection, diagnosis and treatment required for prevent biliary tract complications including biliary stones, or biliary tract malignancy. PBM should be kept in mind in childhood cholangitis and pancreatitis.

Disclosure of interest: “None Declared”
Genetic influence over vitamin d deficiency and bone lose in patients with cystic fibrosis

Tatjana Jakovska-Maretti

1University Pediatric Clinic, Skopje, Macedonia

Objectives and study: Reduced bone mass density (BMD) is frequent in patients with cystic fibrosis (CF). Pathogenesis of CF bone disease is multifactorial. Imbalance between bone formation and degradation in cystic fibrosis (CF) has become an important issue for developing osteopenia. Genetic and environmental factors may play a role in determining the variability of bone mass. Aim: To determine the prevalence and identify determinants of reduced BMD in CF patients.

Methods: The study included 80 CF patients (range 5-36y.). BMD was measured via dual energy-ray absorptiometry (DXA) scans with spinal scores recorded. Vitamin D level was assessed by plasma 25OHD levels (<15 ng/ml) was defined as deficiency. Serum osteocalcin (OC), CTX, 25OHD and PTH were determined by electrohemiluminiscent method.

Results: 50 % of the CF patients with PI had serum vitamin D >20 ng/ml (range 10-44) with no difference of age. There was a significant difference for 25OHD between CF and healthy controls (p<0.05). Low bone mineral density (Z score < -1SD) was found in 31.25% patients and in 10% of them BMD was below – 2SD. 42 CF patients were homozygote for ΔF508 mutation, from them 26.2% have lower BMD (-0.43±0.99SD) and 25OHD was <15 ng/ml in 21.4%. In group with heterozygote for ΔF508 (28 CF patients) low BMD have 32.1% (-0.53±1.13SD), and 25OHD < 15ng/ml have 39.2 %. Ten CF patients have other mutations, 50% have low BMD (-0.45±1.2SD). OC in prepubertal CF patients correlated significantly with the controls indicating a decreased formation rate whereas resorption rate was normal. No significant correlation was found between COLIA1, ESR1 and VDR polymorphisms and BMD. Patients with low BMD had worse BMI, FEV1 and more severe symptoms of CF.

Conclusion: Our results suggest that bone turnover in CF is impaired (bone formation was decreased in children). Reduced bone mineral density in cystic fibrosis is associated with a number of factors including ΔF508 genotype, deficiency of vitamin D, lung disease severity and malnutrition. There was no evidence that the genes under study may modulate bone phenotype in CF.

Disclosure of interest: “None Declared”.
Videocapsule endoscopy confirms the presence of active Crohn's disease in children where magnetic resonance enteroscopy is normal or inconclusive, resulting in subsequent changes of disease management

Alexandra Bobarnac¹, Colette Deslandres², Martha H. Dirks²

¹Chc Esperance, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Montegnee, Belgium
²Chu Sainte Justine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Montreal, Canada

Objectives and study: Both videocapsule endoscopy (VCE) and magnetic resonance enteroscopy (MRE) are key points in classification of the type and severity of inflammatory bowel disease (IBD). In the paediatric population, the growth and puberty delay are essential outcomes in addition to stricture and fistulae development. The ability to accurately assess the small bowel (SB) is crucial for determining optimal patient management. MRE is the current standard of care for disease cartography. VCE recognition of new disease locations in active Crohn's disease may offer earlier and more complete diagnosis, and influence management. Clinical trials of comparison of the 2 techniques prospectively have been limited.

Evaluate the accuracy of VCE in diagnosis of small bowel Crohn’s disease in comparison with MRE, in pediatric patients, and the impact on management.

Methods: Pediatric, retrospective, monocentric study in which we included patients with suspected active Crohn’s disease (new diagnosis or relapse), or IBDU (IBD-unclassified–indeterminate colitis) who had a negative or inconclusive ileocolonoscopy with biopsies, esophagogastroduodenoscopy with biopsies, who had undergone both a VCE and MRE within 12 months from January 2012 to July 2015. 51 patients were identified, which were divided into 2 groups. The indications for VCE in this patients were: suspected IBD, suspected relapsed Crohn disease (CD) or undetermined inflammatory bowel disease (IBDU). All patients had complete endoscopic workup normal or inconclusive for CD. Both exams were done in less then 3 months (32 patients, Group 1) or 3-12 months (19 patients, Group 2) before VCE. For all patients we compared the diagnosis and therapeutic changes after VCE and MRE.

Results: For all 51 patients, MRE couldn't detect CD lesions in 16 (31.4%) cases. 40.6% of patients from Group1 and 15.8% from Group 2, had typical CD lesions on VCE misted by the MRE. The results of VCE alone diagnosed 10 new cases of CD, changed the diagnosis from IBD-U to CD in 1 case and identified 5 cases of active or relapsed CD. For 46.9% patients from Group1 and 63.2% from Group 2, VCE confirmed the absence of CD when the MRE was normal or inconclusive, reassuring the patient’s families.

In the Group1, following the VCE, 6(18.8%) patients started immunomodulators (IM), 1(3.1%) had IM escalade, 5(15.3%) started biologics (B), 1 (3.1%) biologic dose escalade and 2 (6.3%) stopped the treatment. After MRE 3(9.4%) started IM, 2(6.3%) started biologics, no escalade of IM or B. In the Group2, after VCE, 4(21.1%) started B, 3(15.8%) IM, no patient had therapy dose increase. After MRE, 4(21.1%) started IM, no other changes were made after this exam. In all patients, VCE led to a change of the therapeutic decision for 80.4% cases. No complications were noted during the VCE exams.

Conclusion: VCE is an important diagnosis tool in the assessment of the SB in IBD and should be the gold standard for SB CD diagnosis in children. VCE offer a better view of the mucosal lesions cartography and severity. VCE results have a direct impact on management of the disease. Cost analysis on a prospective basis of VCE as first choice in the diagnostic pathway is needed.

Disclosure of interest: “None Declared”.

GASTROENTEROLOGY: Endoscopy

G-P-083
Emergency upper gastrointestinal endoscopy in children in district general hospitals in the UK: time for a rethink?

Amit Saha1, Bim Bhaduri2

1 Kings College Hospital NHS Trust, Paediatric Hepatology, Gastroenterology and Nutrition, London, United Kingdom
2 Maidstone and Tunbridge Wells Hospitals NHS Trust, Department of Paediatrics, Maidstone, United Kingdom

Objectives and study: Emergency upper gastrointestinal endoscopy in district general hospitals (DGHs) in the UK is mainly undertaken involving the management of acute gastrointestinal bleeds in adults. The advent of the European Working Time Directive has seen the gradual disappearance of on-call rotas in the DGHs for patients with acute bleeds in favour of alternative arrangements, usually through the development of managed clinical networks. Its provision and applicability in children in DGHs in the UK is still evolving. We report a case of a two year old boy who was admitted to a DGH with acute ammonia ingestion who underwent an emergency endoscopy by a consultant paediatric gastroenterologist. To the best of our knowledge, this is the first reported case of its kind, and prompts the need for a wider discussion on the provision of such services for children in DGHs in the UK.

Methods: A two year old boy presented to the local district general hospital after having accidentally ingested a household cleaning solution, the main ingredient of which was ammonium hydroxide. This was promptly noticed by his parents and within a few seconds they removed the bottle, rinsed his mouth out with water and gave him some milk to drink. He however was noted to be drooling, and his parents rushed him to the nearest accident and emergency department. Because of the history of ingestion of a corrosive alkali, an emergency endoscopy under general anaesthesia was undertaken by a consultant paediatric gastroenterologist, with an adult upper GI surgeon on standby.

Results: The endoscopy revealed areas of significant corrosion, ulceration and bleeding in the oesophagus and the stomach. There was no corrosive damage seen in the duodenum. The procedure was uneventful, and the child was commenced on treatment with intravenous analgesia, omeprazole and oral sucralfate. He made good clinical progress and within 48 hours of admission, he was back to his normal self, eating and drinking normally, and was discharged home. A repeat endoscopy and an upper GI contrast study was planned after review in a few days time.

Conclusion: Ingestion of household solutions is usually accidental and commonly occurs in children. It can cause immediate pain with burning of the mouth, throat and stomach, followed by abdominal pain, vomiting, haematemesis and dyspnoea. Patients can develop swallowing difficulty and in severe cases haemorrhagic or hypovolemic shock and airway obstruction from laryngeal oedema. Gastric or oesophageal perforation may occur in severe cases from ulceration. Stricture formation is a potential late complication, this occurs between 2 weeks and 2 months post exposure.

Urgent assessment of the airway is crucial, a supra/epiglottic burn with oedema can lead to airway obstruction and early intubation is indicated. Investigations should include early endoscopy but this should be avoided between 5-15 days post exposure as this is when the oesophagus is at its weakest. Late onset sequelae must be managed by specialist paediatric gastroenterologists.

In the child described above, an emergency endoscopy was undertaken within a few hours with prompt initiation of treatment. Early endoscopy helps identify the extent of damage which can guide initial management and also predict long term sequelae. The provision of paediatric emergency endoscopy services in UK district general hospitals remain ill defined and is a subject of discussion.

Disclosure of interest: None Declared.
Biopsy-induced duodenal hematoma is a rare complication favored by hematological disorders

Anais Sierra¹, Emmanuelle Ecochard-Dugelay¹, Marc Bellaiche¹, Bogdana Tilea², Hélène Cavé³, Jerome Viala¹

¹Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris, Departments of Pediatric Digestive and Respiratory Diseases, Paris, France
²Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris, Pediatric Radiology Department, Paris, France
³Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris + Paris-Diderot University + Inserm, Genetics Department + Umr_s1131, Paris, France

Objectives and study: Intraduodenal hematoma (IDH) is an uncommon complication of endoscopic duodenal biopsy which can cause severe obstruction of digestive, biliary or pancreatic tracts. We aimed to analyze the risk factors and the outcome of biopsy-induced IDH in children.

Methods: Between 2010 and 2014, a retrospective chart review was conducted in all children under 18 years of age treated for an IDH. We collected data in our tertiary pediatric center and compared them to controls matched for age, sex and pathology.

Results: Among 2061 upper non-therapeutic endoscopies with duodenal biopsy, 7 IDH occurred in 6 children suspected of graft-versus-host-disease after bone marrow transplantation and in 1 Noonan patient. After a median delay of 48 hours, patients developed an intestinal obstruction, with abdominal pain and vomiting. The diagnosis was confirmed by ultrasound or CT scan. An acute pancreatitis was associated in 3/7 patients. Conservative treatment allowed complete resolution in all patients.

Conclusion: IDH is not a rare complication of endoscopic duodenal biopsy which occurs especially in patients with bone-marrow transplantation. Endoscopists should be especially careful during the duodenal biopsy procedure in these patients. With no reported early perforation due to post-biopsy IDH, the prognosis is good and conservative management generally leads to resolution of the symptoms in 2-3 weeks.

Disclosure of interest: None
A Rare Cause of Iron Deficiency Anemia: Phacomatosis Pigmentovascularis

Asuman Karhan¹, Sibel Ersoy Evans², Pelin Memis³, Hulya Demir¹

¹Hacettepe University, Pediatric Gastroenterology, Ankara, Turkey
²Hacettepe University, Faculty of Medicine, Dermatology, Ankara, Turkey

Objectives and study: Phacomatosis pigmentovascularis (PPV) is a rare congenital disorder characterised by cutaneous vascular and melanocytic lesions. PPV may affect many organ systems and clinical expression may have a wide variability. We report a case of a four-year-old girl who has PPV and was referred to our department due to iron deficiency anemia. This four-year-old girl was diagnosed with phacomatosis cesioflammea (a subgroup of PPV) as she had nevus of ota, nevus flammeus, mongolian spots and nevus anemicus. A blood count test performed due to pallor and heart palpitations and was consistent with anemia as her hemoglobin level was 4.6 g/dl. The patient was thoroughly investigated for anemia, and laboratory tests were consistent with iron deficiency anemia. The patient received an erythrocyte transfusion and iron therapy over three months. Control blood tests showed that the patient was still anemic, even after given iron treatment. An occult blood test with stool was positive. The patient referred to our department with iron deficiency anemia. Endoscopy was performed to investigate the cause of the anemia. An upper endoscopy revealed vascular tortuosity, telangiectasia in the stomach and fragile mucosa. A Doppler ultrasound was performed to determine whether portal venous abnormalities existed, but the ultrasound was normal.

Conclusion: PPV is a rare disorder which coexistence of a pigmented nevus and cutaneous vascular malformations. The diagnosis of this syndrome is primarily clinical and classified into five main groups. To our knowledge, this is the first case of phacomatosis pigmentovascularis in which the patient displays symptoms of iron refractory anemia due to occult gastrointestinal bleeding from vascular lesions in the stomach and the second part of the duodenum.

Disclosure of interest: We have no conflict of interest.
Granular cell tumor of Esophagus in pediatric population of a single center.

Bauraind Olivia¹, Dupont Pierre², Alexandra Bobarnac¹, Bury Françoise¹, Colinet Stephanie¹, Paquot Isabelle¹, Massart Brigitte³

¹Chc, Paediatric Gastroenterology, Liege, Belgium
²Chc, Adult Gastroenterology, Liege, Belgium
³Chc, Anatomopathology Department, Liege, Belgium

Objectives and study: Review (from 04/2011 to 03/2015) of granular cell tumor of esophagus in a pediatric population of a single center. Granular cell tumors (GCT) are rare tumors arising from neurogenic mesenchymal stem cells and can occur in a multitude of anatomic locations and tissue types. 2% of GCT are localized in the esophagus. Granular cell tumor of esophagus are rarely reported in the pediatric population.

Methods: Retrospective study (from april 2011 to march 2015) of 1832 upper GI endoscopies in a pediatric population in a single center.

Results: Two cases of esophagus granular cell tumor (or Abrikossof tumor) are described.

1rst case: a 15-year-old girl was complaining of persisting nausea. Endoscopy showed a yellow intramural lesion of 1 cm at 25 cm from the mouth suggesting granular cell tumor of the esophagus. Duodenal ulcer was also visualised. Histology confirmed the diagnosis of CGT and diffuse cytoplasmic immunoreactivity for PS100 antigen was shown. Ulcus was treated with PPI. At 18 months of follow-up she has no complain of dysphagia or nausea.

2nd case: a 17-year-old girl with developmental delay present recurrent pain when antiH2 (ranidine) was discontinued. Endoscopy showed a yellow nodular lesion at 27 cm from the mouth suggesting CGT and oesophagitis grade A. On echoendoscopy, a hypoechoic submucosal lesion of 11 mm was well limited, with no infiltration of the muscular layer and with no adenopathy. Histology confirmed the diagnosis with diffuse cytoplasmic immunoreactivity for PS100 antigen. A bariumesophagram was normal. At follow-up, she was not developing dysphagia. An endoscopic ultrasound was performed two years later and showed the lesion with the same characteristics and dimensions.

Conclusion: The incidence of esophageal granular cell tumor in our pediatric population is 0,1 %. Most patients are asymptomatic, as our 2 cases, but dysphagia has been described in adults and in an adolescent girl. The endoscopic appearance of yellow intramural lesion is typical. Diagnosis may be confirmed by endoscopic ultrasound of a hypoechoic submucosal lesion. Histology shows granular cells which are PS100 positive on immunohistochemistry. Those tumors are usually benign, with only 2% reports of malignancy in mixed-age studies. Therefore, if the patient is asymptomatic, surgical excision is not recommended and follow-up with endoscopic ultrasonography on every 2 years is advised.

Disclosure of interest: None declared
Use of percutaneous endoscopic gastrostomy in children with primary neurologic disease in the last 10 years

Carlos Ruiz Hernández¹, Belinda García¹, Pablo Ercoli¹, Ecaterina Julio¹, Marcela Alarcón¹, Esperanza Castejón¹, Javier Martín¹, Sergio Pinillos¹

¹Sant Joan de Deu Hospital, Gastroenterology and Nutrition, Barcelona, Spain

Objectives and study: To describe the evolution of patients with primary neurological disease undergoing PEG and compare with patients with other pathologies.

Methods: A descriptive and retrospective review was performed on patients undergoing PEG in the Gastroenterology department in a third level Paediatric Hospital, during 2004-2014. There were included patients younger than 18 years at the time of PEG placement with a follow-up of ≥ 3 months. Two groups of patients were compared. One group with neurological disease (Group A = 105) and another with other pathologies such as digestive, metabolic, oncologic, cardiac, and respiratory diseases (Group B = 105). In both groups the following variables were analyzed: PEG indication such as oropharyngeal dysphagia (OD) and failure to thrive, use of nasogastric tube (NGT) as nutritional support prior to PEG, GERD symptoms before and after PEG (vomiting, irritability, poor feeding, nocturnal cough), need for anti reflux surgery (Nissen type) after PEG due to the failure of medical treatment in GERD. Frequency table with percentages was used to describe categorical variables. The comparison of numerical variables between the two groups was performed by Student test.

Results: Out of a total of 210 patients, 53.3 % (n = 112) were male, with average age of 4.5 years (range 1-17 years). Regarding the indication of PEG, the OD in group A was more prevalent with 76 % (n = 80) than in group B 48.5 % (n = 51) (P = 0.001); unlike with failure to thrive in Group A 22 % (n = 23) and group B 43 % (n = 45) (P = 0.001). The use of NGT as nutritional support was slightly more frequent in group A 71 % (n = 65) than in group B 67% (n= 64) (P = 0.009). GERD symptoms prior to PEG placement is mostly observed in the group A 28.5 % (n = 30) than in group B 15% (n = 16) (P = 0.003); as well as GERD symptoms after PEG placement was more common in group A 39.8 % (n = 41) Group B 16.5 % (n = 17) (P = 0.001). Regarding the need and risk of requiring placement of PEG after anti reflux surgery (Nissen type), no statistical association between the two groups (group A 26 % vs group B 4.7 %) (P = 0.91) was found. The PEG was withdrawn because of the improvement of clinical condition, in a lower percentage in group A 13.3 % (n = 14) than in group B 27 % (n = 28) (P = 0.03). While the use of prophylactic antibiotics prior to PEG was similar in both groups (group A vs group B 62 % vs 68 %); no statistical difference in the risk of immediate complications was found between group A 11.4 % (n = 12) and group B 16 % (n = 17) (P = 0.32); but increased risk of late complications was observed in group A 36 % (n = 38) compared to group B 19 % (n = 20) (P = 0.005)

Conclusion: In children with neurological disease, the DOF is the main indication for PEG. Even though GERD symptoms before and after PEG placement are more frequent than in patients with other diseases, the need for anti reflux surgery remains the same, regardless of the condition of each child. In the long term, a higher risk of late complications and prolonged dependency on gastrostomy appears in the group with neurological disease.

Disclosure of interest: “None Declared”.
Esophageal eosinophilia in pediatrics endoscopies after ten years of analysis

Eríca Rezende¹, Matheus Mickael Neves Rodrigues Lopes¹, Lara Oliveira Gonçalves¹, Cristina Palmer Barros¹, Rogerio Melo Costa Pinto², Gesmar Rodrigues Silva Segundo¹

¹Uberlandia Federal University, Pediatrics, Uberlandia, Brazil
²Uberlandia Federal University, Mathematics, Uberlandia, Brazil

Objectives and study: The purpose of this study and verify the presence of esophageal eosinophilia in the last 10 years in endoscopies performed in children in a Tertiary Hospital and the seasonal distribution in the evaluated months

Methods: This is a retrospective, descriptive, and analytical study, which analyzed all medical records of pediatric patients undergoing Upper Digestive Endoscopy (DE) and Esophageal Biopsy (EB) at the Clinical Hospital of the Federal University of Uberlândia in a period of ten years (2004-2014). The data were obtained from patient records in the medical archives. This study was approved by the Ethics Committee on human research.

Results: According data center, in this period were performed 3595 DE in 3079 patients. After analyze medical records, only 1906 (53%) results from esophageal biopsies were presented in patient records. The examination of biopsies reports showed 290 results with eosinophilia (2 or more Eo/HPF). A total of 125 EB showed levels higher than 15 Eo/HPF, in this group, 63% were male and the mean age was 92 months. The most common endoscopy finds were opacification in 67(54%), erosion in 14 (11%), thickening in 14(11%), traqueilization in 8 (6%), vertical furrows in 6 (5%). There was no statistical difference between the different months evaluated.

Conclusion: The data showed the presence of eosinophilia in 15.2% of BE, while levels associate with eosinophilic esophagitis were found in 6.5% of BE. There was no seasonal difference in the presence of esophageal eosinophilia in the evaluated months. Although the recommendation in childhood is perform esophageal biopsies in all ED, in 46.9% of upper digestive endoscopies there were no report of EB in the medical records.

Disclosure of interest: None Declared.
Guideline for wireless capsule endoscopy in children and adolescents: A consensus document by the SEGHNP (Spanish Society for Pediatric Gastroenterology, Hepatology, and Nutrition) and the SEPD (Spanish Society for Digestive Diseases)

Federico Argüelles-Arias1, Ester Donat2, Ignacio Fernández-Urrien3, Fernanado Alberca4, Federico Argüelles-Martín5, María José Martínez6, Manuel Molina7, Vicente Varea8, Carmen Ribes-Koninckx2

1Hospital Universitario Virgen Macarena, Digestive Unit, Sevilla, Spain
2La Fe Universitari i Politecnic Hospital, Pediatric Gastroenterology Unit, Valencia, Spain
3Complejo Hospitalario de Navarra, Digestive Unit., Pamplona, Spain
4Hospital Virgen de la Arrixaca, Digestive Unit., Murcia, Spain
5Hospital Universitario Virgen Macarena, Pediatric Gastroenterology Unit, Sevilla, Spain
6Hospital Niño Jesús, Pediatric Gastroenterology Unit, Madrid, Spain
7Hospital La Paz, Pediatric Gastroenterology Unit, Madrid, Spain
8Hospital San Joan de Deu., Pediatric Gastroenterology Unit, Barcelona, Spain

Objectives and study: Capsule endoscopy (CE) is an emerging procedure in children. However, contrary to adults, sound studies in the paediatric age range are scarce. Therefore, the aim of this consensus was to establish evidence based guidelines for CE applicability in children.

Methods: A committee of experts, from the Spanish Society of Gastroenterology, Hepatology and Nutrition (SEGHNP) and the Spanish society of digestive pathology (EDPS) reviewed the literature to respond to key questions according to levels of evidence. The evidence level (EL) was graded according to the Oxford Centre for Evidence-Based Medicine system.

When no evidence was available, consensus was reached by voting

The specific queries were: 1) General indications and contraindications, 2) Effectiveness in specific indications (Crohn's disease, obscure gastrointestinal bleeding (OGB) and anemia, polyposis and miscellaneous, 3) Methodology (preparation and administration), 4) Complications, 5) patency capsule and 6) Colon Capsule.

Results: The agreement establishes a series of statements for each question addressed.

So it concludes that age should not be a contraindication for the CE administration; if the patient cannot swallow the capsule it can be administered by endoscopy, under deep sedation, and using a specific release device (basket) for the CE. Crohn's disease is the main indication, unlike adults, with high efficiency for this condition. Also, it is useful in anemia and OGB and the Peutz Jeghers Syndrome. There is little evidence for its use in the diagnosis of other entities although case reports studies show the procedure can be helpful in a wide range of circumstances.

The main complication is the retention of the CE, which should be especially considered in patients with children with Crohn's disease. In these cases, the patency capsule could be helpful in detecting relevant strictures but more studies are needed to support its use. The best way of preparation is by PEG and a liquid diet in terms of cleanliness. However, this regimen does not improve the results of the CE procedure. About Colon Capsule there is one single study showing its safety and efficacy in children.

Conclusion: The CE is a safe and useful procedure in children. The indications are similar to those in adults but the main one is Crohn's disease both for diagnosis and study of disease extension. A relative limitation at this age is the inability to swallow the CE.

Disclosure of interest: none
GASTROENTEROLOGY: Endoscopy

G-P-091

Bowel Preparation For Elective Paediatric Procedures

Morris Gordon¹, Sahira Isaji², Fiona Tyacke²

¹University of Central Lancashire, School of Medicine, Manchester, United Kingdom
²Blackpool Victoria Teaching Hospitals Trust, Paediatrics, Blackpool, United Kingdom

Objectives and study: Adequate bowel preparation is crucial prior to bowel imaging and surgery. A recent Cochrane review focused on preparation for childhood colonoscopy. We carried out a systematic review to summarise the available evidence investigating the optimum bowel preparation agents for all indications in children using the Cochrane Collaboration format.

Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE and CINAHL (Inception – October 2015). Manufacturers were contacted to identify unpublished trials. References of trials were also searched. Abstracts were considered for inclusion if full details to judge inclusion were offered or available from the authors. Randomised controlled trials (RCTs) that compared probiotics against placebo or any other intervention were eligible for inclusion. Data extraction and assessment of methodological quality of included studies were independently performed by two authors. Analysis was completed in accordance with the intention to treat approach.

Results: The search yielded 1957 results and fifteen randomised controlled studies (n = 1459) met the inclusion criteria. Meta-analysis of three studies (n=179) comparing PEG with normal saline found no difference in rate of adequate bowel preparation (RR 1.03 [95% CI 0.96 to 1.10]), however, there were significantly less adverse events in the PEG group (RR 0.36 [95% CI 0.15 to 0.84]). Meta-analysis of two studies with 64 participants comparing polyethylene glycol (PEG) with sodium phosphate showed no significant difference in the quality of bowel preparation (RR 2.44 (95% CI, 0.81 to 7.36). Meta-analysis of three studies (n=241) found no difference between PEG and Sennasoids in adequate bowel preparation (RR 1.12 [95% CI 0.81 to 1.54]). Meta-analysis of two of these studies with 238 participants showed equivocal bowel preparation between sodium picosulphate/magnesium citrate and polyethylene glycol-electrolyte lavage solution (PEG-ELS), but a significantly higher number of patients needed nasogastric tube (NGT) insertion in the PEG-ELS group than the Sodium.

Conclusion: The published evidence based is small and heterogeneous. The evidence suggests that PEG is as effective as other agents, but safer than normal saline. However, PEG does not appear to be as well tolerated as Sodium picosulphate. It is suggested that future research focus on these two agents to determine the optimum balance between efficacy and tolerability in a childhood population.

Disclosure of interest: “None Declared”. Morris Gordon has received travel grants from various pharma companies for travel to scientific meetings. These companies have had no involvement with the planning, completion or write up of this or any other work.
Gastrointestinal bleeding associated with pharmacologic treatment of patent ductus arteriosus in preterm neonates

Gianluca Terrin, Francesca Conte, Mehmet Yekta Once, Etta D'Aquino, Francesca Cautilli, Sara Monaco, Maria Di Chiara, Patrick McNamara, Sinno Simons, Rahul Sinha, Omer Erdeve, Kadir Serafettin Tekgunduz, Mustafa Dogan, Irena Kessel, Cathy Hammeman, Erez Nadir, Sadik Yurtutan, Bonny Jasani, Alan Serdar, Francesco Manguso, Mario De Curtis

1“Sapienza” University of Rome, Department of Pediatrics, Rome, Italy
2Zekai Tahir Burak Maternity Teaching Hospital, Department of Neonatology, Ankara, Turkey
3The Hospital for Sick Children, Department of Neonatology, Toronto, Canada
4Erasmus MC-Sophia Children’s Hospital, Department of Pediatrics, Rotterdam, Netherlands
5167 Military Hospital, Department of Pediatrics and Neonatology, Pathankot, India
6Ankara University School of Medicine Children’s Hospital, Department of Pediatrics, Ankara, Turkey
7Ataturk University Medical Faculty, Department of Neonatology, Erzurum, Turkey
8Pamukkale University, Department of Pediatrics, Denizli, Turkey
9Carmel Medical Center, Department of Neonatology, Haifa, Israel
10Shaare Zedek Medical Center, Hebrew University, Department of Neonatology, Jerusalem, Israel
11Hillel Yaffe Medical Center, Department of Neonatology, Hadera, Israel
12Kem Hospital, Department of Neonatology, Mumbai, India
13Hitit University, Department of Neonatology, Corum, Turkey
14Cardarelli Hospital, Department of Gastroenterology, Naples, Italy

Objective and study: A persistently patent ductus arteriosus (PDA) is a major complication of prematurity. A prompt PDA closure is crucial to reduce related risk of morbidity and mortality. Cyclooxygenase inhibitors (COXi) are the therapy of choice for PDA. However, the use of COXi is characterized by a high risk of gastrointestinal bleeding. Recently paracetamol was proposed as an alternative treatment to reduce side effects of the COX-inhibitors therapy for PDA. We performed a systematic review and meta-analysis of all the available evidence to assess the risk of gastrointestinal bleeding during the treatment of PDA with paracetamol vs. COXi.

Methods: We conducted electronic searches in Medline, Scopus, and ISI web of Knowledge databases, using the following medical subject headings and terms: paracetamol, acetaminophen, and patent ductus arteriosus. Additionally, we performed electronic and manual screening of conference abstracts from international meetings of relevant organizations and manual search of the reference lists of all eligible articles. We considered eligible all studies comparing paracetamol vs. COXi (i.e. ibuprofen or indomethacin), or vs. placebo, for the treatment of PDA. Data regarding safety were collected and analyzed.

Results: Sixteen studies were included: two randomized controlled trials (RCTs) and 14 uncontrolled studies. Quality of selected studies is poor. A meta-analysis of RCT demonstrated a reduction of the risk of gastrointestinal bleeding in subjects receiving paracetamol vs. COXi (2/125 vs 9/125, RR 0.2, 0.1-1.0 95%CI). No data on gastrointestinal bleeding were reported by uncontrolled studies. Contemporarily, the meta-analysis of the data on the efficacy do not demonstrate any difference between the two therapeutic options on ductal closure (Arch Dis Child Fetal Neonatal Ed 2015; fetalneonatal-2014-307312).

Conclusion: The use of paracetamol may reduce the risk of gastrointestinal bleeding in preterm neonates receiving pharmacologic treatment for PDA. These results should be interpreted with caution taking into account the non-optimal quality of the studies analyzed and the limited number of neonates treated with paracetamol so far.

Disclosure of interest: No conflict of interest.
Impact of ethnicity and atopic status on treatment response to Eosinophilic Oesophagitis

Hany Banoub¹, Mashhood Ayaz¹, Sonny Chong¹

¹Queen Mary’s Hospital for Children, St. Helier Hospital, Paediatrics, Carshalton, Surrey, United Kingdom

Objectives and study: Clinical experience in treatment of Eosinophilic Oesophagitis (EoE) showed various response to a standardised treatment. We analysed the histologic treatment response according to racial factors (caucasian vs non caucasian) and atopic status (high IgE versus normal IgE) of our Paediatric case cohort of 32 patients diagnosed between 2004-9.

Methods: Our retrospective case series included 32 paediatric patients diagnosed with EoE. The patients were reviewed and clinical and histological response while receiving treatment and after stopping treatment. Our patients were treated mainly with Fluticasone inhalation to be swallowed in addition to Omeprazole. We modified our treatment over the years to include Montelukast 5 mg/day and antigen avoidance (Target elimination diet based on IgE specific antibody levels).

Response to treatment is subdivided further into complete, partial or no response according to the eosinophils level/hpf.

Results: Our 32 patients are 25 caucasians and 7 non caucasians.

20% of caucasian patients had pretreatment level of Eosinophils 100/hpf, and 16% had Eosinophils levels between 40-50/hpf. This is compared with 28.5% of non caucasians who had pretreatment level of 50/hpf.

44% of caucasians had complete resolution, and 16% had partial resolution of Eosinophils post treatment. This is compared with 28.5% of non Caucasian who had complete resolution.

Of the total 32 patients, 22 had high total IgE (atopic) versus 10 with normal total IgE (non atopic). Complete resolution following treatment in 32%, and partial resolution in 12 % of atopic patients. This is compared with complete resolution in 71% of non-atopic patients.

Conclusion: Caucasian children present with higher histological Eosinophils/hpf but they show better histological response to treatment than non Caucasian children.

Better treatment response in non atopic children. This has the implementation of using targeted elimination diet in the atopic group only.

Disclosure of interest: “None Declared”.
A tertiary care center experience in feasibility and safety of ERCP in infants, children and adolescents

Jasmin Felux1, Ekkehard Sturm2, Andreas Busch2, Emanuel Zerabruck3, Florian Graepler3, Dietmar Stueker3, Nisar Malek3, Martin Götz3

1University Hospital Tuebingen, Internal Medicine I, Tuebingen, Germany
2Childrens Hospital University of Tuebingen, Pediatric Gastroenterology, Tuebingen, Germany
3University Hospital Tuebingen, Internal Medicine I, Tuebingen, Germany

Objectives and study: Compared to adults, ERCP in children is characterized by different indications and potential concerns regarding practical limitations, presumed lower effectiveness and higher risk of side effects. We retrospectively analyzed these characteristics of ERCPs in children aged 0-18 years.

Methods: Fifty-four ERCPs (median 1, range 1-7) were performed in 31 children (mean age 7.6±6.1 yrs; median weight 22kg, range 3.3-142.7 From Jan 2012 – Mar 2015). Indications were discussed in a multidisciplinary team and included suspected choledocholithiasis (n=13), postoperative complications (15), ductal anomalies (including biliary atresia) (14), tumors (10), and PSC (2). High end ultrasonography and/or cross sectional imaging was available for all patients before ERCP. All patients were followed up for at least 3d. Standard duodenoscopes were used in children >20 kg BW, smaller diameter duodenoscopes (min. diameter 7.5mm, working channel 2mm) in smaller children or infants. Similarly, we used .018", .025", and .035" wires.

Results: ERCP in children accounted for 3.3% of our total ERCP caseload. Therapeutic ERCP was performed in 36 children, diagnostic in 18, by ERCP expert endoscopists. Endoscopic papillotomy was performed in 16/54 examinations. General anesthesia was preferred, only in 6/54 interventions (age>16y), conscious sedation was used. In two patients, retrograde access to the papilla was necessary (after Roux-en-Y, duodenostomy). Successful intervention (defined as accurate diagnosis and/or adequate therapy) was possible in 87.0% (47/54 ERCPs), and was more often achieved in older children (mean age 10.9 vs. 4.2 years, median weight 34.0 vs. 8.3kg). Failed cannulation was associated with limited dimensions of infants and young children. 5 complications were recorded (5/54, 9.3%), and included 4 cases of mild pancreatitis (7.4% PEP rate; incl. 2 pts. with aggravation of preexisting pancreatitis) and 1 aggravation of cholangitis in PSC despite antimicrobial prophylaxis. PEP was noted in 0 of 6 children with protective pancreatic stents vs. 4/43 without pancreatic stents. All complications were managed conservatively. No complications were attributed to mechanical stress on the GI tract.

Conclusion: Endoscopists must be aware of a different pathology of pediatric biliary and pancreatic diseases compared to adults. A multidisciplinary team including the endoscopist and the pediatric gastroenterologist should discuss the ERCP indication, findings and conclusions. Accessories for small caliber duodenoscopes are limited, thus limiting peripapillary navigation in infants. Complications were similar to rates reported in adults. In summary, ERCP in children of all ages appears to be safe and frequently effective in selected indications.

Disclosure of interest: None Declared
Flexible endoscopic procedure in children with foreign bodies in the upper gastrointestinal tract

Kaan Demiroren

Yuzuncu Yil University, Pediatric Gastroenterology, VAN, Turkey

Objectives and study: Foreign body ingestion is an important public health problem in some regions of the world. The aim of this study is pointed to this subject and determine the effectiveness of flexible endoscopic procedure.

Methods: One hundred children, admitted for ingestion of foreign body during two and a half years in only one center, who underwent esophagogastroduodenoscopy, were included in this study. A plain radiographic film of the neck, chest and abdomen was obtained in all children. Endoscopic procedure was performed by 9 mm diameter flexible endoscope (Fujinon, Fujifilm, system2500 processors, Japan). Before the endoscopic procedure, anesthesia was administered by either conscious sedation (intravenous midazolam, a dose of 0.1-0.4 mg/kg) or general anesthesia. For the removal of foreign bodies, rat-tooth, alligator-jaw, 3-prong, 4-prong or snare were used as the endoscopic retrieval devices. Overtube was used in some older children.

Results: The mean age of the patients was 4.9 years, and 59% were female. Two patients had undergone an operation of esophageal atresia and one patient had a mental and motor retardation.

Ingested foreign bodies were coin (38%), safety pin (18%), pin (4%), brooch (4%), hair clips (3%), screw (3%), chicken bones (3%), food bolus (2%), sewing needle (2%), wire (2%), discoid battery (2%), screw washer (2%), fish bones (2%), key (1%), ring (1%), button for clothes (1%), chicken skin (1%), sock (1%), magnet (1%), apricot kernel (1%), pencil sharpener (1%), head of a lighter (1%), AA battery (1%), stone (1%), marble (1%), token (1%), cherry stone (1%), teaspoon (1%).

In endoscopic procedure, foreign bodies were seen in upper esophagus (35%), middle esophagus (11%), lower esophagus (3%), stomach (29%), bulb (5%) and second part of duodenum (5%), but were not seen in 12% of the cases.

Foreign bodies in 3% of the patients were pushed to stomach with gastroscope from esophagus and left for spontaneous passage. While 80% of foreign bodies were endoscopically removed, 5% of them could not been removed. Any important complication was developed.

Conclusion: Flexible endoscopic procedure is an effective and safe method for removal of gastrointestinal system foreign bodies in children.

Disclosure of interest: “None Declared”.
Service Evaluation of Bristol Endoscopy

Lakshmi Priya Selvarajan¹, Siba Paul², Dharam Basude³, Bhupinder Sandhu³, Christine Spray³

¹Bristol Royal Hospital for Children, Paediatric Gastroenterology, Bristol, United Kingdom
²Yeovil District Hospital, Somerset, United Kingdom
³Bristol Royal Hospital for Children, Bristol, United Kingdom

Objectives and study: There is a wide variation in the provision of paediatric endoscopy services across units in the UK. Childhood endoscopy is most commonly indicated when the diagnoses of inflammatory bowel disease, coeliac disease or reflux oesophagitis are under consideration.

The aim of our study was to identify the current provision of paediatric endoscopy services in Bristol, UK- the number of endoscopies performed in the last 7 years, the number of abnormal results and the contribution of Inflammatory bowel disease, Coeliac disease and Eosinophilic oesophagitis to our endoscopy workload.

Methods: Data was collected from our endoscopy database from January 2008 to December 2014. Details of all children undergoing endoscopy are prospectively entered with demographic details, indications, macroscopic findings and histopathology results.

Results: On an average, 347 patients underwent endoscopy each year with 476 procedures/year. 66% of our results were abnormal (62-68%), 52% of which, was contributed in diagnosing Inflammatory bowel disease, Coeliac disease and eosinophilic oesophagitis. 10-12% of those with Inflammatory bowel disease had their disease re-assessed. On an average, there were 58 (range 47-72) patients with a new diagnosis of IBD and 8 (range 6-13) with eosinophilic oesophagitis. Endoscopic diagnosis of coeliac disease has reduced from 92 in 2010 to 45 in 2014. We do 15 therapeutic procedures/year on an average.

In 2014, we had 94 elective, 5 extra and 32 emergency lists with an average of 8 lists and 5-6 procedures per month. 35% were from Bristol and the remaining were referred from other hospitals. We had a total of 537 procedures with 159 upper GI endoscopies, 33 colonoscopies and 171 had both the procedures. Our terminal ileum intubation rate was 96%.
### Table:

<table>
<thead>
<tr>
<th>Year</th>
<th>Patients</th>
<th>Procedures</th>
</tr>
</thead>
<tbody>
<tr>
<td>2008</td>
<td>287</td>
<td>364</td>
</tr>
<tr>
<td>2009</td>
<td>298</td>
<td>418</td>
</tr>
<tr>
<td>2010</td>
<td>341</td>
<td>449</td>
</tr>
<tr>
<td>2011</td>
<td>318</td>
<td>438</td>
</tr>
<tr>
<td>2012</td>
<td>425</td>
<td>599</td>
</tr>
<tr>
<td>2013</td>
<td>396</td>
<td>529</td>
</tr>
<tr>
<td>2014</td>
<td>366</td>
<td>537</td>
</tr>
</tbody>
</table>

**Conclusion:** There is a wide variation in the number of procedures each year and there has been a steady increase. More than half of our endoscopic procedures are to diagnose Inflammatory bowel disease, coeliac disease and eosinophilic oesophagitis although there is a downward trend in the endoscopic diagnosis of coeliac disease.

**Disclosure of interest:** “None Declared”.

Vol. 62, Supplement 1, May 2016 270
Endoscopic Findings in Children with Isolated Rectal Bleeding


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
3Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Hospital, Petach Tikva, Israel

OBJECTIVES: Colorectal polyps are among the common etiologies of rectal bleeding in children. Our aim was to assess the causes of isolated rectal bleeding in children, and to analyze the characteristics of colorectal polyps in this cohort.

METHODS: We reviewed all colonoscopic procedures between 2007 and 2015 at the Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Medical Center of Israel. Only patients aged 0-18 years with isolated rectal bleeding were selected for analysis. Children with characteristics of inflammatory bowel disease such as diarrhea, arthritis aphthous stomatitis, peri-anal disease, weight loss, or increased serum inflammatory markers were excluded. Abdominal pain was regarded as a non-specific symptom and was not excluded.

RESULT: Out of 998 colonoscopies, 204 met the inclusion criteria for isolated rectal bleeding. Median age was 8.5 years (IQR 5-14) with 60% males. A total of 88 patients (43%) were found to have colorectal polyps. Solitary polyps, 2-3 polyps and >3 polyps were detected in 75 (85%), 7 (8%) and 6 (7%) patients, respectively. Sixty-nine (92%) of the solitary polyps were located in the left colon, while 3 (4%) were in the transverse colon, and 3 (4%) were in the ascending colon. Of these, only one patient with a right sided polyp had been suspected of a polyposis syndrome a priori. Histologically, 83% of solitary polyps were juvenile, 8% inflammatory, 6% hyperplastic, 1% hamartoma, and 1% were not retrieved. Polyp detection rate did not differ according to age. Other endoscopic findings in patients with isolated rectal bleeding included: normal colonoscopy 57 (28%), eosinophilic colitis 25 (12%) and proctitis 5 (2.5%). Among the patients who underwent a colonoscopy that did not meet the inclusion criteria for isolated rectal bleeding, we found only 7 (0.9%) patients with colorectal polyps.

CONCLUSION: In our cohort, single left sided juvenile polyp is the most common cause of isolated rectal bleeding in all age groups. The small but significant incidence of polyp detection proximal to the splenic flexure justifies a full colonoscopy in isolated pediatric rectal bleeding. Polyps are rare findings in children not presenting with isolated rectal bleeding.
Experience of 19 years in Percutaneous Endoscopic Gastrostomy in children

Marcela Alarcón Gamarra¹, Ecaterina Julio¹, Pablo Ercoli¹, Belinda García¹, Carlos Ruiz Hernández¹, Esperanza Castejón¹, Javier Martín¹, Sergio Pinillos¹

¹Sant Joan de Deu Hospital, Gastroenterology and Nutrition, Barcelona, Spain

Objectives and study: To portray the experience of Percutaneous Endoscopic Gastrostomy (PEG) attached by the Gastroenterology team of a third level Paediatric Hospital to children with diverse diseases.

Methods: Retrospective descriptive study of medical records of patients undergoing PEG attachment during 1996-2014. There were included patients younger than 18 years with a follow-up of ≥ 6 months. Data concerning age, sex, underlying disease, indications, technique, prophylactic antibiotic therapy, tolerance, type of diet, post operatory complications and incidence of gastroesophageal reflux (GERD) were described. Statistics analysis SPSS 15.0 was used.

Results: 318 PEG were carried out. Age average 6.69 years. 53.14% (n=169) was male. The 66.67% (n=212) suffered from severe neurologic disease, 13.52% (n=43) metabolic disease, 6.92% (n=22) oncologic pathology, 17% (n=56) other diseases. The indications were oropharyngeal dysphagia (OD) 68% (n=215), failure to thrive 28% (n=91), preventive nutritional support 6.6% (n=10), access to drug administration 3.14% (n=2). The 61.6% (n=196) needed nasogastric tube (NGT) for enteral nutrition with an average duration of 4.9 months (1 – 18 months). The 93% (n=297) had a normal macroscopically endoscopy and esophagitis a 4% (n=13). 63% (n=213) received prophylactic antibiotic therapy. An 88.6% (n=282) started eating in the first 24 hours with appropriate tolerance. 46.8% (n=149) received exclusive gastrostomy feeding and 45% (n=145) mixed feeding (mouth-PEG). Average time of hospitalization stay was 3.7 days. 14% (n=76) of the PEGs was removed after an average of 32 months since the attachment. The 21% (n=68) presented a suggestive clinic of GERD before the attachment and a 25% (n=80) after it.

A 10% (n=32) required anti reflux surgery after PEG placement. Of these patients, 40.8% (n=13) had GERD symptomatology before gastrostomy attachment and 59.2% (n=19) presented symptoms after it (P<0.05). 78% of the patients with neurologic disease was significantly related to a higher OD percentage (P<0.01) and GERD symptomatology previous to PEG attachment (P<0.09) though not to a higher risk of anti reflux surgery (P=0.41). There is not statistic difference between patients with or without OD and PEG detachment probability in the long run.

The total of complications was 35%, (n=111), precocious 10.4% (n=33), belated 24.5% (n=78), severe 1% (n=4) (n=1 colonic perforation, n=1 peritonitis, n=1 sepsis and another of pneumoperitoneum), minor 14% (n=45). No statistic relationship between the use of prophylactic antibiotic and risk of immediate complications was detected.

Conclusion: It is a simple, fast and safe technique, which provides a nutritional support to children suffering from diverse pathologies. Neurologic diseases and OD are the main diagnosis and the most frequent indication respectively. GERD symptomatology presence is related to a higher incidence of anti reflux surgery after gastrostomy. Although complications are frequent, most of them are mild. The use of prophylactic antibiotic does not seem to decrease the incidence of immediate complications.

Disclosure of interest: None Declared.
Duodenal–Jejunal Bypass Liner- Primary Experience in Morbidly Obese Adolescents, Safety and Efficacy

Matjaz Homan¹, Tadej Battelino², Primoz Kotnik³, Rok Orel⁴

¹University Children's Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia
²University Medical Center Ljubljana, Endocrinology, Diabetes & Metabolism, Ljubljana, Slovenia
³University Children's Hospital, University Medical Centre Ljubljana, Department of Endocrinology, Diabetes and Metabolism, Ljubljana, Slovenia
⁴University Children's Hospital Ljubljana, Department of Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia

Objectives and study: The duodenal–jejunal bypass liner (DJBL) (Endobarrier) is an endoscopic implant that mimics the duodenal–jejunal bypass component of the Roux-en-Y gastric bypass. Studies in adults have shown relevant weight loss and improvement in type 2 diabetes. The aim of this prospective study was to investigate for the first time safety and efficacy of DJBL in severely obese adolescents with obesity complications 6 months after implantation.

Methods: The device was successfully implanted in 10 morbidly obese adolescents out of 12 that underwent the procedure (7 females, mean age 17.9 years (range 16.4–19.2); BMI 42.4 kg/m² (range 39.7–48.8)). Inclusion criteria were; ≥ BMI 35 kg/m² with obesity complications such as hypertension, prediabetes or type 2 diabetes. Metformin was discontinued prior to DJBL placement. The exclusion criteria are described in details at www.ClinicalTrials.gov (NCT02183935). The procedure was performed endoscopically under general anesthesia. Subjects were under observation in the hospital for 2 days following the procedure for possible complications. According to the protocol they were receiving esomeprazole 40 mg BID throughout follow up.

Results: In the safety analyses there were no severe procedure or post procedure related complications. The most frequent adverse events were gastrointestinal: nausea (5/10), abdominal pain (5/10), and diarrhea (2/10) in the first days after implantation. One subject developed cholecystitis 3 months after endoscopy and one patient had transiently elevated pancreatic enzymes. The body weight was measured at 1, 3 and 6 months and decreased at all time frames (-7.0% (range -3.9% to -10.7%), -11.1% (range -2.75% to -19.0%), -11.7% (range -1.3% to -21.7%), respectively). In addition, glucose metabolism significantly improved at 6 months (HOMA-IR decreased by – 3.3 (range -0.9 to -6.5)).

Conclusion: This is the first report on the use of endoscopically placed DJBL in adolescents being followed-up for 6 months. Relevant weight loss was determined in most adolescents and glucose metabolism improved in all. No serious device-related adverse effects were detected.

Disclosure of interest: None Declared.
Inventory on primary prophylaxis in portal hypertension in children in France, Belgium, French speaking Canada and Switzerland

Odile Malet¹, Duché Mathieu², Fabre Alexandre³

¹Centre Médical de Spécialistes, Plan de Cuques, France
²Hôpital Bicêtre, Le Kremlin-Bicêtre, France
³Hôpital de la Timone Enfant, Service de Pédiatrie Multidisciplinaire, and Genius Group, Marseille, France

Objectives and study: Primary prophylaxis in portal hypertension in infants is controversial, despite its efficacy statistically proven in adults, as they are few studies, retrospective for most of them, showing its efficacy on the risk of rebleeding in children. The kind of primary prophylaxis (medical or endoscopic) is also debated, excluding surgery sometimes used in case of portal cavernoma.

Methods: 38 major French speaking hospitals were sent a short questionnaire about their clinical practice in a matter of primary prophylaxis.

Results: 74% (28) returned the questionnaire filled up. 7 of them address their patients to tertiary centres. More than 75% of the 21 centres screen by endoscopy patients attempted with portal cavernoma, biliary atresia, cystic fibrosis and other fibrotic chronic liver disease, in case of clinical, biological or sonographic signs of portal hypertension.

Respectively 67% and 62% of them don’t practise any primary prophylaxis in case of grade 1 varices with red marks or grade 2 varices. Respectively 100% and 90% of them practise sclerotherapy or even better EVL in case of grade 2 varices with red marks or grade 3 varices. In case of oesogastic varices, most of them (48%) don’t practise any prophylaxis and 38% practise gluing. Interestingly, non-cardio selective beta blockers where used by around 20% of the centres in any case.

Side effects were found more severe with sclerotherapy than with non-cardio selective beta blockers or EVL.

Conclusion: it seems that, despite the absence of scientific recommendations, there is a tacit consensus, concerning the need to screen by gastroscopy children suspected of portal hypertension, and to undergo primary prophylaxis in case of threatening varices, preferring EVL to sclerotherapy and non-cardio selective beta blockers.

Disclosure of interest: Non declared
Objectives and study: Colonoscopy of the lower gastrointestinal tract has diagnostic and therapeutic value. This retrospective study aimed to investigate the indications, complications, and diagnostic yield of colonoscopy.

Methods: The application of colonoscopy performed on children younger than 18 years old, between 2010 and 2015 in a referral tertiary center, in the province of Isparta in Turkey was reviewed. Each patient had a bowel preparation of low residue diet for 2 days prior to examination, followed oral sodium phosphate with liquid in the night and on the day before the examination. Bowel cleansing enemas were also performed on the day of the examination. During the examination received conscious sedation with intravenous midazolam (0.1 mg/kg) and ketamine (1 mg/kg), and monitored by pulse oximetry. All colonoscopy procedures were performed with Fujinon EC 530LP IC657K068 video-colonoscope. Data on age, gender, indications, complications, and colonoscopic and final diagnoses were collected and analyzed.

Results: One hundred and thirty six children with 121 colonoscopies and 15 sigmoidoscopies were enrolled. There were 75 boys (55.1%) with a mean age of 11.8 ± 4.1 years (1-18 years). The most common indication was chronic abdominal pain (41.2%, n=56), followed by lower gastrointestinal bleeding (36.7%, n=50), chronic diarrhea (11%, n=15), and iron deficiency anemia (9.5%, n=13). All procedure of 136 patient the cecum was successfully reached in 68 (50%) cases, while the terminal ileum was reached in 46 (33.8%). Biopsies were obtained from 86 (63%) patients during the procedures. Two or more sequential colonoscopies were performed in 15 (11%) cases. All patients of the procedures involved conscious sedation. The average sedation time for the procedure was 21.7±8.4 minutes (5-39 minutes). Conclusive diagnosis relied on endoscopic imaging and/or histology in 82 patients on their first examination, while 39 had negative findings. Finally, all children were 90 patient (66%) with a conclusive diagnosis in colonoscopy; including nonspecific colitis (21%, n=29), polyp (17%, n=23), inflammatory bowel disease (7.3%, n=10) and the others, while 46 had negative findings (Table). There were no major procedure related complications in any of the patients.

Table: Indications for colonoscopy or sigmoidoscopy and the diagnostic yields

<table>
<thead>
<tr>
<th>Indications</th>
<th>Patient no. (%)</th>
<th>Diagnostic yield</th>
<th>Patient no. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic abdominal pain</td>
<td>56 (41.2)</td>
<td>Nonspecific colitis 21 (15.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Polyp(s) 3 (2.2)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD 2 (1.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Others* 9 (6.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative 21 (15.4)</td>
<td></td>
</tr>
<tr>
<td>Lower gastrointestinal bleeding</td>
<td>50 (36.7)</td>
<td>Polyp(s) 20 (14.7)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD 2 (1.5)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Others* 9 (6.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Nonspecific colitis 2 (1.5)</td>
<td></td>
</tr>
<tr>
<td>Condition</td>
<td>Count (%)</td>
<td>Diagnosis</td>
<td>Count (%)</td>
</tr>
<tr>
<td>----------------------------</td>
<td>------------</td>
<td>---------------------</td>
<td>------------</td>
</tr>
<tr>
<td>Chronic diarrhea</td>
<td>15 (11)</td>
<td>Nonspecific colitis</td>
<td>6 (4.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>IBD</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Other*</td>
<td>4 (2.9)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Iron deficiency anemia</td>
<td>13 (9.5)</td>
<td>IBD</td>
<td>2 (1.5)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Others*</td>
<td>6 (4.4)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Negative</td>
<td>5 (3.8)</td>
</tr>
<tr>
<td>Body weight loss</td>
<td>1 (0.8)</td>
<td>Negative</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td>Intestinal gas</td>
<td>1 (0.8)</td>
<td>Negative</td>
<td>1 (0.7)</td>
</tr>
</tbody>
</table>

*Anal fissure, angiodysplasia, hemorrhoids, parasite, preparation quality adequate, IBD; Inflammatory Bowel Diseases.

**Conclusion:** Chronic abdominal pain is the most common indication for pediatric colonoscopy. Pediatric colonoscopy is the most effective procedure for diagnosing pediatric lower gastrointestinal bleeding and chronic diarrhea.

**Disclosure of interest:** “None Declared”.
Bowel Preparation before Colonoscopy for Children: Comparison of Efficacy of Three Different Methods

Seyed Mohsen Dehghani¹, Hazhir Javaheirizadeh²

¹Shiraz University of Medical Sciences, Pediatrics, Gastroenterohepatology Research Center, Shiraz, Iran
²Shiraz University of Medical Sciences, Shiraz, Iran

Objectives and study: Colonoscopy is an important diagnostic and therapeutic procedure. Adequate bowel preparation is mandatory. Several regimens were discussed in the literature. Among the drugs which has recently used, polyethylene glycol is one of the most popular agents.

The aim of this study was to compare efficacy of three different methods for one day preparation before colonoscopy.

Methods: This study included children with the range of ages (2-21) who had an indication of colonoscopy. Exclusion criteria were based on the history of previous surgery, parental disagreement, and patients who did not use preparation protocol. Three methods for bowel preparation were studied: 1- Polyethylene glycol only; 2- Polyethylene glycol and bisacodyl suppositories; 3- Polyethylene glycol plus normal saline enema. Boston Bowel Preparation Score was used for evaluation of preparation. SPSS version 16.0 (Chicago, IL, USA) were used for data analysis.

Results: In this study 83 cases completed the bowel preparation completely. Acceptable bowel preparation in 24 (85.71%), 36 (94.73%), and 14 (82.35%) of cases in PEG, PEG+ bisacodyl, and PEG+ normal saline enema groups respectively. PEG+ bisacodyl suppositories was more effective than PEG+ Normal saline for the preparation of the first segment (P=0.05). For 2nd and 3rd segment of colon, Boston Bowel Preparation score was higher in PEG + bisacodyl suppositories compared to other regimens, but this difference was not statistically significant.

Conclusion: There was no significant difference between one day colonoscopy regimens in terms of bowel preparation score. Lowest score was seen in PEG + Enema group compared to other group.

Disclosure of interest: None Declared.
Small Bowel Diaphragmatic Disease

Shishu Sharma1, Mike Thomson2, Richard Lindley3
1Sheffield Children's NHS Foundation Trust, Gastroenterology, Sheffield, United Kingdom
2Sheffield Childrens NHS Foundation Trust, Sheffield, United Kingdom
3Sheffield Childrens NHS Foundation Trust, Paediatric Surgery, Sheffield, United Kingdom

Objectives and study: Small bowel diaphragmatic disease (SBDD) is a rare complication of small bowel enteropathy secondary to the use of non-steroidal anti-inflammatory drugs. Idiopathic SBDD is a rare entity in itself and it has not been widely reported in paediatric population. We present here a 33 month old girl who was diagnosed with SBDD by wireless capsule endoscopy (WCE) and further managed effectively by trans oral double balloon enteroscopy (DBE) and mini-laparotomy-assisted enteroscopy (LAE).

A 33 month old girl presented with a 1 year history of microcytic hypochromic anaemia with hypoalbuminaemia of unknown origin, requiring 5 blood transfusions over this period. No PR blood or melaena were identified. Night sweats and intermittent facial/pedal oedema were seen. The parents were second cousins. Racial background:

Initial normal/negative investigations at the referring hospital included: FBC; LFTs; clotting screen, B12, folate, fat soluble vitamin levels, thalassemia screen, electrophoresis, autoantibody/ANA screen, thyroid function tests, coeliac screen, ASOT, mycoplasma, EBV screen, parvovirus screen. Quantiferon, serum compliments, trypase, stool pancreatic elastase and urine neuroblastoma screens. The stool tests were negative for bacteria, ova cysts and parasites on multiple occasions but was positive for faecal occult blood. She also had an echocardiogram to rule out constrictive pericarditis.

The bone marrow aspirate and trephine biopsy at the referring hospital were suggestive of iron deficiency anaemia. She had low serum ferritin (3ug/L) and iron levels (1umol/L), needing intravenous iron infusion. Her urinary iron levels were normal, which ruled out renal iron loss.

Urine dipstix showed intermittent non-nephrotic range proteinuria and abdo ultrasound suggested nephrocalcinosis.

Faecal calprotectin was raised on more than one occasion precipitating the referring hospital to perform oesophagogastroduodenoscopy, ileocolonoscopy and a Meckels’ scan, which were all normal except for mild chronic gastritis.

On referral to the gastrointestinal bleeding centre WCE was performed and this showed SBDD with ulceration associated with multiple narrow strictures/bands. Subsequent DBE and then LAE revealed 23 stenosing ulcerated concentric band type lesions over a 70cm span of small bowel 180 cm distal to the pylorus. (Video slides/ pictures)

The diseased section of small bowel was resected under the same anaesthetic. The infectious disease team review ruled out tropical disease. Histopathology showed non-specific superficial ulcers of the mucosal surface with no evidence of vasculitis, CMV or inflammatory bowel disease, leading to a final diagnosis of idiopathic small bowel diaphragmatic disease.

Methods: A case report

Results: To the best of our knowledge this is the second reported case of poorly understood paediatric idiopathic SBDD. Our centre published the first ever case report of SBDD in a 5 year old girl in 2012. The differential diagnosis of SBDD is NSAID-precipitated ulceration, Crohn’s disease, vasculitis, intrauterine insults, CMV, tuberculosis and eosinophilic enteritis.

Conclusion: This case highlights the importance of WCE and DBE/pan-enteroscopy in managing difficult cases of chronic intestinal blood loss.

Disclosure of interest: None declared
GASTROENTEROLOGY: Endoscopy

G-P-104

Use of oesophageal stent and trans thoracic T-tube in a case of oesophageal perforation post button battery ingestion.

Shishu Sharma¹, Mike Thomson², Sean Marven³, Govind Murthi³

¹Sheffield Childrens NHS Foundation Trust, Gastroentrology, Sheffield, United Kingdom
²Sheffield Childrens NHS Foundation Trust, Sheffield, United Kingdom
³Sheffield Childrens NHS Foundation Trust, Paediatric Surgery, Sheffield, United Kingdom

Objectives and study: There are many household battery-operated items in a modern home that contribute to the availability of button batteries to young children. The children may mistake them for sweets or pills, leading to inadvertent ingestion. We present here an interesting case of button battery ingestion, managed by using esophageal stent and trans thoracic T-tube.

Case report: A 2 year old girl presented after 1 hour following ingestion of a 20mm lithium ion button battery. This was removed using a rigid oesophagoscope within 2 hours of stipulated time. A 5cm long segment of necrosis and erosive damage to the mucosal surface was noted on the posterior aspect of the oesophagus 15cm from the incisors. She was then admitted for observation and was planned for discharge the following day. Prior to discharge after 22 hours post-ingestion her clinical state deteriorated and a left sided tension pneumothorax was noted which was treated by urgent needle decompression followed by intubation and chest drain insertion. Clinical suspicion of an oesophageal perforation was confirmed by an upper GI contrast showed leakage into the mediastinum revealing an 8-10mm perforation approximately 20 cm from the incisors. A temporary metallic oesophageal stent (covered Comvi® fully covered biliary shunt 10mm X 60mm) was placed across the perforation endoscopically with a plan to replace this in a week. Total parenteral nutrition was also commenced on day 3 post ingestion.

On day 10 post-ingestion it was planned to replace the metallic stent with Polyflex transheo-bronchial fibre stent, but a contrast chest CT prior to the procedure showed a longitudinally oriented defect extending from the oesophagus into the left pleural space, measuring almost 14 mm in coronal section and approximately 5 mm in AP diameter. This was considered to unamenable to stent alone. Therefore a decision was made for endoscopic removal of the original stent combined with thoracotomy and insertion of a ZOF® T-tube extending from oesophagus to outside the chest wall. A serratus muscle flap was raised and split to wrap around oesophagus. The left chest drain was removed simultaneously.

On day 52 post-ingestion the T-tube was removed under direct endoscopic vision and a tissue repair glue (Tissel®) was injected into the artificial fistula. Subsequently two Instinct® endoclips were also applied to the residual defect in the oesophageal wall. Intraoperative contrast X-ray identified oesophageal integrity and no leak. (Figure)

She was discharged home on day 56 post-ingestion and a repeat upper oesophagoscopy on day 66 post-ingestion showed complete healing of the perforation.

Methods: A case report

Results: The outcome of button battery ingestion is potentially catastrophic and a very high index of suspicion should exist amongst front line medical staff with a very low threshold for radiological examination. Oesophageal arrest of the battery is an endoscopic emergency necessitating removal immediately.

It would seem intuitive that an urgent review of preventive measures such as education around their storage and safe disposal, and child-proof packaging be advocated on a national level.

Conclusion: A case is made for the establishment of a Europe wide Helpline, equivalent to the National Battery Ingestion Hotline in the US, to advise general public.

Disclosure of interest: None declared
A comparison of the sedation with midazolam-ketamine versus propofol-fentanyl during upper GI endoscopy in children

Ulas Emre Akbulut¹, Sedat Saylan², Bilal Sengu², Gulgun Elif Akcali², Engin Erturk³, Murat Cakir⁴

¹Kanuni Training and Research Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
²Kanuni Training and Research Hospital, Anesthesiology and Intensive Care Medicine, Trabzon, Turkey
³Karadeniz Technical University Faculty of Medicine, Anesthesiology and Intensive Care Medicine, Trabzon, Turkey
⁴Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey

Objectives and study: The best sedation procedure with minimal side effects providing the best comfort both for the patient and the endoscopist during the upper gastrointestinal endoscopy of children is under discussion. The aim of this study was to compare the efficacy and safety of midazolam plus ketamine versus fentanyl plus propofol administered to children undergoing UGE and to determine the most appropriate sedation protocol.

Methods: This prospective, randomized, single-blind study was conducted in the department of Pediatric Gastroenterology, Hepatology and Nutrition at the Kanuni Training and Research Hospital. Patients were randomly divided into Groups A and B. The midazolam (0.1 mg/kg) plus ketamine (1 mg/kg) combination was given to Group A, and the fentanyl (0.1 µg/kg) plus propofol (1 mg/kg) combination was given to Group B for sedation. All patients were monitored for peripheral oxygen saturation, heart rate (HR), respiratory rate, and RSS during the procedure. The start and end of the process were recorded after providing appropriate sedation. Complications during the procedure were recorded. The time between the end of the process and departure from the endoscopy unit (the recovery time) were recorded. Complications during the recovery time were recorded.

Results: The processes started without an additional dose of the drug for 118 patients (99.1%) in group A and for 101 patients (84.8%) in group B (p = 0.001). Average ketamine given to the patients in Group A was 1.03 ± 0.15 mg / kg and average propofol given to the patients in Group B was 1.46 ± 0.55 mg / kg. None of the patients stopped the operation in Group A but 1 patient (0.8%) had to discontinue the operation in Group B. 27 patients in Group A (22.7%) and 41 patients (34.5%) in Group B had complications during the procedure (p = 0.044). Complication during the recovery rates of Group A (110 patients, 92.4%) was significantly higher than Group B (48 patients, 40.3%) (p = 0.001). In addition, the recovery time of Group A was significantly higher than Group B (78.85 ± 25.47 vs. 34.46 ± 14.50min, p = 0.01).

Conclusion: Our study demonstrated that midazolam-ketamine and fentanyl-propofol combinations provide effective sedation of children during UGE. In children, UGE procedures can be quite comfortable when using the midazolam-ketamine combination. However, adverse effects related to ketamine were observed during the recovery.

Disclosure of interest:
1. Ulas Emre Akbulut,
   Title: M.D.
   Email: ulasemre@hotmail.com
   Conflicts: Ulas Emre Akbulut reported no conflicts of interest

2. Sedat Saylan,
   Title: M.D.
   Email: sedatsaylan@yahoo.com
   Conflicts: Sedat Saylan reported no conflicts of interest
3. Bilal Sengu,
   Title: M.D.
   Email: drbilalsengu@hotmail.com
   Conflicts: Bilal Sengu reported no conflicts of interest

4. Gulgun Elif Akcali,
   Title: M.D.
   Email: geaksoy@yahoo.com
   Conflicts: Gulgun Elif Akcali reported no conflicts of interest

5. Engin Erturk,
   Title: Asst. Prof.
   Email: engin_md@yahoo.com
   Conflicts: Engin Erturk reported no conflicts of interest

6. Murat Cakir,
   Title: Prof.
   Email: muratcak@hotmail.com
   Conflicts: Murat Cakir reported no conflicts of interest
Evaluation of esophageal pathology in children who underwent esophagogastroduodenoscopy

Ulas Emre Akbulut¹, Elif Sag², Murat Cakir³

¹Kanuni Training and Research Hospital, Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
²Karadeniz Technical University, Faculty of Medicine, Trabzon, Turkey
³Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey

Objectives and study: Data concerning the prevalence of esophageal pathologies in children, and their relations with age and sex and symptoms, are limited. The purpose of this study was to investigate the prevalence, etiology and endoscopic and histopathological characteristics of esophageal pathologies in children.

Methods: Patients aged 1-17 and undergoing esophagogastroduodenoscopy in our unit between May 2009 and June 2015 were investigated retrospectively. Patients’ ages, sex, symptoms and endoscopic findings were recorded from their medical files. At statistical analysis, the Independent Two Sample t test was used for normally distributed variables in two-group comparisons and the Mann-Whitney U test for non-normally distributed variables. The chi square test was used to compare categoric variables.

Results: Pathology was present in the esophagus of 335 patients (10.8%) (endoscopic in 205, histopathological in 12 and both endoscopic and histopathological in 118). Esophageal pathology was more common in patients aged over 10 (p<0.001, OR: 1.65, 95% CI: 1.31-2.08). A higher prevalence of pathology in the esophagus was determined in patients with reflux (89, 26.5%, p<0.001, OR: 7.58, 95% CI: 5.61-10.25) and dysphagia (10, 2.9%, p<0.001, OR: 7.01, 95% CI: 3.00-16.35). Histopathological anomaly was determined in all patients with hiatal hernia (n=8), and histopathological anomaly was also more common with high-grade esophagitis determined endoscopically.

Conclusion: This study revealed the diagnostic importance of esophagogastroduodenoscopy in patients aged over 10 with reflux and dysphagia, and that histopathological anomalies are more common in the presence of hiatal hernia and high-grade esophagitis determined endoscopically.

Disclosure of interest:
1. Ulas Emre Akbulut,
   Title: M.D.
   Email: ulasemre@hotmail.com
   Conflicts: Ulas Emre Akbulut reported no conflicts of interest
2. Elif Sag
   Title: M.D.
   Email: drturkmen@mynet.com
   Conflicts: Elif Sag reported no conflicts of interest
3. Murat Cakir,
   Title: Prof.
   Email: muratcak@hotmail.com
   Conflicts: Murat Cakir reported no conflicts of interest
Endoscopic and Histological Findings in Children with Recurrent Abdominal Pain with and without Helicobacter Pylori Infection

Daniela Jojkic-Pavkov¹, Matilda Djolai²

¹Institute for Child and Youth Health Care of Vojvodina, Department of Gastroenterology, Hepatology and Nutrition, Novi Sad, Serbia
²Clinical Center of Vojvodina, Pathology and Histology, Novi Sad, Serbia

Objectives and study: The objective of our study was to identify the prevalence of recurrent abdominal pain (RAP) among pediatric gastroenterological patients and to identify the main characteristics of endoscopic and histological findings in children with RAP with and without Helicobacter pylori infection.

Methods: Over a period of 5 years a total of 900 children aged 2-18 were hospitalized at our department. Of these, 67 had RAP and were included in our study. The inclusion criteria were: age 2-18 years and abdominal pain recurring minimum once a month during 3 months, regardless of the pain intensity. None of the patients with RAP had previously received any treatment for RAP. The patients were divided into a study group with H. pylori infection (Hp+) and a control group without H. pylori infection (Hp-). Both groups underwent upper endoscopy (esophagogastroduodenoscopy). H. pylori infection was diagnosed on the basis of at least 2 of 4 available methods: 1) rapid urease test (helico test), 2) histological examination of mucosal biopsy for helico-like organisms (HLO), 3) microscopic examination of biopsy specimens of antral gastric mucosa for HLO and 4) classical urease test for H. pylori. Data was analyzed using methods of descriptive and inferential statistics.

Results: Among the 67 patients with RAP, 35 (52.2%) were Hp+ (girls:boys=77.1%:22.9%) and 32 were Hp- (girls:boys =79.7% :20.3%). The mean age of patients with RAP was 14.73 ± 2.25 (±SD) (range 9.00 - 17.92). Hp+ and Hp- patients with RAP had similar age. Comparison of endoscopic findings of the antral mucosa in Hp+ and Hp- patients did not show significant differences as regards the presence of hiperemia (p=0.439), whereas nodularity of the antral mucosa was statistically significantly more frequent in Hp+ patients ($\chi^2=15.019$, $p<0.001$). Mucosal hyperemia and nodularity of the corpus region was not statistically significantly more frequent in Hp+ patients. Endoscopic findings of the duodenal mucosa was most commonly normal in both groups, and pathological findings were few. However, histopathological examination of the antral mucosa in Hp+ patients showed chronic active gastritis in 77.1% and chronic inactive gastritis in 22.9 %, whereas there were no normal findings. In Hp- patients, chronic inactive gastritis was found in 34.4 % and normal findings in 65.6%. Histopathological examination of the mucosa of the corpus region showed chronic active gastritis, chronic inactive gastritis and normal results in 57.1%, 40% and 2.9% of Hp+ patients, respectively and in 0%, 12.5% and 87.5% of Hp- patients, respectively. In Hp+ patients, acute and subacute duodenitis was found in 31.3 %, chronic duodenitis in 65.6 % and normal findings in only 3.1% of patients. In Hp- patients acute and subacute duodenitis was found in 10% and chronic duodenitis in 90.0% . No normal histopathologic finding was found in the Hp- group.

Conclusion: The most common endoscopic finding in patients with RAP was hyperemia, and nodularity was the most common in those who were Hp+. The endoscopic findings corresponded with chronic active gastritis in Hp+ patients and histopathologic findings were normal in Hp- patients. Although endoscopic findings of the duodenal mucosa were most frequently normal, histopathological analysis showed the presence of a form of duodenitis in both Hp+ and Hp- patients.

Disclosure of interest: None declared.
How much is the effect of helicobacter pylori in children with gastrointestinal hemorrhage?

Derya Altay¹, Tanju Basarrı Ozkan², Taner Ozgur², Aysegul Otuzbir², Nilufer Ulku Sahin²

¹Fırat University Faculty of Medicine, Pediatric Gastroenterology, Elazıg, Turkey
²Uludag University Faculty of Medicine, Pediatric Gastroenterology, Bursa, Turkey

Objectives and study: Gastrointestinal hemorrhages, alarm findings of childhood, is among the issues to be investigated carefully. The aim of this study was to evaluate the prevalence of H.pylori infection in pediatric patients admitted with upper gastrointestinal hemorrhage.

Methods: In this study, 81 pediatric patients who followed up with upper gastrointestinal hemorrhage in our clinic between January 2010 and April 2014 were included and their medical files were retrospectively analyzed. Patients were divided into two groups: Group 1; younger than 10 years and Group 2; older than 10 years. P values <0.05 were considered statistically significant.

Results: 81 of the 1164 patients who underwent endoscopic evaluation were admitted with upper gastrointestinal hemorrhage. Four of 34 patients (11.7%) in Group 1 and 16 of 47 patients (34%) in Group 2 were positive for H. pylori infection histopathologically. While gastric ulcers were detected in six patients in Group1 (17.6%) and in eight patients in Group 2 (17%), all the patients with duodenal ulcer were in Group 2. Positivity of H.pylori infection in over 10 years of age group was statistically significant (p=0.02).

Conclusion: Upper gastrointestinal hemorrhages accompanied by H.pylori were more common in patients older than 10 years. But no statistical correlation was shown between H.pylori infection and gastrointestinal hemorrhage.

Disclosure of interest: None Declared.
Are there any factors associated with chronic helicobacter pylori negative gastritis?

Efrat Broide

1 Assaf Harofeh, Tel Aviv, Israel

Objectives and study: Chronic gastritis in children is a common finding and has many etiologies including Helicobacter pylori infection. The rate of Helicobacter pylori positive gastritis (Hp+ gastritis) has been declining over the years. As a result, Helicobacter pylori negative gastritis (Hp- gastritis) has become more prevalent. The objectives of this study were: I. to investigate the prevalence of Hp- gastritis in children. II to characterize the demographic, clinical and histological features of this disorder compared to Hp+ gastritis. III to explore whether there are any predictors associated with Hp- gastritis.

Methods: The medical records of children aged between 1 and 18 years that underwent elective esophagagogastroduodenoscopy at Assaf Harofeh Medical Center in Israel were retrospectively reviewed. Demographic, clinical, endoscopic and histologic features were analyzed. Gastric biopsies were taken from two sites (two from antrum and two from corpus) and graded using the Updated Sydney System. Hp+ gastritis was defined by the presence of Hp by histology (H&E, Gimsa or immunohistochemistry staining).

Results: Out of 184, 66.3% (122) had chronic gastritis; 60.7% (74) had Hp- gastritis. Children with Hp- gastritis were younger (p=0.003), less Arabic origin (p=0.011) and had less abdominal pain (p=0.02). Nodular gastritis was found to be less frequent in Hp- gastritis (6.8%) compared to Hp+ gastritis (35.4%) p<0.001. Most (95.8%) children with Hp+ gastritis had pan-gastritis compared to only 50% of the Hp- gastritis group (p<0.001). The presence of neutrophils (activity of gastritis) was recorded in the minority of children (9.5%) while was prominent in the Hp+ gastritis (83.3%) (p<0.001), with specificity of 90.5%, sensitivity of 83.3%, NPV of 89.3% and PPV of 85.1%. Mononuclear infiltrates was less prominent in Hp- gastritis (p<0.001). In contrast to Hp+ gastritis, lymphoid follicles, surface epithelial damage, mucous depletion and erosions were significantly less typical to Hp- gastritis in children. The presence or absence of Coeliac disease in HP- gastritis had no impact on the histological findings.

Conclusion: Hp- gastritis is a common etiology for chronic gastritis in the pediatric population. This entity is significantly different endoscopic and histologic and typically is milder and less active compared to Hp+ gastritis. The clinical implications and prognosis of this entity is still unknown. Follow up and further investigation of those children are needed.

Disclosure of interest: "None Declared".
Associations between Helicobacter pylori infection and Body Mass Index in children: Any relation between Obesity and Helicobacter pylori?

Gunsel Kutluk¹, Nevzat Aykut Bayrak², Burcu Volkan³, Esra Polat⁴, Osen Ari⁵, İpek Yıldız Ozaydın⁶

¹Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Diyarbakır State Hospital, Pediatric Gastroenterology, Diyarbakır, Turkey
³Erzurum State Hospital, Pediatric Gastroenterology, Erzurum, Turkey
⁴Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
⁵Kanuni Sultan Süleyman Education and Research Hospital, Pediatrics, Istanbul, Turkey
⁶Kanuni Sultan Süleyman Education and Research Hospital, Pathology, Istanbul, Turkey

Objectives and study: A number of publications in adults and children have suggested that Helicobacter pylori (H.Pylori) infection may have a potential role in decreasing the likelihood of obesity. In this study we aimed to find out the prevalence of H.Pylori infection and its relation between body mass indexes (BMI) of the subjects.

Methods: Children aged 2–18 years undergoing an esophagogastroduodenoscopy were retrospectively evaluated. Gastric histology, clinical features and calculated BMI for age and gender were recorded. Patients were divided into 4 groups according to their BMI z-scores as malnutrition, normal, overweight and obese. H. pylori was determined by histopathologic examination. Data were analyzed in order to measure the association between BMI z-scores and H.pylori infection.

Results: Among a total of 1641 endoscopies, 1054 cases (54.2% female, 9.8±4.7 years, mean BMI z-score: 0.28±1.5) were eligible for the study. Overall H.Pylori infection rate of our cohort was 40.8% (n=430, 52.8% female, 10.3±4.2 years). There was no difference for age and sex between H.Pylori positive and negative groups. BMI z-score was also statistically indifferent between groups (-0.24±1.5 vs. -0.34±1.3). H.pylori infection rate was 37.8% (51/135) in malnutrition group, 44.3% (316/714) in normal group, 33.6% (36/107) in overweight group and 27.6% (27/98) in obese group. Being obese was significantly correlated with lesser H.Pylori infection rate (χ²:13.43, p<0.01). By univariate analysis, after adjustment with age, sex and BMI z-scores, H.pylori infection rate was significantly related with age only (F:3.66, p<0.01).

Conclusion: Although we found an inverse correlation between H. pylori infection rate and obesity in our study, after univariate analysis, we could not state that H. pylori infection decreases the prevalence of obesity in children. As the pathogenesis of obesity is multifactorial, further studies with a heterogeneous cohort and long-term prospective follow-up are needed to explicate this relationship.

Disclosure of interest: “None Declared”.
**Antibiotic resistance by Helicobacter pylori in a Portuguese pediatric population**

Gisela Silva¹, Joao Nascimento¹, Jean-Pierre Gonçalves¹, Fernando Pereira¹, Rosa Lima¹, Helena Maria Moreira Silva¹

¹Centro Hospitalar Do Porto, Pediatric Gastroenterology, Oporto, Portugal

**Objectives and study:** The prevalence of Helicobacter pylori infection in Portugal is high. The increasing prevalence of antimicrobial resistance, mainly for clarithromycin, undermines the success of treatment. Today, several antibiotic schemes are available for eradication treatment. The aim of study is to determine the local pattern of first-line antimicrobials resistance and the eradication rate.

**Methods:** Prospective cohort study of H.pylori infected patients (positive histological and cultural exams) followed in Centro Hospitalar do Porto from January of 2013 to September of 2015. Patients with previous treatment for H.pylori or previous gastric surgery, severe systemic illness, use of a PPI or H2 receptor antagonist in the last 6 weeks were excluded. Susceptibility to the four antibiotics, amoxycilin, metronidazole, clarythromicin, and levofloxacin were analyzed by E-test (phenotypic resistance). Point mutations that confers clarithromycin resistance was surveyed (genotypic resistance). Eradication of H.pylori infection was defined by a negative urea breath test or fecal antigen 6 - 8 weeks after finishing of treatment.

**Results:** From a total of 45 H. pylori infected patients, 6 were excluded because they had previous H. pylori treatment or severe systemic disease. 53,8% were female. Median age of infection was 15 yrs (3-17yrs). The most common endoscopic finding was nodular gastropathy (in 64,1% of patients). The eradication regimen used in all patients combined the use of three antibiotics for 14 days. 88,6% of the patients completed the treatment. The resistance rate to amoxycilin and levofloxacin was 7,7% and to clarithromycin 26,9%. There was no resistance to metronidazole. The rate of genotypic resistance to clarythromicin was 34,3%. There was an eradication rate of 95,8%.

**Conclusion:** The authors found a high resistance rate of H. pylori to clarithromycin. This factor should determine a change in local current treatment, contraindicating the use of clarithromycin as a first-line treatment for H. pylori infection in children.

**Disclosure of interest:** None Declared.
Complaints, endoscopic and histopathological findings in patients with Helicobacter pylori infection and their correlation with each other

Gunsel Kutluk¹, Tugce Kalayci², Seyma Murtezaoglu², Nermin Gunduz³

¹Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
²Kanuni Sultan Süleyman Education and Research Hospital, Pediatrics, Istanbul, Turkey
³Kanuni Sultan Süleyman Education and Research Hospital, Pathology, Istanbul, Turkey

Objectives and study: In countries with high prevalence rate of Helicobacter pylori (H.pylori), the bacteria commonly acquired during the first years of life and may lead to complications such as chronic infection, gastritis, peptic ulcers and gastric cancer. There is no significant clinical state indicating H.pylori infection in pediatric population. In this study, most common complaints, endoscopic and histopathological findings in children with H.pylori infection were evaluated and their correlation with each other was explicated.

Methods: Patients between 3-18 years, applied to the hospital with dyspepsia, epigastric pain, reflux symptoms, developmental delay, anemia and suspected gastrointestinal (GI) bleeding and underwent upper GI endoscopy were enrolled in this study. Gastric antrum and corpus biopsies were performed in all patients during endoscopy for rapid urease test and histopathological examination. Sydney classification was used to evaluate H.pylori intensity, activity of gastritis, chronic inflammation, atrophy and intestinal metaplasia. Demographical properties, complaints, endoscopic findings and Sydney scores of the patients were recorded.

Results: A total of 339 patients (183 female) were enrolled in the study. The most common complaints were dyspepsia and epigastric pain. 90% of the patients had antral pathology, 78% of which was nodularity. Relation between dyspepsia, epigastric pain and antral nodularity is found to be statistically significant. In histopathological examination, intensity score of H.pylori is found to be increasing with the age. Rapid urease test was positive in 90.2% patients, and negative in 9.8% patients. Relation between rapid urease test and the intensity of H.pylori was statically significant. Relations between detected morphological changes in the antrum and the intensity of H.pylori, activity and chronic inflammation scores were statistically significant (p=0.009, p=0.017, p=0.031, respectively). Intestinal metaplasia (IM) and gastric atrophy (GA) was present in 7.1% and 6.2% of the patients respectively. No relation was found between IM or GA with the intensity of H.pylori, endoscopic findings and complaints.

Conclusion: The most common complaints of children with H.pylori infection were epigastric pain and dyspepsia. There were significant relations with this complaints, antral morphological changes and with the intensity of H.pylori, and the intensity of H.pylori, increases with age. Since these complaints were related with antral morphological changes and these changes were related with activity of gastritis, chronic inflammation and increased intensity of H.pylori, early eradication can be recommended in these children in order to prevent from long term complications.

Disclosure of interest: None Declared.
Correlation between helicobacter pylori colonization and obesity in pediatric population

Hadar Moran-Lev¹, Ronit Lubetzky², Dror Mandel³, Shlomi Cohen¹

¹"Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology Unit, Tel Aviv, Israel
²"Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Pediatrics, Tel Aviv, Israel
³"Dana-Dwek" Children's Hospital, Tel Aviv Medical Center, Neonatology, Tel Aviv, Israel

Objectives and study: Helicobacter pylori (HP) is one of the most common bacterial pathogens in humans, generally acquired during childhood. The correlation between HP and obesity has not been thoroughly investigated. Our aims in this study is to assess the correlation between overweight/obesity and HP colonization in pediatric population.

Methods: HP colonization in 70 symptomatic children was determined after gastric biopsies during esophagogastroduodenoscopy. Anthropometric measurements, socio-demographic characteristics and medical history were recorded.

Results: The results are presented in table 1. In brief, mean age of participants was 12.41±3.16 years, 58% were female. Among the entire group 24% were obese or overweight. HP colonization rate was 31%. There were no statistically significant differences between the groups (HP positive or negative) in terms of age, gender, clinical and sociodemographic characteristics. The prevalence of obesity was significantly lower in patients with HP colonization compared to children with normal biopsy (P<0.018) Table 1.

Table 1: Characteristics of all patients, HP infected VS. Non infected children

<table>
<thead>
<tr>
<th></th>
<th>All patients (n=70)</th>
<th>HP positive (n=22)</th>
<th>HP negative(n=48)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>12.41±3.16 (range 5-18)</td>
<td>11.31±3.38 (range 5-16)</td>
<td>12.91±2.96 (range 5-18)</td>
<td>NS</td>
</tr>
<tr>
<td>Gender (female:male)</td>
<td>42:28</td>
<td>12:10</td>
<td>30:18</td>
<td>NS</td>
</tr>
<tr>
<td>Mode of delivery (CS %)</td>
<td>12 (17%)</td>
<td>4 (18%)</td>
<td>8 (16%)</td>
<td>NS</td>
</tr>
<tr>
<td>Breastfeeding (month)</td>
<td>3.87±5.83 (range 0-30)</td>
<td>3.84±5.63 (range 0-24)</td>
<td>3.89±5.41 (range 0-30)</td>
<td>NS</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>70 (100%)</td>
<td>22 (100%)</td>
<td>48 (100%)</td>
<td>NS</td>
</tr>
<tr>
<td>Nausea and vomiting</td>
<td>14 (20%)</td>
<td>7 (18%)</td>
<td>7 (14%)</td>
<td>NS</td>
</tr>
<tr>
<td>Obese/overweight</td>
<td>17 (24%)</td>
<td>2 (11%)</td>
<td>15 (31%)</td>
<td>0.018</td>
</tr>
<tr>
<td>Rooms in residency</td>
<td>4.26±1.26 ( range 2-7)</td>
<td>4.03±1.3 ( range 2-6)</td>
<td>4.37±1.23 ( range 2-7)</td>
<td>NS</td>
</tr>
<tr>
<td>Nom. of siblings</td>
<td>1.93±1.19 (range 0-5)</td>
<td>2.05±1.31 (range 0-4)</td>
<td>1.88±1.15( range 0-5)</td>
<td>NS</td>
</tr>
</tbody>
</table>
Conclusion: This study demonstrates an inverse relation between HP colonization and overweight/obesity among symptomatic children from similar socioeconomic and geographic background. The exact mechanism explaining this "protective" effect of HP colonization upon weight is yet to be determined.
GASTROENTEROLOGY: Peptic disease and helicobacter pylori

G-P-114

inhaled air analyzer Helicosens - a new device for detection of Helicobacter pylori infection

abkari mohamed¹, Kawtar Driouiche²

¹Hopital Abderrahim Elharouchi Chu Ibn Rochd , Gastroenterology Unit, Casablanca, Morocco
²Abderrahim Elharouchi Hospital Ibn Rochd University Hospital, Gastroenterology Unit, Casablanca, Morocco

Objectives and study: Many methods have been developed to detect Helicobacter pylori infection. Moreover, in developing countries, for socioeconomic reasons, most infected children are not diagnosed and/or treated for H. pylori infection. To circumvent these difficulties, a non-invasive test with reliability for all age groups of children and adolescents is required. Inhaled Air Analyzer HelicoSense is a new test for diagnosis of Infection with Helicobacter pylori. This method of HP detection is based on measurement of ammonia concentration in exhaled air. The aim of this study was to evaluate the properties of the HelicoSense gas analyzer as a non-invasive method for detection of H. pylori, in comparison with histological diagnosis.

Methods: This prospective study involved 152 children (age between 3 and 14 years) with symptoms of H. pylori infection. All patients received two types of explorations: Upper Gastrointestinal Endoscopy with histological diagnosis, and HelicoSense gas analyzer for noninvasive electrochemical detection of H. Pylori in exhaled air. The principle of operation of this new method is based on assay of the gas content in the air exhaled by the patient. Diagnosis is carried out by measuring of the ammonia concentration in the exhaled air of a patient after the intake of a fluid – a water solution of normal isotopic composition urea.

Results: Of 152 children recruited, there were 112 H. pylori positive cases, a prevalence of 73.7%. The main reason for performing endoscopy was epigastric pain in 83 patients (54.6%) followed by vomiting (39.4%), and hematemesis (13.8%). 44.6% of the H pylori positive cases exhibited nodularity of the antral mucosa. 30.3% had antral hyperemia and three patients (2.6%) had erosive gastritis. In the gastric antrum, most patients had moderate chronic inflammatory activity. Mild glandular atrophy was found in only 16%. The Helicosens test was positive in 111 cases (96.4% sensitivity) and it was negative in 41 cases (92.5% specificity) with 3 false-positive and 4 false-negative results.

Conclusion: The Helicobacter pylori infection diagnosis method with HelicoSense device is precise, non-invasive and it is easy to use. It is a rapid test (performed within 10 minutes), safe and comfortable for surveyed patients.

Disclosure of interest: None Declared
Heart rhythm and conduction disorders in children with complicated duodenal ulcer

Viachaslau Dzmitrachkou1, Kseniya Yurchyk1, Volha Dzmitrachkova2

1Belarusian State Medical University, Minsk, Belarus
2Belarusian State Medical College, Minsk, Belarus

Objectives and study: Peptic ulcer disease can lead to arrhythmias, due to the influence of the vagus nerve. The main objective of our study was to determine the frequency of heart rhythm and conduction disorders in children with complicated duodenal ulcer.

Methods: 68 patients (7 - 17 years old) with complicated duodenal ulcers, admitted to our Department of Gastroenterology, were examined (group 1). Patients were assigned to upper endoscopy, electrocardiography (ECG), Holter monitoring. The control group comprised of 40 healthy subjects (group 2).

Results: Complications of duodenal ulcer included: deformed duodenal bulb (95,8%), bleeding (2,1%), duodenal obstruction (2,1%). Heart rhythm and conduction disorders were observed in 77,9% of cases in children with ulcer and in 12,5% - in control group (p<0,001). Most frequent arrhythmias in group 1 were caused by the changes of sinus node function: unstable sinus rhythm (42,9%), sinus bradycardia (28,6%), atrial ectopic rhythm (19,0%), sinus tachycardia (9,5%). Conduction disorders included intraventricular conduction blocks (85,7%), first-degree atrioventricular block (14,3%). Other ECG changes identified in this group of children were: early ventricular repolarization syndrome (17,0%), short QT syndrome (5,7%), WPW syndrome (3,8 %), ventricular pre-excitation syndrome (3,8 %). Heart rhythm and conduction disorders in group 2 included unstable sinus rhythm (60,0%), atrial ectopic rhythm (20,0%), early ventricular repolarization syndrome (20,0%), intraventricular conduction blocks (60,0%; p<0,05 compared with group 1).

Conclusion: Heart rhythm and conduction disorders occur more often in patients with complicated duodenal ulcer, than in healthy children. Some of the identified cardiac arrhythmia may affect the systemic hemodynamics, which necessitates a dynamic observation of this group of patients.

Disclosure of interest: None Declared.
Helicobacter pylori in the pediatric population in the health area of a tertiary hospital: microbiological diagnosis and antimicrobial susceptibility

MCarmen Rivero de la Rosa¹, Zoraima Martínez Martos², María Murillo Murillo², Mónica Ballestero Téllez², Federico Argüelles Martín¹, Álvaro Pascual²

¹Hospital Universitario Virgen Macarena, Pediatric Gastroenterology and Nutrition, Seville, Spain
²Hospital Universitario Virgen Macarena, Seville, Spain

Objectives and study: Helicobacter Pylori infection whose incidence is increasing in children, can cause injuries to the gastric mucosa with the risk in adulthood of developing metaplasia of the mucosa and even MALT lymphoma or gastric carcinoma. It is recommended that treatment with a combination of an inhibitor of proton pump and antibiotics such as amoxicillin, metronidazole, clarithromycin or tetracycline. The aim of this study is to evaluate the ability of culture for the preservation of the sample, determine the relationship between the results of histopathology, culture antral biopsy and the breath test and the prevalence of pathogen resistance to antibiotics in pediatric population of our health area.

Methods: 186 cases between November 2010 and February 2014 were studied retrospectively. Suspecting infection with endoscopy was performed at least 2 take biopsy samples of gastric antrum and fundus preserved in a sterile tube with saline serum and analyzed in less than 1 hour by Gram stain, culture samples and study of antimicrobial susceptibility. Sensitivity to amoxicillin, clarithromycin, metronidazole and tetracycline were studied. Retrospectively, we obtained data from the medical records of patients, the results of histopathology, endoscopy and previous test breath.

Results: Of the 186 cases studied H. pylori was isolated in 43 (23%) The average age was 9.7 years (4-13). In cases where the culture was positive in, all but one biopsy as gastritis and neutrophilic immunological activity associated with H. pylori (98%) were reported. In 31 cases, the previous urea breath test was positive (72%), 1 negative, and 11 patients did not undergo (26%). Of the 43 cases, in 13 the infection was eradicated after a first treatment (30%). In 7 cases (16%) were detected resistance: 3 to clarithromycin, 1 metronidazole and 3 to clarithromycin plus metronidazole, so that 14% of all showed resistance to clarithromycin and 9% metronidazole. No ampicillin or tetracycline resistance were found. Of the 7 cases with resistance, 3 relapsed despite correct treatment according to the antibiogram. The 6 remaining required a second treatment for eradication despite absence of resistances (5 of which nevertheless treatment was modified).

Conclusion: H. pylori culture remains difficult and isolated only in 23% of samples. There is a very high correlation between the result of the histopathology, urea breath test and isolation in culture of H. pylori in gastric biopsy specimens of the pediatric population. In the last four years, the rate of resistance to clarithromycin (16%) is higher than metronidazole (9%). All cases were sensitive to ampicillin and tetracycline. Despite the absence of resistance, 14% of patients required more than one treatment cycle to achieve eradication.

Disclosure of interest: None Declared.
Helicobacter pylori in the oral cavity of children

Damla Aksit¹, Serap Akyuz¹, Binnur Kıratlı², Merve Usta³, Nafiye Urganci³, Aysen Yarat⁴

¹Marmara University, Faculty of Dentistry, Department of Pediatric Dentistry, Istanbul, Turkey
²Marmara University - Faculty of Dentistry, Biochemistry, Istanbul, Turkey
³Sisli Hamidiye Etfal Training and Research Hospital, Pediatric Gastroenterology, Istanbul, Turkey
⁴Marmara University, Basic Medical Sciences, Department of Biochemistry, Istanbul, Turkey

Objectives and study: The aim of this study was to demonstrate the presence of H. pylori in the dental plaque and saliva which are proposed as reservoir for gastric H. pylori of dyspeptic and healthy children respectively and to evaluate the association of oral colonization of this bacteria with gastric infection.

Methods: Seventy patients with dyspeptic complaints, aged between 5-16 years who have undergone upper gastrointestinal system endoscopy formed the study group. Control group included thirty healthy children in the same age group. Oral clinical examination and collection of saliva (2 ml) and supragingival dental plaque samples were performed. H. pylori was detected in dental plaque and saliva through a real-time PCR system.

Results: Among 70 children who underwent endoscopy 12 were gastric H. pylori (-) and 58 were gastric H. pylori (+) histopathologically. The real-time PCR identified H. pylori in the dental plaque samples of 8 (66.7%) among 12 gastric H. pylori (-) children, 45 (77.6%) among 58 gastric H. pylori (+) children and 5 (16.7%) among 30 control group. The real-time PCR also identified H. pylori in the saliva samples of 9 (75%) among 12 gastric H. pylori (-) children, 44 (75.9%) among 58 gastric H. pylori (+) children and 12 (40%) among 30 control group.

Conclusion: In both dental plaque and saliva specimens the detection rate of H. Pylori in dyspeptic group was higher than control group. In gastric (+) and (-) group the detection rates of H. pylori in dental plaque and saliva samples were similar. Our results indicate that the presence of H. pylori in the oral cavity is not associated with the gastric infection. H. pylori can occur in the oral cavity aside and independently from the stomach. High rates of H. pylori identified in the dental plaque and saliva specimens indicate that the oral cavity is a source of bacterium for the transmission of infection by the oral route.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Peptic disease and helicobacter pylori

G-P-118

Validation of quick Helicobacter pylori stool antigen test in children
Nicolas Kalach1, Gosset Pierre2, Dehecq Eric3, Papadopolos Stephane4, Spykerelle Claire5, Dupont Christophe6, Raymond Josette6
1St Vincent de Paul Hospital, Lille, France
2Département D’anatomopathologie, Hôpital St Vincent de Paul, Ghicl, Lille, France
3Département de Microbiologie, Hôpital St Philibert, Ghicl, Lille, France
4Département D’anatomopathologie, Hôpital St Vincent de Paul, Ghicl, Lille, France
5Clinique Pédiatrique Saint Antoine, Hôpital St Vincent de Paul, Groupement des Hôpitaux de L’institut Catholique de Lille (Ghicl), Lille, France
6Service de Gastroentérologie Pédiatrique, Hôpital Necker-Enfants-Malades, Université Paris Descartes, Paris, France
7Université Paris Descartes, Department de Microbiologie, Hôpital Cochin, Paris, France

Objectives and study: In children, the reference method of Helicobacter pylori (H. pylori) infection diagnosis is based on upper GI endoscopy with gastric biopsy-based-methods, i.e. histology, culture, rapid urease test (RUT), and PCR. These are invasive, explaining the need for a validated noninvasive method: detection of H. pylori antigen in the stools (SD-test) may use a quick one-step immuno-chromatographic technique.

Aim: To assess the performances of a quick, noninvasive, immuno-chromatographic, SD-test (ALERE®, Jouy-En-Josas, France) for the diagnosis of H. pylori infection in children.

Methods: From March 2014 to September 2015, 158 children (89 girls, 69 boys), median age (range) of 8.5 yrs. [8 m- 17 yrs.], with clinical signs suggesting gastritis were enrolled. Children having receiving antibiotics and/or anti-acid (PPI or anti-H2) during the last 4 weeks were not enrolled. An upper GI endoscopy was performed in all with 3 antrum & 3 corpus biopsy-specimens for: 1) histology (up-dated Sydney classification), 2) RUT, 3) culture with antimicrobial susceptibility testing, 4) real-time quantitative PCR (qPCR). Stools were also collected from all children for SD-test. The performances of the SD-test were compared to the positivity of the reference method, i.e. a positive H. pylori status, defined by the positivity of culture alone, or at least two-other biopsy-based-methods among histology, RUT and PCR. A negative H. pylori status was defined by the concordant negativity of all diagnostic biopsy-based-methods.

Results: Among 158 enrolled children, 135 were H. pylori-negative (85.4%) & 23 H. pylori-positive (14.6%). Among the 23 H. pylori-positive children, culture was positive in 22 cases (1 false negative), histology in 23 cases (1 false-negative & 1 false-positive), RUT in 13 cases (10 false negatives), qPCR in 24 cases (1 false-positive), & SD-test in 25 cases (2 false-negatives & 4 false-positives). In 2 patients, SD-test was negative despite positive culture & qPCR (low bacterial load of 10^3 & 10^4copies). For 4 patients SD-test was positive with all other tests negative. The performances of different tests were as the follow:

- SD-test: 95% IC sensibility (Se) 91.3% (86.9-95.6), specificity (Sp) 97% (94.3-99.6), positive predictive value (PPV) 84% (78.2-89.7), negative predictive value (NPV) 98.5% (96.6-100). A test performance (TP) was 96.2% (93.2-99.1).
- Histology: Se 95.7 (92.5-98.8), Sp 99.3 (97.9-100), PPV 95.3 (91.9-98.6), NPV 99.3 (97.9-100), TP 98.7 (96.9-100).
- RUT: Se 56.5 (48.7-64.2), Sp 100, VPP 100, VPN 93.1 (89.1-97), TP 93.6 (89.7-97.4).
- Culture: Se 95.7 (92.5-98.8), Sp 100, VPP 100, VPN 99.3 (97.9-100), TP 99.3 (97.9-100).
- qPCR : Se 100, Sp 99.3 (97.9-100), VPP 95.8 (92.6-98.9), VPN 100, TP 99.3 (97.9-100).

Conclusion: The SD-test (ALERE®) is a concordant, reliable, quick, & specific test with an excellent NPV for the detection of H. pylori infection in children.

Disclosure of interest: no conflict of interest.
Vitamin B12 (Cobalamin) deficiency and Helicobacter Pylori infection in children.

Sarit Peleg¹, Ron Shaoul², Raanan Shamir³

¹Emek Medical Center, Pediatric Gastroenterology, Afula, Israel
²Meyer's Children's Hospital, Rambam Medical Center, Haifa, Israel
³Schneider's Children's Medical Center Of Israel, Pediatric Gastroenterology and Nutrition Unit, Petach Tikva, Israel

Objectives and study: Helicobacter Pylori (HP) infection has been implicated in the etiology of iron deficiency anemia (IDA). Recently it was suggested that in adults, HP infection is a possible trigger for autoimmune gastritis, in a form of molecular mimicry. Thus, it is plausible that HP is involved in the early stages of pernicious anemia (PA), leading to severe gastric atrophy and contributing to depletion of vitamin B₁₂ stores. No other studies in the pediatric age group were found in a search of the English literature.

The aim of our study was to determine the prevalence of cobalamin deficiency in children with HP positive gastric biopsies compared to healthy children without HP infection.

Methods: 80 consecutive children (ages 2-18) referred for endoscopy were enrolled. Children known to have chronic diseases were excluded. Assessment of HP infection was documented by assessment of antrum and corpus biopsies. Laboratory work up included a complete blood count, serum iron, transferrin, ferritin, vitamin B₁₂, anti-parietal antibodies and gastrin levels.

Results: Of the 80 children, 30 were found to be HP positive (37.5%). Mean age was similar for HP positive and HP negative children. Mean Vitamin B₁₂ levels were 530±268pg/ml in the HP positive group compared to 502±242pg/ml in the group of children without HP infection. Serum gastrin levels were 72.1±81.3 in the HP positive group compared to 53.9±55.7 in the group of children without HP (p<0.01). IDA was found in 6 children (7.5%), three (6%) in the HP positive group and 3 (10%) in the group without HP infection. None of the study participants had anti-parietal antibodies or gastric atrophy.

Conclusion: Our results suggest that currently, neither IDA nor vitamin B₁₂ deficiency are associated with HP infection in Israeli children. Whether high gastrin levels in the HP positive group are associated with atrophic gastritis in later life could not be determined due to the short follow up period.

Disclosure of interest: “None Declared”.

High Helicobacter pylori resistance to clarithromycin and metronidazole in Turkish Children

Sevim Cakar¹, Yeşim Öztürk¹, Ebru Demiray Gürbüz², Tuba Becerikli², Özlem Yılmaz²

¹Dokuz Eylül University, Faculty of Medicine, Department of Pediatric Gastroenterology, İzmir, Turkey
²Dokuz Eylül University, Faculty of Medicine, Department of Medical Microbiology, İzmir, Turkey

Objectives and study: Antimicrobial resistance of H.pylori is a growing problem in developing countries. We have limited data about antibiotic resistance rates in our children with H.pylori infection. We aimed to assess the primary resistance to clarithromycin, metronidazole and amoxicillin in dyspeptic children with H.pylori infection.

Results: Seventy-eight (97.5%) of 80 patients were H. pylori positive by real-time PCR. Thirty-two of 80 (40.0%) were positive by culture. Twenty-nine of 78 (37.2%) patients had clarithromycin-resistant (14 of 29 had mixed infection) H.pylori strains in antrum and/or corpus biopsy specimens by real-time PCR. In 32 culture positive patients, 13 (40.6%) and 14 (43.8%) had clarithromycin-resistant H.pylori strains in antrum and/or corpus biopsy specimens by E-test and real-time PCR. All mutations were A→G transition at positions 2142/2143. Resistance determined by E-test to clarithromycin (MIC≥1µg/mL), metronidazole (MIC>8µg/mL) and amoxicillin (MIC>0.5µg/mL) were 40.6%, 37.5% and 0.0%, respectively.

Conclusion: Monitoring of H.pylori resistance to antibiotics used in the therapy is necessary. The high resistance rates found in our study should exclude clarithromycin and metronidazole based H.pylori standard eradication therapy in our region.

Disclosure of interest:
None Declared
Detection of Clarithromycin Resistance and 23S rRNA Gene Point Mutations Using the Method Polymerase Chain Reaction at Paraffin Blocks for Children with Helicobacter Pylori Infection in Manisa Region, Western Turkey

Yeliz Cagan Appak¹, Horu Gazi², Semin Ayhan³, Beyhan Cengiz Özyurt⁴, Semra Kurutepe⁵, Erhun Kasırga¹

¹Celal Bayar University School of Medicine, Department of Paediatric Gastroenterology, Manisa, Turkey
²Celal Bayar University, Clinical Microbiology, Manisa, Turkey
³Celal Bayar University School of Medicine, Department of Pathology, Manisa, Turkey
⁴Celal Bayar University School of Medicine, Department of Public Health, Manisa, Turkey
⁵Celal Bayar University School of Medicine, Department of Microbiology, Manisa, Turkey

Objectives and study: Helicobacter Pylori (H. pylori) resistance to clarithromycin has increased throughout the world and therefore the success of eradication treatment decreases. This study aims to evaluate H. pylori with clarithromycin resistant genotypes in Manisa region, Turkey.

Methods: 200 patients, who received diagnosis of H. pylori infection histopathologically, were included in the study. Polymerase chain reaction (PCR) method was applied to determine the clarithromycin resistance rate and resistance genotypes at the histologic sections prepared from antrum biopsies that had been embedded in paraffin after detection by formalin. Three major point mutations responsible for clarithromycin resistance (A2143G, A2142G, A2142C) in the 23S rRNA gene of H. pylori were detected.

Results: 63.5% of the patients were girls and 36.5% were boys and their mean age was 13.24(±2.99) years. 79% of the patients underwent upper gastrointestinal system (GIS) endoscopy due to dyspepsia, 10% due to anemia, 8.5% due to abdominal pain and 2.5% due to GIS bleeding. Clarithromycin resistance was defined for 9.5% of the patients. 5% of the patients with clarithromycin resistance had A2143G mutation, 4.5% A2142G mutation; none of the patients had A2142C mutation. A meaningful correlation was not set between upper GIS endoscopy indications and detection of clarithromycin resistance (p=0.38). All of the clarithromycin resistant patients had gastritis, only four of them had duodenal ulcers. But there was no statistically significant relationship between clarithromycin resistance mutation and peptic ulcer (p=0.28) or gastritis (p=0.08)

Conclusion: Clarithromycin can be used as a first step treatment in the eradication of H. pylori for the children in our region; if the treatment fails for some patients, clarithromycin resistance and especially A2143G mutation should be considered.

Disclosure of interest: None Declared
GASTROENTEROLOGY: Peptic disease and helicobacter pylori

G-P-122

The Effect of Helicobacter pylori Eradication on Functional Dyspepsia in Turkish Children: Cost of Diagnosis and Treatment

Aysel Ünlüsoy Aksu¹, Güldal Yılmaz², Ödül Eğritaş Gürkan¹, Sinan Sarı¹, Buket Dalgıç¹

¹Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
²Gazi University, Pathology, Ankara, Turkey

Objectives and study: There are few studies about the endoscopic examinations performed in pediatric patients with functional dyspepsia (FD), the effect of the treatment of Helicobacter pylori (H. pylori) in FD and the cost of all these procedures. The primary aim of this study is the evaluation of the effect of H. pylori eradication on dyspepsia symptom scores in children with functional dyspepsia and costs of all procedures for diagnosis and treatment regimens.

Methods: One hundred and fifty dyspeptic children (ages 8-18 years, mean 13.3 ± 2.84 years; 30% male), who symptomatically fulfilled the Rome III criteria for FD, were enrolled to this prospective study. The patients’ severity and incidence of eight cardinal dyspepsia symptoms in the latest two months were scored on the Likert scale. The symptoms were also assessed at first visit and at the 8th and 16th weeks. Upper gastrointestinal endoscopy (UGE) was performed on all patients. H. pylori negative patients have received proton pump inhibitor (PPI) treatment for eight weeks and H. pylori positive patients have received amoxicillin and clarithromycin for 10 days and PPI therapy for eight weeks. The costs of UGE and the tests for the presence or absence of H. pylori were calculated according to the fee system of Turkish social insurance and universal health insurance in 2012-2013.

Results: Forty nine (33%) children were classified in the H. pylori positive group and 101 (67%) children were classified in the H. pylori negative group. H. pylori was higher in the antrum than in the corpus, and 67.3% of patients had an endoscopic picture of antral nodular gastritis in the H. pylori positive group. For the antrum biopsy specimens, the κ coefficient was 0.87 (almost perfect) for the concordance of histologic diagnosis of H. pylori and urease test. In the H. pylori negative and positive groups, dyspepsia symptom scores improved after treatment compared with pre-treatment (P<0.05). Dyspepsia symptom scores were not statistically different after treatment and eight weeks after completion of treatment between the two groups. H. pylori was eradicated in 30 patients (61%) and H. pylori was not eradicated in 19 patients (39%). In the H. pylori - eradicated group; all dyspepsia symptoms scores decreased after the treatment; and five scores were lower in the H. pylori - eradicated group than the H. pylori - uneradicated group. Also eight weeks after completion of treatment; 6 of 8 scores were lower in the H. pylori - eradicated group than in the H. pylori - uneradicated group. H. pylori negative and positive dyspepsia diagnosis and therapy yields an average costs of 274.5 Turkish Liras (TL, approximately $152.5) and 351.6 TL (approximately $195.5) respectively per child in 2012-2013 years in Turkey.

Conclusion: The concordance of endoscopic and histologic descriptions was poor. In contrast, the concordance of histologic and urease test was almost perfect, so using only the urease test is the most cost-effective management strategy. Although the cost of tests used for the diagnosis of H. pylori in functional dyspeptic patients is high, the dyspepsia symptom scores decreased with the eradication therapy in our study and eradicating H. pylori infection would give long-term benefit by preventing development of peptic ulcer and gastric cancer. So we conclude that H. pylori should be investigated and eradicated in FD.

Disclosure of interest: None Declared.
Objective s and study: This study aimed to determine the incidence of oesophageal eosinophilia in southwestern area of the region of Madrid, analyzing the relationship between eosinophilia and the most common pollens measured in annual absolute counts (Olea, Platanus, Poaceae, Artemisia, Urticaceae, Cupressaceae and Quercus) and seasonal variations in these pollen counts. We hypothesized that a relationship between them could exist in addition to other environmental factors.

Methods: A multi-center retrospective observational descriptive study of the incidence of oesophageal eosinophilia in children aged under 15 years in the southwestern area of the region of Madrid. 254 cases diagnosed with confirmed oesophageal eosinophilia based on standard clinicopathologic criteria between 2002 and 2013 were included. The clinical data collected include age, sex, clinical presentation and diagnosis date. To test for statistical significance, the relative risk (RR) estimate was performed using negative binomial regression models to assess the association between seasonal analysis of the relationship between the oesophageal eosinophilia incidence and absolute characteristics of age, sex and clinical presentation presented.

Results: 192 were male (75.6%), age range 6 months to 14.99 years old (median 9). Symptoms at presentation were: oesophageal impaction 23.6% (n=60); dysphagia 22% (n=56); gastroesophageal reflux-like symptoms 44.9% (n=114); abdominal pain, faltering growth and others 4.3% (n=11); 5.1% were asymptomatic (n=13). We estimated the incidence of cases per 100,000 under 15 year old children / year (from 2002-2013): 0.81; 1.5; 0.37; 3.17; 3.07; 4.36; 6.87; 7.19; 8.38; 9.05; 9.14; 9.68. The overall analysis of the relationship between the oesophageal eosinophilia incidence and absolute counts of pollen types analysed both annually and at times of pollination revealed a RR> 1 for all pollens, though only Platanus showed a statistically significant difference (p <0.05).

Conclusion: The average incidence of oesophageal eosinophilia in our region has increased by 19% each year between 2002 and 2013. The characteristics of age, sex and clinical presentation presented.

GASTROENTEROLOGY: Gastroenterology other

G-P-123

Pollen count and incidence of oesophageal eosinophilia in southwestern area of the region of Madrid: is there a relationship?

Enrique La Orden Izquierdo1, Sonia Fernández Fernández2, Josef Barrio Torres3, Mª Luz Cilleruelo Pascual4, Carolina Gutierrez Junquera4, Gonzalo Botija Arcos5, Enrique Medina Benitez6, Beatriz Martínez Escribano6, Luis Grande Herrero7, Ana I. Rayo Fernández2, Gloria Rodrigo García6, Enrique Salcedo Lobato9, Carmen Miranda Cid9, Myriam Herrero Álvarez10, Nieves Romero Hombrebueno11, Mercedes Sebastián Planas12, Ignacio Macillo Fernández13, Javier Subiza Garrido Lestache14, Pedro Urruzuno Tellería6, Alfonso Barrio Merino15, Javier Manzanares López-Manzanares6, Enriqueta Román Riechmann9

1Hospital Universitario Infanta Elena , Paediatric Gastroenterology Unit, Valdemoro, Madrid, Spain
2Hospital Universitario Severo Ochoa, Paediatric Gastroenterology Unit, Leganés, Madrid, Spain
3Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
4Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
5Hospital Universitario Fundación de Alcorcón, Paediatric Gastroenterology Unit, Alcorcón, Madrid, Spain
6Hospital Universitario 12 de Octubre, Paediatric Gastroenterology, Madrid, Spain
7Hospital Universitario de Getafe, Paediatric Gastroenterology Unit, Getafe, Madrid, Spain
8Hospital Universitario Infanta Cristina, Paediatric Gastroenterology Unit, Parla, Madrid, Spain
9Hospital Universitario Doce de Octubre, Paediatric Gastroenterology, Madrid, Spain
10Hospital Universitario Rey Juan Carlos, Paediatric Gastroenterology Unit, Mostoles, Madrid, Spain
11Hospital Universitario del Tajo, Paediatric Gastroenterology Unit, Aranjuez, Madrid, Spain
12Hospital Universitario de Móstoles, Paediatric Gastroenterology, Móstoles, Madrid, Spain
13Hospital Universitario Fundación Jiménez Díaz, Epidemiology and Biostatistics, Madrid, Spain
14Clinica Subiza, Allergy and Clinical Immunology, Madrid, Spain
15Hospital Universitario Fundación Alcorcón, Paediatric Gastroenterology Unit, Alcorcen, Madrid, Spain
here are presented here are consistent with those of other reports. This increase may be related to *Platanus* pollen counts (among other environmental factors), with higher incidence occurring during pollination. According to this model, a 9.8% increase in the risk of developing oesophageal eosinophilia is expected for every 1,000 unit increase in *Platanus* pollen counts.

**Disclosure of interest:** None Declared.
Clinical profile of esophageal eosinophilia: multicenter study of the southwest area of Madrid.

Sonia Fernández Fernández¹, Ana I. Rayo Fernández¹, Carolina Gutierrez Junquera², Enrique de la Orden Izquierdo³, Mª Luz Cilleruelo Pascual², Enrique Medina Benítez⁴, Josefa Barrio Torres⁵, Gloria Rodrigo García⁶, Pedro Urruzuno Tellería⁴, Carmen Miranda Cid⁷, Gonzalo Botija Arcos⁸, Luis Grande Herrero⁹, Mercedes Sebastián Planas¹⁰, Iván Carabaño Aguado¹¹, Ana Isabel Ruiz Díaz¹², Encarna Lancho Monreal¹³, Javier Manzanares López-Manzanares¹, Enriqueta Román Riechmann²

¹Hospital Universitario Severo Ochoa, Paediatric Gastroenterology Unit, Leganés, Madrid, Spain
²Hospital Universitario Puerta de Hierro-Majadahonda, Pediatric Gastroenterology Unit, Majadahonda, Madrid, Spain
³Hospital Universitario Infanta Elena, Pediatric Gastroenterology, Valdemoro, Madrid, Spain
⁴Hospital Universitario 12 de Octubre, Paediatric Gastroenterology, Madrid, Spain
⁵Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
⁶Hospital Universitario Infanta Cristina, Paediatric Gastroenterology Unit, Parla, Madrid, Spain
⁷Hospital Universitario Infanta Cristina, Pediatric Gastroenterology, Parla, Madrid, Spain
⁸Hospital Universitario Fundación de Alcorcón, Paediatric Gastroenterology Unit, Alcorcón, Madrid, Spain
⁹Hospital Universitario de Getafe, Paediatric Gastroenterology Unit, Getafe, Madrid, Spain
¹⁰Hospital Universitario de Móstoles, Paediatric Gastroenterology, Móstoles, Madrid, Spain
¹¹Hospital Universitario Rey Juan Carlos, Pediatric Gastroenterology, Móstoles, Madrid, Spain
¹²Hospital de El Escorial, Pediatric Gastroenterology, San Lorenzo de El Escorial, Madrid, Spain
¹³Hospital Universitario del Tajo, Pediatric Gastroenterology, Aranjuez, Madrid, Spain

Objectives: Eosinophilic esophagitis (EoE) is a chronic inflammatory disorder, confined to the esophagus, characterized by esophageal dysfunction and eosinophilic-predominant inflammation of esophageal mucosa (≥ 15 eosinophils per high-power field, eos/hpf). Other causes of esophageal eosinophilia should be excluded, specifically proton pump inhibitor-responsive esophageal eosinophilia. The objective of this study is to describe clinical, endoscopic, and histologic features in patients with esophageal eosinophilia, the compliance with ESPGHAN guidelines for the diagnosis of EoE and the frequency of response to proton pump inhibitor (PPI) treatment.

Methods: We prospectively enrolled new patients with esophageal eosinophilia diagnosed between September 2014 and September 2015 in twelve Hospitals of the southwest area of Madrid. Clinical profile of the patients was analyzed, as well as the compliance with ESPGHAN guidelines (high dose PPI treatment for 8 weeks) prior to diagnosing EoE. Frequency and characteristics of responders and nonresponders were analyzed.

Results: Seventy-eight patients (71% males, 2-15 years) were included. Regarding clinical outcomes, 52.3% reported abdominal pain, 37.1% food impaction, 26.9% vomiting and 25.6% dysphagia. About 45% of children reported clinical symptoms with specific foods, the most frequently involved were meat, milk and rice. Median delay in diagnosis of esophageal eosinophilia was 11.2 months. Regarding allergic background, 39% had asthma, 25% had food allergy and 69.4% had aeroallergen sensitization. There was no association between symptoms and histological severity. Fifty-six patients (71.8%) received high dose PPI trial, histological response was observed in 28 children (50%) and 28 were finally diagnosed with EoE. Clinical symptoms were similar in both groups (Table 1). There were no significant differences in atopic background, food allergy, aeroallergen sensitization and pretreatment endoscopic score between both groups. The mean pretreatment peak eosinophil count was higher in EoE than in PPI responsive esophageal eosinophilia (PPI-REE) patients (52.2± 32.6 vs 32.03±25.62; P=0.04).

Table: Clinical Characteristics of PPI-REE and EoE patients

<table>
<thead>
<tr>
<th>Clinical Characteristics</th>
<th>EoE (n=28)</th>
<th>PPI-REE(n=28)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>18</td>
<td>18</td>
</tr>
<tr>
<td>Chest pain</td>
<td>8(28.6%)</td>
<td>5 (17.9%)</td>
</tr>
</tbody>
</table>

Vol. 62, Supplement 1, May 2016 302
<table>
<thead>
<tr>
<th>Condition</th>
<th>Count (Percentage)</th>
<th>Comparison Count (Percentage)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Food impaction</td>
<td>12 (42.9%)</td>
<td>12</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>12 (42.9%)</td>
<td>13 (46.4%)</td>
</tr>
<tr>
<td>Dysphagia</td>
<td>13 (46.4%)</td>
<td>11 (39.3%)</td>
</tr>
<tr>
<td>Vomiting</td>
<td>7 (25%)</td>
<td>10 (35.7%)</td>
</tr>
</tbody>
</table>

Atopic state:  
- Asthma: 12 (12)  
- Food allergy: 8 (8)  
- Aeroallergen sensibilization: 8 (9)

**Conclusion:** The great majority of children with esophageal eosinophilia received PPI trial according with ESPGHAN guidelines, and 50% responded to high dose PPI treatment. There were no significant differences in clinical profile, pre-treatment endoscopic score and atopic background between both groups. Pretreatment mean peak eosinophil count was significantly higher in nonresponders to PPI.

**Disclosure of interest:** None Declared.
Evaluation of patient/parent satisfaction of a newly established Paediatric Gastroenterology Ambulatory Unit (PGAU).

Aikaterini Kakotrichi¹, Neil Shah¹, Sara Sider¹, Eleni Volonaki¹, Sibongile Chadokufa¹, Bonita Huggett¹, Fevronia Kiparissi¹

¹Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom

Objectives and study: Our aim was to evaluate patient/parent satisfaction for the newly established rapid access ambulatory unit. The Paediatric Gastroenterology Ambulatory Unit (PGAU) was established 18 months ago, aiming to provide rapid access and hence improving the quality of care of patients. It was designed for current patients that are deteriorating and newly diagnosed ones. The ambulatory facilities comprised clinical reviews, laboratory and radiology investigations, as well as dietetic and CNS reviews.

Methods: A previously validated, modified and anonymous questionnaire was used; it was distributed to the parents/patients for completion after the consultation. The form included 19 questions and the answers provided were either qualitative values (i.e. poor to excellent) or quantitative (i.e. from a numerical scale 0 to 10). It also provided the opportunity to offer free comments. Parameters examined included evaluation of the pre-appointment administration, staff attitude and courtesy, medical and nursing care and overall satisfaction with the service.

Results: The data were prospectively collected over a one-month period. 52 out of 60 questionnaires were successfully completed. Out of 52, 15 (28.8%) were completed by patients and 37 (71.2%) by parents, 37 were female (71.2%) and 12 were male (23%), 3 (5.8%) did not comment. The administration booking process was scored 5 (very good) on a range of 1 being poor to 6 being excellent. The staff attitude and courtesy was evaluated as excellent for the doctors (5.62), nurses (5.63) and Allied Health Professionals- AHPs (5.60) respectively, on a scale from 1 being very poor to 6 being excellent. On a scale from 1 rated as ‘no confidence’ and 3 rated as ‘yes definitely confident’, the confidence and trust were rated 2.90 for doctors, 2.88 nurses and 2.89 AHPs. 94.2% of patients/parents thought that the ‘right amount’ of information was given to them about the condition, diagnosis and treatment; 5.8% thought that information given was either ‘not enough’, ‘too much’ or ‘didn’t know’. Overall, the average score for the degree of overall satisfaction with regard to all of the services provided, was nine 9 (very good) on a scale from 1 (very poor) to 10 (excellent). Lastly, in the friends and family test, 90% were extremely likely to recommend PGAU to other families.

Conclusion: The evaluation of the newly established PGAU services revealed high patient and parent satisfaction levels and has been found to be an excellent model of delivering care that could be used within other settings.

Disclosure of interest: “None Declared”
Non-communicable chronic diseases: the role of neonatal characteristics

maria elisabetta Baldassarre¹, Antonio Dimauro¹, Silvio Tafuri¹, Nicola Laforgia¹

¹University of Bari-Policlinico Hospital, Biomedical Science and Human Oncology- Neonatology and Nicu Section, Bari, Italy

Objectives and study: Non communicable chronic disease are still the major cause of mortality and morbidity. Neonatal characteristics could early influence their development. Aim of our study was to evaluate the influence of selected neonatal characteristics on non-communicable chronic disease development during life.

Methods: a questionnaire was assessed to evaluate the influence of cesarean section, breastfeeding and prematurity on development of non-communicable chronic disease as asthma and allergy, celiac disease, type I and II diabetes, overweight and obesity. The questionnaire was distributed by means of an online form linked to a Facebook page. Data were analyzed using EXCEL and STATA.

Results: 6379 people participated to our survey (5106 (80%) female, mean age 25.6 ± 9.9). About three in ten (29.9%) were born by cesarean section. 36.7% received exclusive breastfeeding until 6 month of life. 1091 (17.1%) subjects were born prematurely at a mean gestational age of 34.7± 3.4 weeks. 7.7 % of responders have a family history of celiac disease, 13.5 % of diabetes (1 or 2) and 35.6 % of allergy, 2048 (32.1%) subjects reported asthma or allergy, 239 (3.7%) celiac disease, 101 (1.6%) type II diabetes and 51 (0.8%) Type I diabetes. 1318 (20.7%) reported a BMI >25 and in particular 349 (5.5%) were obese. Cesarean section resulted not associated to development of asthma and allergy, celiac disease, type I and II diabetes, overweight and obesity. Our study revealed an inverse association between breastfeeding and risk of asthma and allergy (OR=0.49; p=0.002), type II diabetes (OR=0.63; p=0.023), overweight (OR=0.74; p=0.014) and obesity (OR=0.60; p<0.0001). No association was found related to type I diabetes and celiac disease. Preterm births was not associated to development of asthma and allergy, celiac disease, type I and II diabetes but seems to have a protective role on overweight (OR=0.69; p=0.015) and obesity (OR=0.65; p=0.012) development.

Conclusions: many neonatal and parental characteristics could influence non-communicable chronic disease development during life. These characteristics could have a direct or indirect influence on neonatal gut establishment with subsequent health implications later in life. Further longitudinal studies are needed to confirm our conclusions

Disclosure of interest: None Declared.
Clinical Features of Appendicitis in Early Childhood: Comparison with Late Childhood Onset

Chun Woo Song¹, Myung Seok Shin², Jae Young Kim¹

¹Chungnam National University Hospital, Pediatrics, Daejeon, Rep. of South Korea
²St. Mary's Hospital, Pediatrics, Daejeon, Korea, Rep. of South

Objectives and study: In toddler and preschool age, a diagnosis of appendicitis is a challenge for the practitioner due to an uncommon event, frequent atypical presentation, and rapid progress of complications. The goal of this study was to clarify the clinical features and assess the scoring systems in this age group.

Methods: We retrospectively collected data on 113 patients below 10 year of age who were confirmed acute appendicitis based on the surgical and pathologic findings from June 2010 to May 2015. Enrolled subjects were divided into two groups according to age as group I (preschool≤5year, n=32) and group II (5<prepuberal age≤10 years, n=81). Medical records were analyzed as clinical presentations, interval between symptoms onset to diagnosis, laboratory findings, pediatric appendicitis score (PAS) and modified Alvarado score (MAS).

Results: Mean age was 4.3±1.1 years in group I and 8.7±1.3 years in group II. The most common symptom was abdominal pain in each group (93.8% vs. 98.8%). Other presenting symptoms were fever (71.9%), vomiting (65.6%), RLQ localization (43.8%) and diarrhea (6.3%) in preschool age and RLQ localization (79.0%), vomiting (70.4%), fever (35.8%), and diarrhea (18.5%) in prepuberal age, retrospectively. The occurrence of fever and RLQ localization were significant between two groups (p=0.006, 0.002), but those of RLQ tenderness and rebound tenderness were not different. The mean delay from onset of symptoms to diagnosis was significant different between the groups (2.08±1.79 days vs. 1.27±1.00 days, p=0.003). Of laboratory results, CRP was only significant between the groups (8.13±7.67 mg/dL vs. 3.56±4.81 mg/dL, p=0.003). PAS and MAS were significantly different between the groups (4.87±1.84 vs. 6.06±1.64, 4.71±1.68 vs. 5.82±1.43; p=0.003, 0.002, respectively). Perforation and abscess formation were more frequently presented in group I than group II (53.1% vs. 21.0%, 40.6% and 3.7%, p<0.001, <0.001, respectively).

Conclusion: This data shows that acute appendicitis in early childhood is rapid often represents non-typical symptoms, more severe progress and higher incidence of complications. The PAS and MAS may seem to be a weak tool in evaluating appendicitis in early childhood. Modified or adjusted scoring system might be warranted for tool in diagnosing early childhood onset acute appendicitis.

Disclosure of interest: None Declared
Availability of low dose CT in the diagnosis of appendicitis in childhood and comparison of abdominal USG and standard dose CT

In Seok Lim, Kyung Hoon Lee, Dae Yong Yi

1Chung-Ang University Hospital, Department of Pediatrics, Seoul, Rep. of South Korea

Objectives and study: Acute appendicitis is the most common abdominal disease in pediatrics that requires surgical procedure. Diagnostic accuracy of acute appendicitis gets higher while negative appendectomy rate gets lower as imaging techniques has developed. Ultrasonography (USG) is considered as safe diagnostic method, however, its diagnostic accuracy is variable due to operator dependent and it is difficult to apply in obese patients. Computed tomography (CT) scan should be careful to prescribe due to radiation hazard, which is why interest in low dose CT has increased recently. Most studies in the past were performed in young adults or adolescents; moreover there has been no clinical study for childhood, especially early age. Therefore, we evaluated usefulness and accuracy of low dose CT in diagnosis of childhood with acute appendicitis and compared it to abdominal USG and standard dose abdominal CT.

Methods: 484 childhood patients younger than 10 years old who were presented to Chung-Ang University Hospital between March 2005 and December 2014 and examined and/or treated for acute appendicitis were recruited for this study. The subjects were divided into 4 groups according to performed radiologic methods; low dose CT group, abdominal USG group, standard dose CT group and USG + standard dose CT group. The subjects were categorized according to age classification and BMI.

Results: Of patients evaluated with radiologic methods, surgical procedure was performed in 312 patients after diagnosis of acute appendicitis. (low dose CT; 90, USG; 40, standard dose CT; 167, and USG + standard dose CT; 15). The low dose CT was contributive tool in appendicitis, and there was no significant difference by comparison with USG or standard dose CT in sensitivity (94.4% vs 95.0% & 95.2%, $P=0.879$), specificity (96.4% vs 80.0% & 97.5%, $P=0.025$), positive predictive value (96.6% vs 92.7% & 98.8%, $P=0.031$) and negative predictive value (94.1% vs 85.7% & 90.7%, $P=0.944$). In perforated patients, the low dose CT was diagnosed all patients. Both early childhood and middle childhood were effectively diagnosed using low dose CT. In comparison according to obesity, low dose CT was useful and represented similar results to USG and standard dose CT in all BMI groups.

Conclusion: Low dose CT is effective and relatively accurate in diagnosis of acute appendicitis in childhood, as well as early age or obese patients. Also, there was not insufficient irrespective of early age or obesity. Therefore, the low dose CT could be the effective diagnostic method for acute appendicitis in childhood as well as adolescents.

Disclosure of interest: The authors have indicated they have no potential conflicts of interest to disclose.
GASTROENTEROLOGY: Gastroenterology other

G-P-129

Anastomotic ulcerations in short bowel syndrome: an unsolved problem

Filippo Torroni¹, Paola De Angelis¹, Luigi Dall'Oglio¹, Erminia Romeo¹, Roberto Tambucci¹, Chiara Grimaldi¹, Antonella Diamanti¹, Teresa Capriati¹, Dominique Hermans², Pietro Bagolan¹, Fabio Fusaro³

¹Bambino Gesù Children’s Hospital, Rome, Italy
²Saint Luc Hospital - Université Catholique de Louvain, Brussels, Belgium
³Bambino Gesù Children’s Hospital, Neonatal Surgery, Rome, Italy

Objectives and study: Anastomotic ulceration (AU) may be an unsuspected and potential life threatening complication in patients affected by short bowel syndrome (SBS) after intestinal resection and anastomosis. The aim of the study is to analyse risk factors, diagnosis, treatment and outcome of AU in SBS patients.

Methods: Clinical records from pediatric patients affected by SBS followed in two European institutions between 1995 and 2015 have been reviewed. Data analysis included primary diagnosis, age of bowel resection, length of remnant bowel, presence of ileocecal valve, age at diagnosis, symptoms, endoscopic and histologic findings, therapies, outcome.

Results: Seven patients (5 boys, 2 girls) presented an AU. Underlying diseases were necrotising enterocolitis (NEC) in 4, gastroschisis in 2 and multiple intestinal atresia in one. The mean age at AU diagnosis was 6.2 years (range 10 months – 17.5 years). The mean intestinal length was 63.8 cm (range 30-150 cm). Ileocecal valve was resected in 5/7 patients. Principal symptoms included occult bleeding and chronic iron-deficiency anemia in 4, acute anemia in 2 and life-threatening intestinal bleeding in one. All AU were diagnosed by endoscopy (5 colonoscopy, 1 enteroscopy, 1 small bowel capsule endoscopy). Five AU were located at the ileocolonic, 1 ileo-ileal and 1 colocolonic anastomosis. Histology showed a polymorphous nonspecific inflammatory infiltrate in 5 patients.

During the first endoscopic check, two patients required balloon hydrostatic dilations of a stenotic anastomosis; one relapsed and needed surgical resection for chronic bleeding; the other patients underwent two successful dilations.

Six out of 7 patients received medical treatments at onset: 1 patient antibiotics + cholestyramine, 3 patients antibiotics + budesonide, 1 patient antibiotics + mesalazine, 1 patient only antibiotics; one patient needed emergency endoscopic treatment by argon plasma for life-threatening severe acute AU hemorrhage. One patient, received also platelet gel on AU for moderate acute bleeding, during medical treatment.

One patient underwent surgical enterostomy for recurrent chronic anemia, resistant to several courses of medical treatment, without evidence of AU active bleeding.

All patients are free of symptoms in a mean follow-up of 14 months (range 3 - 24 months).

Conclusion: In SBS patients with chronic anemia not explained by malabsorption AU should keep in mind. In our population ischemic causes (NEC and gastroschisis), could explain AU. A combined medical, endoscopical and surgical treatment is mandatory to control symptoms. Because of small case series, long-term follow-up from different referral centres could be necessary to define the best approach.

Disclosure of interest: none declared
Screen Postpartum Depression in Pediatric Gastroenterology: Time Has Come.

Gokhan Baysoy1, Gizem Ondalıkoglu2

1Istanbul Medipol University School of Medicine, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
2Istanbul Medipol University School of Medicine, Pediatrics, Istanbul, Turkey

Objectives and study: Postpartum depression (PPD) causes suffering of mother and adversely effects the growth and development of the infant. Important portion of the infants in the pediatric gastroenterology outpatient clinics have functional/physiological conditions such as infantile colic and physiological reflux. Although these symptoms disappear in time they might impose extra stress on the mother. In this study, we sought to determine impact of the functional/physiological conditions in the infants below 1 year of age on the postpartum depression.

Methods: This study was carried out in pediatric gastroenterology outpatient clinic from June 2015 to December 2015. Mothers of infants under 1 year of age were included. Eligible mothers were requested to fill a questionnaire including a validated Turkish version of Edinburgh Postpartum Depression Scale and demographic data including age of mother, number of children, previous depression history and perceived family support. A score of 12 or higher was accepted as postpartum depression.

Results: A total of 164 mothers were included. Mean age of mothers and infant were 30±4.8 years and 4.4±3.0 months respectively. Prevalence of depression was found to be 36.6% (n=60). There was a weak but significant correlation between number of the children and PPD score (r=0.2, p=0.04). Previous history of depression was related to the presence of PPD (p=0.03). Age of mother and infant, and perceived support level was not related to PPD. Infants with functional/physiological conditions consisted of 29.3% (n=48) of the outpatients. Prevalence of depression in functional/physiological group was 31.3%, and in organic disease group was 38.8%.

Conclusion: Prevalence of postpartum depression is high in pediatric gastroenterology outpatient clinic. Organic diseases don’t cause significant increase in prevalence of depression. Given the negative effect of PPD on the health of the infant and the harmful effects of the underlying disease, PPD in gastroenterology outpatient clinic might have even worse effects on the long term compared to well children. Postpartum depression screening should be a part of every pediatric gastroenterology examination. Effects of PPD and the treatment on the symptoms of infants with functional/physiological conditions should be investigated.

Disclosure of interest: Gokhan Baysoy: None declared, Gizem Ondalıkoglu: None declared.
The burden of gastrointestinal diseases on admissions to general paediatrics: 15-years follow-up of 4500 children.

Jake Mann¹, Paul Carter², Suresh Chandran², Hardeep Uppal², Rahul Potluri³
¹University of Cambridge, Paediatrics, Cambridge, United Kingdom
²Acalm Study Group, London, United Kingdom
³Acalm Study Group, Manchester, United Kingdom

Objectives and study: Gastrointestinal diseases are frequent indications for admission to general paediatric departments. In the context of resource-limited healthcare it is important to minimise the number and duration of admissions, particularly from chronic conditions. This study aimed to identify gastrointestinal conditions associated with long admissions or frequent re-admissions under general paediatrics, to facilitate targeting of future resources.

Methods: 15-years follow-up data from 2000-2014 from 9 general paediatrics units in the United Kingdom. Patient’s diagnoses were identified using ICD-10 diagnostic codes, which was linked to hospital length of stay and admissions data. Patients with the following diagnoses were identified: appendicitis, cholecystitis, Coeliac disease, constipation, Crohn’s disease, eating disorders, gastritis, non-specific abdominal pain, and ulcerative colitis.

Results: During 15-years follow-up, there were 275961 children admitted to general paediatrics units (52% male, mean age 2.6 years). 4429 children were diagnosed with one of 9 common GI disorders (as listed above). Mean length of stay for the population was 2.8 days, with mean 4 re-admissions. Eating disorders had the longest length of stay (mean 6.5 days), with mean 11 re-admissions. This was followed by Crohn’s disease, which had a mean length of stay of 4.1 days with mean 21 re-admissions. Ulcerative colitis and non-specific abdominal pain had a high frequency of re-admission (18 and 19, respectively) but short duration of stay (2.6 and 2.2 days, respectively).

Table:

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>Number of children</th>
<th>Mean age (years)</th>
<th>Mean length of stay (days)</th>
<th>Mean number of re-admissions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appendicitis</td>
<td>1055</td>
<td>12</td>
<td>3.1</td>
<td>7</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>13</td>
<td>16</td>
<td>2.6</td>
<td>10</td>
</tr>
<tr>
<td>Coeliac disease</td>
<td>48</td>
<td>10</td>
<td>1.4</td>
<td>16</td>
</tr>
<tr>
<td>Constipation</td>
<td>2405</td>
<td>5</td>
<td>2.8</td>
<td>8</td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>80</td>
<td>12</td>
<td>4.1</td>
<td>21</td>
</tr>
<tr>
<td>Eating disorders</td>
<td>73</td>
<td>13</td>
<td>6.5</td>
<td>11</td>
</tr>
<tr>
<td>Gastritis</td>
<td>676</td>
<td>6</td>
<td>2.0</td>
<td>8</td>
</tr>
<tr>
<td>Non-specific abdominal pain</td>
<td>48</td>
<td>13</td>
<td>2.2</td>
<td>19</td>
</tr>
<tr>
<td>Ulcerative colitis</td>
<td>38</td>
<td>13</td>
<td>2.6</td>
<td>18</td>
</tr>
</tbody>
</table>

Conclusion: Eating disorders and Crohn’s disease result in a high number of admissions with long lengths of stay. Interventions to prevent admission should be targeted at these conditions to reduce pressure on general paediatric units.

Disclosure of interest: The authors have no conflict of interest to declare.
Non-invasive monitoring of regional tissue oxygenation in newborns using near-infrared spectroscopy

Laura Olariu¹, Gabriela Olariu², Sebastian Olariu², Oana Belei³, Otilia Marginean¹

¹University of Medicine and Pharmacy "Victor Babeș", Pediatrics, Timisoara, Romania
²Timisoara Municipal Hospital, Neonatology, Timisoara, Romania
³University of Medicine and Pharmacy Victor Babes, First Pediatric Clinic, Timisoara, Romania

Objectives and study: Near-infrared spectroscopy (NIRS) is a noninvasive method for monitoring in real-time regional tissue oxygenation status. NIRS has the ability to continuously and simultaneously monitor tissue perfusion in various organs without interrupting daily care. Research has demonstrated its usefulness in monitoring cerebral, intestinal and renal perfusion, in detection of potential ischemic episodes.

The objective of the study was to compare which of the two parameters used by the NIRS method are faithful for detecting changes in tissue perfusion in various diseases in newborns.

Methods: NIRS method was applied, using as parameters somatic regional oxygen saturation (rSO2S), cerebral saturation (rSO2C) and cerebro-somatic oxygenation ratio (ROCS) to a group of 30 newborns with gestational age (GA) between 24-39 weeks, birth weight between 600-3100 grams, from day 3 until day 21 of life, over a 1-5 day period required for causal diagnosis, in which we clinically presumed a decrease in mesenteric blood flow. The group included 12 newborns with ulceronecrotic enterocolitis (NEC), 6 newborns with intrauterine growth retardation (IUGR), 6 newborns with congenital heart malformation (CHM) and 6 infants with sepsis. rSO2S and ROCS were compared with each other to determine which of the two parameters are faithful for detecting changes in tissue perfusion. To verify statistical hypothesis which states that there are significant differences regarding rSO2S value and ROCS depending on the type of the disease were used ANOVA statistical tests, Bonferroni option and Pearson correlation.

Results: In the NEC group the rSO2S average was 40.37 compared with 44.94 for CHM group, 51.86 in IUGR group and 53.08 for the sepsis group. The ROCS average achieved was 0.59 for NEC, 0.68 in CHM group, 0.97 in sepsis group and 0.73 for IUGR. No statistically significant differences were found for rSO2S (F = 1.69, p = 0.18, p > 0.05) inside the group and between groups values but were significant for ROCS (F = 2.82, p = 0.04, p < 0.05).

Conclusion: The study shows that continuous noninvasive monitoring with NIRS technology can show that impaired intestinal perfusion increases with decreasing GA. Decreases of the two parameters are influenced by GA (rSO2S: p = 0.008; ROCS: p = 0.03). The lowest values of intestinal perfusion are in NEC (rSO2 = 40.37, ROCS = 0.59), followed by CHM (rSO2S = 44.94, ROCS = 0.68), IUGR (rSO2S = 51.86, ROCS = 0.73) and sepsis (rSO2S = 53.08, ROCS = 0.97). rSO2S value is less statistically significant (F = 2.82, p = 0.18) compared with ROCS (F = 2.82 p = 0.04) in patients with NEC compared to those with CHM, sepsis or IUGR. ROCS is the most accurate parameter in determining intestinal perfusion changes and the use of NIRS remains a very good method for early detection of lower intestinal perfusion in various diseases.

Disclosure of interest: None Declared.
Ten years after a successful intestinal transplantation: what is their life?

Lorenzo Norsa¹, Girish Gupte², Esther Ramos Boluda³, Francisca Joly⁴, Olivier Corcos⁴, Jacques Pirenne⁵, Gustaf Herlenius⁶, Florence Lacaille⁷

¹Hopital Necker Enfants Malades, Gastroentérologie Hépatologie et Nutrition Pédiatriques, Paris, France
²Birmingham Children’s Hospital, Hepatology, Birmingham, United Kingdom
³University Hospital La Paz, Madrid, Spain
⁴Beaujon Hospital, Clichy, France
⁵University Hospitals Leuven, Leuven, Belgium
⁶Sahlgrenska University Hospital, Goteborg, Sweden
⁷Hopital Necker Enfants Malades, Paris, France

Objectives and study: Intestinal transplantation (ITx) is a difficult procedure, it can lead to physical or psychological sequelae. Aim is evaluate graft function, impact on life and psychosocial status in long term survivors.

Methods: Using the Network for Intestinal failure and Transplantation in Europe (NITE), we enrolled all European patients, who received ITx before 18 years of age and enjoy a good function after 10 years or more of follow-up.

Results: 38 patients with mean age of 18 years were enrolled from 5 centers. 1 needs parenteral nutrition while 7 are on complementary enteral nutrition for feeding disorders. 6 patients had 5 or more stools a day, and 3 are experiencing stool incontinence. 1 patient has a gastrostomy and 4 an ileostomy. The mean standard deviation for height is -1.2 and -1.1 for weight. In the last 2 years 50% had endoscopy and 29% stool balance study. In the last year 11 patients needed hospitalization for complications and 22 in the last 5 years, with a medium stay of 19 days in 5 years. Most frequent complications were acute diarrhea and infections. 53% of patients are taking 5 or more drugs daily. Special medical or psychological assistance is needed in 9 and 11 patients. Regarding personal life 31 patients are in training and 3 are working; 29 patients are living with parents. 2 have alcohol and drugs addiction, 1 have been in prison and one is morphine dependant.

Conclusion: In patients with good long term graft function we observed a significant burden of health care. Only a few of them needed nutritional support, due to feeding disorders, few had still a stoma. However bowel movements can be a problem in few, number of drugs is still high in most. One third needed emergency hospitalization recently and more than half in the last five years. Majority of patients is still dependent from parents but they are still young. More than half of them need a special medical or psychological assistance and some developed frightening addictions. These long term results should help us to prevent and treat these problems in the future.

Disclosure of interest: None Declared.
Specificity of infant gastric digestive conditions: new in vivo data from preterm

Samira De Oliveira1, Amélie Deglaire1, Olivia Ménard1, Amandine Bellanger2, Yann Le Gouar1, Emelyne Dirson3, Gwénaele Henry1, Candice Perrier1, Patrick. Pladys2, Didier Dupont1, Claire Bourlieu4

1Inra - Agrocampus Ouest, Umr1253 Science et Technologie du Lait et de L’œuf, Rennes, France
2Chu Rennes, Service de Pédiatrie, Rennes, France
3Chu Rennes, Lactarium, Unité Nutrition et Diététique Infantile, Rennes, France
4Umr Stlo 1253 Inra-Agrocampus Ouest, Bioactivity and Nutrition, Rennes, France

Objectives and study: The digestive functions are immature during the first months of life, especially for preterm newborns (i.e. motility, enzymatic and secretory functions). The gastric digestion of complex colloidal emulsions such as human milk and infant formulas is a key step which will further modulate nutrient absorption and infant nutrition. Factors such as gastric acidification, emptying rate and enzyme outputs are key parameters that play a role in the kinetics of hydrolysis and the disintegration of these emulsions, and may be influenced by the nature of the meal and the age of the infant. The purpose of this study was to characterize gastric contents and physiological parameters of preterm infants in fasting state or after ingestion of raw, pasteurized or pasteurized-homogenized human milk.

Methods: In vivo study was conducted at Rennes Hospital on preterm infants fed by a nasogastric tube (NCT02112331). Newborns were included in two independent groups determining the type of meals: A) raw and pasteurized human milk; B) pasteurized and pasteurized-homogenized human milk. Gastric contents were collected twice a day, over six day. Gastric contents were collected before meal ingestion and 35, 60 or 90 min after meal ingestion. Gastric volume and pH were measured. Lipase activity was determined by titration of released free fatty acids from tributyrin (pH-stat technique, at pH 6 and pH 8, at 37°C). Gastric emptying rates and ratio of meal to secretions were determined using two different meal markers: total fatty acids for the lipid phase and taurine for the liquid phase. The markers were quantified respectively by gas and cation-exchange chromatography.

Results: Infants from group A (n=12) were 16 to 53-day old at the first day of the study. On average (±SD), birth weight was 1.4 ± 0.3 kg and gestational age 29.6 ± 1.0 weeks. In group A, fasting gastric volume was 1.4 ± 1.6 mL/kg of body weight and fasting pH was 3.7 ± 1.0 (range: 1.7 to 5.6). Gastric acidification was not impacted by meal (p > 0.05). On average, pH values of gastric digesta were 6.0 ± 0.6, 5.2 ± 0.7 and 4.4 ± 0.8 at 35, 60 and 90 min after ingestion, respectively. These data confirm the neonates’ limited capacity of acidification but also suggest the impact of frequent feeding. Still in group A, at 35 min of digestion the gastric volume was higher for pasteurized than for raw human milk (p < 0.05). Similar trends were observed in group B and will be further discussed. Some lipase activity was measured in the fasting state; in postprandial aspirates the activity depended on the meal ingested. The estimation of gastric emptying rates and ratio of meal to secretions determined by lipid or liquid markers is an original approach. Values differed depending on the marker, revealing a non-homogeneous emptying of the emulsion. It has been demonstrated (Marciani et al., 2007) that emulsions that are destabilized in the gastric compartment can modulate the hormonal feedback (cholecystokinin).

Conclusion: This study presents a unique set of data illustrating the specificity of preterm infants’ gastric digestive conditions. Understanding the physiological environment in the infant gastric tract is essential to optimize nutrition and oral drug delivery. Moreover, these data will be useful to develop relevant in vitro models of infant digestion.

Disclosure of interest: None declared.
Evaluation of microencapsulated sodium butyrate effects in young patients with newly diagnosed IBD – preliminary results.

Agnieszka Gawronska¹, Izabella Łazowska-Przeorek¹, Katarzyna Karolewska-Bochenek¹, Maria Kotowska¹, Marcin Banasiuk¹, Jarosław Walkowiak², Piotr Albrecht¹, Aleksandra Banaszkiewicz¹

¹Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Warsaw, Poland
²Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Sciences, Poznan, Poland

Objectives and study: Increasing number of reports emphasize the key role of short-chain fatty acids (SCFAs) in gastrointestinal diseases therapy. The aim of the study was to assess the efficacy of microencapsulated sodium butyrate (MSB) supplementation in young patients with newly diagnosed IBD.

Methods: This was a multi-center, randomized, double blind, placebo controlled study. Sixty-three patients aged from 6 to 18 years with newly diagnosed Crohn’s disease (CD) or ulcerative colitis (UC) treated with standard therapy used in IBD were enrolled to the study. All patients randomly, on the basis of computer generated randomization list, received MSB (at dose 150 mg) or placebo twice daily, orally, for 12 weeks. Clinical evaluation was based on Pediatric Crohn Disease Activity Index (PCDAI) for CD and Pediatric Ulcerative Colitis Activity Index (PUCAI) for UC, and was performed at baseline and 12 weeks. A PCDAI score ≤10 for CD and a PUCAI score <10 for UC were defined as remission.

Results: Therapeutic success defined as remission, scoring in both PCDAI and PUCAI scale below 10, gained 55.6% of all patients in MSB group and 68.8% in placebo group. The difference between groups was not statistically significant, p=0.41. In group of patients with CD, after twelve weeks PCDAI scoring decreased by 21.5 points vs. 30 points in placebo group, p=0.0896. In patients with UC, PUCAI scoring decrease by 32.5 vs. 35 points, respectively. There was not statistically significant difference between patients with CD and UC.

Conclusion: Twelve weeks supplementation of MBS did not appear to be effective in young patients with newly diagnosed IBD. Further clinical studies with large number of patients are necessary to judge its role in gastrointestinal diseases therapy.

Disclosure of interest: None Declared.
Efficacy of a micronised, dispersible ferric pyrophosphate in children with anemia associated with inflammatory bowel disease

Agnieszka Wegner1, Grazyna Mierzwa2, Sabina Wiecek3, Anna Korlatowicz- Bilar4, Maciej Dadalski5, Bartosz Korczowski3, Jaroslaw Kierkus5

1Public Children's Clinical Hospital, Warszawa, Poland
2Nicolaus Copernicus University Collegium Medicum , Chair of Vascular and Internal Diseases,, Bydgoszcz, Poland
3Medical University of Silesia, Department of Paediatrics, Katowice, Poland
4Children's Hospital, Departament of Paediatrics, Gastroenterology and Rheumatology, Szczecin, Poland
5The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland
6State Hospital No 2, University of Rzeszow, Department of Pediatrics and Pediatric Gastroenterology, Rzeszow, Poland

Objectives and study: Anemia is one of the most frequent complications of inflammatory bowel disease (IBD) in children. Iron deficiency is the most important cause of anemia in Crohn's disease and ulcerative colitis patients. Oral iron supplementation has been the main form of the treatment for anemia in IBD. However, this treatment is associated with the high risk of side effects. In addition to that, oral iron may exacerbate the inflammation of the intestinal tissues.

The aim of the study was to assess the therapy efficacy and the frequency of side effects in patients with the anemia during IBD, treated the ferric pyrophosphate.

Methods: A prospective, randomized, multicenter trial was conducted in a group of 37 children (15 girls, 21 boys) aged 13.54±2.7 years (mean±SD), with inflammatory bowel disease (19 Crohn Disease, 18 ulcerative colitis) and the iron deficiency anemia. The patients were randomly assigned to start treatment with the micronised, dispersible ferric pyrophosphate in the dose 60 mg (group 1) or micronised, dispersible ferric pyrophosphate in the dose 120 mg (group 2) for a period of 90 days. Clinical disease activity assessment and blood analysis were performed on days 0 and 90 of the trial.

Results: 34 /37 patients completed the study. During the trial the hemoglobin, hematocrit, ferritin and TIBC scores were increased in both groups with statistical significance (p<0.05). The iron level was increased with statistical significance in group 2 but not in group 1.

There were no statistical significant differences in comparison this parameters from group 1 and 2 in the 90 day of the study.

During the trial there were no SAE. 13 patients from group 1 reported the side effects (7-stomachache, 3- nauseas, 2- constipation). In group 2 – 7 patients reported the side effects (3-stomachache, 3- nauseas, 1- constipation). The difference between groups was not statistically significant.

3 patients didn’t complete the trial. Reasons for not completing the study were: withdrawal of consent (1 patient from group 2), relapse of the disease and stopped taking ferric pyrophosphate (1 patient from group 1, 1 patient from group 2).
Table:

<table>
<thead>
<tr>
<th></th>
<th>Day 0 Mean±SD</th>
<th>Day 90 Mean±SD</th>
<th>Group 1 Mean±SD</th>
<th>Day 90 Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>11.42±0.92</td>
<td>12.13±1.33</td>
<td>Hemoglobin</td>
<td>11.67±1.4</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>34.8±2.5</td>
<td>37.05±3.72</td>
<td>Hematocrit</td>
<td>35.58±3.99</td>
</tr>
<tr>
<td>Ferrum</td>
<td>40.73±28.64</td>
<td>55.76±44.27</td>
<td>Ferrum</td>
<td>43.52±22.75</td>
</tr>
<tr>
<td>TIBC</td>
<td>368.36±114.11</td>
<td>309.57±55.88</td>
<td>TIBC</td>
<td>333.11±51.25</td>
</tr>
</tbody>
</table>

**Conclusion:** Ferric pyrophosphate is effective and safe in children with IBD anemia.

**Disclosure of interest:** No
Natural history of paediatric Inflammatory Bowel Disease-Unclassified: single tertiary UK centre experience

Ahmed Kadir¹, Ylenia Perone², Fevronia Kiparissi², Neil Shah², Keith Lindley², Eleni Volonaki²

¹Great Hormond Street Hospital, Paediatric Gastroenterology, London, United Kingdom
²Great Ormond Street Hospital, London, United Kingdom

Objectives and study:

Inflammatory bowel disease - Unclassified (IBD-U) refers to patients with chronic colitis who lack characteristic features of Crohn’s disease (CD) or ulcerative colitis (UC). Children are more likely to be diagnosed with IBD-U compared to adults, with a progressively lower frequency of IBD-U with an increase in the age at diagnosis of IBD but data on the evolution of IBD-U with time are lacking. We aimed to investigate the natural history of children initially diagnosed with IBD-U in a single tertiary centre over a ten-year period.

Methods:

All patients referred to our Paediatric Gastroenterology unit between January 2004 and December 2014 with initial diagnosis of IBD-U were identified from our electronic database. Clinical, endoscopic, histological and radiological information at diagnosis and follow up were retrieved from patients records and analysed retrospectively.

Results:

From 637 children with IBD, 389 were diagnosed initially as Crohn’s disease, 159 were diagnosed with ulcerative colitis, 35 children were diagnosed with EOIBD and 30 children (6.1 years to 17.1 years) were diagnosed initially with IBD-U. Out of the 30 patients during a follow up time lag of 2-10 years only 6 (18%) patients were diagnosed with CD and 2 (6%) with UC whereas 26 (76%) children remained IBDU. The reclassification was done on the basis of repeat histology.

Conclusion:

Our study suggest that in our population the incidence or diagnosis of IBD – U was low as compared to diagnosis of CD and UC. The change of the diagnosis of IBD-U to CD or UC over time was considered to be because of disease evolvement as the histopathologist used the same criteria on different occasions.

Disclosure of interest: None
Faecal Calprotectin as a Biomarker of Intestinal Inflammation in Children younger than 5 years old.

Aikaterini Kakotrichi\(^1\), Eleni Volonaki\(^2\), Neil Shah\(^3\), Alexsandra Zambrano Perez\(^1\), Soledad Montoro Romero\(^3\), Sara Sider\(^2\), Sibongile Chadokufa\(^2\), Bonita Huggett\(^2\), Fevronia Kiparissi\(^1\)

\(^1\)Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom
\(^2\)Great Ormond Street Hospital for Children Foundation Trust, Gastroenterology, London, United Kingdom
\(^3\)Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom

**Objectives and study:** The aim of the study was to evaluate the use of faecal calprotectin (FC) as a biomarker of intestinal inflammation in children younger than 5-years old with gastrointestinal symptoms, and its correlation with very early onset inflammatory bowel disease (VEOIBD). FC is an established non-invasive biomarker of neutrophilic intestinal inflammation, which correlates closely with endoscopic activity in inflammatory bowel disease (IBD) and may differentiate IBD from functional disorders. Increased faecal excretion of FC has been reported in IBD, with the cut-off of 50 µg/g established in adults and children older than 4-years old, depicting increased neutrophil migration into the gut lumen across inflamed mucosa.

**Methods:** FC samples were collected over a 2-year period. Data were collected and analysed retrospectively and included children younger than 5-years old with gastrointestinal symptoms (abdominal pain, loose stool, PR bleeding, failure to thrive), suspected IBD or other gastrointestinal disorders. Values above 50 µg/g were considered high. The patients subsequently were selected for upper endoscopy and ileo-colonoscopy, according to medical history, physical examination, FC values and high inflammatory markers (i.e. ESR, CRP, PLT). The results were correlated with the histopathological findings.

**Results:** 219 patients were analysed, and 82 (37.4%) had an FC higher than 50 µg/g. In the high FC group, 34 patients (41.5%) had endoscopies; 8 patients (23.5%) were diagnosed with VEOIBD and the remaining 26 were non-IBD (i.e. cow’s milk protein allergy, multiple food allergies, autoimmune diseases, immunological diseases). The median FC was 225.5 µg/g (range 50-3000 µg/g). The median FC concentration was significantly higher in the IBD group (416 µg/g, range 203-3000) compared to the non-IBD group (215 µg/g, range 50-3000) (p= 0.023). The optimal FC cut-off value for IBD diagnosis was 197 µg/g in ROC-curve analysis, with sensitivity of 87.5% and specificity of 70%. After exclusion of patients younger than 12 months, both sensitivity and specificity increased (87.5% and 75.5% respectively; p= 0.008). IBD diagnosis was not confirmed in any of the patients younger than 12 months, despite high FC levels. Interestingly, 1 out of the 8 patients with positive histology (12.5%) had a negative FC.

**Conclusion:** The role of FC as a biomarker in IBD has been widely investigated in children above 4-years old. Our data show that the existing cut-off level of 50 µg/g is inaccurate for children younger than 5-years old and a higher level (197 µg/g) is more appropriate for this population. Negative samples may not exclude IBD and clinical criteria should be considered to proceed with endoscopy. Larger prospective multicentre studies are required to define fully the role of FC in this age group.

**Disclosure of interest:** “None Declared”
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-139

Maintenance of remission in paediatric Crohn disease using mesalazine monotherapy: a single centre experience

Ben Hope¹, Amit Saha², Thangarajah Anthi², Vadamalayan Babu²

¹King’s College Hospital Centre for Paediatric Liver, Gastroenterology and Nutrition, London, United Kingdom
²King’s College Hospital, Paediatric Liver, Gastroenterology and Nutrition, London, United Kingdom

Objectives and study: Mesalazine is a 5-aminosalicylic acid (5-ASA) used to induce and maintain remission in inflammatory bowel disease (IBD). It is metabolised to its active form by the intestinal mucosa, thus more useful in treating ulcerative colitis (UC) than transmural Crohn disease (CD). There is little published evidence that mesalazine is effective in maintaining remission in paediatric CD. We report our experience in the use of mesalazine as sole therapy after initial induction therapy in paediatric CD.

Methods: A retrospective electronic case note review was performed for all children diagnosed with CD and prescribed mesalazine monotherapy after successful induction therapy between 2009 – 2014 at King’s College Hospital Centre for Paediatric Liver, Gastroenterology and Nutrition. Phenotype at presentation was described according to Paris criteria. Disease activity at diagnosis and at 3, 6 and 12 months was documented using the paediatric Crohn disease activity index (PCDAI) and faecal calprotectin (FC).

Results: A total of 19 children (11 males) were suitable for this study. The mean age at diagnosis was 12 years. Four children had ileal disease, 8 ileo-colonic disease and 6 colonic disease. 18 had only inflammatory disease, while one child had strictures at the time of diagnosis. For induction therapy 9 had exclusive enteral nutrition and 9 systemic corticosteroids. One child had neither, and was prescribed mesalazine as induction therapy. The number of children in remission on mesalazine alone was 18, 14 and 5 at 3, 6 and 12 months respectively. The commonest reason to start additional therapy was ongoing disease activity. Adverse effects were rare, leading to cessation of the drug in only one child.

Conclusion: A proportion of CD patients will enter a significant period of remission while taking mesalazine as sole maintenance drug. The beneficial effect of mesalazine in CD does not appear to be restricted to those with disease limited to the colon. Our results suggest a role for mesalazine in paediatric CD.

Disclosure of interest: None
Prevalence of thromboembolism in pediatric patients with inflammatory bowel disease-data from the CEDATA-GPGE registry

Andrea Deutschmann1, Jan De Laffolie2, Claudia Wendt2, Antje Ballauff3, Rolf Behrens4, Carolin Blümi5, Martin Claßen5, Almuthe Christine Hauer1, Sibylle Koletzko7, Martin Laaß8, Thomas Lang9, Stephan Wirth10

1Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria
2University of Giessen, Department of General Pediatrics and Neonatology, Giessen, Germany
3Helios-Klinikum Krefeld, Kinderklinik, Krefeld, Germany
4University of Erlangen, Hospital for Children and Adolescents, Erlangen, Germany
5Kinderklinik Marburg, Department of Pediatrics, Marburg, Germany
6Klinikum Links der Weser, Bremen, Germany
7Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, München, Germany
8Medical Faculty Carl Gustav Carus, Technische Universität Dresden, Children’s Hospital, Dresden, Germany
9University Hospital Regensburg, Department of Paediatrics and Juvenile Medicine, Regensburg, Germany
10Universität Witten-Herdecke, Universitätsklinikum, Helios Klinikum Wuppertal, Children’s Hospital, Wuppertal, Germany

Objectives and study: In patients with inflammatory bowel disease (IBD) the risk of thromboembolism (TE) is increased, representing a relevant cause of morbidity and mortality. In contrast to other extraintestinal IBD manifestations (i.e. arthritis or uveitis), TE receives much less attention because of its low incidence. Pediatric epidemiological data are scarce, but an incidence of TE of 0.4-0.9 % in hospitalized children with IBD has been reported.

Methods: A retrospective analysis of TE cases as documented in the German-Austrian pediatric IBD registry “CEDATA-GPGE” was performed. For all patients with signs of TE a questionnaire was filled in by the treating pediatric gastroenterologist.

Results: Between 2004 and 2013, 4153 patients (age 0-18 years) with IBD were registered in “CEDATA-GPGE”. In total, we identified 12 patients with TE. Median age at diagnosis was 10 years (ys), median age at manifestation of TE was 13 ys with a median latency to TE of 2 ys. The prevalence was 0.3% with more girls than boys affected (f:m = 7:5). Eight patients were diagnosed with ulcerative colitis (UC); 5/8 had a pancolitis (Paris Classification E4), in three, disease extension is unknown. All three patients with Crohn’s disease (CD) had colonic disease (Paris classification L3, L2L4a, and L2L4b, respectively). One patient was diagnosed with IBD-unclassified. At TE manifestation, median PUCAI in 5/8 patients was 35 and median PCDAI 30. Median Hb-level in 8/12 patients was 8.9 g/dl. Most often venous sinus thrombosis (VST) was reported. In one patient myocardial infarction and VST occurred simultaneously. Information on medication was available in 10/12 patients: 7/10 received prednisolone. Immobilisation was attributed to play a role in occurrence of TE. One patient had a peripheral venous catheter placed at the site of thrombosis. 9/12 patients underwent a thrombophilia-screening. In one patient activated protein C-resistance, in two patients protein S deficiency was found, one of them presented with a right ventricular thrombus. One patient with VST suffers still from focal epilepsy.

Conclusion: Our study suggests that children with IBD have a substantial risk for TE. Identified risk factors such as anemia, colonic disease, intake of prednisolone, immobilisation, central or peripheral venous catheter access, and familial thrombophilia should be considered when managing pediatric IBD as well as preventive measures for those hospitalized (i.e. early mobilization, use of compression stockings). Initiation of pharmacologic thromboprophylaxis is a challenging decision as there are no published trials for the efficacy and safety of primary pharmacologic thromboprophylaxis in children with UC or CD.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016
Diagnostic and prognostic value of auto and anti-microbial antibody profiles in paediatric inflammatory bowel disease patients

Anna Maria Peter1, Diana Reznik2, Michael P. Horn3, Susanne Schibli2, Johannes Spalinger4, Christiane Sokollik5

1Children’s Hospital, Inselspital, University of Berne, Paediatric Gastroenterology, Hepatology and Nutrition, Berne, Switzerland
2Children’s Hospital, University of Berne, Paediatric Gastroenterology, Hepatology and Nutrition, Berne, Switzerland
3University Institute of Clinical Chemistry, University of Berne, Centre for Laboratory Medicine, Berne, Switzerland
4Children’s Hospital, Inselspital, University of Berne and Children's Hospital Lucerne, Paediatric Gastroenterology, Hepatology and Nutrition, Berne, Switzerland
5Paediatric Gastroenterology, Hepatology and Nutrition, Bern, Switzerland

Objectives and study: The prevalence of inflammatory bowel disease (IBD) in Switzerland is 1:500, with a rising incidence in children over the last few years. Up to 20% cannot be classified in the main subtypes Crohn’s Disease (CD) and Ulcerative Colitis (UC), although correct classification is important for prognosis, risk stratification and treatment.

The aim of this study was to evaluate the diagnostic and prognostic value of auto as well as anti-microbial antibodies in a paediatric cohort.

Methods: We retrospectively retrieved clinical data from diagnosis of IBD until the age of 18 or last date of follow-up and completed the antibody profiles (consisting of cANCA, pANCA, ASCA, PAB) of all patients in stored sera. Disease location and behaviour was classified according to the Paris Classification at time of diagnosis.

Results: 61 paediatric IBD patients were included (28 with CD, and 33 UC). 12 (43%) suffering from CD were ASCA IgA and IgG positive, but only 2 (6%) of the UC (p = 0.003). However, 6 (18%) of the UC were either ASCA IgA or IgG positive. 11/16 (68%) CD with ileocolonic disease were ASCA positive with a positive predictive value (PPV) = 68%, a sensitivity (TPR) of 73%, specificity (SPC) of 61%, and a positive likelihood ratio (LR+) of 1.8. 5/7 (71%) CD who ever used Infliximab were ASCA positive.

PAB positivity was found in 10 (36%) CD and in 7 (21%) UC (p = 0.258). Both CD with stricturing disease (B2) were PAB positive.

19 sera from the UC showed pANCA positivity by indirect immunofluorescence (IIF) but only 4 (14%) sera from CD (p < 0.001).

2 CD and 9 UC were positive for cANCA determined by IIF as well as proteinase 3 (PR3)-ANCA. However, none of them presented with features of vasculitis. Remarkably 15 (45%) UC were PR3-ANCA positive whereas only 2 (7%) sera from CD (p = 0.001). PR3-ANCA positivity in UC patients reached a PPV of 88%, with a TPR of 45% and a high SPC of 92%, the LR+ was 5.6.

PR3-ANCA positivity compared with xANCA (also called atypical pANCA) positivity shows a PPV of 100%, a TPR of 73% and the extraordinary SPC of 100%.

Conclusion: As previously known pANCA positivity was more common in UC than CD and ASCA positivity in CD than UC. ASCA and PAB positivity seem to predict a more complicated disease course in CD expressed by more stricturing disease and an increased need for Infliximab. Importantly, PR3-ANCA positivity was strongly associated with UC and therefore may be used as a new diagnostic marker in paediatric IBD patients.

Disclosure of interest: None Declared.
The role of environmental exposure and nutritional habits in development of inflammatory bowel disease in pediatric population

Anna Stochel-Gaudyn¹, Agnieszka Koziół-Kozakowska¹, Agata Wasilewska¹, Paweł Jagielski², Krzysztof Fyderek¹
¹Jagiellonian University Medical College, Department of Pediatrics, Gastroenterology and Nutrition, Cracow, Poland
²Jagiellonian University Medical College, Health Nutrition Department, Faculty Health Science, Cracow, Poland

Objectives and study: Inflammatory bowel disease (IBD) is a group of chronic inflammatory conditions of colon and small intestine, characterized by periods of remission and exacerbation. The clinical symptoms are mixed, unknown initial cause and multifactorial etiology being the common feature. According to the current knowledge environmental exposure and nutritional habits next to immunological and genetic factors may play an important role in the development of IBD. Aim: To assess the environmental exposure and eating habits of children with newly diagnosed IBD compared to healthy controls.

Methods: A prospective cohort study consisted of 41 children with newly diagnosed IBD (17 boys and 27 girls) and 20 healthy children (9 boys and 11 girls) as control group. In the IBD group 27 patients were diagnosed with CD and 14 with UC. The mean age for both groups was 11 years. Every study participant completed an authorial questionnaire estimating their exposure to environmental pollution and a food frequency questionnaire (FFQ) estimating their eating habits. In the IBD population the questionnaire was taken at the moment of diagnosis and covered one month prior to diagnosis.

Results: The exposition to environmental pollution was greater among IBD children then among those from control group, more of them lived on urbanized territory (70% vs 10%) and near ironworks (19.5% vs 10%) and electrical power and heating stations (34.1% vs 10%). The diet of pediatric patients with IBD didn't cover the daily nutritional recommendations, especially in reference to vegetables, fiber and dairy products. The only vegetables eaten on daily basis were tomatoes (56% of IBD children), compared to rare consumption of green vegetables such us salad or brussels sprouts (only 3% of IBD children). There was a high consumption of fruit in both groups, but still it didn't cover the daily recommendations. Only 40% of IBD children consumed dairy products on daily basis whereas in control group it was 70% of children. Consumption of fast food products was higher in IBD group compared with controls (80% vs. 56%).

Conclusion: Based on our study children with newly diagnosed IBD were more frequently exposed to environmental pollution then healthy children from the control group, which may suggest this factor as an important one in the etiology of disease development. Eating habits were poor among IBD children lacking diary and fiber products, whereas the consumption of processed food such as fast food was quite high in this group, which may also contribute to the development of IBD. Finally low consumption of fruit and vegetables among pediatric IBD patients may also influence the course of the disease since the presence of prebiotics is essential to the proper functioning of the gastrointestinal tract.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 322
Assessment of IMPACT III Emotional and Social Functioning Domain Scores in Adalimumab-Treated Paediatric Patients with Crohn’s Disease

Amy Grant¹, Anthony Otley², Johana Escher³, Jeffrey Hyams⁴, Jen-Fue Ma⁵, Gabriela Alperovich⁵, Andreas Lazar⁶, Anne M. Robinson⁵, Anthony W. Wang⁵, Samantha Eichner⁵

¹Iwk Health Centre, Nova Scotia, Canada
²Iwk Health Centre and Dalhousie University, Nova Scotia, Canada
³Erasmus MC-Sophia Children’s Hospital, Rotterdam, Netherlands
⁴Connecticut Children’s Medical Centre, Hartford, United States
⁵Abbvie Inc., North Chicago, United States
⁶Abbvie Deutschland GmbH & Co. Kg, Ludwigshafen, Germany

Objectives and study: IMPACT III is a validated, disease-specific health-related quality of life (HRQoL) questionnaire for children with inflammatory bowel disease. Using the re-categorized tool, we assessed the effect of adalimumab (ADA) on social and emotional function and examined the consistency of changes in individual questions within these domains in patients (pts) enrolled in IMAgINE 1 trial.

Methods: IMAgINE 1 was a 52-week (wk) trial of ADA that enrolled 6-17 year (yr)-old pts with moderate to severe CD (baseline [BL] PCDAI >30) who failed/were intolerant to conventional therapy. Pts experiencing disease flare/non-response could move to blinded weekly (EW) ADA after wk 12, followed by open-label (OL) EW ADA for continued flare/non-response. The IMPACT III questionnaire was administered to pts ≥10 yr at BL; the range for each individual question is 0-100; higher scores represent better QoL. Total IMPACT III scores were normalized (sum of responses divided by number of questions answered), each domain score was normalized (sum of responses for each question within domain divided by total number of questions answered). Change from BL at wks 12, 26, and 52 in the score for each domain and in individual IMPACT III questions were reported. Last observation carried forward (LOCF) was used to account for missing data (post-BL), pts who discontinued, or who moved to OL EW ADA.

Results: A total of 172 pts in IMAgINE 1 were analyzed (54.7% male, median PCDAI: 40, median CRP: 1.2 mg/dL, and mean IMPACT III total score: 57 at BL). Mean emotional and social domain scores at BL were 54 and 72, respectively. Statistically significant improvements were observed for both domain scores and some individual questions in each domain as early as week 12, and were sustained to week 52 (Table).
Table:

<table>
<thead>
<tr>
<th>Domain</th>
<th>Mean changes from baseline</th>
<th>Mean changes from baseline</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean baseline score</td>
<td>Week 12&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Emotional functioning domain</td>
<td>54</td>
<td>10&lt;sup&gt;***&lt;/sup&gt;</td>
</tr>
<tr>
<td>How much does it bother you that you have an illness that does not just go away?</td>
<td>39</td>
<td>14&lt;sup&gt;***&lt;/sup&gt;</td>
</tr>
<tr>
<td>How often do you think it is unfair that you have IBD?</td>
<td>51</td>
<td>7&lt;sup&gt;***&lt;/sup&gt;</td>
</tr>
<tr>
<td>During the past 2 weeks, were you ever angry that you have IBD?</td>
<td>62</td>
<td>16&lt;sup&gt;***&lt;/sup&gt;</td>
</tr>
<tr>
<td>Do you think too many rules or limits are placed on you because of your IBD?</td>
<td>60</td>
<td>11&lt;sup&gt;***&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup>Note that data were missing for two patients at week 12, but data were available for those patients at weeks 26 and 52

**p<0.01, ***p<0.001 for mean change from baseline to weeks 12, 26, or 52 was determined by one sample t-test

Conclusion: ADA treatment was associated with early and substantial HRQoL improvements in children with CD, as indicated by statistically significant mean increases in emotional and social functioning domain scores and in most individual questions in each domain.

Disclosure of interest: Grant: None declared; Otley, Conflict with: Janssen, AbbVie, Nestle; Escher, Conflict with: MSD, Janssen Biologics, AbbVie; Hyams, Conflict with: Janssen Orthobiotech, AbbVie, Celgene, EnteraHealth, Pfizer, Soligenix, Takeda, AstraZeneca; Maa, Alperovich, Lazar, Robinson, Wang, Eichner, Conflict with: are AbbVie employees, and may own AbbVie stock and/or options
Malignancy and mortality in paediatric onset inflammatory bowel disease

Maria Joosse1, Lissy de Ridder2, Dan Turner3, David Wilson4, Sibylle Koletzko5, Javier Martin de Carpi6, Ulrika Fagerberg1, Christine Spray4, Małgorzata Sladek7, Ron Shaoul10, Daniela E. Serban11, Eletheria Roma12, Jiri Bronsky13, Salvatore Cucchiara14, Gábor Veres15, Frank Ruemmele16, Marina Alo17, Paolo Lionetti17, Iva Hojsak18, Kajsa Kolho19, Ieuan Davies20, Genevieve Veereman21, Christian Braegger22, Eunice Trindade23, Anne Wewer24, Almuthe Christine Hauer25, Arie Levine26

1Erasmus Medical Center, Laboratory of Pediatrics, Rotterdam, Netherlands
2Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands
3Shaare Zedek Medical Center, Genius Group, Jerusalem, Israel
4University of Edinburgh, Child Life and Health, Edinburgh, United Kingdom
5Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, München, Germany
6Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain
7Centre for Clinical Research, Västmanland Hospital, Department of Pediatric Gastroenterology, Västerås, Sweden
8Bristol Royal Hospital for Children, Department of Pediatric Gastroenterology, Bristol, United Kingdom
9Polish-American Children's Hospital, Jagiellonian University Medical College, 9department of Pediatrics, Gastroenterology and Nutrition, Cracow, Poland
10Rambam Hospital, Pediatric Gastroenterology, Haifa, Israel
11Iuliu Hatieganu' University of Medicine and Pharmacy, Department of Pediatric Gastroenterology, Cluj-Napoca, Romania
12University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
13Second Faculty of Medicine, Charles University and University Hospital Motol, Department of Pediatric Gastroenterology, Prague, Czech Republic
14Sapienza University of Rome, Pediatrics and Childhood Neuropsichiatry, Rome, Italy
15Semmelweis University, Ist Department of Pediatrics, Budapest, Hungary
16Hôpital Necker Enfants Malades, 16department of Pediatric Gastroenterology, Université Paris Descartes, Sorbonne Paris Cité, Aphp. , Paris, France
17Meyerchildren's Hospital, Pediatric Gastroenterology, Meyerchildren's Hospital, Florence,, Italy
18Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
19Children's Hospital, University Central Hospital and University of Helsinki, Department of Pediatric Gastroenterology, Helsinki, Finland
20University Hospital of Wales, Department of Pediatric Gastroenterology, Cardiff, United Kingdom
21Free University Brussels, Brussels, Belgium
22Children's Research Centre, University Children's Hospital, Zurich, Switzerland
23Hospital São João, Porto, Portugal
24University Hospital Hvidovre, Hvidovre, Denmark
25Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria
26Wolfson Medical Center, Holon, Israel

Objectives and study: The tendency 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 this multinational collaboration, we aim to quantify the risk of malignancy and mortality within PIBD to better define the risk/benefit ratio of our new therapeutic strategies.

Methods: In a prospective population based survey for 3 years (Jan 2014-Jan 2017) we aim to identify all cases of cancer and mortality occurring in patients in case IBD was diagnosed <19 years of age. The survey is conducted in Europe (20 countries), USA, Canada, New Zealand and Israel. National representatives informed adult and pediatric gastroenterologists from their country half-yearly to report any cancer or mortality PIBD case in the previous 6 months including exposure to medications, causes of death and type of malignancy. Patients are eligible if manifestation of malignancy and/or mortality occurred <26 years of age. Our primary endpoint is cause of mortality in...
PIBD <19 years; secondary endpoints are risk of cancer and mortality in PIBD <26 years and identification of risk factors for cancer and mortality.

Results: Over a period of 18 months, we identified 23 cases of cancers and 13 deaths in 33 children (13 males (ulcerative colitis, n=9, Crohn's disease, n=21, IBD unclassified, n=3) at a median age of 12.9 years (IQ range 10.7-14.5). The most common malignancies were hematopoietic tumours (n=11). Patients that developed a malignancy had been exposed to thiopurines (n=12), biologics (n=1), combination therapy of immunomodulator and biologic (n=5) and other medications (n=5). Causes of mortality were infectious (n=5), cancer (n=4), other non-IBD related disease (n=2) or unknown (n=2). Medications used at time of fatal infection were thiopurines (n=1), biologics (n=1), combination therapy of immunomodulator and biologic (n=1), unknown (n=1) and none (n=1). Primary sclerosing cholangitis (PSC) was present in 8 cases (24%, 3/8 died).

Conclusion: Contrary to previous study by our group, the current data set does not show increased mortality primarily among UC patients. Infectious cases continue to be the most common cause for mortality. PSC seems to be the most prominent identifiable risk factor for malignancy and poor outcomes this far. By identifying malignancy and mortality cases in 24 countries we will capture more data than previously acquired regarding the worst outcomes in IBD, enabling us to understand the scale of the problem and to evaluate how many cancers actually cause mortality.

Disclosure of interest: This study is supported by ECCO and ESPGHAN.
The Effect of Colectomy in the Course of Inflammatory Bowel Disease

Aysel Ünlüsoy Aksu¹, Neslihan Gürcan Kaya¹, Sinan Sarı¹, Odül Eğritaş Gürkan¹, Ramazan Karabulut², Buket Dalgıç¹

¹Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
²Gazi University, Pediatric Surgery, Ankara, Turkey

Objectives and study: The aim of this study was to evaluate the effect of colectomy during the course of inflammatory bowel disease (IBD) and its post-operative complications. Indications for colectomy included life-threatening bowel perforation and/or bleeding, toxic megacolon, worsening of symptoms despite medical treatment, side effects associated with the chronic use of corticosteroids and/or immunosuppressive agents, growth retardation, and dysplasia.

Methods: Thirty nine patients were diagnosed with colitis between 1999 and 2014 in our department in a tertiary center. Indications of colectomy, clinical and laboratory findings before and after colectomy, and colectomy-related complications were evaluated retrospectively.

Results: Colectomy was performed in 13 patients. In all patients, the indication for colectomy was poor response to medical therapy. The mean age of patients was 9.3 ± 5.9 years (range, 1.5–15.5 years), and 8 (62%) were male. Before colectomy, all patients received 5-aminosalicylic acid, corticosteroids, and azathioprine. Cyclosporin and/or infliximab were used in 5 patients as step-up or rescue therapies before colectomy, but they failed as well. The median score for the pediatric ulcerative colitis activity index was 60 (range, 30-75) at the time of surgery. The median time between IBD diagnosis and colectomy was 12 months (range, 3-78 months). Total colectomy plus ileoanal anastomosis was performed in 10 patients, and subtotal colectomy was performed in 3 patients. Although there was no statistical difference, weight, height, and BMI z-scores improved, hemoglobin level increased, and thrombocyte, CRP, and ESR levels decreased after colectomy (p > 0.05). Median follow-up was 41 months (range, 4–184 months). Complications observed after colectomy and subsequent management is shown in Table 1. Two patients with subtotal colectomy and one patient with total colectomy required post-operative immunosuppressive therapy. Loperamid failed to restore defecation frequency and stool inconsistency on long-term follow-up of 6 patients with ileoanal anastomosis. Only one patient died from postoperative sepsis. Chronic granulomatous disease was confirmed in one patient with an ileoileal fistula after surgery. Also, an IL-10 receptor gene mutation was found in one patient after subtotal colectomy. Sclerosing cholangitis was diagnosed in one patient 2.5 years after colectomy.

Table 1. Complications observed after colectomy and subsequent management.

<table>
<thead>
<tr>
<th>Complication after colectomy</th>
<th>n</th>
<th>Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stool inconsistency</td>
<td>6</td>
<td>Loperamide</td>
</tr>
<tr>
<td>Stricture of ileoanal anastomosis</td>
<td>3</td>
<td>Bougie dilatation</td>
</tr>
<tr>
<td>Perirectal abscess</td>
<td>1</td>
<td>Antiobiotics and surgical drainage</td>
</tr>
<tr>
<td>Wound infection</td>
<td>2</td>
<td>Antiobiotics</td>
</tr>
<tr>
<td>Rectal bleeding</td>
<td>3</td>
<td>Symptomatic treatment</td>
</tr>
<tr>
<td>Ileoileal fistula</td>
<td>1</td>
<td>Surgery</td>
</tr>
<tr>
<td>Postoperative ileus</td>
<td>1</td>
<td>Clinical follow-up</td>
</tr>
</tbody>
</table>
**Conclusion:** Colectomy performed in patients who were refractory to immunosuppressive therapy, at our institution. Colectomy improved clinical and laboratory findings by alleviating inflammation, and restored growth and development of children. It relieved patients from immunosuppressive therapy. A great concern may be given to the patients who need immunosuppressive therapy after colectomy because they may suffer from an immune deficiency and/or immune dysregulation disorder. Complications seen after surgery were tolerable, for the most part.

**Disclosure of interest:** None Declared.
Laparoscopic Colectomy for Ulcerative Colitis with Associated Auto-Immune Liver Disease and Portal hypertension

Babu Vadamalayan¹, Bhanu Bhanu Lakshminarayanan², Emer Fitzpatrick², Maryanne Samyn², Ashish Desai³, Joseph Nun-Mensah², Niyi Ade Ajayi¹

¹King's College Hospital, Paediatric Liver, Gi and Nutrition Centre, London, United Kingdom
²King's College Hospital, London, United Kingdom
³King's College Hospital, Paediatric Surgery, London, United Kingdom

Objectives and study:

Laparoscopic colectomy for ulcerative colitis (UC) is well established. However, patients with UC and auto-immune liver disease (AILD) pose unique management and technical challenges. This is particularly true of those with established variceal disease. We report our laparoscopic experience in this rare group of patients.

Methods: Patients with UC and AILD who underwent surgery were retrospectively reviewed since 2009. Data regarding age at surgery, pre-operative work up, operative procedure and operative times were noted.

Results: 10 patients with UC and AILD were identified in the study period. 5 patients (4 male, median age of 16 years) underwent total colectomy (3 laparoscopic, 2 open of which 1 was done as a combined procedure with liver transplant [LT]). Of the other 5 patients, 4 underwent LT. 1 patient with severe varices in whom laparoscopic colectomy (LC) was considered too hazardous is awaiting colectomy which will be carried out at the same time as LT. Of the 3 patients who underwent LC, Propanalol was used to lower portal pressures in 1 pre-operatively. Haemostasis was achieved in all using LigaSure ™ for vessel sealing. The mean operative time was 300 minutes (240 – 400 minutes). There were no immediate complications. One patient required revision ileostomy for obstructive symptoms one week after LC and subsequently underwent a laparoscopic J pouch anal anastomosis. One other patient had ileorectal anastomosis 1 year after LC.

Conclusion:

1. UC and AILD progressing at different rates in the same patient may pose unique management challenges
2. Safe colectomy may not be feasible without LT in those with the most severe variceal disease
3. With suitable pre-operative preparation, laparoscopic colectomy is feasible and safe in selected patients with UC and AILD

Disclosure of interest:
“None Declared”.
Usefulness of Magnetic Resonance Enterography in Assessement of Small Bowel Diseases in Children with Crohn's Disease

Barbara Iwańczak¹, Ewa Nienartowicz², Elżbieta Krzesiek³

¹Wroclaw Medical University, Department of Pediatrics, Gastroenterology and Nutrition, Wroclaw, Poland
²Copper Health Center, Diagnostic Imaging Laboratory, Lubin, Poland
³Medical University Wroclaw, Department of Pediatrics, Gastroenterology and Nutrition, Wroclaw, Poland

Objectives and study: According to the Porto criteria for diagnosis of inflammatory bowel disease (IBD) in children it is necessary to perform endoscopic procedures and imaging studies of the small intestine. Magnetic Resonance enterography (MR enterography) is a new method of small bowel imaging, which does not expose the patient to ionizing radiation. The aim was to assess the usefulness of MR enterography in the diagnosis of lesions in the small bowel in children with Crohn's disease (CD).

Methods: We analyzed 62 children with CD (31 girls, 31 boys) aged 5.5 to 18 years, (mean age 13.6). The diagnosis was based on the Porto criteria. The average duration of disease was 2.3 years. In all children MR enterography according to the Giles et al. protocol was performed. The results were compared with the clinical manifestation of the disease and the location of endoscopic lesions using Paris classification.

Results: In 18 children (29%), diagnosis was made before 10 years of age (A1a), in the remaining 71% after 10th year of age but before 17th (A1b). Endoscopically ileo-cecal location (L1) was found in 11.3% of the children and MR enterography showed small bowel involvement in all of them. Endoscopic abnormalities located exclusively in the colon (L2) were found in 40.3% of the children, and in 36% of them MR enterography also showed lesions in the small intestine. Inflammatory changes in the large intestine and the terminal ileum (L3) were found in 25.8% of the children, and in 62.5% of them MR enterography showed changes in the small bowel. In 22.6% of the children endoscopy of the lower part of the alimentary tract was incomplete (did not include the terminal ileum); in as many as 71.4% of the patients from this group, MR enterography revealed inflammatory changes in the small intestine. From all patients with endoscopic lesions localized only in the large intestine and patients with incomplete endoscopy, in 48.7% MR enterography allowed to visualize inflammatory changes also in the small intestine. 53 patients (85.5%) presented non-stricturing and non-penetrative form of CD (B1), and 54.7% of them demonstrated inflammatory changes in the small intestine in MR enterography. 14 patients with B1 form (22.6%) demonstrated also penetrating perianal changes. From 6 patients (9.7%) with stricturing form of CD (B2), changes in MR enterography were observed in 83.3% of them. Patients with both stricturing and penetrating form of CD (B2, B3) accounted for 4.8% of all patients with CD, and in 66.6% of them in MR enterography abnormalities were visible. Perianal changes (p) occurred in 54.8% of children, and 54.6% of them revealed inflammatory abnormalities in MRI. 20 children (32.3%) presented growth failure (G1); in 65% of them MR enterography revealed abnormalities.

Conclusion: 1. MR enterography is a non-invasive, safe method of small intestine imaging, well tolerated by children
2. It is a complementary to endoscopy procedure, useful for the diagnosis of CD
3. In about half of the patients with CD, in whom endoscopic abnormalities were limited to the large intestine or who had an incomplete endoscopy, MR enterography revealed changes also in the small intestine.

Disclosure of interest: Barbara Iwańczak “None Declared”. Ewa Nienartowicz “None Declared” Elżbieta Krzesiek “None Declared”
Combination of 2 biologicals in pediatric Crohn’s disease with paradoxical psoriasis due to TNF alfa inhibitors.

Christine Olbjørn¹, Jon Bergreen Rove¹, Jørgen Jahnsen²

¹Akershus University Hospital, Department of Pediatric and Adolescent Medicine, Lørenskog, Norway
²Akershus University Hospital, Department of Gastroenterology, Lørenskog, Norway

Objectives and study: Pediatric Crohn’s disease (CD) is an aggressive disease, and biologic therapy is often needed. Side effects of biological treatment with TNF inhibitors include psoriasis and psoriasis-like skin rashes. The clinical presentation can be severe with psoriatic lesions resistant to topical treatments. Ustekinumab, a fully human anti-interleukin-12/23 monoclonal antibody, is the first drug of a new class of biologic therapy approved for the treatment of moderate-to-severe plaque psoriasis. There is limited experience with combination treatment with a TNF-inhibitor and ustekinumab.

Methods: We describe our experience with combination treatment with infliximab and ustekinumab in six pediatric CD patients who developed psoriasis resistant to topical treatment with corticosteroids.

Results: Six patients, three girls and three boys, aged 10 to 17 years, developed psoriasis while on maintenance treatment with infliximab for CD. Four of them received either azathioprine or methotrexate as co-medications. They had been treated for a median of 2 years (0.5-6 years) when psoriasis of the scalp and face occurred with additional palmoplantar psoriasis in one boy and anogenital psoriasis in one girl. Four patients developed severe hair loss. All were referred to a dermatologist and treated with topical medications and corticosteroids without adequate response. In two patients infliximab was switched to adalimumab and thereafter to certolizumab pegol, but the psoriasis persisted. Treatment with TNF inhibitors and immunosuppressants were discontinued and monotherapy with ustekinumab was initiated. The psoriatic skin lesions and hair loss were resolved. However, their CD flared, and treatment with steroids, total parenteral nutrition and antibiotics was not sufficient. Re-treatment with infliximab was started and remission was achieved, but within two months their psoriasis reoccurred. Ustekinumab therapy was again initiated without stopping infliximab and with the combination of these drugs both the psoriasis and the CD went into remission. One of the girls with scalp psoriasis and hair loss had TNF inhibitor treatment stopped while azathioprine was continued and ustekinumab was initiated. The psoriasis was resolved and her CD has stayed in remission. The 3 other patients were started on ustekinumab without stopping infliximab, all of them having significant improvement of psoriasis with their CD in stable remission. Immunosuppressants were stopped before starting combination treatment with the two biologics. We have not seen any serious adverse events. The girl with anogenital psoriasis experienced a bacterial skin infection and an otitis externa, both which were successfully treated with antibiotics.

Conclusion: Pediatric CD patients dependent on infliximab who develop recalcitrant psoriasis can be successfully treated with additional ustekinumab. The safety should, however, be addressed in long-term follow-up studies.

Disclosure of interest: “None declared".
Adalimumab treatment for luminal inflammatory pediatric Crohn’s disease: Long-term single center experience

Cynthia Popalis1, Claudia Tersigni1, Thomas Walters1, Peter Church1, Karen Frost1, Aleixo Muise1, Anne Griffiths1
1The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada

Objectives and study: Real-world experience with infliximab in children treated for luminal inflammatory Crohn’s disease (CD) demonstrates that durability of responsiveness is enhanced by concomitant immunomodulation (IM) (Church, 2014; Grossi, 2015), but pediatric studies comparing adalimumab (ADA) with and without IM have not been performed. We reviewed the effectiveness of ADA treatment in achieving short and long-term clinical remission and the effect of concomitant IM on durability of response in a single-center cohort.

Methods: From 2007 to 2014 at SickKids, Toronto, 106 children (63% male; median age 14.3 yrs, IQR 12.8-15.8) with luminal inflammatory CD (25% L1; 16% L2, 59% L3) received standard 2 dose ADA induction according to body weight, either to treat active CD (n=96) or as maintenance therapy (n=10) following other active treatments (steroids 1; enteral nutrition 4; infliximab 5). Median duration of diagnosed CD at initiation was 22 months. 64 (60%) were anti-TNF naïve; the remainder had prior secondary loss of response (LoR) and/or intolerance to infliximab. Responders, as judged by physician global assessment (PGA) and Pediatric Crohn’s Disease Activity Index (PCDAI), continued regularly scheduled maintenance injections +/- IM. Records were retrospectively reviewed to extract: PGA of continued response/remission vs. loss of response (LoR), PCDAI, levels of ADA and antibodies. Linear growth and follow-up colonoscopic and imaging data were recorded.

Results: Rates of clinical response (>/= 20 drop in PCDAI) and remission (PGA quiescent and PCDAI <10) following induction therapy in anti-TNF naïve and infliximab-experienced patients treated for active disease are shown in Table. Clinical remission was achieved more often in those patients that were anti-TNF naïve, 83% vs 62% (p=0.02).

Responders and those in remission at ADA initiation (n=92; anti-TNF naïve: 60) continued ADA as every other week maintenance. Concomitant IM was given more often to those with prior infliximab (50%) vs anti-TNF naïve (23%). During the first year of follow-up, 19% of patients escalated to weekly dosing to maintain clinical remission. During follow-up of median 20.7 months (IQR 11.7-35.2), 17 patients (7 (12%) of anti-TNF naïve; 10 (31%) of prior infliximab) discontinued ADA, 1 due to unsatisfactory primary response; 8 due to intolerance; 8 due to secondary LoR.

Table:

<table>
<thead>
<tr>
<th></th>
<th>All (n=96)</th>
<th>Prior infliximab exposure (n=37)</th>
<th>Anti-TNF naïve (n=59)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response, N (%)</td>
<td>83 (86.4)</td>
<td>28 (75.7)</td>
<td>55 (93.2)</td>
</tr>
<tr>
<td>Remission, N (%)</td>
<td>72 (75.0)</td>
<td>23 (62.2)</td>
<td>49 (83.1)</td>
</tr>
<tr>
<td>Non-Response, N (%)</td>
<td>13 (13.5)</td>
<td>9 (24.3)</td>
<td>4 (6.8)</td>
</tr>
</tbody>
</table>

Conclusion: In this cohort of pediatric patients treated with ADA for luminal inflammatory CD, response is greater and more durable in anti-TNF naïve patients than in those with prior secondary LoR to infliximab. If first anti-TNF, ADA response appears durable, even given as monotherapy, but this important question should be further addressed in a prospective randomized controlled trial of ADA +/- IM.

Disclosure of interest: CP, none declared; CT, none declared; TDW, Jansen, Abbvie; PCC, Jansen, Abbvie; KF, none declared; AMM, Regeneron; AMG, Jansen, Abbvie.
Similarity of Clinical Outcomes and Golimumab Pharmacokinetics in Adult and Pediatric Patients with Moderate to Severe Ulcerative Colitis Treated with Subcutaneous Administered Golimumab

Dan Turner, Genevieve Veereman, Jeffrey Hyams, Anne Griffiths, Daphne Chan, Omoniyi J Adedokun, Lakshmi Padgett, Richard Strauss

1 Shaare Zedek Medical Center, Genius Group, Jerusalem, Israel
2Free University Brussels, Brussels, Belgium
3Connecticut Children’s Medical Center, Hartford, United States
4The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
5Janssen Research and Development, LLC, Spring House, United States

Objectives and study: Pediatric patients with moderate-to-severe ulcerative colitis (UC) who fail 5-ASAs, corticosteroids, and immunomodulators have limited alternative approved treatment options. Golimumab is a subcutaneous (SC) anti-tumor necrosis factor (anti-TNF) agent with potential to offer such patients a safe, effective, and convenient treatment option. The pharmacokinetics (PK), efficacy, and safety of golimumab was evaluated in pediatric patients with moderate to severe UC in the PURSUIT PEDS PK study and compared to results from the adult UC phase 3 study.

Methods: PURSUIT PEDS PK is a multicenter open-label study with a PK portion (Week 0-14) and a study extension (Week 14-126); we report here results through Week 14. Patients aged 2-17 years with moderate to severe UC (Mayo score 6-12, endoscopy subscore ≥2) who previously failed steroids or immunomodulators, and were naïve to anti-TNF treatment were enrolled. Patients received SC golimumab induction at Week 0 and 2 by weight (<45kg [90→45mg/m²]; ≥45kg [200→100mg]). At Week 6, Mayo clinical responders continued golimumab maintenance q4w (<45kg [45mg/m²]; ≥45kg [100mg]). Key outcome measures included PK, immunogenicity, efficacy, safety; exposure-response relationships were also evaluated. Results: Please copy and paste the corresponding text here.

Results: Thirty-five patients enrolled and received ≥1 dose of golimumab. At baseline, the mean±SD age, weight, and duration of disease were 13.4±3.2 years (Range 6-17), 51.7±22.7 kg (Range 19.7-134.0) and 2.4±3.1 years (Range 0.2-16.0), respectively. Patients had moderate-to-severe disease activity (mean±SD: Mayo score 8.1±1.8 [Range 6-12], PUCAI score 48±17 [Range 15-80], CRP level 10.1±23.9 mg/L [Range 0.1-116.0]).

At Week 6, 60% and 42.9% of patients achieved clinical response and clinical remission, respectively, as evaluated by Mayo score and 34.3% achieved PUCAI remission. Mucosal healing was achieved in 54.3% of patients and 22.9% achieved complete healing. At Weeks 2, 4, and 6, respectively, mean serum golimumab concentrations in pediatric patients (6.5 µg/mL, 6.5 µg/mL, and 2.6 µg/mL) were similar to those observed in adults who received 200→100mg induction (6.4, 5.6, 2.1, 1.8 µg/mL). Through Week 6, the incidence of antibodies to golimumab (6.3% vs 4.3%) using a drug tolerant assay were comparable between pediatric and adult patients, respectively. Serum golimumab concentrations were positively associated with efficacy outcomes; this relationship was generally comparable between pediatric and adult patients.

Through Week 14, 94.3% of patients reported ≥1 AE; 8.6% had an AE leading to discontinuation; 37.1% reported infections (none serious); 17.1% reported injection site reactions (all mild); 31.4% reported SAEs (majority were UC flares). No opportunistic infections, malignancies or deaths were reported.

Conclusion: Golimumab was generally well tolerated in this small open-label study of pediatric patients with UC. The PK, efficacy, and safety outcomes observed were comparable with those previously reported in the golimumab adult UC phase 3 study.

Disclosure of interest: D Chan, O Adedokun, L Padgett, R Strauss: Employees of Janssen
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-151

Osteopontin in paediatric patients with IBD

Diana Reznik¹, Anna Maria Peter¹, Michael P. Horn², Susanne Schibli¹, Johannes Spalinger³, Christiane Sokollik¹

¹Children’s Hospital, University of Berne, Paediatric Gastroenterology, Hepatology and Nutrition, Berne, Switzerland
²University Institute of Clinical Chemistry, University of Berne, Centre for Laboratory Medicine, Berne, Switzerland
³Children’s Hospital, Lucerne, Paediatric Gastroenterology, Hepatology and Nutrition, Lucerne, Switzerland

Objectives and study: Inflammatory bowel disease (IBD) affects around 0.2% of the population in Switzerland and 10-20% are diagnosed during childhood. Classification into its subtypes Crohn’s Disease (CD) and Ulcerative Colitis (UC) is not possible in up to 20% at time of diagnosis, however a correct classification has important prognostic and treatment consequences. Osteopontin (OPN), which is essential for the Th1 immune response associated with CD, may thus provide additional information. Previously it has been shown that OPN levels correlate with disease activity in children with Langerhans cell histiocytosis, as well as in adults with IBD. The aim of this study was to evaluate OPN as a diagnostic and/or predictive marker in paediatric IBD.

Methods: We retrospectively analysed clinical and laboratory data of paediatric IBD patients and correlated them with OPN, anti-Saccharomyces cerevisiae antibody (ASCA), perinuclear/cytoplasmic anti-neutrophil cytoplasmic antibody (p-/c-ANCA) and exocrine pancreatic antibody (PAB) measurements.

Results: We included 61 patients, 29 with CD (17 boys, median age 11 years, median follow up time 4.5 years) and 32 with UC (15 boys, median age 11.3 years, median follow up time 2.33 years). OPN did not differ between age groups. Mean serum OPN were not significantly different between CD (15.87 ng/ml ± 12.26) and UC (13.19 ng/ml ± 10.84) (p=0.369). OPN levels did neither correlate with laboratory inflammatory markers (CRP, ESR, thrombocytes, albumin) nor with PCDAI and PUCAI scores, nor with disease location, extension and behaviour. Furthermore, OPN levels were independent of ASCA, ANCA and PAB antibody status. OPN levels did not predict the need of TNF-alpha antibody treatment during follow up, as marker of disease severity. Even though the OPN levels changed over time, as assessed in multiple OPN measurements in 9 patients, there was no correlation between OPN levels and disease activity at time of sampling.

Conclusion: To our knowledge, this is the first study examining a potential diagnostic and predictive role of OPN in paediatric IBD patients. In contrast to adult studies, OPN values did not differ between CD and UC, did not correlate with disease activity, and did not predict severity of the disease course. Despite promising results in adults, we could not derive a beneficial role of OPN as an additional serum marker in paediatric IBD patients.

Disclosure of interest: None Declared
Effectiveness of induction therapy of ulcerative colitis in children with biosimilar infliximab – 1.5 year of experience.

Dorota Jarzębicka¹, Joanna Sieczkowska¹, Anna Plocek², Aleksandra Banaszkiewicz³, Agnieszka Gawronska⁴, Ewa Toporowska-Kowalska², Jarosław Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
²Medical University of Łódź, Department of Paediatric Allergology, Gastroenterology and Nutrition, Lodz, Poland
³The Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
⁴Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Warsaw, Poland

Objectives and study: Incidence of inflammatory bowel diseases in children is still rising. Biological treatment with infliximab in ulcerative colitis (UC) is introduced in case of inefficacy of standard therapy. European Medicines Agency (EMA) in 2013 approved two biosimilar infliximab products for marketing in the European Union (EU). The aim of the study was to retrospectively assess the effectiveness of biosimilar infliximab in paediatric UC.

Methods: Fifteen patients treated with biosimilar INF (CT-P13, Remsima) between 03.2014 – 10.2015 in 3 academic hospitals in Poland were included to the study. Disease activity and laboratory tests were assessed before therapy and at week 14 (after 3 induction doses).

Results: Median age of patients at diagnosis was 12.52 years (range 2.9-16.68). Five patients had been treated with anti-TNFalpha before and remaining 10 patients were anti-TNF naive. Mean PUCAI before first infliximab dose was 47.7 (range 5-80) vs. 24.3 (range 0-65) at Week 14. There was good clinical response in 7/14 (50%) patients observed (one patient still during induction therapy) and 5 out of 14 patients (5/14; 33%) obtained clinical remission. We observed one allergic reaction during infusion.

Conclusion: Clinical response after induction therapy with biosimilar infliximab in paediatric UC is observed in up to 50% of patients.

Disclosure of interest: J. Kierkus – Lecture fee(s): speaker fees from Egis, MSD and AbbVie
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-153

Immunogenicity of biosimilar infliximab in children with colitis ulcerosa- single centre experience

Dorota Jarzębicka¹, Joanna Sieczkowska¹, Grzegorz Oracz¹, Monika Meglicka¹, Maciej Dadalski¹, Jarosław Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Biosimiliar Infliximab was approved in Poland in Jan 2014, with the same indications for treatment as original Infliximab. Immunogenicity of biosimilar in comparison with originator, in clinical trials in rheumatology, seems to be comparable.

Methods: Patients with colitis ulcerosa who were qualified to biological therapy with biosimilar Infliximab and gave permission to take blood sample for assessment of drug level and presence of anti-TNF antibodies by ELISA were enrolled to the study. PUCAI (Paediatric Ulcerative Colitis Activity Index), patients characteristics, laboratory value were recorded.

Results: 8 patients with colitis ulcerosa (4 M, 4 F) were enrolled to the study. In these group in 6 patients authors observed clinical response for the treatment. There were 2 patients without clinical response (PUCAI 55 and 90; after the third and second doses, respectively), although they had therapeutic drug level (10.4 ug/ml and 6.7 ug/ml) with low antibodies level (0.0 ng/ml and 0.07 ng/ml). In case of one patient was observed positive antibodies level – 14.1 ng/ml, with subtherapeutic drug level. This patient presented clinical remission (PUCAI 0). Statistical analysis, in the Spearman’s test, shown statistical significant correlation between level of antibodies and ESR (-0.83) - it was strong negative correlation. Also between drug level and ESR (0.82) and albumin (0.9). Correlation between drug level and ESR or albumin were strong positive correlation.

Conclusion: First assessment does not suggest higher immunogenicity of biosimilar infliximab in paediatric patients with colitis ulcerosa. Further analyses on the bigger group of patients are needed.

Disclosure of interest: J. Kierkus – Lecture fee(s): speaker fees from Egis, MSD and AbbVie
GASTROENTEROLOGY: Inflammatory bowel disease

Value of laboratory parameters in determining of endoscopic exacerbation of Crohn's disease in children

Elena Roslavtseva¹, Maria Venedictova², Ekaterina Tsimbalova², Anton Anoushenko², Alexander Potapov²

¹Scientific Center for Children’s Health, Healthy and Sick Child Nutrition Dep., Moscow, Russian Federation
²Scientific Center for Children’s Health, Gastroenterology, Moscow, Russian Federation

Objectives and study: Recurrent nature of Crohn’s disease requires constant and careful monitoring of disease activity. Assessment of exacerbation can be done at various levels, such as clinical, laboratory (hematological parameters, level of faecal calprotectin), endoscopic and histological ones.

Methods: The study included 126 children with Crohn’s disease, aged 2 months - 18 years (mean age 11.6 ± 0.6 years). Based on PCDAI, all patients were divided into 2 groups: group I - clinical remission (PCDAI <10), group II - clinical exacerbation (PCDAI > 10). In order to identify the most significant diagnostic laboratory markers (haemoglobin, haematocrit, white blood cells count, erythrocyte sedimentation rate (ESR), albumin, C-reactive protein (CRP), fibrinogen, IgG, IgM, IgA, fecal calprotectin) for determining endoscopic exacerbation, ROC-analysis and multivariate correlation analysis of clinical laboratory parameters were held. Endoscopic disease activity was determined by the level of SES-CD index.

Results: Correlation analysis of laboratory parameters with the endoscopic picture in children with the clinical exacerbation (group I) determined weak correlation between SES-CD index and levels of haemoglobin (R =0.23), the number of white blood cells (R =0.27), platelet count (R =0.42), ESR (R =0.37), albumin (R =0.28); level of IgA (R =0.23). Levels of CRP (R =0.26) and fecal calprotectin (R =0.29) showed p <0.05. In the group of patients in remission (II), only fecal calprotectin had significant correlation with SES-CD (R =0.50), p <0.008..

Conclusion: The maximum diagnostic accuracy in predicting of endoscopic exacerbation was the level of fecal calprotectin (AUC = 0.766) 390 mg/g with the sensitivity of 85% and specificity of 66%.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 337
Transition clinic in inflammatory bowel disease: a two centre model

Erminia Romeo\textsuperscript{1}, Ornella Ricca\textsuperscript{2}, Giulia Angelino\textsuperscript{3}, Simona Filoni\textsuperscript{3}, Filippo Torroni\textsuperscript{3}, Simona Faraci\textsuperscript{3}, Francesca Rea\textsuperscript{3}, Paola Tabarini\textsuperscript{4}, Valentina Giorgio\textsuperscript{2}, Luigi Dall'Oglio\textsuperscript{3}, Antonio Gasbarrini\textsuperscript{2}, Edoardo Borrelli\textsuperscript{2}, Franco Scaldaferri\textsuperscript{2}, Paola De Angelis\textsuperscript{3}

\textsuperscript{1}Bambino Gesù Children’s Hospital, Irccs, Inflammatory Bowel Disease Group, Rome, Italy
\textsuperscript{2}General Hospital Agostino Gemelli, Gastroenterology Unit, Rome, Italy
\textsuperscript{3}Bambino Gesù Children’s Hospital, Digestive Surgery and Endoscopy Unit, Rome, Italy
\textsuperscript{4}Bambino Gesù Children’s Hospital, Clinic Psychology Unit, Rome, Italy

Objectives and study: Transition clinic programs from pediatric inflammatory bowel disease (IBD) centres to adult centres are an emerging challenge. Many factors may affect this step: sex, age, psychological aspects. First end point of the present study was to evaluate the efficacy of the proposed transition model. Secondary end point was to evaluate the predictive factors of failure.

Methods: Proposed model was based on three meetings every four-six weeks: the first in pediatric centre (Bambino Gesù Children’s Hospital); the second one in adult centre (Agostino Gemelli General Hospital), with both pediatric and adult gastroenterologists; the last one in adult centre with only adult gastroenterologists. During the first visit, the pediatric gastroenterologist proposed the transition; during the second meeting pediatric gastroenterologist introduced the patient to the adult gastroenterologist; in the third visit, the adult gastroenterologist proposed the own follow up program. Questionnaires (General, GQ, transition clinic, TCQ, IBD yourself, self efficacy, VAS based) were used. Inclusion criteria were: patients with ulcerative colitis (UC) or Crohn’s disease (CD) with low disease activity or remission. Transition was considered successful if three steps were reached form patients.

Results: Twenty patients were enrolled; age 18-25 years (mean age 20.2, M/F 12/8; UC/CD 10/10). Eleven/20 (55%, 8 M/3 F) immediately accepted the second check at adult gastroenterology centre. Five patients refused transition and 4 patients delayed the transition. Three patients (F)/11 refused follow up in the proposed centre. In eight patients (40%, 8 M) this model was successful. Patients ready to transition knew their disease better than who did not accept transition at IBDQ test. IBDQ was higher in transited patients than not transited. Young patients who interrupted the transition program felt more independent at VAS-based questionnaire. Patients who completed the transition program totalized higher scores in the resilience scale, had better scores of wellbeing perception and had lower anxiety scores.

Conclusion: Proposed transition program seems to be feasible. Overall patient seems to be ready to transition, but they are not sufficiently confident in knowledge about IBD. Patients resistant or failing were more likely female, with high self-efficacy scores, lower confidence in adult gastroenterologist and worse wellbeing perception. Working with these variables with psychologists dedicated on IBD is needed.

Disclosure of interest: None Declared.
Pancreas and bowel: a causal or random linkage?

Federica Ferrari¹, Eva Epifani¹, Fortunata Civitelli¹, Marina Aloï², Emanuele Casciani¹, Franca Viola², Salvatore Cucchiara²

¹Sapienza University of Rome, Rome, Italy
²Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy

Objectives and study: Extraintestinal manifestations are common in inflammatory bowel disease (IBD). Pancreatic involvement in pediatric patients with IBD could be often a silent condition. The prevalence of acute pancreatitis (AP) in children is about 5.1% in ulcerative colitis (UC) and 4.5% in Crohn Disease (CD). Asymptomatic pancreatic hyperenzimemia (PH) has been described in 6%-to-16% of IBD patients. The aim of our study was to describe the prevalence of pancreatic enzymes increase and imaging findings in a pediatric UC population. We have also analysed the possible relationship between PH and therapy, UC disease activity and extension.

Methods: We retrospectively reviewed data of all pediatric patients with UC, followed in our Unit from 2010 to 2014, who had presented at least one episode of PH (serum amylase ≥100 IU/L and/or lipase ≥60 IU/L) from the diagnosis. Demographic and clinical data included: sex and age, the lag time between the onset of the first episode of PH and UC diagnosis; presence or absence of typical abdominal pain; UC extension according to Paris classification; Paediatric Ulcerative Colitis Activity Index (PUCAI). Laboratory tests included blood count, C-Reactive Protein (CRP), cholesterol, triglycerides, liver enzymes. All patients underwent abdominal ultrasound (US) and, in some cases, magnetic resonance cholangiopancreatography (MRCP). AP was diagnosed according to 2 out of 3 INSPIRE criteria.

Results: We found 45 (39%) out of 115 children with UC, (22 males; median age 10 years, range 1-19) who had at least one episode of PH (mean amylase 114,42±57,63 U/L; mean lipase: 217,73±292,27 U/L); 29 (64,4%) patients were asymptomatic, while 16 (35,5%) had abdominal complaints. Only 8 patients (17,7%) met diagnostic criteria of AP. The median lag time period between the episode of PH and UC diagnosis was 10.5 months (range 1-168). In 24 (53%) patients UC was in remission; 10 (22%), 9 (20%), 2 (4%) had mild, moderate and severe disease, respectively. Furthermore, 86% of patients had a pancolitis, while 9% and 5% presented left colitis and proctitis, respectively. Among 45 patients con PH, 3.1% were taking Methotrexate, 12.1% Azathioprine, the 54,50% Mesalazine, 21.2% sulphasalazine and 9.1% was off-therapy. At US, 8 (17,7%) patients showed increase of gland volume and only one of them pancreatic duct dilation. Among 22 patients who performed MRCP, 13 (59%) showed increased pancreas volume with altered lobular architecture, especially in pancreas body and tail. Five (22,7%) patients showed also irregular contour of pancreatic duct. In one patient pancreas divisum was detected. The 46% of children presented radiologic changes in both US and MRCP. There was no statistical correlation between amylase levels and PUCAI (p = 0.027); while PUCAI correlated with lipase levels (p <0.05). The extension of disease was correlated both with lipase (p <0.05) and amylase levels (p <0.05).

Conclusion: In our study 39% of a pediatric population with UC showed at least one episode of alteration of pancreatic enzymes, but rarely fulfilled diagnostic criteria of AP. This finding was not related to disease activity, although most of children had a framework of pancolitis, and did not correlate with administered drugs. In conclusion, pancreas seems to be another target organ of the intestinal inflammation occurring in UC. We recommend investigation of pancreatic function and imaging in UC children.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Inflammatory bowel disease

Aminosalicylates and pediatric UC: use and efficacy at one year from diagnosis, results from the Pediatric IBD Italian registry.

Federica Nuti1, Giulia Tringali1, Erasmo Miele2, Massimo Martinelli3, Stefano Martelossi3, Giovanna Zuin4, Patrizia Alvisi5, Salvatore Pellegrini6, Vittorio Romagnoli7, Graziella Guariso8, Salvatore Cucchiara9, Marina Aloi9

1Sapienza University Rome, Rome, Italy
2Federico II University, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
3Institute for Maternal and Child Health - Irccs "Burlo Garofolo", Trieste, Italy
4Ospedale Dei Bambini Vittore Buzzi, Milan, Italy
5Ospedale Maggiore , Bologna, Italy
6Policlinico Universitario G Martino, Messina, Italy
7Ospedale Salesi, Ancona, Italy
8Università Degli Studi DI Padova, Padova, Italy
9Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy

Objectives and study: Aminosalicylates (5-ASAs) are an essential therapeutic tool for pediatric UC. Nonetheless, data regarding their efficacy in pediatric patients is scarce. The aim of this multicenter study was to evaluate the use and efficacy of 5-ASAs in a large pediatric UC population.

Methods: Data were obtained from the Pediatric IBD Italian Registry, a prospective registry including children aged <18 years diagnosed from 2009.

The primary outcome was to evaluate corticosteroid (CS) and rescue therapy (immunomodulants, biologics or colectomy) free remission according to PUCAI at 1 year (FU) of oral 5-ASAs, introduced within 30 days from diagnosis (± concomitant CS).

Secondary outcomes were to evaluate the frequency and use of rescue therapies and the influence of the patients’ baseline characteristics on the following clinical outcome

Results: Of the 427 newly diagnosed pediatric UC patients included in the registry, 252 met the inclusion criteria and 161 (70 males, 43.5%) had complete data and were included in the study. Mean age at diagnosis was 10.6 ± 3.9 years. Disease location according to Paris classification was E1 5.6%, E2 30.4%, E3 12.4%, E4 51.5%. Mean PUCAI at diagnosis was 33 ± 18. The majority of patients presented with a mild (42.2%) to moderate (42.8%) disease, 5.6% presented with a severe disease. CSs were introduced joint to 5-ASA in 55.3% of patients; the majority of these patients (55/91, 60%) presented with a pancolitis at diagnosis.

At FU 68 (42.2%) patients were in CS and rescue therapy free remission. Of the remaining patients, 63 (39.1%) required a rescue therapy and 43 (26.7%) were on 5-ASA treatment but not in remission.

The main rescue therapy introduced was azathioprine (53/63 patients, 84%), in the remaining patients infliximab was used in 5/63 patients (8%) and only 2 patients underwent colectomy (3%). The main disease location at diagnosis for the rescue therapy group was E4, no difference between mean PUCAI and sex or age at diagnosis and use of CS was found between the rescue therapy or no rescue therapy group of patients (Table).
Table: Baseline characteristics of patients necessitating rescue therapy at 1 year from diagnosis (pts:patients, CS:corticosteroid).

**Conclusion:** Fifty nine percent of newly diagnosed UC introduced 5-ASAs as primary maintenance therapy. 5-ASAs were capable to obtain CS and rescue therapy free remission in 42% of patients at one year. The patients with pancolitis at diagnosis where more likely to receive a rescue therapy during this first year of follow-up.

**Disclosure of interest:** no disclosure of interest to declare
Mortality and cancer in paediatric inflammatory bowel disease in Scotland 2005-2013

Fiona Cameron¹, Richard Russell², Sabari Loganathan³, David Wilson¹

¹University of Edinburgh, Child Life and Health, Edinburgh, United Kingdom
²Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
³Royal Aberdeen Children’s Hospital, Paediatric Gastroenterology, Aberdeen, United Kingdom

Objectives and study: The long term risks of cancer and mortality in paediatric-onset inflammatory bowel disease (PIBD) are unknown with few population based studies and most evidence provided by case series. It is critical that further data is provided in order to inform clinicians and families about risks of both the disease, and treatment as PIBD is often associated with a more severe phenotype, often requiring immunosuppressive treatment. Therefore, the aim of this retrospective study is to characterise the risk of cancer and mortality in population-based cohort of PIBD patients.

Methods: All cases of mortality and cancer in PIBD patients cared for in paediatric services (<18 years) in Scotland were collected retrospectively from 01.01.2005 to 31.12.13. Details were collected on PIBD disease course, medications, cause of death/cancer and relation to IBD/IBD treatments and outcome. In 2011, Scotland had a population under 16 years of just under 1 million and the incidence of PIBD 2003-2013 was 9.4/100,000/year.

Results: Four cases were recorded between 2005 and 2013 of cancer/death, 2 male and 2 female. The median age at diagnosis of PIBD was 12 years (range 9.0-15.4) with median age of event (cancer/death) of 14.4 years (range 11.7-18.0). Three cases died; one male diagnosed with Crohn’s disease (CD) age 14 years and on azathioprine for 2.5 years died of gamma hepatosplenic T cell lymphoma aged 18 years having never recieved anti-TNF therapy. One female died aged 12 years due to volvulus 11 months post pouch having been diagnosed with UC 2 years previously. One female died aged 12 years from an unrelated chronic lung disease secondary to a left sided congenital hernia having been diagnosed with IBDU 3 years prior to her death and was recieving corticosteroids. One case of acute myeloblastic leukaemia was reported in a 16 year old male who had been diagnosed with CD 4 years prior and been treated with azathioprine for 3 years. The patient was successfully treated with a bone marrow transplant and fully recovered, not requiring any further treatment for his CD at last follow up. With the small number of patients affected meaningful comparison with standardised population cancer and mortaility rates was not thought to be meaningful.

Conclusion: Death and cancer were rarely observed in this cohort. Both cancers developed in teenage males with CD on thiopurines. Unlike other studies, no deaths were related to infective causes although this may be related to small numbers in this study. As treatment algorithms have changed in recent years with increasing use of anti-TNF therapy and other immunosuppression, further prospective data collection is required to determine future trends allowing clinicians to better inform their decision making.

Disclosure of interest: Dr Richard K Russell has received speaker’s fees, travel support, or has performed consultancy work with: MSD Immunology, Nestle, AbbVie, Dr Falk, Takeda, Napp, Mead Johnson, Nutricia and 4D Pharma.
The prevalence of growth failure and short stature in paediatric onset Crohn’s disease

Firas Rinawi1, Amit Assa1, Tal Almaguer2, Corina Hartman1, Yael Mozer - Glassberg1, Vered Nachmias Friedler1, Yoram Rosenbach1, Ari Silbermintz1, Noam Zevit3, Raanan Shamir3

1Schneider Children’s Medical Centre of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach-Tikva, Israel
2Haemek Medical Centre, Afula, Israel, Paediatric Endocrine Unit, Afula, 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: Growth failure is not uncommon in children with Crohn's disease (CD). However, the rate of short stature at final height is not well characterized. Our aim was to determine the prevalence of growth failure at diagnosis and short stature at adulthood in patients with paediatric onset CD.

Methods: We performed a retrospective analysis of the Schneider Paediatric Inflammatory Bowel Disease (SPID) cohort. Height Z-scores of 459 children (ages 2-18 years) at diagnosis of CD and of 319 patients who reached the age of 20 years during follow-up were retrieved and compared to a cohort (n=58,228) representing the general population attending primary care clinics and matched for age and gender (control group). Growth failure at diagnosis and short stature at adulthood was defined as height Z-score for age ≤ -2.

Results: Mean height Z-score at diagnosis of CD was -0.53±1.14 compared with -0.04±1.08 in the control group (P<0.001). Prevalence of childhood growth failure was 9.2% (42/459) and 3.4% (1964/57349) in CD patient and in controls, respectively (P<0.001). Mean final adult height Z-score in the SPID cohort was -0.36±1.07 with adulthood short stature prevalence of 6% (19/319) compared with -0.27±0.98 and 4.4% (39/879) in the controls (p=0.188 and 0.279 respectively).

Conclusion: Despite the substantial prevalence of growth failure reported among children with CD, our data suggest that most of these patients attain normal height as adults. These findings could be attributed to early diagnosis and appropriate management of CD.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-160

Investigating the small bowel in pediatric Crohn’s disease: prospective comparative study between small intestine contrast ultrasonography and magnetic resonance imaging

Fortunata Civitelli¹, Salvatore Oliva¹, Marina Aloï¹, emanuele casciani², Franca Viola¹, Francesca Maccioni², Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
²Sapienza University of Rome, Emergency Radiology, Rome, Italy
³Sapienza University of Rome, Radiological Sciences, Oncology, and Pathology, Rome, Italy

Objectives and study: Magnetic resonance imaging (MRI) is considered the gold-standard for evaluation of small bowel (SB) in Crohn’s disease (CD). However, MRI is expensive, requires a strong compliance and a considerable amount of oral contrast to distend intestinal lumen. Small Intestine Contrast Ultrasonography (SICUS) is non-invasive, low cost and generally well-tolerated by pediatric patients (pts). We aimed to compare the diagnostic accuracy of SICUS and MRI in detecting presence, site and extension of SB disease and in assessing strictures in pediatric CD.

Methods: children with suspected CD or relapse of a known CD were prospectively enrolled. All underwent SICUS, MRI and ileo-colonoscopy, performed by different operators blinded to other results. The SB was subdivided into: jejunum, ileum, terminal ileum (TI). The concordance (k) between the two techniques for presence of lesions was calculated. For TI, sensitivity (SE) and specificity (SP) were also assessed, with ileo-colonoscopy as reference standard. One-way ANOVA with Kruskal-Wallis post-test was applied to compare the extension (cm) of disease in the different segments.

Results: 66 pts (median age 13; range 7-18), 23 suspected, 43 known CD were included. The overall k for presence of SB lesions was 0.94 (ES 0.06; 95%CI 0.8-1). The k for segments was: jejunum, 0.67 (ES 0.1, 95%CI 0.4-0.8), ileum, 0.91 (ES 0.06, 95% CI 0.76-1), TI 0.91 (ES 0.06; 95%CI 0.8-1). SE and SP (%) of SICUS and MRI for TI lesions were 98,100 and 93, 92, respectively. There was no difference in the assessment of disease extension between SICUS and MRI (p NS). The overall k for strictures was 0.62 (ES 0.1, 95% CI 0.4-0.8). SE and SP(%) of SICUS and MRI for TI strictures were 100, 100 and 92, 87, respectively. MRI provided 7 false positive results, not detected at SICUS nor confirmed at endoscopy.

Conclusion: the diagnostic performance of SICUS is comparable to that of MRI in pediatric CD. SICUS might represent a first-line tool in pediatric CD, able to reduce costs and to post-pone or even avoid more invasive and expensive investigations.

Disclosure of interest: None declared
Objectives and study: Upper and lower endoscopy with histology together with imaging of the small bowel is the gold standard for the diagnosis of inflammatory bowel disease (IBD) in children and adolescents. Due to high costs and invasive nature of these techniques, accurate selection of patients is mandatory. We aimed to assess the accuracy of non-invasive tests including fecal calprotectin (FC), blood inflammatory markers (BIM) and bowel ultrasound (US) alone or in combination as first level investigations in children with suspected IBD.

Methods: Consecutive patients referred to our Unit for a clinical history compatible with IBD were enrolled during a 3-year period. All underwent FC (Calprest®, Eurospital), C-reactive protein [CRP], erythrocyte sedimentation rate [ESR] and bowel US as first investigations. Endoscopy with biopsies was the gold standard for diagnosis. At US pathological findings were: BWT>3 mm, BW vascularity, loss of stratification, enlarged mesenteric nodes. Multiple logistic analysis with stepwise method considering IBD diagnosis as dependent variable was conducted. Sensitivity (SE), specificity (SP), positive and negative predictive values (PPV and NPV) of laboratory and US parameters alone or in combination were analyzed according to the final diagnosis.

Results: 100 patients (58 males, median age 12) were enrolled. The final diagnosis was IBD in 69 (57 CD, 12 CU) other than IBD in 31. Mean values of CRP, ESR, FC and BWT were higher in IBD vs non-IBD patients (p<0.001) (Table 1). Multiple logistic analysis showed that independent variables predictive of IBD were: FC (OR 44.8; p<0.01), BWT (OR 20.4, p<0.001) and ESR (OR 9; p<0.05). The combination of 3 or 2 parameters was more frequent in IBD patients (p<0.01). Table 2 shows SE, SP, PPV, NPV of these parameters alone or in combination.

Table 1:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>IBD</th>
<th>NON-IBD</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRP</td>
<td>17.7 ± 19</td>
<td>3.5 ± 6</td>
<td>0.001</td>
</tr>
<tr>
<td>ESR</td>
<td>40 ± 22</td>
<td>17 ± 11</td>
<td>0.001</td>
</tr>
<tr>
<td>CALPROTECTIN (ug/g)</td>
<td>292 ± 287</td>
<td>19.2 ± 10</td>
<td>0.001</td>
</tr>
<tr>
<td>BWT (mm)</td>
<td>6 ± 2.3</td>
<td>2 ± 0.6</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 2.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SE (%)</th>
<th>SP (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FC</td>
<td>94</td>
<td>89</td>
<td>94</td>
<td>89</td>
</tr>
<tr>
<td>ESR</td>
<td>75</td>
<td>89</td>
<td>93</td>
<td>65</td>
</tr>
<tr>
<td>BWT</td>
<td>94</td>
<td>83</td>
<td>88</td>
<td>57</td>
</tr>
<tr>
<td>2 (at least 2 of 3)</td>
<td>96</td>
<td>94</td>
<td>97</td>
<td>92</td>
</tr>
<tr>
<td>2 (FC + BWT)</td>
<td>91</td>
<td>100</td>
<td>100</td>
<td>86</td>
</tr>
<tr>
<td>3 (FC + BWT + ESR)</td>
<td>71</td>
<td>100</td>
<td>100</td>
<td>64</td>
</tr>
</tbody>
</table>
Conclusion: the combination of FC, BIM and bowel US may help to select children needing further invasive procedures and allow to avoid or delay endoscopy in patients with negative initial diagnostic work-up.

Disclosure of interest: None declared
Health care transition of patients with pediatric onset Inflammatory Bowel Disease: a Pilot Survey.

Giovanna Alfano¹, Salvatore Guercio Nuzio², Marco Poeta¹, Dario Di Salvo², Claudia Mandato³, Marina Tripodi¹, Annamaria Staiano⁴, Fabiana Castiglione⁵, Antonio Cuomo⁶, Carolina Ciacci⁷, Pietro Vajro⁸

¹University of Salerno, Department of Medicine and Surgery, Pediatric Section, Baronissi (Sa), Italy ²Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi (Sa), Italy ³Aorn Santobono-Pausilipon, Pediatrics, Naples, Italy ⁴Federico II University, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy ⁵Federico II University of Naples, Department of Clinical and Experimental Medicine, Gastroenterology Unit, Naples, Italy ⁶Umberto I Hospital, Nocera Inferiore (Sa), Section of Gastroenterology, Nocera Inferiore (Sa), Italy ⁷University of Salerno, Department of Medicine and Surgery, Section of Gastroenterology, Baronissi (Sa), Italy ⁸Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi, Italy

Objectives and study: Data on health care transition of patients with pediatric onset Inflammatory Bowel Disease (IBD) from Pediatrician/Pediatric Gastroenterologist (PGE) to Adult Gastroenterologist (AGE) settings are still scarce. Here we report on the evaluation of management procedures/outcomes of IBD young patients in the real life of a Southern Italy region, where a centralized and structured IBD transition program started only recently.


Results: The response rate was 80.8% (21 of 26 eligible patients). Mean age at transfer was 19.3 y; a clinical and/or laboratory disease activity was present in 52% (lab 14%; clinical + lab = 38%). Globally, 81% felt mostly/completely prepared to transition, although only <10% had at least one pediatric visit without their parents before the transfer and none received written transition explanatory materials. A relationship was found between perceived preparation and number of specific transition preparation items received (r = 0.5141, p 0.017). Patients who had a ≥ 6mo interval (gap) between the last visit to the PGE and the first to the AGE (14%) were less satisfied (p 0.030), had a worse self-assessment of IBD related well-being at the time of transfer (p 0.046), and also found one or more of the following difficulties: limited information provided by the PGE (p 0.046), worries in identifying the AGE (p 0.032), and insufficient communication between PGE and AGE (p 0.046). The 13 patients (62%) who had participated to the structured regional IBD clinic transition program felt more supported by the PGE (p 0.046) and more satisfied (p 0.003), and had a better self-assessment of IBD related well-being at the time of transfer (p <0.001) and also thereafter (after 1 year p = 0.005), than the remaining patients. With a gap between pediatric and adult care <6mo, patients tended to perceive having a better health care continuity (p=0.06).

Conclusion: Data of our pilot study show that future efforts should aim at reducing the time interval in health transition visits from PGE to AGE, and also implementing structured regional clinic transition programs for adolescents/young adults with pediatric onset IBD.

Disclosure of interest: None Declared.
Evaluation of Autonomic Nervous System Functions in Children with Inflammatory Bowel Disease in Remission Phase

Günesel Kutluk1, Helen Bornaun2, Kazım Oztarhan2, Nuh Yılmaz3, Tugce Kalaycı4

1Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Gastroenterology, Hepatology and Nutrition, Istanbul, Turkey
2Kanuni Sultan Süleyman Education and Research Hospital, Pediatric Cardiology, Istanbul, Turkey
3Mustafa Kemal University School of Medicine, Pediatric Cardiology, Hatay, Turkey
4Kanuni Sultan Süleyman Education and Research Hospital, Pediatrics, Istanbul, Turkey

Objectives and study: Ulcerative colitis (UC) and Crohn disease (CD) are inflammatory bowel diseases (IBD) with unknown cause and mechanism, and characterized with chronic inflammation. Many factors such as genetic and environmental factors, immune dysfunction, stress and infectious agents play role in etiology. Recent studies show in IBD, chronic inflammation, stress, medications and malnutrition lead to develop autonomic nervous system (ANS) dysfunction, especially increased sympathetic nervous system activity and deterioration of heart rate variability, correspondingly. In our study, we evaluated the effect of IBD on ANS functions by using noninvasive electrophysiological parameters like heart rate variability (HRV) in young patients.

Methods: Out of IBD patients between the ages of 3 and 18, 35 were enrolled in the study, who have been followed-up in our pediatric gastroenterology department within remission phase for at least 12 months. Thirt-five age and sex matched healthy individuals were chosen as the control group. Clinical and laboratory parameters of all the individuals were evaluated. Previous structural heart disease was excluded with physical examination and echocardiographic assessment. Twenty-four hours Holter electrocardiography monitorization was performed in patient and control groups. Time and frequency based parameters was used in obtained ECG records. Results of both of the groups were compared separately for day and night with mean values of NN, SDNN, SDNN-i, SDANN, RMSSD and pNN50 parameters.

Results: The study group had 15 UC and 20 CD patients; and sex and age matched 35 healthy children. The mean age was 11.96 ±4.47 in patients and 12.01±4.2 in controls, with 51.4% (N=18) female and 48.6% (N=17) male individuals. Minimal and mean heart rate was significantly higher and the mean RR interval was significantly lower in patients comparing to controls. Besides, out of time dependent HRV parameters, SDNNday, SDNNtotal and SDANN indexes were significantly lower in patients (p<0.05), in addition, out of frequency dependent HRV parameters, VLF and LF were also significantly lower (p<0.05) in this group. Even though individuals in patient group were in remission, we determined deterioration in standard autonomic function tests, and this condition was considered as affected autonomic nervous system. We found no statistical difference in parameters between CD and UC groups in our study.

Conclusion: We believe that this study helped us to achieve important results on early evaluation of ANS functions in IBD. Even in remission phase, some of the time and frequency dependent HRV parameters were found significantly different in patient group, when comparing with control group. In other words in children with IBD, parasympathetic activity was significantly decreased comparing with control group; while sympathetic activity was more active and heart rate was significantly higher. Since this autonomic dysfunction we found in young IBD group may be related with increased cardiac morbidity and mortality in older age, we believe that long term cardiac follow-up might be necessary in this group of patient.

Disclosure of interest: None Declared.
Prevalence and Evaluation of Predictors of Poor Outcome in Paediatric Crohn’s Disease Patients -data from the CEDATA-GPGE registry

Jan de Laffolie¹, Yenny Kho¹, CEDATA Study Group

¹University Giessen, General Pediatrics and Neonatology, Giessen, Germany

Objectives and study: Regarding the treatment of paediatric Crohn’s Disease (CD) a strategic paradigm shift towards intensified therapy with early use of immunomodulators was recently proposed if “predictors of poor outcome (POPO)” were present. These are (1) deep colonic ulcerations on endoscopy, (2) persistent severe disease despite adequate induction therapy, (3) extensive disease, (4) marked growth retardation (>2.5 Height SDS), (5) severe osteoporosis, (6) structuring and penetrating disease at onset and (7) severe perianal disease. CEDATA GPGE is a registry in for pediatric IBD patients in Germany and Austria since 2004. The main objective was to characterize CEDATA GPGE patients using the proposed criteria and to compare therapy and outcome.

Methods: All CD patients entered into CEDATA-GPGE within three months of initial diagnosis and with at least one follow up within the first three months were included. Of all seven criteria proposed, five are contained in CEDATA-GPGE data, while deep ulceration on endoscopy and presence of osteoporosis are not sufficiently addressed (POPO 1 & 5).

Patients with positive criteria were compared to other patients, considering disease presentation, therapy, course of disease and outcome parameters (severe growth retardation, fistula or stenosis, sustained remission, surgery, extraintestinal manifestation, immunomodulators or biologicals).

Results: Since 2004, 4339 patients (age 0-18 years) with IBD were registered in “CEDATA-GPGE”, 2574 patients diagnosed with CD and, 978 patients included in the study. In 706 patients (72.2%) at least one criterion was found. 522 (53.4%, 3) showed extensive disease (L3 with or without upper GI involvement), 15 (1.5%, 4) patients had severe growth retardation (<-2.5 SDS), 29 patients (3%, 6) penetrating or structuring disease.

Compared to POPO negative patients, the group of positive patients is younger (12.8 (10.3-14.9) vs 13.5 (11.2-15.2) median (P25-P75) years, p=0.002), PCDAI is higher. History of Loss of performance in school was significantly more frequent (43.0 vs 36.4%, p=0.03), while other symptoms were not statistically significant.

For Surgery, there was high specificity for criteria 4 and 6 (each >95%) with relatively high sensitivity in POPO 3 for growth retardation, development of abscess, stenosis or fistula, extraintestinal manifestation and lack of sustained remission (>= one year) specificity was high in POPO 4, 6 and 7 (each >90%). Predicting use of immunomodulators and biologicals POPO 4, 6 and 7 showed also considerable specificity (>90%).

Negative predictive value was considerable high for all criteria when predicting surgery (>90%) and development of abscess, stenosis or fistula or the use of biologicals (>80%) and low for lack of sustained remission for all criteria (40%) or therapy with immunomodulators (33%).

Conclusion: The identification of predictors for disease course and potential criteria for risk stratification are important prerequisites for treatment optimization. Predictors of poor outcome were common in CEDATA-GPGE.

Disclosure of interest: None declared
Patient Registry CEDATA - GPGE - a collaborative development of an enhanced online platform to facilitate quality improvement

Björn Schwarz1, Jan de Laffolie2, Christian Thomae3, Keywan Sohrabi3, CEDATA Study Group

1Technische Hochschule Mittelhessen University of Applied Sciences, Faculty of Health Science, Giessen, Germany
2University Giessen, General Pediatrics and Neonatology, Giessen, Germany
3Technische Hochschule Mittelhessen University of Applied Sciences, Faculty of Health Science, Giessen, Germany
4University Giessen, Germany

Objectives and study: CEDATA-GPGE is a prospective, multi-center registry for pediatric inflammatory bowel disease (IBD) patients in Germany and Austria, established by the Society for Pediatric Gastroenterology and Nutrition of German speaking countries (GPGE) in 2004. In order to support and improve patient care comprehensive data concerning course of disease (UC, CD, IBD-U) and care is collected using online case report forms. The currently used software suffers from deficiencies regarding accessibility, usability and use of modern web technologies. Insufficient documentation and maintainability are hindering further developments of the current system.

Methods: To avoid a lengthy reengineering process which would still not enable to address all known issues it was decided to completely rewrite the CEDATA-GPGE web portal software. In close communication with participating centers an agile development process was introduced, allowing to solve research-relevant problems in addition to technical issues. A platform for project-management and controlling as well as structured communication was provided to allow a methodologically sound development process. In addition, changes to the software are integrated into the runtime environment daily via a continuous integration solution.

Results: Modern web technology makes up the core of the rewritten online portal. Freely available open source components, such as the Ruby on Rails framework, the Bootstrap web-framework and the PostgreSQL database system were used to achieve a consistent, stable and secure user experience within the prototype software. The database-backend was restructured to lessen the time and resource requirements for future modifications. In addition, a foundation was established to allow the inclusion of additional features providing direct benefits for patients and reporting institutions.
Conclusion: Initial feedback concerning the software redesign as provided by participating centers and physicians was very positive. Possibilities to further enhance the software with features like automatic generation of clinical reports, laboratory interface, and more comprehensive visualizations were recognized to provide major benefits for reporting physicians and patients by providing vital information at the point of care. Usability improvements are likely to improve the number of contributions as well as the overall data quality. The conceptual design of a data migration plan for existing data sets is currently under investigation in order to integrate the new software into daily routine as soon as possible.

Disclosure of interest: None Declared
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-166

Tolerance and effectivity of preparation to magnetic resonance enterography with 3% sorbitol solution in children with IBD.

Joanna Sieczkowska¹, Dorota Jarzębicka¹, Beata Marcinska², Monika Meglicka¹, Grzegorz Oracz¹, Elżbieta Jurkiewicz¹, Jaroslaw Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
²The Children’s Memorial Health Institute, Department of Diagnostic Imaging, Warsaw, Poland

Objectives and study: Magnetic resonance (MR) is an imaging technique of choice to assess small bowel in diagnosis of inflammatory bowel disease (IBD). To successfully perform MR it is obligatory to distend small bowel. Sufficient distension of the gut is achieved by oral contrast agent (enterography) or with use of naso-duodenal tube (enteroclysis). So far there is no guidelines of bowel preparation for MR enterography which regulate amount and type of contrast sufficient for good bowel distention. The aim of our study was to detect toleration and efficacy in bowel distention of 3% sorbitol solution as contrast for MR enterography in children with IBD.

Methods: 58 patients who had magnetic resonance enterography were included to the study. Amount of 3% sorbitol solution for enterography depended on children’s age. Patients started bowel preparation 2 hours before examination. Children younger than 12y old were obligatory to drink 35ml 3% sorbitol mixed in 200ml water. Older patients drank 45ml in 200ml water and 50ml in 200ml water for 12-15y old and older than 15 y old, respectively. After that patient were asked to drink every 10-15min clean water to properly fulfil small bowel.

Results: 7/58 (12%) patients presented intolerance to sorbitol solution. 4 (6,9%) experienced vomiting, 3 (5,3%) had diarrhoea after contrast adjustment. As a result of severe vomiting in case of 1 patient MR was not performed and for another one study was stopped. Segmental, not sufficient small bowel distention were observed in 21,1% and in 17,5% cases MR showed lesions suggested inflammation which could be false positive results. There was found strong statistically significant correlation between these two variables. However magnetic resonance enterography in 94,8% shown good distention of terminal ileum.

Conclusion: Bowel preparation for magnetic resonance enterography was generally good tolerated. Ileum terminale was successfully evaluated in 94,8%. However in 21,1% cases was observed segmental insufficient small bowel distention.

Disclosure of interest: None Declared
Efficacy of biosimilar infliximab induction therapy in paediatric patients with Crohn’s disease - 1.5 year of experience.

Joanna Sieczkowska¹, Anna Plocek², Aleksandra Banaszkiewicz³, Dorota Jarzębicka¹, Agnieszka Gawronska⁴, Ewa Toporowska-Kowalska², Jaroslaw Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
²Medical University of Łódź, Department of Paediatric Allergology, Gastroenterology and Nutrition, Lodz, Poland
³The Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
⁴Department of Pediatric Gastroenterology and Nutrition, Medical University of Warsaw, Warsaw, Poland

Objectives and study: Infliximab biosimilars has been approved in therapy of IBD paediatric patients by extrapolation of indications of originator. The aim of the study was to assess the efficacy of induction therapy with biosimilar in Crohn’s disease paediatric patients.

Methods: This study had been performed in 3 Polish hospitals. All patients with Crohn’s disease who had biological therapy with biosimilar applied between 03.2014-07.2015 were enrolled to the study. The patients received induction doses of biosimilar 5mg/kg at week 0, 2, 6. The change in PCDAI (Paediatric Crohn’s Disease Activity Index) scoring was primary endpoint in the assessment of efficacy. Patients characteristics, previous history of anti-tumor necrosis factor administration, response and remission to treatment and adverse drug reaction were also analysed.

Results: 36 children (19 M, 17 F) were enrolled to the study. Mean age at diagnosis was 11.8 (12.2: 0.8-17.1). 17 patients were anti-TNF naive and 9 had previous anti-tumor necrosis factor treatment. Mean PCDAI before first biosimilar dose was 49.7 (median 52.5; 5-87.5) vs. 10.1 (5; 0-47.5) Week 14. Clinical response and remission after 3 initial doses were achieved in 32/36 (88.9%) and 26/32 (72%) patients, respectively. Two patients didn’t complete induction therapy. We observed one allergic reaction during second biosimilar infusion which led to treatment discontinuation.

Conclusion: Induction therapy with biosimilar in Crohn’s disease paediatric patients is effective and safe.

Disclosure of interest: J Kierkus reports having received speaker fees from Egis, MSD and AbbVie
Immunogenicity after switching from reference infliximab to biosimilar in children with Crohn disease.

Joanna Sieczkowska¹, Dorota Jarzębicka¹, Grzegorz Oracz¹, Monika Meglicka¹, Maciej Dadalski¹, Jarosław Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Infliximab biosimilars’ immunogenicity has been assessed in several clinical trials in rheumatology. Basing on these studies, biosimilars have been approved to be used in the same indications as originator. Due to their lower price and better availability there is sometimes necessity to switch patients to biosimilar infliximab during the course of biologic therapy. The aim of the study was to compare products’ immunogenicity before and after switching.

Methods: Paediatric patients with Crohn’s disease who had switch from reference infliximab to biosimilar in the course of therapy were enrolled to the study. All of them were sampled for assessment of drug level and presence of anti-TNF antibodies (ATI) with ELISA tests within the time of switching and 5 dose of biosimilar. PCDAI (Paediatric Crohn’s Disease Activity Index), patients characteristics, laboratory data were recorded and related to drug and ATI concentrations.

Results: 16 CD patients (11 M, 5 F) were enrolled to the study. Mean age was 12,7 (14,1; 3,7 – 17,4). 14 out of 16 patients had therapeutic level of IFX (>1,5 μg/ml) at time of switching and 7 of them presented positive ATI concentration (>2ng/ml). 1 patient had subtherapeutic concentration of IFX with presence of ATI, and 1 presented with undetectable concentration of IFX (<0,035μg/ml) with negative ATI (< 2ng/ml). There were no significant correlations between IFX level, presence of ATI and disease activity and laboratory data (albumin, CRP). Assessment of immunogenicity after switching has been performed in 15 patients. All 15 patients had therapeutic IFX concentrations and only 4 out of 15 had ATI >2ng/ml and higher antibody concentration corresponded to lower drug concentration. No significant correlation between drug level and laboratory data was identified.

Conclusion: This is the first study regarding immunogenicity in paediatric Crohn’s disease patients who had switching from originator to biosimilar infliximab performed. No attributes of higher immunogenicity after switching were found. Further analyses are needed.

Disclosure of interest: J Kierkus reports having received speaker fees from Egis, MSD and AbbVie
Immunogenicity of pertussis booster vaccination in adolescents with inflammatory bowel disease: a controlled study

Aleksandra Banaszkiewicz1, Agnieszka Gawronska1, Beata Klincewicz2, Anna Kofla3, Urszula Grzybowska-Chlebowczyk4, Ewa Toporowska-Kowalska5, Ilona Małecka6, Joanna Stryczynska-Kazubksa7, Wojciech Feleszko8, Izabella Lazowska-Przeorek9, Katarzyna Karolewska-Bochenek1, Maria Kotowska9, Janusz Slusarczyk10, Jarosław Walkowiak2, Andrzej Radzikowski9, Urszula Demkow11, Piotr Albrecht9

1The Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
2Poznan University of Medical Sciences, Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland
3Wrocław Medical University, Department of Pediatrics, Gastroenterology and Nutrition, Wrocław, Poland
4Medical University of Silesia, Department of Pediatrics, Katowice, Poland
5Lodz Medical University, Department of Allergology, Gastroenterology and Nutrition, Lodz, Poland
6University of Medical Sciences Poznan, Department of Health Promotion, Poznan, Poland
7University of Medical Sciences Poznan, Department of Pediatric Gastroenterology and Metabolic Diseases, Poznan, Poland
8The Medical University of Warsaw, Department of Pediatric Respiratory Diseases and Allergy, Warsaw, Poland
9Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
10Medical University of Warsaw, Department of Public Health, Warsaw, Poland
11Medical University of Warsaw, Department of Laboratory Diagnostics and Clinical Immunology of Developmental Age, Warsaw, Poland

Objectives and study: There is a paucity of data on immune response to pertussis vaccine in patients with inflammatory bowel disease (IBD). The aim of the study was to evaluate the immunogenicity and safety of booster pertussis vaccination in adolescents with IBD compared to healthy controls.

Methods: This was a multi-center, prospective and controlled study on adolescents with IBD aged 11-18 years with no history of pertussis booster immunization after the age of 6 years or documented pertussis infection. The subjects for the study belonged to one of the following groups: patients with IBD on no immunosuppressive therapy, those on biological therapy and/or immunomodulators, and healthy controls. The study population received one intramuscular injection of Boostrix® that is tetanus toxoid, reduced diphtheria toxoid and acellular pertussis vaccine. The primary outcome measure was adequate vaccine response defined as post-vaccination concentration ≥11 µg/mL measured between 4 and 8 weeks after the vaccination. The evidence of local and systemic adverse effects for three days after the vaccine was registered.

Results: A total of 138 subjects (111 patients and 27 controls) completed the study course. The rate of seroconversion was higher in IBD patients compared to controls measured 4-8 weeks after vaccination (89.2% vs. 74%, p=0.02). There was no significant difference in the rate of seroconversion between IBD patients treated and non-treated with immunosuppressive drugs (89.2% vs.87.2%, p=0.37). There were no serious adverse events related to the vaccine during the study.

Conclusion: Pertussis booster vaccination was both immunogenic and safe in adolescents with IBD.

Disclosure of interest: All following authors Aleksandra Banaszkiewicz, M.D., Ph.D., Agnieszka Gawrońska, M.D., Ph.D. Beata Klincewicz M.D., Ph.D., Anna Kofla M.D., Ph.D., Urszula Grzybowska-Chlebowczyk, M.D., Ph.D., Ewa Toporowska-Kowalska M.D., Ph.D., Ilona Małecka M.D., Joanna Stryczynska-Kazubksa M.D., Ph.D., Wojciech Feleszko M.D., Ph.D., Izabella Lazowska-Przeorek, M.D., Ph.D., Katarzyna Karolewska-Bochenek, M.D., Ph.D. Maria Kotowska, M.D., Ph.D., Janusz Slusarczyk, M.D., Ph.D., Prof., Jarosław Walkowiak M.D., Ph.D., Andrzej Radzikowski, M.D., Ph.D., Prof., Urszula Demkow M.D., Ph.D. Prof., Piotr Albrecht, M.D., Ph.D. declare no conflict of interest.
Clinical response and reported experience of adolescent newly diagnosed Crohn’s Disease patients treated with exclusive enteral nutrition: A single centre experience

Katie Keetarut¹, Sara McCartney², Charles Murray², Fevronia Kiparissi³

¹University College London Hospital, Nutrition and Dietetics, London, United Kingdom
²University College London Hospital, Department of Gastroenterology, London, United Kingdom
³Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom

Objectives and study: To assess the clinical response in newly diagnosed adolescent Crohn’s disease (CD) patients to exclusive enteral nutrition (EEN) and reported patient experience following EEN in a single tertiary gastroenterology centre over a 3 year period.

Methods: Retrospective review of dietetic and clinical notes on sequential patients newly diagnosed with CD using the PCDAI aided by histology and laboratory pathology. All patients were started on a 6 week course of either elemental or polymeric feeds.

Results: 25 patients (7 females 18 males) median age 15.7 years diagnosed with CD. Disease distribution using the Paris classification A1b were isolated colonic disease (n=6), isolated upper disease coexistent with L3 (L4a n=5), isolated terminal ileal disease (L1 n=3), isolated upper disease coexistent with L2 (n=2), isolated upper disease coexistent with L1 (n=3) ileocolonic (n=4), isolated colonic and perianal (L2p n=1), upper disease distal to ligament of Treitz (n=1).

Excluding for patients who required combination therapy from outset (n=2) and non-compliant patients (n=2) 14/21 (67%) reached clinical remission after 6 weeks of EEN using the PCDAI (n=2 ElementalO28 Extra Liquid, n=12 Modulen IBD). All patients were treated with azathioprine. 13 patients took the feed orally and 1 required a nasogastric tube (NGT).

7/21 (33%) failed to reach remission (n=1 Fresubin Energy, n=2 Ensure Plus Juce/Milkshake style, n=2 ElementalO28 Extra Liquid, n=2 Modulen IBD). All were treated with prednisolone. 4 patients continued on EEN for 6 weeks for nutrition support (n=3 NGF n= 1 orally). A median weight gain of 1.4kg versus 6.2kg in oral versus NGT group respectively.

Post treatment questionnaires were given to all patients who completed 6 weeks EEN (n=18) measuring responses on a rating scale from strongly agree/agree to disagree/strongly disagree as follows:

I found the diet easy to follow (13/18 versus 5/18), I was given enough MDT support (18/18 versus 0/18), I would consider using EEN in future flare ups (13/18 versus 5/18), I found the drinks palatable (11/18 versus 7/18) I was able to manage the full volume (13/18 versus 5/18).

12/18 disagree/strongly disagree to at least one statement. 8/12 missed eating food, 6/12 missed mealtimes with families/friends, 5/12 felt excluded at mealtimes. 4/18 reported experiencing unpleasant side effects including diarrhoea 3/4 or nausea/hunger/low energy 2/4.

Conclusion: Our study suggests EEN is an effective treatment for newly diagnosed adolescent CD with 14/21 (67%) reaching clinical remission. The majority of patients had some difficulty following EEN but reported side effects were less common. Comments included suggestions to improve the taste of feeds. Despite this the majority of patients managed the EEN orally but significant improvements in weight were only found in those patients fed via NGT.

Disclosure of interest: None Declared
circulating inflammatory cytokine profiles in children with newly diagnosed ibd: determining trends in ulcerative colitis and crohn’s disease patients

alice foster¹, Edie Dullaghan², leanna yee², kevan Jacobson³

¹Bc children's hospital, vancouver, canada
²Centre for drug and research development, vancouver, canada
³Bc children's hospital, pediatric gastroenterology, vancouver, canada

Objectives and study: it is hypothesized that a component of inflammatory bowel disease (IBD) pathogenesis involves dysregulation of the immune system and an associated inflammatory response. Signaling proteins such as cytokines and chemokines are one mechanism responsible for driving this process. Limited knowledge is currently available on the cytokine profiles seen in pediatric IBD patients. The aim of this study is to define cytokine signatures in newly diagnosed pediatric IBD patients using MesoScale technology.

Methods: this prospective study included patients who were newly diagnosed with IBD at BC children's hospital between January 2012 and June 2013. Patients were between 6 and 17 years-old and had either not yet started on therapy, or were within the first two weeks of initiation of a 5-ASA compound. Healthy controls were also recruited as a comparator group. Plasma levels of cytokines were measured using multiplex assays manufactured by MesoScale Discovery.

Results: twenty-nine patients with IBD (16 Crohn’s disease (CD), 13 ulcerative colitis (UC)) and 23 healthy controls (HC) were enrolled and completed cytokine testing. When compared to HC, UC patients had significant elevations in IL-8, IL-13 and IL-17 (p<0.05). In addition, those with moderate to severe UC also had elevations of IL-5 and IL-23. In contrast, CD patients had significant differences in IFN-γ IL-6, IL-8, IL-17 and TNF-α when compared to HC (p<0.05). When CD patients were analyzed according to severity, only those with mild disease differed with respect to TNF-α and IL-17. A direct comparison of CD to UC cytokine profiles showed a significant dissimilarity between both IFN-γ, with higher levels in CD, and IL-13, with higher levels in UC.

Conclusion: there is variation in plasma cytokine distribution patterns seen in newly diagnosed pediatric CD and UC patients along with healthy control subjects. Improved understanding of these differences may help explain the heterogeneous nature of IBD, and provide potential targets for therapy and inflammatory signatures for monitoring disease response to therapy. Further research is needed to characterize IBD biomarkers and understand their utility in the management of IBD.

Disclosure of interest: None Declared
Fermentation capacity of gut microbiota of patients with inflammatory bowel disease compared with healthy controls

Yunqi Koh1, Mhairi McGowan1, Daniel Gaya2, Douglas Morrison3, Richard Hansen4, Richard Russell5, Konstantinos Gerasimidis1

1University of Glasgow, Human Nutrition/School of Medicine, Glasgow, United Kingdom
2National Health Service, Department of Gastroenterology, United Kingdom
3Suerc, East Kilbride, United Kingdom
4National Health Service, Department of Paediatric Gastroenterology, Hepatology & Nutrition, Glasgow, United Kingdom
5Royal Hospital for Children, Department of Paediatric Gastroenterology, Hepatology & Nutrition, 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 project 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 8 carbohydrate/fibres (maize starch, pectin, raftilose, wheat bran, cellulose). Aliquots were taken at 0, 4, 24 and 48 hours. Faecal SCFA (butyrate, propionate and acetate) concentration (umol/g) was measured with Gas Chromatography

Results: Five IBD participants and four matched HC were recruited. Following 24h batch cultures, total SCFA, acetate (Figure 1) and butyrate tended (p<0.100) or were significantly lower in IBD participants than in healthy controls (p<0.05) and for the majority of the fibre substrates tested:
- [Butyrate, umol/g, IBD vs HC; wheat bran: 8.7 vs 36.4, p=0.022; cellulose: 4.0 vs 8.2, p=0.070; raftilose: 18.4 vs 58.3, p=0.048, apple pectin: 15.7 vs 42.6, p=0.066; Maize starch: 13.5 vs 51.2, p=0.044];
- [Total SCFA, umol/g, IBD vs HC; wheat bran: 74.3 vs 268, p=0.029; cellulose: 32.3 vs 77.2, p=0.012; raftilose: 133 vs 330, p=0.102, apple pectin: 122 vs 461, p=0.031; Maize starch: 80.3 vs 300, p=0.028];
- [Acetate, umol/g, IBD vs HC; wheat bran: 45.8 vs 124.5, p=0.039; cellulose: 15.8 vs 39.7, p=0.055; raftilose: 66.6 vs 135, p=0.176, apple pectin: 91.9 vs 273, p=0.052; Maize starch: 48.2 vs 151, p=0.023]. No significant differences were observed for propionate concentration or the production profile (% proportional ratio) or SCFA.

Conclusion: This pilot data suggest that the microbiota of IBD patients has a lower capacity to breakdown fibre, compared to healthy people. The findings of this work should be replicated in larger populations and be complemented with the use of next generation sequencing

Disclosure of interest: None declared
Comparison between calprotectin and high motility group box 1 (HMGB1) protein as fecal biomarkers of intestinal inflammation in pediatric and adult patients with inflammatory bowel disease

Francesca Palone¹, Roberta Vitali¹, Salvatore Cucchiara², Renata D’Incà³, Alessandro Armuzzi⁴, Brigida Barberio³, Daniela Pugliese⁴, Carla Felice⁴, Anna Dilillo², Maurizio Mennini², Laura Stronati⁵

¹Enea, Radiobiology and Human Health, Rome, Italy
²Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
³University of Padova, Surgical, Oncological and Gastroenterological Sciences, Padova, Italy
⁴Catholic University of Rome, Internal Medicine, Rome, Italy
⁵Sapienza University of Rome, Cellular Biotechnology and Hematology, Rome, Italy

Objectives and study: Ileocolonoscopy is the gold standard for monitoring disease activity in patients with inflammatory bowel disease (IBD). However, it is invasive, costly, and time-consuming. Thus, stool markers are being increasingly used and, among them, the fecal calprotectin (FC) level is probably the most widely adopted. We have recently shown that fecal high mobility group box 1 (HMGB1) protein may be considered a novel biomarker of both high- and low-grade intestinal inflammation and of mucosal healing (1,2).

We aimed at assessing the reliability of HMGB1 protein as a fecal biomarker by analyzing its levels in larger cohorts of pediatric as well as adult IBD patients and correlating values to those obtained with FC test.

Methods: 85 pediatric patients with IBD (49 with Crohn’s disease (CD), 36 with ulcerative colitis [UC]), 119 adult patients (57 with CD; 62 with UC) and two age-matched control groups (37 children and 63 adults) were enrolled for the study at three IBD referral Centers. Calprotectin and HMGB1 levels were analyzed on fecal samples by ELISA (Calprest Eurospital) and western blot, respectively.

Results: Fecal HMGB1 and FC were both significantly increased by comparing pediatric and adult patients and respective controls (CD: p<0.001, UC; p<0.001). When patients were stratified according to the endoscopic disease severity (UC Mayo Endoscopic Sub-Score e CD: SES-CD), a significant correlation was found between HMGB1 as well as FC and endoscopic scores (r Spearman in a range between 0.60 and 0.84, p<0.01, for CD and UC for both fecal markers). Finally a significant correlation between HMGB1 and FC values in pediatric and adult populations was detected (r Spearman: 0.60, 0.72, respectively).

Conclusion: These results confirm that fecal HMGB1 protein is a reliable marker of intestinal inflammation, useful to monitor pediatric and adult IBD, and has a sensitivity comparable with that of FC


Disclosure of interest: None Declared
Oral implementation of exclusive enteral nutrition (EEN) with Modulen IBD is good tolerated method of therapy to induce remission and to normalize nutritional status and growth velocity in children with active Crohn's disease (CD)

Malgorzata Matuszczyk, Monika Meglicka, Piotr Landowski, Beata Sordyl, Elzbieta Czkwianianc, Joanna Bierla, Bozena Cukrowska, Jaroslaw Kierkus

Objectives and study: The aim of treatment with EEN in children with active CD is both to reduce the inflammation and to optimize the nutritional status. Modulen is the industrial diet created especially for patients with IBD. It differs from standard polymeric formula not only by the flavour but also by the content of antiinflammatory cytokines (TGF-β) and medium-chain triglycerides. These features can play an important role in the context of induction of mucosal healing and weight/growth gain in the combination with the good oral acceptance of such treatment.

Methods: Twenty children (male/female: 14/6) in median age of 14 years with active CD were treated for 6 weeks by EEN with Modulen IBD. Based on the Paris Classification among 100% of them the disease was localized in the illeum terminale, in 5% the colon and in 5% the upper gastrointestinal tract were also involved. The daily caloric intake was established depending on age and nutritional status. Disease activity (measured by PCDAI score), intensity of inflammation (reflected by fecal calprotectin concentration, measured by the ELISA) and nutritional status were assessed at baseline and at 4 week after the end of treatment. At the final point the tolerance of nutrition therapy was evaluated as well. The statistical significance for PCDAI and calprotectin concentration was measured by the Wilcoxon signed-rank test.

Results: The mean reduction of PCDAI was statistically significant (from 26.3 ± 13.2 with the range of 57.5-10 to 7.8 ± 11.6 with the range of 52.5-0, p=0.05). Full remission (reflected by PCDAI<10) was achieved in 65%, clinical response in 30% and no response in 5% of children. The anti-inflammatory effect of therapy was stated based on the mean reduction of fecal calprotectin concentration (from 3380 mg/kg ± 7746 with the range of >30000-28 to 1046,6 mg/kg ± 1219 with the range of 4006-25, p=0.05). The flavour acceptance of Modulen IBD was observed - in the 95% of patients the oral intake of the industrial formula was successfully realized during the whole duration of therapy. EEN was generally well tolerated - initially in 20% of patients the symptoms of industrial diet's intolerance were recorded, but they receded within the first days of therapy. At baseline the 30% of children was undernourished, that was reflected by BMI below 3 percentile on WHO charts. In all patients the improvement of BMI status was stated. The mean increase of BMI was 0.91 kg/m²±0.4 and it was greater in the undernourished group (1.19 kg/m² vs 0.62 kg/m²). In two-thirds of malnourished children the BMI status met the normal value after treatment. Before the introduction of EEN in 25% of patients the deficit of growth was observed, based on growth below 3 percentile on WHO charts. The growth gain was obtained in 55% of the study participants and among 80% in the group with initially growth failure. The mean increase of growth was 1cm ± 1.1 and it was greater in the group with impaired growth (1.5 cm vs 08 cm).

Conclusion: Based on our experience the six-week course of EEN with Modulen IBD is an effective method of treatment in children with active CD, that induces remison, reduces inflammation and normalizes the nutritional status. The observation of good oral tolerance of the nutritional plan, without
the necessity of naso-gastric tube insertion, is the additional benefit with particular importance in pediatrics.

**Disclosure of interest:** 1. J. Kierkus and M. Matuszczyk report having received speaker fees from Nestle. 2. Modulen IBD had been provided by Nestle Poland
Listeria meningitis in a child with Crohn’s disease: An important complication of immunosuppression

Maria Fotoulaki1, Maria Ioannidou1, Olga Tsiatsiou2, Eleni Papadimitriou2, Maria Eboriadou3, Emmanuel Rolilides2

1Aristotle University of Thessaloniki, 4th Department of Paediatrics, Papageorgiou Hospital, Thessaloniki, Greece
2Hippokration Hospital of Thessaloniki, Paediatric Infectious Disease Unit, Thessaloniki, Greece
3Aristotle University of Thessaloniki, 4th Department of Paediatrics Papageorgiou Hospital, Thessaloniki, Greece

Objectives and study: Listeria monocytogenes, although uncommon cause of illness in the general population is an important pathogen in individuals with impaired cell-mediated immunity including neonates, pregnant women, elderly persons and transplant recipients. TNF-α is a critical component of the immune response against intracellular agents like L. monocytogenes. Recent reports have implicated immunosuppressive therapy, such as the monoclonal antibody neutralizing the biologic action of tumor necrosis factor-alpha (TNF-α) infliximab, in the development of severe Listeria infections, particularly sepsis and meningitis. Infliximab is an effective therapy for Crohn’s disease.

Methods: We report a case of L. monocytogenes meningitis in a child receiving infliximab and corticosteroids for Crohn’s disease.

Results: The patient was a 13-year-old female on iatrogenic immunosuppression with infliximab and corticosteroids, who presented 7 days after last infliximab infusion with fever, headache, diplopia, malaise and pain in the abdomen. Neurological examination revealed a somnolent patient although responsive to verbal commands, confused, disoriented with evidence of nuchal rigidity. The abdomen was slightly tender with normal bowel sounds. Her laboratory results were notable for an elevated CRP. Chest X-ray and computed tomography of the brain were normal. A lumbar puncture revealed cloudy spinal fluid, white cell blood count of 970/mm³ with 80% neutrophils, 23mg/dl glucose and 86mg/dl protein. Empirical treatment for CNS infection with ceftriaxone and acyclovir was started; ampicillin was added due to immunocompromised state of the patient. Cerebrospinal fluid culture and PCR were positive for L. monocytogenes. Treatment was continued with ampicillin alone for 16 days plus gentamicin for the first seven days. By day 16 due to a rash (the patient had a history of ampicillin allergy), ampicillin switched to trimethoprim-sulfamethoxazole, thereby completing a total of three weeks of active antimicrobial therapy. She recovered completely without any neurological sequelae three months after the event. No epidemiological source of Listeria was implicated.

Conclusion: Serious infections due to L. monocytogenes may occur in patients that are immunosuppressed by corticosteroids and infliximab. As this organism is notably resistant to third generation cephalosporins frequently used in CSF infections, physicians should be aware of the possibility of this complication in patients with Crohn’s disease and should consider aggressive early diagnosis and treatment with ampicillin.

Disclosure of interest: None Declared.
Feasibility and effectiveness of a psycho-educational program in adolescents with Inflammatory Bowel Disease (IBD)

Maria Maragkoudaki, GEORGE CHOULIARAS, ALEXANDRA PAPADOPOULOU, MARIA CHRISTAKI

First Department of Pediatrics, University of Athens, Children's Hospital “agia Sofia”, Athens, Greece
Division of Gastroenterology, Hepatology & Nutrition, First Department of Pediatrics, University of Athens, Children's Hospital “agia Sofia”, Athens, Greece, Athens, Greece
Postgraduate Program of Stress Management and Health Promotion, University of Athens, Athens, Greece

Objectives and study: Adolescents with IBD have been reported to be at risk for psychological problems such as anxiety and depression and are prone to school absenteeism, stress related symptoms, medication adherence problems, all of which may affect their quality of life and disease outcome. The basic approach remains the standard medical care although a biopsychosocial approach may be a more integrated model of dealing with this disease. The aim of this study was to assess the feasibility of a multi-component psycho-educational program in adolescents with IBD and to investigate whether life style modifications and stress management techniques affect quality of life, depressive symptoms, stress and physical activity of the patients. Sixteen adolescents (mean age 12.8 years; 8 males) with IBD (6 with UC and 10 with CD) from a total number of 56 adolescents (30 with CD; 26 with UC), seen at a single IBD outpatient clinic during 12 consecutive months, agreed to participate in the study and were randomized to either an intervention or a control group.

Methods: Intervention consisted of 6 (30-40 min each) weekly sessions and included promotion of healthy life style (information about CNS-GUT axis, sleep hygiene, Mediterranean diet, moderate exercise); education in stress management techniques (guided imagery, diaphragmatic breathing and progressive muscle relaxation); and promotion of positive thinking (information about the connection between cognitions, emotions and actions, about cognitive distortions and exercise in cognitive techniques).

Depression (using the Children Depression Inventory score; CDI), stress and health scores (using self-rated Likert type scales 0-10), physical activity (using pedometer) and quality of life (using the IMPACT III questionnaire) were all assessed at baseline and after finishing the program. Both groups received standard medical care during the study period.

Results: A significant improvement in CDI scores (Cohen’s d=1.027) and an increase in the physical activity (p=0.045) were found in the intervention group compared to controls. Stress and IMPACT III scores were similarly changed in both groups while health scores were weakly (Cohen’s d coefficient: 0.37) improved in the intervention group.

Conclusion: Multi component psycho-educational programs are feasible in adolescents with IBD and effective in decreasing depression risk and improving physical activity of the patients thus, should be incorporated in the care of adolescents with IBD where appropriate.

Disclosures: “None Declared”.
Predicting outcome of pediatric Crohn’s disease: role of clinical, endoscopic and imaging findings at the diagnosis

Marina Aloi1, Fortunata Civitelli1, Salvatore Oliva1, Emanuele Casciani2, Giulia D’Arcangelo2, Alessia Spatoliatiore, Franca Viola2, Salvatore Cucchiara1

1Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
2Sapienza University of Rome, Rome, Italy

Objectives and study: Aims of this study were to evaluate the predictive value of clinical, laboratory endoscopic and imaging factors at the diagnosis for the risk of surgery and complicated disease course in children with Crohn’s Disease (CD)...

Methods: In this single-centre, prospective, longitudinal study, children newly-diagnosed with CD were enrolled and followed for 3 years. At baseline all patients underwent a clinical evaluation (Pediatric Crohn Disease Activity Index, PCDAI), laboratory exams [including C-Reactive Protein (CRP) and Erythrocyte Sedimentation Rate (ESR)], Magnetic Resonance Imaging (MRI) and ileocolonoscopy. Disease location and behavior were defined according to Paris classification. Simple endoscopic score for Crohn’s disease (SES-CD) was used to evaluate the severity of endoscopic lesions. Rate of surgery at maximum follow up was the primary outcome evaluated.

Results: 50 patients (64% males, median age 12.7±2.9 years) were enrolled. Mean SES-CD at the diagnosis was 15.3±10.6. A SES-CD graded as severe (>15) was present in 20/50 (40%) patients. MRI showed ulcers in 7/50 (14%) patients, stenosis in 20/50 (40%), pre-stenotic bowel dilation in 14/50 (28%), abscesses in 3/50 (6%) and fistulas in 7/50 (14%). The presence of stenosis at ileocolonoscopy (p=0.009) and fistulae at MRI (p=0.05) correlated with the need of resection surgery at follow-up. At a multivariate analysis, penetrating disease [r 0.65(0.40 to 0.81); p<0.0001], perianal involvement [0.41 (0.15 to 0.62); p=0.002], stenosis at ileocolonoscopy [r 0.30 (0.03 to 0.53); p=0.02] and fistula at MRI [r 0.41 (0.15 to 0.62); p=0.002] at the diagnosis increased the surgical risk at follow-up, while inflammatory behavior (B1) (r -0.4 (-0.6 to -0.1); p=0.006) and ESR>25 mm/h (r -0.3 (-0.5 to -0.03); p=0.03) were negatively associated.

Conclusion: Penetrating behavior and perianal disease at the diagnosis along with the presence of stenosis at ileocolonoscopy and fistulae at MRI are independent predictive factors of the surgical risk in children with CD. An inflammatory behavior and high ESR seem to correlate with a milder disease course.

Disclosure of interest: None Declared.
Assessing iron status in children with inflammatory bowel disease: beyond absolute iron deficiency

Maijolijn Akkermans1, Mirjam Vreugdenhil1, Danielle Hendriks2, Anemone van den Berg2, Joachim Schweizer3, Hans van Goudoever4, Frank Brus1

1Juliana Children's Hospital/Haga Teaching Hospital, Paediatrics, The Hague, Netherlands
2Juliana Children's Hospital/Haga Teaching Hospital, Paediatric Gastroenterology, The Hague, Netherlands
3Willem-Alexander Children's Hospital/Leiden University Medical Centre, Paediatric Gastroenterology, Leiden, Netherlands
4Vu University Medical Centre, Paediatrics, Amsterdam, Netherlands

Objectives and study: Iron deficiency (ID) in children with inflammatory bowel disease (IBD) is either an absolute (depleted iron stores) or a functional deficiency ('iron-restricted erythropoiesis' caused by inflammation). The differentiation between these two types of ID is important because they require a different therapeutic approach. Zinc protoporphyrin (ZPP) and red blood cell distribution width (RDW) are two parameters of iron-restricted erythropoiesis. Studies using these parameters to differentiate between absolute and functional ID are scarce. The aim of this study was to evaluate the prevalence of and risk factors for absolute and functional ID in paediatric IBD patients while using ZPP and RDW.

Methods: We evaluated the iron status and medical charts of 59 paediatric IBD patients in a secondary hospital in the Netherlands. Absolute ID (AID) was defined as a serum ferritin <15µg/l in the absence of infection (defined as CRP <10mg/l). Iron deficiency anaemia (IDA) was defined as IDA in combination with anaemia. Functional ID (FID) was defined as ZPP >70µmol/mol haem and/or a RDW >14%, in patients without AID. Anaemia of chronic disease (ACD) was defined as FID in combination with anaemia. These definitions were based on criteria of the World Health Organization.

Results: AID and FID were found in 19 (32.2%) and 32 (80%) patients, respectively. The prevalence of IDA and ACD was 27.1% and 20%, respectively. AID and IDA were both associated with a shorter disease duration.

Conclusion: Absolute and functional ID are common in paediatric IBD patients and this differentiation is important because of therapeutic consequences. Furthermore, AID is associated with a shorter disease duration.

Disclosure of interest: None Declared.

GASTROENTEROLOGY: Inflammatory bowel disease

G-P-178
Ileo-cecal Crohn's disease is associated with early strictureing and poor medical outcomes in children

Massimo Martinelli\textsuperscript{1}, Caterina Strisciuglio\textsuperscript{2}, Francesca Paola Giugliano\textsuperscript{1}, Marialuisa Andreozzi\textsuperscript{1}, Annamaria Staiano\textsuperscript{1}, Erasmo Miele\textsuperscript{1}

\textsuperscript{1}Federico II University, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
\textsuperscript{2}Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy

Objectives and study: Localized ileo-cecal disease (L1 according to Paris classification) is a specific CD phenotype whose prevalence and natural history in pediatric age is not well characterized. The aims of this study were to evaluate the natural history of children with ileocecal CD at diagnosis and to compare the outcomes of medical therapy in ileocecal CD children with pediatric patients showing different CD localizations.

Methods: We retrospectively reviewed charts of children diagnosed with CD at our referral center from January 2005 to December 2014. Only patients with luminal CD and with a minimum follow-up of 6 months were included in the study. Demographic characteristics, disease localization according to Paris classification, behaviour at diagnosis, change of behaviour during the follow-up, induction therapy and need for treatment escalation, including immunosuppressants (IM), biologics, endoscopic/surgical therapies, were collected. Patients were then divided into 2 groups: Group 1: patients with localized ileocecal CD at diagnosis; Group 2: all remaining luminal CD patients.

Results: Seventy-four children affected by CD were identified, of whom 23 (31%) with a localized ileocecal CD (median age: 17 yrs; range: 9.4-18; M/F: 15/8) and 51 (69%) with other luminal localizations (median age: 15.9 yrs; range 6.5-18; M/F: 30/21). Among the 51 children of group 2 CD localization was: Ileal (L1) (n=11, 21.6%), colonic (L2) (n=10, 19.6%), ileocolonic (L3) (n=28, 54.9%) and Upper GI (L4a-b) (n=11, 19.6%). Median follow up was 49.5 months (range: 6-154). Median age at diagnosis was not significantly different between the two groups (12.8 yrs vs 10.5 yrs; p=0.1), as well as induction therapy [Group 1- Enteral nutrition (EN): 13/23 (56.5%), EN+Steroids: 7/23 (30.4%) and steroids: 3/23 (13%); Group 2- EN: 39/51 (76.5%); EN+Steroids: 3/51 (5%) and steroids: 9/51 (17.6%); p=0.1]. Eight out of 23 children of group 1 presented with stricturing behaviour at diagnosis versus none of Group 2 (p<0.001); overall, 16 out of 23 patients (69.5%) developed a stricture during disease course versus 3/51 (5.8%) of group 2 (p<0.001). Twenty out of 23 children of Group 1 presented with strictureing behaviour at diagnosis versus none of Group 2 (p<0.001); overall, 16 out of 23 patients (69.5%) developed a stricture during disease course versus 3/51 (5.8%) of group 2 (p<0.001). Twenty out of 23 (87%) patients with ileocecal CD started an IM [Azathioprine (AZA):17 (85%); Methotrexate (MTX): 3 (15%) versus 21 out of 51 children of Group 2 [(AZA: 19 (39.1%); MTX: 2 (9.6%)] (p<0.001). Moreover, a higher number of patients of Group 1 needed to switch to another IM when compared with Group 2 [10/20 (50%) vs 4/21 (19%); p=0.05]. A higher number of children with ileocecal disease started biologics with a trend towards statistical significance [7/23 (30.4%) vs 7/51 (13.7%); p=0.08]. Nine out of 23 (39.1%) children of Group 1 underwent surgery or endoscopic dilation compared with 2 out 51 (3.9%) patients of group 2 (p<0.001). Seven out of 9 patients (77.7%) of group 1 had a sustained remission after surgical procedure with a median follow-up of 28 months (range 7-42 months).

Conclusion: Patients with localized ileocecal CD show a more severe disease, including early strictureing and need for therapy escalation. During disease course most of these children undergo surgery. Our data suggest that patients with ileocecal CD should receive a top-down strategy and that early elective surgery as a first line treatment should be evaluated in future studies.

Disclosure of interest:
M. Martinelli: none declared
C. Strisciuglio: none declared
F.P. Giugliano: none declared
M. Andreozzi: none declared
A. Staiano: none declared
E. Miele: none declared
**GASTROENTEROLOGY: Inflammatory bowel disease**

G-P-180

**Assessing mucosa state in children with Crohn’s disease using faecal calprotectin**

Monika Meglicka¹, Michal Szczepanski¹, Maciej Dadalski¹, Jaroslaw Kierkus¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Paediatrics, Warsaw, Poland

**Objectives and study:** Faecal calprotectin (FC) is a good marker in monitoring mucosal healing in adults with Crohn’s disease (CD). Its concentrations in faeces is related to state of mucosa observed in endoscopy. Only few studies in paediatric CD patients concern the role of FC in monitoring mucosal healing. In this study we wanted to assess the usefulness of FC in monitoring and predicting mucosal mucosa state in population of paediatric CD patients.

**Methods:** 68 patients with CD (F 26, M 42, ±12.51 years) were involved to the study and had elective colonoscopy performed, FC level and haematocrit (HT) within a week before endoscopy measured. Each patient had also paediatric Crohn’s disease activity index (PCDAI) calculated. Mucosa status was assessed during endoscopy with simple endoscopic score for Crohn's disease (SES-CD). Full mucosal healing was defined as SES-CD=0. We have identified two subgroups: those with full mucosal healing, and patients with inflamed gut mucosa. The receiver operating characteristic curve (ROC) was used as a statistical method to establish cut-off points. The cut-off points are FC level for simple model and probability threshold for the logistic regression. The area under the curve (AUC) assesses the differentiation quality of the study group based on the model score. To increase specificity at high sensitivity the logistic regression with other predictors was made. The final model was selected using cross-validation.

**Results:** AUC for the simple model was 0.86. The selected cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation was 59 μg/g with specificity 0.94 and sensitivity 0.56. When sensitivity was outweighed over specificity the cut-off point was 1442 μg/g with specificity 0.36 and sensitivity 0.94. With logistic regression on FC, CRP, HT and PCDAI the AUC was 0.85, and we could discriminate our patient with specificity 0.50 and sensitivity 0.94.

**Conclusion:** FC is a good marker of mucosal healing in monitoring of children with CD. FC below 59 μg/g enable us to select 56% of patients with full mucosal healing. Logistic regression with FC, HT and PCDAI let us select 50% of patients with inflamed mucosa. Using these two methods, step by step, we could discriminate 44% of patients with unknown mucosa status, that require endoscopy.

**Disclosure of interest:** None Declared
Evaluation of the nutritional status in our pediatric patients with inflammatory bowel disease at diagnosis

Natàlia Egea, Gemma Pujol, Karina Rosales, Alejandra Gutierrez, Dolores Garcia, Víctor Vila Miravet, Sergio Pinillos Pison, Javier Martin de Carpi

1Hospital Sant Joan de Déu, Gastroenterology, Barcelona, Spain
2Hospital Sant Joan de Déu, Gastroenterology and Nutrition, Barcelona, Spain
3Hospital Sant Joan de Déu, Pediatric Gastroenterology, Barcelona, Spain

Objectives and study: To evaluate the nutritional status and assess the eating habits in a cohort of paediatric inflammatory bowel disease (PIBD) patients at diagnosis, in order to establish an individualized nutritional recovery plan.

Methods: Data of 84 patients (48 boys; 44 CD, 40 UC) diagnosed with PIBD in our hospital (July 2012 - November 2015) were collected. Mean age at diagnosis: 12 years (range 18 months-17 years). Collected data were: anthropometric parameters (weight, height, skin folds), nutritional index (Muscle Mass Index -MMI-, Waterlow Index -WI-) and scan to determine nutritional status such us bioelectrical impedance. Likewise, eating habits were assessed by a food frequency questionnaire (FFQ) and according to the validated EnKid study.

Results: 73.7% of patients had lost weight before diagnosis. Of these, 33.3% have less than 10% weight loss, 22.6% lost between 10-15% and 17.8% of patients lost more than 15% of their previous weight. According to the WI, 26% presented with a normal nutritional status, 26% were overweight or obese and 47% had some kind of malnutrition (27% mild, 18% moderate, 2% severe). We observed a greater percentage of undernourished CD patients as compared to UC ones (60/40). 13% of the patients followed at the time of diagnosis a low quality nutritional diet, 50% of patients needed to improve the eating pattern to suit the Mediterranean diet whereas 37% maintained good dietetic habits.

Conclusion: More than a half of our patients present with weight loss at the time of diagnosis with malnutrition being more frequent in CD patients as compared to UC patients. Regarding the eating habits, more than a half of the patients should improve some aspects of their diet and strengthen guidelines of a balanced diet. A small percentage of the patients have wrong eating habits that should be modified. Nutritional status assessment at the time of diagnosis is quite helpful in order to establish an individualized nutritional treatment and to give dietetic recommendations, either with traditional food or enteral nutrition. A close dietetic control during the follow-up should influence the re-education of eating habits and reinforce a balanced diet of PIBD patients.

Disclosure of interest: None declared.
5-year review of IBD management in children with autoimmune liver disease; a single-centre experience

Natalia Nedelkopoulou1, Marianne Samyn2, Nedim Hadzic1, Maesha Deheragoda3, Anil Dhawan1, Babu Vadamalayan1

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
3King’s College Hospital, Institute of Liver Studies, London, United Kingdom

Objectives and study: The association between inflammatory bowel disease (IBD) and autoimmune liver disease (AILD) has been well established. We present our experience in the course and management of IBD in pediatric patient with concomitant AILD.

Methods: The records of pediatric patients with AILD who underwent endoscopic assessment between 2010-2015 were reviewed. The type of GI/liver disease, the interval between diagnoses and the course of the diseases were documented.

Results: 29 patients (19M) aged 4-17y (median age 12y) were identified. In all patients, IBD and AILD were confirmed with endoscopy, liver biopsy and positive autoantibodies. 8 had endoscopic reassessment for known IBD; 7/8 had ulcerative colitis (UC) and 1/8 Crohn’s disease. In 4 patients the diagnosis of AILD (3 AISC/1 AIH type 1) preceded that of IBD. The course of IBD/AILD was severe in 2 requiring biologics (IFX, Humira, Golimumab, Vedolizumab). Out of the 2 patients with severe IBD/AILD, 1 underwent liver transplantation (OLT) and colectomy at the same time and 1 can’t have colectomy due to advanced portal hypertension and is awaiting TIPS procedure. 1 patient with mild UC (right-sided) received liver transplantation (OLT) for AISC. The patient was re-transplanted for acute Budd-Chiari and died of multi-organ failure. 1 patient with mild indeterminate colitis received OLT for AISC and died of sarcoma. Follow-up since initial diagnosis of AILD ranged from 8-14y (median 10y).

Of the 8 patients who had endoscopy for known IBD, 2 had been diagnosed with IBD/AILD at the same time (AISC/UC) and in other 2, AILD followed the diagnosis of IBD within 1-3y (1 Crohn’s /AIH and 1 with UC/AISC). Follow-up ranged from 6-10 years (7.7y). 3 patients had mild IBD with 1-2 flares on standard immunosuppression (5ASA, Azathioprine, MMF, Prednisolone 5mg) and normal or mildly deranged LFT. 1 had difficult-to-control Crohn’s/AIH and received biologic therapy and OLT. 21 patients underwent diagnostic endoscopy between 2010-15. 17 were diagnosed with UC ( pancolitis 16, left-sided colitis 1), 2 with Crohn’s and 2 with indeterminate colitis. 12/21 had an established AILD; AISC/UC (5), AIH type 1/UC (4), AISC/ Crohn’s disease (1), indeterminate colitis/AIH type 1 (2). 6 had severe, difficult to control IBD, requiring biologics (IFX, Humira) and colectomy was performed in 2 patients. 4 of the patients with severe IBD have deranged liver function tests (AST 75-116, gGT 174-254). 6 with mild IBD had 0-3 flares. LFT are normal in 2, mildly deranged in 2 and 2 patient received OLT for AIH type 1.

Of the 21 patients with diagnostic endoscopy, 9 were first diagnosed with IBD and then AILD. Follow-up since diagnosis of IBD ranged from 3m-2y (median 1.75y). IBD has been in remission (0-1 flares) in 6 patients, whereas 3 with AISC have steroid dependent UC requiring biologics. All 9 patients have normal LFT.

Conclusion: In our cohort, the course of IBD has been mild with uncomplicated AILD in 11/29 (38%). Patients with pancolitis resistant to standard treatment had IBD following AILD diagnosis in 67% of cases with severe IBD. These patients may require colectomy/liver transplantation that can be challenging due to the risk of bleeding and should be performed in centres with special expertise. The clinical presentation of IBD in pediatric patients with AILD on immunosuppressive treatment may not be typical resulting in delayed diagnosis and complicated disease. Early diagnosis with ileocolonoscopy is essential.

Disclosure of interest: None

Vol. 62, Supplement 1, May 2016
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-183

Adalimumab as First Line Biologic Therapy is Effective and Well Tolerated by Children with Crohn's Disease

Nkem Onyeador¹, Theodoric Wong¹, Susan Protheroe¹, Wolfram Haller¹, Lisa Whyte¹, Ronald Bremner¹, Rafeeq Muhammed¹

¹Birmingham Children's Hospital NHS Foundation Trust, Birmingham, United Kingdom

Objectives of study: Infliximab and Adalimumab are the two anti Tumor Necrosis Factor (TNF) alpha agents licensed for use in children with Crohn’s disease (CD) in the UK. We have compared the efficacy, safety and patient acceptance of treatment with Adalimumab as first line anti TNF alpha agent to treatment with Infliximab.

Methods: We have collected clinical and laboratory data from patient notes and electronic case records of all patients with Crohn’s disease who are currently receiving anti TNF therapy. Results: 21 patients with Crohn's disease were started on Adalimumab as the first line anti-TNF alpha treatment compared to 101 patients receiving Infliximab as the first line anti TNF alpha therapy. All patients were receiving Adalimumab using a pen device at home. All Infliximab infusions were given in the hospital. Active luminal Crohn’s disease was the indication to start Adalimumab in 19/21 (90%) patients. 88/101 (87%) patients were started on Infliximab for active luminal Crohn’s disease. 2/ 21 (10%) patients on Adalimumab switched treatment to Infliximab due to patient preference. 20/101 (20%) patients switched treatment from Infliximab to Adalimumab (11 due to loss of response, 6 due to infusion reaction and 3 due to patient preference). 3/21 (14%) patients on Adalimumab switched treatment to Infliximab due to patient preference. 20/101 (20%) patients needed switching of biologic treatment from Infliximab to Adalimumab. 17/20 (85%) patients on Adalimumab treatment were in clinical remission compared to 70/81 (86%) patients receiving treatment with Infliximab. Results are summarised in Table 1. No malignancy was reported in any patients.

Table 1: Comparison of patients with Crohn’s disease receiving Adalimumab and Infliximab as first line anti TNF alpha therapy

<table>
<thead>
<tr>
<th>Patients receiving Adalimumab</th>
<th>Patients receiving Infliximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>21</td>
</tr>
<tr>
<td>Patients on co-immunosuppression</td>
<td>16/21 (76%)</td>
</tr>
<tr>
<td>Patients needing dose/frequency escalation</td>
<td>3/21 (14%)</td>
</tr>
<tr>
<td>Patients needing switching of biologic treatment</td>
<td>2/21 (10%) (patient preference)</td>
</tr>
<tr>
<td>Clinical remission</td>
<td>17/20 (85%)</td>
</tr>
<tr>
<td>Clinical response</td>
<td>3/20 (15%)</td>
</tr>
<tr>
<td>Cost of 6 months treatment</td>
<td>£6000 (Adalimumab induction 160/80 mg followed by)</td>
</tr>
</tbody>
</table>
Conclusion: Treatment with adalimumab as first line biologic agent is safe and effective and well accepted by children with Crohn’s disease. We hope that this information would be useful for children and parents to make an informed decision about the choice on anti TNF alpha treatment.

Disclosure of interest: Dr Rafeeq Muhammed 7th author has conflict with MSD Immunology, Abbvie, Dr Falk, Tillotts Pharma, Nestle, Takeda and Pfizer.
Altered mucosal expression of microRNAs in pediatric patients with inflammatory bowel disease

Nóra Judit Béres¹, Zoltán Kiss¹, Dániel Szűcs³, Katalin Eszter Müller¹, Áron Cseh¹, Zsófia Sztupinszki¹, Gábor Lendvai³, Andras Arato¹, Erna Sziksz¹, Ádám Vannay¹, Attila Szabo¹, Gábor Veres³

¹Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary
²University of Szeged, Department of Pediatrics and Pediatric Health Care Center, Szeged, Hungary
³Semmelweis University, MTA-SE Tumor Progression Research Group, Budapest, Hungary
⁴MTA-SE, Pediatrics and Nephrology Research Group, Budapest, Hungary

Objectives and study: Non-coding small RNA-s, called microRNAs (miRs) came recently into focus as promising novel research targets offering possible new insights into the pathogenesis of inflammatory bowel disease (IBD). Since the diagnosis of IBD is reasonably challenging, there is an urgent need to identify new disease biomarkers. Therefore, the aim of the present study was to identify a pediatric IBD specific miR profile and to analyze the network connection of differently expressed miR and their target genes in Crohn’s disease (CD) and ulcerative colitis (UC).

Methods: Illumina small RNA sequencing was performed on fresh-frozen macroscopically inflamed (CD inflamed, n=4) and intact, non-inflamed (CD intact, n=4) colonic biopsies of therapy-naïve children with CD and control patients (C, n=4). Selected miRNAs were further investigated by real-time reverse transcription PCR using an extended number of patients (CD inflamed, n=15, CD intact, n=10, UC, n=10, C, n=10). Network connection of differentially expressed miRs and target genes in pediatric IBD according to the MiRTarBase database and publicly available microarray data were performed (E-GEOD-57945) along with Gene Ontology (GO) analysis on the common genes.

Results: MiR profiling of colonic samples identified 148 miRs that were dysregulated in the inflamed mucosa compared to the intact mucosa of IBD patients. 22 miRs were differently expressed in the intact mucosa of CD patients in comparison to controls. Expression of miR-18a, -21, -31, -99a, -99b, -125a, -126, -142-5p, -146a, and -223 were elevated in both CD and UC samples as compared to the controls. Expression of miR-100, -150, -142-3p, and -185 were elevated in the inflamed mucosa of CD patients compared to the controls, but not to patients with UC. Moreover, the expression of miR-20a, -100, -221, -204, and -185 were elevated in the intact mucosa of CD patients in comparison to controls. Expression of miR-141 and -204 were decreased in the inflamed intestinal mucosa compared to the intact counterpart of CD patients and controls. The enrichment analysis resulted in 50 major GO terms, and the most abundant terms are the regulation of apoptotic process, response to wounding, response to bacterium, immune response, cell proliferation, adhesion, migration and activation, blood vessel development, regulation of gene expression, cell-cell signaling.

Conclusion: We demonstrated a characteristic colonic miR pattern in pediatric patients with IBD. The target gene screening, annotation and enrichment analysis identified several IBD-related functional groups, providing further evidence for the specificity of miR profile and underlining the potential importance of these regulatory elements in the pathomechanism of pediatric IBD.

Disclosure of interest: None Declared.

This work was supported by grants OTKA-K105530, -K108688, -PD105361, LP008/2015
Young IBD patients should receive a combotherapy (IS and IFX) until the 3rd infusion of Infliximab to reduce the risk of acute infusion reactions.

Christine Martinez-Vinson¹, Olivier Courbette¹, Camille Aupiais², Jerome Viala³, Jean-Pierre Hugot¹

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

Objectives and study: Administration of Infliximab (IFX) is associated with a well recognised risk of acute infusion reaction. The aim of this observational retrospective study is to assess the risk of acute infusion reactions according to patient's Anti-infliximab antibodies (ATI) status and the relationship of immunomodulators.

Methods: This is a single center observational retrospective study of pediatric patients who were treated with IFX for Inflammatory bowel disease (IBD) from 2002 to 2014 as a first line biotherapy. Data included age, sex, underlying disease, IFX therapy duration before the infusion reaction, ATI's, trough levels of infliximab (TRI), Imunosuppressive (IS) associated therapy and rates of remission.

Results: 147 patients less than 18 years old with IBD were treated with IFX during the period. 87.7% were Crohn's disease (CD), 16.3% Ulcerative colitis (UC). The reasons for starting anti-TNF therapy were failure of IS therapy in 61.9%, perianal disease in 25.9%, severe colitis in 12.2%. A median of 15 infusions (4-65) were analysed per patient with a total of 2258 infusions. Median age at the initiation of IFX was 14 years. 87.1% (127) patients achieve remission at the 3rd infusion (2-5). 9 patients (6%) developed an acute infusion reaction, at the 8th infusion (5-9). The patients in the group with reaction were 10.6 years old (9.1-12.6) whereas in the group without reaction they were older : 14 (12-15.4). 17.9% of patients under 11 years old experienced an acute infusion reaction whereas only 3.4% of patients equal or more than 11 years old experienced it. 78.8% of the patients in the group with reaction were girls, 41.7% in the group with no reaction. TRI was lower in the group with reaction (1 versus 4,8 in the group with no reaction). ATI were higher in the group with reaction 78% versus 39% in the group with no reaction (p=0.03). IS therapy was significantly associated with no infusion reaction (61.6% patients with no infusion reaction were still receiving IS therapy at the 3rd reaction versus 0% in the group with infusion reaction, p<0.01).

Conclusion: The presence of ATI is associated with a significantly higher risk of acute infusion reactions. Young patients, and specially girls, less than 11 years old are at high risk of infusion reactions. Concomitant IS therapy reduces significantly the risk of infusion reactions. In conclusion, young patients less than 11 years old should receive a combotherapy (IS and IFX) until the 3rd reaction to reduce the risk of infusion reactions.

Disclosure of interest: None declared.
Tacrolimus has a transient efficacy for the treatment of refractory Crohn disease colitis in children

Oriane Truffinet¹, Christine Martinez-Vinson¹, Jean-Pierre Hugot¹, Jerome Viala¹

¹Robert-Debré Hospital. Assistance Publique-Hôpitaux de Paris, Departments of Pediatric Digestive and Respiratory Diseases, Paris, France

Objectives and study: Tacrolimus is an immunosuppressive agent which has been used to control severe ulcerative colitis. Rare adult studies suggested that tacrolimus could control refractory Crohn disease (CD) relapse. Our aims were to analyze efficacy and safety of tacrolimus on refractory CD colitis in children.

Methods: We retrospectively studied children treated by oral tacrolimus for CD colitis which was refractory to steroids and infliximab. The response (PCDAI decrease ≥15 and PCDAI ≤30) and the remission (PCDAI ≤10) were analyzed at 2, 4, 12 and 24 months after induction. The secondary mains were the tacrolimus blood level and occurrence of adverse effects.

Results: Eight refractory CD children (3 girls. Median age of 14 years; 9.5-18 years) were collected. The median PCDAI was 58.7 (32.5-65) before tacrolimus treatment. The overall response rates were 6/8, 3/7, 2/4, 2/4 and 1/2 and 2/4 with a remission rate of 4/8, 0/7, 0/5, 2/4, 0/2 at M2, M4, M6, M12 and M24 respectively. At M2, the PCDAI scores were lower than at induction (Median 11.2; P = 0.004) with a mean whole plasma level of tacrolimus of 8.75 ng/mL (5.9-10 ng/mL). Adverse events occurred in 6/8 patients, including renal dysfunction, insulin-dependent diabetes, paresthesia, and tremor. Tacrolimus interruption was required in 2 cases (renal dysfunction and diabetes).

Conclusion: in selected cases, tacrolimus controlled refractory CD colitis in 75% of children. But its transient effect needed other immunosuppressive agents after few months. The adverse events are frequent but easily controlled by withdrawal or interruption of treatment.

Disclosure of interest: None
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-187

Serum hepcidin concentration in children with inflammatory bowel disease (IBD)

Paulina Krawiec¹, Elżbieta Pac-Kożuchowska¹, Agnieszka Mroczkowska-Juchkiewicz¹, Agnieszka Pawłowska-Kamieniak¹, Katarzyna Kominek¹, Beata Melges¹

¹Medical University of Lublin, Department of Paediatrics, Lublin, Poland

Objectives and study: Hepcidin is a major regulator of iron homeostasis and mediator of innate immunity. Iron deficiency down-regulates hepcidin, increasing intestinal iron absorption and release of iron from stores. In contrast, inflammation increases expression of hepcidin, leading to hypoferremia and iron-restricted erythropoiesis. Current data on hepcidin expression in IBD are limited and conflicting. We aimed to assess serum hepcidin concentration in IBD children compared to healthy children and correlate hepcidin with iron status parameters and inflammatory markers.

Methods: The study group comprised 75 children with IBD, including 46 (61%) with ulcerative colitis and 29 (39%) with Crohn’s disease. Twenty-one healthy children were enrolled to the control group. Patients with blood transfusion and iron supplementation in the three previous months were excluded from the study. All children underwent blood tests including complete blood count, high sensitivity C-reactive protein (hsCRP), erythrocyte sedimentation rate (ESR), interleukin-6 (IL-6), iron, ferritin, transferrin and transferrin saturation. The study was approved by the local bioethical committee.

Results: Mean serum hepcidin concentration was significantly decreased in IBD children (5.98ng/mL) compared to healthy controls (10ng/mL) (p=0.03). Hepcidin concentration did not differ significantly between patients with Crohn’s disease (6.9±4.5 ng/mL) and ulcerative colitis (5.4±5.3ng/mL) (p=0.07). In children with IBD, 17 (23%) had iron deficiency without anaemia and 38 (50%) had anaemia including 27 (36%) with iron deficiency anaemia, 6 (8%) with anaemia of chronic disease with iron deficiency and 5 (7%) with anaemia of chronic disease. Hepcidin was significantly decreased in IBD children with iron deficiency (4.9±3.2ng/mL) compared to IBD children without iron deficiency (7.9±7ng/mL) (p=0.05) and healthy controls (10.5±10ng/mL) (p=0.03). In anaemic children with IBD serum hepcidin (5.3±4.4ng/mL) was significantly reduced compared to healthy controls (p=0.04), but comparable to non-anaemic IBD children (6.6±5.6ng/mL) (p=0.1). Serum hepcidin was positively correlated with ferritin in IBD children (p=0.007, R =0.3) and healthy controls (p=0.003, R=0.6). However, there were no correlations between hepcidin and serum iron, transferrin, transferrin saturation, inflammatory markers i.e. hsCRP, ESR, Il-6 and IBD activity indices.

Conclusion: In our cohort of IBD children serum hepcidin concentration was significantly decreased in IBD children compared to healthy controls. Hepcidin levels correlated positively with ferritin, but not with inflammatory markers. These results may suggest that in our cohort hepcidin was regulated predominantly by the iron storage level.

Disclosure of interest: None Declared.
Outcomes in a prospective cohort of newly diagnosed children with Crohn’s disease treated with exclusive enteral nutrition

Gregory Williams¹, Minal Patel², Laura Jellis², Edward Giles², Ian Sanderson³, Protima Amon³

¹School of Medicine and Dentistry, Queen Mary University of London, London, United Kingdom
²The Royal London Hospital, Barts Health NHS Trust, London, United Kingdom
³Blizard Institute, Queen Mary University of London, Immunobiology, London, United Kingdom

Objectives and study: Exclusive enteral nutrition (EEN) is recommended as induction therapy for active Crohn’s disease (CD). It is well established that enteral nutrition has strong anti-inflammatory effects when given exclusively for 6-8 weeks. This study reports on the efficacy of EEN upon disease activity and growth in children newly diagnosed with CD.

Methods: A prospective assessment of all children diagnosed with CD between 1st March 2014 and 31st October 2015 who were commenced on enteral diet for 6 weeks, in a single tertiary paediatric gastroenterology centre. Primary outcome measures were weight change and disease activity (Paediatric Crohn’s Disease Activity Index: PCDAI). Secondary outcomes were relapse and the use of immunomodulatory therapy.

Results: Thirty children (Females 17; Mean age: 12.5 years) were commenced on EEN with a mean follow-up of 294 days. Twenty-one children completed the prescribed period of EEN (70%) and these all achieved clinical remission. Children responding to EEN all took the feeds orally and gained an average of 4.4 ± 2.4kg with mean PCDAI decreasing from 32.1 ± 11.6 to 8.5 ± 8.9 after 6 weeks. 13/30 (43%) relapsed during follow-up with a mean time to relapse from diagnosis of 5.9 months. All 13 of these children were started on azathioprine during the follow-up period, with a mean starting time of 6.9 months following diagnosis.

Conclusion: EEN induced remission in 70% of children with newly diagnosed CD. In addition to inducing remission, EEN improved weight gain. This is in keeping with published data. Further studies are required to determine whether these benefits are sustained longer-term.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-189

Can infliximab treatment for pediatric inflammatory bowel disease be safely stopped? Results from a single center cohort retrospective study.

Hiba Makhoul¹, Liat Pritzker¹, Ron Shaoul²

¹Rambam Medical Center, Haifa, Israel
²Rambam Hospital, Pediatric Gastroenterology, Haifa, Israel

Objectives and study: Biological treatment, especially with anti TNF agents, has become standard of care in pediatric inflammatory bowel disease. Nevertheless, there are no clear guidelines in both adult and pediatric literature how long biologic treatment should be continued. Since there are concerns on the long term safety of these agents, especially in children, proper and clearer guidelines are mandated.

The study retrospectively investigated the efficacy and safety of infliximab treatment in IBD pediatric patients, and specifically assessed an established protocol for infliximab administration based on clinical experience at Rambam medical center that consisted of 3 induction doses and 3 maintenance doses as long as the patient was in remission at the 6th dose.

Methods: the study reviewed the charts of 46 children with the diagnosis of IBD who mostly received infliximab infusion according to the specified protocol. The primary end point was the ability to maintain remission after 6 doses and the secondary end point was the induction of remission after reintroducing infliximab for those who relapsed. Remission was defined as normal laboratory tests and normal clinical scores (PUCAI/PCDAI).

Results: we have found that under this protocol of infliximab treatment; 3 induction doses and 3 maintenance doses, 76.5% and 70% of the children with CD and UC, respectively, underwent into remission. The median infliximab doses for achieving and maintaining remission was 6.5 and 7 for Crohn disease and ulcerative colitis respectively. The length of remission varied between patients; 3-72 months (mean 20.8±19.1 months), while the majority maintained remission for over 12 months. For those who relapsed and were reintroduced to infliximab infusions (10 patients), 3(30%) achieved remission.

Conclusion: infliximab is a successful and a safe treatment for induction and maintenance of remission in pediatric IBD patients. The suggested protocol has been proven to be efficient and safe in the majority of the children.

Disclosure of interest: This study was funded by a grant from Janssen Israel.
Rapid Infliximab infusions are generally well-tolerated in children with inflammatory bowel disease - an Australian perspective.

Caitlin Glover¹, Linny Phuong²

¹Department of Paediatrics, Monash University, Melbourne, Australia
²Department of Paediatrics, Monash Children's Hospital, Melbourne, Australia

Objectives and study: Infliximab (IFX) is commonly used in children with inflammatory bowel disease (IBD). IFX has most frequently been infused in children with IBD over at least 2 hours. Rapid infusions (given over 1 hour) have been used in adults with IBD in several large studies with no significant increase in adverse events reported. The aim of this study was to compare the tolerability and side-effect profile of IFX administered to children over 1 hour with the longer historical (≥2 hours) infusion time in one of Melbourne’s two tertiary paediatric gastroenterology centres.

Methods: We performed a retrospective case-notes review on all patients currently attending the IBD clinic at Monash Children’s Hospital who were receiving Infliximab according to our rapid infusion protocol (RP), which consists of the first four infusions over 2 hours, with 2 hours of monitoring, then subsequent infusions over 1 hour. To be included in the study the children had to have been given IFX according to both the historical protocol and the RP so as to act as their own controls. Those children who were commenced on the RP when their IFX began were excluded.

Results: Between 2011 and 2013, twenty-eight children receiving IFX fulfilled inclusion criteria for the study, median age at diagnosis 13 years, (range, 8-15 years). All children had a diagnosis of Crohn’s disease. 27/28 patients (96%) had mild self-limiting, or no side-effects with the transition, 1/28 developed anaphylaxis requiring intramuscular adrenaline with subsequent full recovery and then cessation of treatment.

Conclusion: Careful monitoring is still mandatory, given the small risk of side-effects, but as has previously been demonstrated in adult data, most children tolerate conversion to rapid infusions with no adverse outcomes. This reduction in hospital time may facilitate reduced disruption to a patient’s education.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: Inflammatory bowel disease

G-P-191

Pediatric Crohn's Disease and its Disability Over Time: a Study Performed With a New Pediatric Lémann Index. Data from a Tertiary Pediatric IBD Center

Serena Arrigo1, Giorgia Bodini2, Paola Diana1, Edoardo Giovanni Giannini2, Edoardo Savarino3, vincenzo savarino2, Arrigo Barabino1

1I. G. Gaslini, Pediatric Gastroenterology and Endoscopy Unit, Genoa, Italy
2Genoa University, Department of Internal Medicine, Gastroenterology Unit, Genoa, Italy
3Padua University, Department of Surgery, Oncology and Gastroenterology - Gastroenterology Unit, Genoa, Italy

Objectives and study: Crohn's disease (CD) is a chronic and progressive condition that, due to disease complication, leads to surgical resection in the majority of cases. Recently, a panel of expert developed the Lémann Index (LI), a new tool aimed to assess the progressive bowel damage due to disease course. The aim of LI is to assess structural bowel damage due to CD based on stricturing lesions, penetrating lesions and surgical resection. However, in the pediatric population we should also take into account also peculiar characteristics, such as intestinal length and the pattern of growth of the patient. The aim of our study was to measure the LI in a pediatric cohort at diagnosis as well as the trend of LI during time.

Methods: We chose segments of 10 cm for small bowel, instead of 20 cm as proposed in adults. Moreover, we decided to adjust the final score considering growth failure, using different values based on weight and height Z-scores at diagnosis and at the last evaluation. We called this new score pediatric LI (P-LI).

We retrospectively selected 50 consecutive pediatric patients who were firstly diagnosed at our hospital by abdominal Magnetic Resonance Imaging, colonoscopy and upper GI endoscopy, and in case of perianal disease, a pelvic magnetic resonance imaging. Patients were aged between 6 to 17 years. We evaluated the P-LI at diagnosis and calculated the difference between P-LI at diagnosis and at the last pediatric outpatient visit or at transition to adult outpatient.

Results: We included a total of 50 CD pediatric patients (24 male, median age 18 years, range 11-27, median age at diagnosis 11.5 years, range 6-17) who were followed-up for a median of 46 months (range 4-120). Among them, 32 (64%) patients had at least a stable P-LI during the follow up, whereas 18 (36%) had an increase in P-LI during time. Considering the overall population there was no statistical significant difference between median P-LI at beginning and at the end of follow up (5.8, range 0.6-18.8 vs 2.5, range 0.0-33.8, P=0.7). Subdividing patients who underwent surgical resection (n=13, 26%) and those who did not (n=37, 74%) we found a significant difference between median P-LI at the beginning and at the end of follow up in both groups (6.2, range 1-18.8 vs 16.7, range 8.3-33.8, P=0.001; 5.6, range 0.6-17 vs 1.2, range 0-20.5, P<0.001) with a disease regression in the no surgery group. Moreover, analyzing data from patients who utilized anti-TNF therapies (n=24, 48%), we found no significant difference between P-LI at the beginning and at the end of follow up (6.1 range 1-17 vs 3.6, range 0.0-31.7, P=0.85).

Conclusion: Our data suggest that the P-LI we devised is a useful tool to evaluate CD in the pediatric population and to assess disease progression. In children avoid a surgical resection is extremely important because medical therapy is able to reverse or halt the disease progression.

Disclosure of interest: None Declared.
Neutrophil Extracellular Traps in Pediatric Inflammatory Bowel Disease

Yehonatan Gottlieb1, Ronit Elhasid2, Sivan Berger-Achituv2, Eli Brazowski3, Shlomi Cohen4

1“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Research Laboratory for Pediatric Hemato-Oncology, Tel Aviv, Israel
2“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Department of Pediatric Hemato-Oncology, Tel Aviv, Israel
3“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pathology, Tel Aviv, Israel
4“Dana-Dwek” Children’s Hospital, Tel Aviv Medical Center, Pediatric Gastroenterology Unit, Tel Aviv, Israel

Objectives and study: The pathogenesis of inflammatory bowel disease (IBD) is multifactorial and characterized by chronic active intestinal inflammation. The contribution of neutrophils to this process is controversial. Upon activation neutrophils release fibers composed of chromatin and granule proteins termed neutrophil extracellular traps (NETs). NETs trap and kill microbes, activate dendritic cells and T cells, and are implicated in autoimmune and vascular diseases.

Methods: In this retrospective study, we aimed to examine the presence of NETs in intestinal biopsies from pediatric IBD patients and their relationship to disease characteristics. Twelve biopsies were taken at diagnosis from the small bowel and colon of pediatric Crohn’s and ulcerative colitis patients and compared to those of healthy controls. The biopsies were labeled for neutrophil elastase, myeloperoxidase, DNA, chromatin and histones in order to identify and quantify NETs. NETs ratio was determined by calculating the ratio between neutrophils elastase labeled area (excluding the non-stimulated neutrophils) and the total tissue area.

Results: Of the 12 pediatric IBD patients, there were 7(58%) females, average age was 12.2±3.4 years, range 5-16, 6 had Crohn’s disease and 6 ulcerative colitis. NETs were identified in all 12 patients but not in the biopsies of healthy controls. The average NETs ratio was higher in Crohn’s disease (41%) than in ulcerative colitis patients (23%), but it did not reach statistical significance. No differences were found between disease severity, disease location and NETs ratio.

Table: Table 1: Baseline characteristics of the study population.

<table>
<thead>
<tr>
<th>Disease location</th>
<th>Crohn’s Disease</th>
<th>Ulcerative Colitis</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>N</td>
<td>6</td>
<td>6</td>
<td></td>
</tr>
<tr>
<td>Age at diagnosis (yr)</td>
<td>12.5(6-13.4)</td>
<td>11.9(5-15)</td>
<td></td>
</tr>
<tr>
<td>Males (%)</td>
<td>3(50%)</td>
<td>2(33.3%)</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Disease location</th>
<th>CD(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ileal (L1)</td>
<td>2</td>
</tr>
<tr>
<td>Colonic (L2)</td>
<td>0</td>
</tr>
<tr>
<td>Ileocolonic (L3)</td>
<td>4</td>
</tr>
<tr>
<td>L4a</td>
<td>3</td>
</tr>
<tr>
<td>L4b</td>
<td>0</td>
</tr>
</tbody>
</table>
**Disease location** | **UC (%)**
--- | ---
E1: ulcerative proctitis | 1
E2: left-sided UC | 0
E3: extensive | 0
E4: Pancolitis | 5

<table>
<thead>
<tr>
<th>Test</th>
<th>Cases</th>
<th>Controls</th>
</tr>
</thead>
<tbody>
<tr>
<td>ASCA</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>pANCA</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>NETs average</td>
<td>0.41</td>
<td>0.23</td>
</tr>
</tbody>
</table>

**Conclusion**: This study, for the first time, demonstrates the presence of NETs in pediatric IBD patients with either Crohn's disease or ulcerative colitis. Their contribution to disease pathogenesis remains to be unrevealed.
Audit on Thiopurine metabolites in children receiving Thiopurines for Inflammatory Bowel Disease

Sian Copley¹, Paul Bellis¹, Christine Maville¹, Clare Smith¹, Su Bunn¹, maureen LAWSON¹

¹Great North Children's Hospital Rvi, Paediatric Gastroenterology, Newcastle Upon Tyne, United Kingdom

Study: Thiopurines 6-mercaptopurine and its nitroimidazole derivative Azathioprine are routinely used for the management inflammatory bowel disease (IBD) in children. Azathioprine is non-enzymatically metabolised to 6-mercaptopurine; which is then enzymatically metabolised to 6-thioguanine nucleotides (6TGN) and by thiopurine methyltransferase (TPMT) to 6-methylmercaptopurine (6MMPN). 6TGN and 6MMPN levels are used to determine likelihood of therapeutic response. In the presence of normal TPMT activity the most effective dosing appear to be 2-2.5mg/kg of Azathioprine or 1-1.5mg/kg of 6-mercaptopurine.

Objectives: To determine if in the presence of normal TPMT enzyme activity effective dosing resulted in optimal levels of 6TGN and 6MMPN at 4 weeks. Enabling early recognition of non-responders and limiting the need for repeated dose changes secondary complications of myelosuppression and hepatotoxicity.

Methods: Retrospective review of 6TGN and 6 MMPN levels, 4 weeks following the commencement of either Azathioprine at 2-2.5mg/kg/dose or 6-mercaptopurine at 1-1.5mg/kg dose in children with IBD at the Great North Children’s Hospital Newcastle upon Tyne. Children under the age of 17 years at the end of December 2015 or over the age of 5 years at the time of diagnosis were included in the study. Children were excluded from the study if:
- TPMT enzyme activity was either low or high or had not been quantified prior to commencing azathioprine or 6-mecaptopurine,
- Treatment included biologics or calcineurin inhibitors within 2 months of commencing thiopurines
- Delay in obtaining 6TGN or 6MMPN levels
- Children with low 6TGN levels with either normal or low 6MMPN levels were excluded from the study as in most cases compliance with medication could not be ascertained.

Results: Of our cohort of 200 children currently receiving thiopurines; 80 children were identified with normal TPMT activity
- 36 Female 44 Male Age range 5-16 years
- All children received either 1.8-2.5mg/kg of azathioprine or 0.9-1mg/kg of 6-mercaptopurine as a single daily dose.
- All children were initially commenced on Azathiopurine. A few children were switched from azathioprine to 6-MP due to side effects such as nausea and headaches, within 10 days of commencing therapy.
- All children had 6TGN and 6MMPN levels obtained 4 weeks from initiating therapy.
- 72.5% had levels within the normal range after 4 weeks of thiopurine therapy.
- 27.5% had levels above the normal range
- 15% of children had high 6TGN levels. 25% of which developed myelosuppression necessitating the temporary withdrawal of therapy. Thiopurines were recommenced at a lower dose following improvement in white cell count.
- 12.5% of children had raised 6MMPN levels, however there was no evidence of hepatotoxicity
- There were no cases of clinical pancreatitis

Conclusion: Normal levels of TPMT enzyme activity is associated widely variable clinical response. These results suggest that at current recommended dosing 3.7% of children had evidence of drug toxicity necessitating temporary drug withdrawal. The numbers are small and would require validation.
in a much larger multicentre study, but, the variation in the percentage of children with levels above the normal range and the children with biochemical evidence of toxicity suggests further studies are required to quantify the level of these metabolites and their clinically relevance.

Disclosure of interest: Conflict of interest - None Declared
Incidence of both Crohn’s disease and ulcerative colitis is continuing to rise and is higher in the city population

Siba Paul, Jim Hart, Bhupinder Sandhu

Bristol Royal Hospital for Children, Paediatric Gastroenterology, Bristol, United Kingdom
Royal Devon and Exeter Foundation Trust, Paediatrics, Exeter, United Kingdom

Objectives and study: The first prospective national survey of paediatric Inflammatory Bowel Disease (pIBD) in the UK documented an incidence of 5.2/100,000 children per year. A higher incidence was noted in the north (Scotland: 6.5) as compared to the south (England: 5.2) and Ireland (4.4). This prospective study aimed to:

(i) document any change in incidence of pIBD in the SWE from 2003 to 2014
(ii) document any difference in incidence of pIBD in the city of Bristol population compared to the whole of southwest England (SWE)

Methods: Bristol is the single specialist paediatric gastroenterology centre for SWE to which all children (aged 0–16 years) suspected of having IBD from the 12 paediatric centres are referred for endoscopy. Prospective data was collected on all new pIBD cases between 2003 – 2014 including types of IBD, gender and postcode address for the City of Bristol.

Results: 615 new cases of pIBD were diagnosed over a 12 year period (2003 – 2014). Male (n=361) to female (n=254) ratio was 1.4:1. The cumulative incidence rates over two consecutive 6 year periods for the city of Bristol were much higher than the whole SWE: 9.5 per 100,000 versus 5.0 per 100,000 (2003-2008) and this increased to 10.6 versus 6.2 (2009-2014). Cumulative incidence increased for all subtypes of IBD: Crohn’s disease (CD) increased from 3.06 (2003-2008) to 3.63 (2009-2014), Ulcerative Colitis (UC) 1.6 to 1.96 and IBD-unclassified (IBDU) 0.36 to 0.57. Figure below shows the overall rising incidence for both UC and CD in SWE.

![Graph showing incidence of pIBD cases over 12 years in Bristol and SWE](image-url)
**Conclusion**: Cumulative incidence of IBD over two consecutive 6 year periods increased from 5.0 (2003 – 2008) to 6.2 (2009-2014) in SWE. This was noted for both CD and UC with male preponderance. This study documents significantly higher incidence in the city population suggesting environmental factors have a role.


**Disclosure of interest**: “None Declared”.

Not just another Crohn’s disease

Siba Paul¹, Dharamveer Basude¹

¹Bristol Royal Hospital for Children, Paediatric Gastroenterology, Bristol, United Kingdom

Objectives and study: Bowel carcinomas are considered to be extremely rare in children; incidence in the UK between 2009 – 2011 was 0.1 – 0.3 per 100,000 children aged 0 – 14 years with equal sex preponderance¹. The aim of this paper is to highlight two rare cases of bowel carcinoma diagnosed at endoscopy who presented with initial symptoms suggestive of Crohn’s disease.

Methods: Patient #1 aged 14 years male presented with 5-weeks history of right iliac fossa pain, intermittent loose stools and weight loss. Patient #2 aged 15 years male presented with 3-months history of recurrent abdominal pain, occasional loose stool and weight loss. Both patients were initially reviewed by surgeons as suspected appendicitis (patient #1 underwent laparoscopy with normal appendix), had normal blood inflammatory markers and abnormal findings on small bowel MRI scan. Both patients underwent urgent endoscopic assessment with biopsies; these are shown in figures below.
Results: Patient #1 was diagnosed with B-cell non-Hodgkin's lymphoma (Burkitt’s lymphoma) and underwent chemotherapy with complete cure. Patient #2 got diagnosed with primary colorectal adenocarcinoma. He underwent multiple surgical interventions and resections and chemotherapy. He developed multi-organ metastasis and died 13 months after initial diagnosis. Burkitt’s lymphoma is endemic in Africa and has an excellent 5-year survival of 90%. Colonic adenocarcinoma has a dismal prognosis of 2.5 – 7% survival at 5-years and despite radical surgery with 2/3rd of cases die by 1-year.

Conclusions: Significant abdominal pain and weight loss with normal inflammatory markers were the prominent features in both the cases and these should raise suspicion of bowel carcinoma. Although these are extremely rare, they present with unusual endoscopic findings which requires appropriate biopsy samples to process urgently for histological diagnosis.


Disclosure of interest: “None Declared”
Fecal calprotectin in monitoring IBD patients: useful or not?

Silvia Salvatore¹, Giorgio Ottaviano¹, Paola Wagner¹, Serena Arrigo², Arrigo Barabino²

¹University of Insubria, Varese, Italy
²Ospedale Gaslini, Genova, Italy

Objectives and study: Fecal calprotectin is a reliable non-invasive inflammatory marker to help in discriminate between functional gastrointestinal disorders and inflammatory bowel diseases (IBD) in children. Its clinical usefulness during the follow up of pediatric IBD patients and optimal cut-off to predict endoscopic relapse still need to be determined but could be relevant to reduce unnecessary invasive procedures. The aim of this study consisted in determining the diagnostic accuracy of fecal calprotectin at relapse of pediatric IBD patients.

Methods: We retrospectively evaluated the correlation between fecal calprotectin (FC) and clinical, biological, radiological and endoscopic data of 47 consecutively enrolled IBD pediatric patients (22 Crohn’s disease, 28 Ulcerative Colitis, mean age 10.5 years). Timing of calprotectin determination after the diagnosis of IBD was based on individual disease history and clinician judgement. We used a high sensitive enzyme-linked immunosorbent assay (ELISA, Calprest®, Eurospital, Trieste, Italy), as previously reported in other studies, with a manufacturer indicated normal cut-off value of 50 mcg/g.

Statistical analysis was first performed using Student t test and determination of significant differences with a confidence interval (CI) of 95%. Linear regression was used to highlight any significant correlation between FC and different parameters (age, endoscopic score, clinical score), with p value significant < 0.05. Finally, ROC (Receiver Operator Characteristic) curves were built to determine the optimal cut-off values.

Results: We analyzed 223 FC determination with a mean of 5 FC determination for each patient (range 1-12). FC values were significantly higher in patients with a clinical relapse assessed by PUCAI/PCDAI scores (mean 587.5, CI95%; 453.3-721.6) compared to patients with remission score (339.0 µg/g, CI95%; 261.3-461.7). We found a mild, but significant (r= 0.22, p < 0.001) rise of FC value related to the increase of the scores with a cut-off value of clinical score-based relapse of 488 µg/g, (sensibility 57.1%, specificity 81.2%) but in 30 cases above this value the PCDAI/PUCAI score was 0 (5 showed an active disease at endoscopy) and area under ROC curve was of 0.70, suggesting moderate diagnostic accuracy. Endoscopies were performed concomitantly with (only) 59 FC determinations during the follow-up. We observed a significant (p < 0.05) difference of FC values in patients with normal endoscopies (275.5 µg/g, CI95%; 151.0-399.9) when compared to patients with active disease (645.6 µg/g, CI95%, 433.7-857.5). Disease localization did not influence FC values, although we found a (not significant) trend to higher FC values in patients with pancolitis with respect to a more limited disease.

Conclusion: FC may offer an additional tool to clinical scores to identify which IBD patients may postpone endoscopic reassessment. The proper cut-off of FC during the follow-up and possible influence of different IBD factors (Crohn versus Ulcerative colitis, structuring versus penetrating or inflammatory phenotype, individual ratio of increase) need to be further explored in a large prospective study.

Disclosure of interest: None Declared.
Post surgical relapse of Crohn's disease in pediatric population of a tertiary center

Simona Faraci¹, Erminia Romeo², Francesca Rea³, Filippo Torroni³, Tamara Caldaro³, Anna Chiara Contini³, Giulia Angelino³, Bronislava Papadatou³, Giovanni Federici di Abriola², Luigi Dall'Oglio², Paola De Angelis²

¹Bambino Gesù Children Hospital, Digestive Endoscopy and Surgery Unit, Rome, Italy
²Digestive Endoscopy and Surgery Unit, Bambino Gesù Children's Hospital, Irccs, Rome, Italy, Rome, Italy
³Gastroenterology Unit, Bambino Gesù Children's Hospital, Irccs, Rome, Italy, Rome, Italy

Objectives and study: Post-surgical relapse of Crohn's disease (CD) is common according to international literature (65– 90% within 12 months and 80–100% within 3 years). Prevention of postoperative relapse remains debated in pediatric patients, while in adulthood better codified; post-surgical treatment has been recently suggested in ECCO/ESPGHAN guidelines of 2014. Aim of this study was to assess the incidence of postoperative relapse in patients operated and followed at our center.

Methods: From 1999 to 2015, 52 patients with complicated CD underwent surgery at Digestive Surgery and Endoscopy Unit of Bambino Gesù Children's Hospital of Rome. Sex, age at surgery, extension of disease and disease behavior ("Montreal classification"), indications for surgery, perianal disease, type of surgery (resection and/or strictureplasty), treatment, postoperative clinical course and relapse, and endoscopic follow-up were evaluated. Patients were divided, according to risk factors, into: low risk (non-smoking, stenosis less than 10 cm, more than 10 years of time before the first intervention), moderate risk (long-inflammatory stenosis or fibrous stenosis > 10 cm and a short time to surgery, less than 10 years after diagnosis), high risk (more than two surgeries, penetrating/perforating disease, complicated post-operative course, habitual smoking), as in adult patients' classification. All patients received antibiotic therapy for 3 months and began post-surgical therapy (mesalazine, azathioprine, adalimumab, Infliximab, thalidomide) within 3 months after surgery. Relapses were considered at endoscopy. All patients underwent endoscopy within a year.

Results: Of 52 patients (range 4-20 years; F/M: 19/33), 27 underwent intestinal resection, 23 strictureplasty (11 Mikulicz technique; 12 Michelassi), 2 patients both resection/strictureplasty. According Montreal classification, disease was: A1,L3,B2 in 91% of patients, A1,L3,B3 in 5%; A1,L3-p in 4%. Indications to surgery were recurrent obstructive symptoms. After surgery, 33 patients had endoscopy; 3 of these are recently operated and haven't been endoscopically checked yet; other patients underwent endoscopy between 6 months and 1 year. Relapses were evidenced in 18 out of 30 patients (60%) in endoscopic follow up; 5/18 (27.7%) relapsed patients were asymptomatic. During post-operative follow up, 22/30 patients (73%) modified previous medical therapy, in 11 of these with more aggressive drugs (5 immunosuppressors: 4 relapsed, 6 biologic therapies: 2 relapsed), without significative differences between patients treated stronger than others. According risk factors, patients in follow up were divided into: 22 high risk (73%), 8 patients moderate (27%); 13 out of 22 high risk patients, patients relapsed (59%), 5 out of 8 patients with moderate risk relapsed (62%).

Conclusions: Endoscopy must be considered within the first year after surgery in order to assess relapse also in asymptomatic patients and to guide treatment adaption. Medical therapy after surgery should be started early, but in our small series no differences were shown in more aggressive treatment. Percentage of relapse in our series is affected by younger "age", that is a high risk factor and an important discriminating variable in determining the possibility of relapse.

Disclosure of interest: None Declared.
Aseptic splenic abscesses can precede paediatric inflammatory bowel disease (pIBD) well before manifestation of the disease - 2 case report

Tania Ahmad1, Fevronia Kiparisi1, Keith Lindley2, Sirwan Hadad3

1Great Ormond Street Hospital, Gastroenterology, London, United Kingdom
2Great Ormond Street Hospital for Children NHS Foundation Trust, Pediatric Gastromotility, London, United Kingdom
3Royal Marsden Hospital, Surgery, Surrey, United Kingdom

Objectives and study: Splenic abscesses have been reported in adult IBD at diagnosis and as a complication. Only one case series in adolescent patients over the age of 15 years is available in the literature with only one patient out of seven subsequently diagnosed with IBD 2 years later.

Aim: To report 2 cases of subsequently diagnosed IBD, with the initial presentation of aseptic splenic abscesses.

Methods: Retrospective case review of 2 patients referred for further investigations with initial diagnosis of aseptic splenic abscesses.

Results: Case 1: A four-year-old girl born at term treated conservatively for one year for possible gastroesophageal reflux disease but otherwise well was referred to her local hospital for recurrent episodes of pyrexia. An abdominal Ultrasound Scan (USS) showed multiple micro splenic abscesses. She had a partial response to empirical antibiotics with reduction in size of the abscesses as confirmed on repeat USS, and her fever improved. As there were ongoing lesions, a splenic biopsy was performed which showed several non-caseating giant cell granulomata. At that point stool calprotectin was found to be raised. Endoscopies showed mild chronic gastritis and patchy inflammation with aphthous ulceration in terminal ileum. A wireless capsule endoscopy showed scattered small aphthous ulcers throughout the small bowel. She was then commenced on Modulen IBD and Azathioprine, which led to complete resolution of her splenic abscesses.

Case 2: A 14-year-old girl was referred for prolonged episodes of fevers, abdominal pain and profound lethargy with a positive family history of IBD (brother with UC). An abdominal USS showed multiple hypoechoic lesions within the spleen consistent with splenic abscesses, confirmed on MRI scan. An upper and lower endoscopy showed minor changes, not specific for IBD. Aspiration of the splenic aspirates did not grow organisms. She continued to spike temperature up to 40°C despite courses of broad-spectrum antibiotics. Her fever eventually settled on oral steroids, and repeat USS showed no residual splenic lesions. She represented one year later with now loose stool, weight loss and lethargy. Repeat abdominal USS showed multiple new hypoechoic lesions, and repeat upper and lower endoscopy showed chronic active pancolitis consistent with a diagnosis of UC. Her clinical symptoms resolved on steroids, Mesalasine and Azathioprine; however, she continues to have aseptic splenic lesions.

Conclusion: In paediatric patients with presumed infectious splenic lesions, without gastrointestinal symptoms and not responding to antibiotic treatment, extraintestinal manifestation of pIBD should be considered and investigated to prevent delayed diagnosis.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016
An Audit of Exclusive Enteral Nutrition use in Crohn’s Disease

Rowena Mills, Theo Wong

1Birmingham Children’s Hospital, Gastroenterology, Birmingham, United Kingdom

Objectives and study: Exclusive enteral nutrition (EEN) is a well established induction therapy in paediatric Crohn’s disease and is recommended as first line treatment for intestinal luminal Crohn’s disease by ESPGHAN. Our aim was to retrospectively audit EEN prescribing for newly diagnosed Crohn’s disease against the 2014 ESPGHAN guidelines.

Methods: A proforma was devised covering demographics, biochemistry, disease location, disease severity (assessed by Paediatric Crohn’s Disease Activity Index (PCDAI)), whether EEN was offered and commenced, achievement of remission, reason for EEN failure and alternative treatment. Patients with newly diagnosed Crohn’s disease at a tertiary referral pediatric hospital were identified over a 12 month period. Their medical and dietetic cases notes were retrospectively analysed.

Results: Eighty-two patients were diagnosed with inflammatory bowel disease and 38 patients were given a definitive diagnosis of Crohn’s disease by the end of 2014. Twenty-three were males (59%) and the mean age was 12.6 years. Ten were inpatients at the time of diagnosis. The mean CRP was 31, ESR 36 and albumin 36. The most common disease location was large bowel in 36 patients, followed by small bowel in 36 patients, upper gastrointestinal tract in 16, and peri-anal in 10 patients. Twenty-seven patients had a (PCDAI) score of greater than or equal to 30. EEN was offered to 24 patients (63%). Three of these patients refused EEN; one preferred steroids and two did not tolerate EEN. Of the 17 patients who did not start EEN, 11 commenced steroids (65%) followed by infliximab for 3(18%). Of the 21 patients who started EEN, 9 completed 6 weeks (43%) and 8 of those achieved remission (89%). The main reason for non-completion of EEN was intolerance and ongoing symptoms (42%). All non-completers commenced steroids as an alternative treatment. There was no significant statistical difference in all parameters between completers of EEN and non-completers, however completers tended to be older (p=0.145) had a lower CRP (p=0.22), ESR (p=0.15), and PCDAI score. Of the 14 patients not offered EEN, 7 had no documented discussion regarding EEN (50%), 3 had an alternative initial diagnosis, 3 had severe disease and one was clinically well.

Conclusion: ESPGHAN guidelines in offering EEN to appropriate patients were followed in 72% of cases. Remission with EEN was achieved in 21% of all patients, however in those who completed a 6 week course this was 89%. Strategies in increasing clinician uptake of EEN as first line treatment and increasing tolerability of EEN may help achieve greater success of EEN as a standard therapy in this group of patients.

Disclosure of interest: None declared
Variation in the treatment of new onset pediatric IBD among phenotypically similar patient subgroups in Canada: a cross-sectional analysis of the Canadian Children IBD Network Inception Cohort.

Thomas Walters1, David Mack2, Hien Huynh3, Anthony Otley4, Jennifer DeBruyn5, Colette Deslandres6, Wael El-Matary7, Kevan Jacobson8, Mary Sherlock9, Kevin Bax10, Ernest Seidman11, Jeffrey Critch12, Peter Church1, Eric Benchimol13, Matthew Carroll14, Eytan Wine14, Mohsin Rashid15, Johan Van Limbergen15, Anne Griffiths1

1The Hospital for Sick Children, Inflammatory Bowel Disease Centre, Toronto, Canada
2Children's Hospital of Eastern Ontario, DIV Gi, Ontario, Canada
3The University of Alberta, Ibd Department, Edmonton, Canada
4Iwk Health Centre, DIV Gi, Halifax, Canada
5Alberta Children's Hospital, DIV Gi, Calgary, Canada
6Chu Sainte Justine, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, Montreal, Canada
7Children's Hospital Research Institute of Manitoba, DIV Gi, Winnipeg, Canada
8Bc Children's Hospital, Pediatric Gastroenterology, Vancouver, Canada
9Mcmaster Children's Hospital, DIV Gi, Hamilton, Canada
10Children's Hospital of Western Ontario, DIV Gi, London, Canada
11Montreal Children's Hospital, DIV Gi, Montreal, Canada
12Janeway Children's Health & Rehabilitation Centre, DIV Gi, St John's, Canada
13Children's Hospital of Eastern Ontario, Ottawa, Canada
14Stollery Children's Hospital, University of Alberta, Edmonton, Canada
15Iwk Health Centre, Halifax, Canada

Objectives and study: Treatment of pediatric onset Crohn’s disease (CD) at first presentation varies internationally. Exclusive enteral nutrition (EEN) is recommended as first-line treatment in European guidelines (Ruemmele JPGN 2014), but is uncommon as initial treatment in the United States. As part of its inception cohort study, the Canadian Children IBD Network (a joint partnership of the CIHR and CH.I.L.D Foundation) is undertaking to identify variation in the nationwide demographic and phenotypic spectrum and treatment of IBD, so that outcomes among similar subgroups of young patients can be longitudinally tracked.

Methods: Between April 2014 and November 2015 consenting families of children and adolescents aged <= 17.0 yrs presenting to Network sites (n=12 academic centers) coast to coast with new onset Crohn’s disease (CD) or ulcerative colitis (UC) were prospectively enrolled. Data were collected using a series of standardized reporting forms and questionnaires, and stored electronically on a centralized database. Individual site data leading to phenotypic labeling of type of IBD were centrally reviewed. Treatment was at the discretion of pediatric gastroenterologists at each site.

Results: Among the first 500 subjects (58% male; CD: 61%, UC: 32%, IBD-U: 7%), median age at presentation (13.0 yrs; IQR 11-15) was similar between diagnostic groups but duration of symptoms prior to diagnosis was significantly longer in CD (5 mths, IQR 2-12 mths) vs UC (2 mths, IQR 1-5 mths) (p<0.001). UC presented with bloody diarrhea in 85%, while abdominal pain predominated in CD (88%). As part of diagnostic evaluation, the ileum was intubated at colonoscopy in 88%. All but 3% (4% UC; 2%CD) had the ileum evaluated by diagnostic imaging if it was not endoscopically visualized. Disease involvement at diagnosis was generally extensive in both UC (pancolonic: 72%, extensive: 12% left-sided: 16%) and CD (ileocolonic: 61%; colonic: 21%; ileal: 18%) but rarely complicated at diagnostic assessment (fibrostenotic: 8%, internally penetrating: 2%). Perianal fistulizing disease was present in 15% of CD subjects. Overall, 71% UC patients received steroids as initial treatment and 25% received 5-ASA. In contrast, EEN was initial treatment in 39% of CD patients; 36% received corticosteroids and 14% anti-TNF. Initial treatment choice varied depending on diagnosis and disease location (Table). Colonic CD showed the greatest variability in first treatment choice.
**Table:**

<table>
<thead>
<tr>
<th>Treatment</th>
<th>UC: Left Sided</th>
<th>UC: Extensive</th>
<th>CD: Ileal</th>
<th>CD: Colonic</th>
<th>CD: Ileocolonic</th>
</tr>
</thead>
<tbody>
<tr>
<td>5-ASA/SASP</td>
<td>65%</td>
<td>19%</td>
<td>12%</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Steroids</td>
<td>30%</td>
<td>77%</td>
<td>33%</td>
<td>44%</td>
<td>32%</td>
</tr>
<tr>
<td>EEN</td>
<td></td>
<td>50%</td>
<td>19%</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>a-TNF</td>
<td>4%</td>
<td>14%</td>
<td>12%</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Methotrexate</td>
<td></td>
<td>3%</td>
<td>3%</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>5%</td>
<td></td>
<td></td>
<td></td>
<td>8%</td>
</tr>
</tbody>
</table>

**Conclusion:** Anatomic localization of IBD influences initial treatment in both UC and CD. The comparable utilization of corticosteroids and EEN in CD involving the ileum (+/- colon) in Canada sets the stage for comparison of long-term outcomes following an initial nutritional versus drug based approach to treatment.

**Disclosure of interest:** “None Declared”.
Faecal microbiomes of paediatric patients with inflammatory bowel disease

Tina Kamhi Trop¹, Bojana Bogovič Matijašić², Tanja Obermajer², Irena Rogelj², Rok Orel¹

¹University Children’s Hospital Ljubljana, Department of Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia
²Biotechnical Faculty, University of Ljubljana, Institute of Dairy Science and Probiotics, Department of Animal Science, Rodica, Slovenia

Objectives and study: Microbiota composition of faecal samples of paediatric patients with active inflammatory bowel disease (IBD) was assessed to determine the main differences in microbial composition between inflammatory bowel disease patients and non-IBD controls (functional gastrointestinal disorders).

Seventy-nine children and adolescents (aged ≤18 years) were included into our study, 24 with Crohn’s disease (CD), 16 with ulcerative colitis (UC), and 39 controls (irritable bowel syndrome). Faecal samples were collected before initiating treatment in de novo patients with IBD and before changing the treatment in patients with relapsing active disease.

Methods: Selected bacterial groups in faecal samples were quantified by plate counting (lactobacilli, bifidobacteria, enterobacteria, coliform bacteria, E. coli, enterococci, staphylococci) and/or by qPCR (all bacteria, Bifidobacterium, Bacteroides-Prevotella group, Clostridium leptum group, Clostridium coccoides group, Enterobacteriaceae group, Faecalibacterium prausnitzii, and Enterococcus faecalis).

Total faecal bacterial DNA was isolated by Maxwell 16 System and Maxwell 16 Tissue DNA Purification Kit (Promega, USA).

Results: Plate counting revealed a higher count (CFU/g) of Enterococcus in Crohn’s disease patients compared to controls (p=0.015). Differences in CFU/g of Enterobacteriaceae, Lactobacillus, Bifidobacterium, E. coli, coliforms, or Staphylococcus were not significant.

qPCR analysis showed significantly higher concentrations of Clostridium leptum group in control samples as compared to CD (p=0.014). It also showed a significantly higher amount of DNA specific for all bacteria, Cl. coccoides, and F. prausnitzii in controls compared to UC (p=0.029, p=0.009, and p=0.025, respectively). On the contrary, the abundance of Enterobacteriaceae (p=0.034) and E. faecalis (p=0.046) was lower in controls compared to UC.

The amounts of Bacteroides/Prevotella or Bifidobacterium determined by qPCR did not differ among the three studied groups.

Conclusion: Our study confirmed the results of previous studies of faecal microbiota in paediatric inflammatory bowel disease showing significantly altered composition of microbiome structure of Crohn’s disease and ulcerative colitis patients as compared to that in non-IBD controls.

Disclosure of interest: None Declared.
NOX1 loss-of-function genetic variants in patients with inflammatory bowel disease

Tobias Schwerd1, Robert V. Bryant1, Sumeet Pandey1, Melania Capitani1, Laween Meran2, Jean-Baptiste Cazier3, Jon Jung Wei1, Peter Sullivan4, Astor Rodrigues4, Simon Travis1, Alexio M. Muise5, Vivian Li2, Holm H. Uhlig6

1University of Oxford, Translational Gastroenterology Unit, Oxford, United Kingdom
2Mrc National Institute for Medical Research, Division of Stem Cell Biology and Developmental Genetics, London, United Kingdom
3The Wellcome Trust Centre for Human Genetics, Oxford, United Kingdom
4University of Oxford, Department of Paediatrics, Oxford, United Kingdom
5The Hospital for Sick Children, Division of Gastroenterology, Hepatology, and Nutrition, Toronto, Canada
6University of Oxford, Translational Gastroenterology Unit and Department of Paediatrics, Oxford, United Kingdom

Objectives and study: Defects in epithelial barrier function predispose to inflammatory bowel disease (IBD) in humans and cause intestinal inflammation in animal models. Genetic risk variants for IBD in loci linked to genes relevant for epithelial integrity have been identified by genome wide association studies (e.g. GNA12, HNF4A, MUC19 or XPB1). In addition, there is an increasing group of monogenic defects associated with significant impairment of epithelial barrier function. Reactive oxygen species (ROS) generated by nicotinamide adenine dinucleotide phosphate (NADPH) oxidase complexes are crucial for host defense. Whereas the role of the NADPH oxidase 2 (NOX2) complex is well established for production of the anti-microbial oxidative burst in phagocytes, the role of epithelial-expressed NOX1 complex for IBD is unclear.

Methods: We performed whole genome sequencing in a patient with very early onset IBD and revealed a defect in the gene encoding NADPH oxidase 1 (NOX1). Expression of NADPH oxidases and their subunits were determined in the human gastrointestinal tract. ROS production of the intestinal epithelium was characterized using nitroblue tetrazolium chloride on ex-vivo colonic biopsies. The functional impact of the identified genetic defect was evaluated in cell lines, primary ex-vivo colonic biopsies and patient-derived organoid cultures. The impact of the NOX1 variant was functionally compared to the common NOX1 polymorphism p.D360N (rs34688635).

Results: We identified a novel NOX1 missense mutation in a patient with very early onset ulcerative colitis-like intestinal inflammation. The patient was diagnosed with IBD unclassified at the age of 5 years. His disease progressed from proctitis to pancolitis and required anti-TNF medication. The identified mutation is at an evolutionarily highly conserved amino acid position and affects the transmembrane region of the NOX1 molecule in all isoforms. NOX1 expression follows a gradient from ileum to the distal colon and is highly expressed in the colonic epithelium. Within colonic crypts, NOX1 constitutively generates high level ROS. Expression of the mutated NOX1 in cell lines, ex-vivo colonic explants as well as primary patient derived colonic organoid cultures showed defective ROS production. Additional variants in NOX1 diminished the generation of NOX1-derived ROS to various degrees.

Conclusion: Our data suggest that NOX1 produces colonic brush border superoxide within the colonic crypts. Loss-of-function variants in NOX1 reduce ROS production at the interface between the colonic epithelium and luminal microbes.

Disclosure of interest: “None Declared”
Faecal calprotectin a useful non-invasive biologic marker for infliximab therapy in paediatric inflammatory bowel disease

Tracee Reid¹, Dhamyanthi Thangarajah¹, Babu Vadamalayan¹, Ben Hope¹

¹Paediatric Liver, Gi and Nutrition Centre, Kings College Hospital Foundation Trust, London, United Kingdom

Objectives and study: Faecal calprotectin (FC) is a biomarker of intestinal inflammation in inflammatory bowel disease (IBD), (1). FC in adult IBD has been shown to predict response to biological therapy, (2). There is little data on the response of FC to infliximab (IFXB) therapy in paediatric IBD. The aim of this study is to report on the response of FC levels to infliximab induction therapy, in paediatric IBD.

Methods: A retrospective electronic case note review was performed of children with a diagnosis of IBD requiring escalation in their immune modulation to IFXB therapy, between January 2011 and January 2015, at our paediatric tertiary gastrointestinal centre. Disease specific parameters were reported. FC and PCDAI/PUCAI prior to induction therapy were documented, normal reference range is was defined as <60µg/g. Change in FC, PCDAI and PUCAI were documented post induction. Indications for escalation to biological therapy as per ESPGHAN guidelines, (3). Descriptive statistics are presented, as this is a small dataset; change in FC, PCDAI and PUCAI presented as median with interquartile range [IQR].

Results: 14 children (9 males) with IBD (CD: 10, UC: 4) were identified, with a mean age of 15.7±2.1 years, mean duration of disease is 4.3±3.8 years, disease site; CD 7 ileo-colonic, 4 colonic, 7 had penetrating disease. All patients with UC had pancolitis.

In CD median FC / PCDAI 662.5 [147.1 to 1404.0] µg/g / 32.5 [23.1 to 43.8], in UC median FC / PUCAI 597.0 [334.0 to 1052.0] µg/g / 20.0 [12.5 to 60.0] respectively.

On completion of induction the median FC / PCDAI in CD was 421.5 [67.0 to 774.5] µg/g / 21.3 [1.9 to 26.9] respectively. The median change in FC / and change in PCDAI after induction therapy was -409.5 [-754.3 to -14.0] µg/g / -8.75 [-34.4 to -5.0].

On completion of induction the median FC / PUCAI in UC was 820.0 [673.3 to 1368.0] µg/g / 20.0 [7.5 to 40.0] respectively. The median change in FC / change in PUCAI was 385.5 [-19.3 to 488.0] / -10 [-41.3 to -1.25].

Conclusion: FC is a useful marker to predict response to IFXB induction therapy in CD. However in UC the response of FC is less clear. Further studies are needed to investigate response to IFXB and FC after therapy is established i.e. 6 months and 1 year and correlate this to IFXB serum levels.


Disclosure of interest: None Declared.
Non-invasive markers for diagnosis and determination of the severity of ulcerative colitis in children - preliminary study

Urszula Daniluk¹, Irena Werpachowska¹, Milena Krasnodebska¹, Dariusz Lebensztejn¹

¹Medical University of Bialystok, Bialystok, Poland, Department of Pediatrics, Gastroenterology, Allergology, Bialystok, Poland

Objectives and study: Ulcerative colitis (UC) represents inflammatory bowel disease characterized by chronic diarrhea and rectal bleeding and susceptibility to gut wall remodeling induced by chronic inflammation. The diagnosis of UC and proper classification of disease activity is usually challenging and requires invasive tests, like colonoscopy. Therefore, the aim of our study was to determine the usefulness of new non-invasive markers representing gut mucosal damage (Metalloproteinase-9, MMP-9) and remodeling (tissue inhibitor of metalloproteinase-1, TIMP-1), gut wall fibrosis (Galectin-3) and gut wall inflammation (calprotectin) in diagnosis of UC in children. Furthermore, the usefulness of MMP-9, TIMP-1 and Galectin-3 to predict severity of UC was evaluated.

Methods: Serum and fecal MMP-9, TIMP-1 and Galectin-3 and fecal calprotectin concentrations were measured with ELISA in 16 children with UC and 15 controls. Disease activity was determined with pediatric ulcerative colitis activity index (PUCAI). The performance of each marker with references to serum C-reactive protein, erythrocyte sedimentation rate, complete blood count, endoscopic activity and clinical activity index was assessed by computing correlations. The cut-off levels, specificity and sensitivity were calculated using receiver operating characteristic (ROC) analysis.

Results: UC children demonstrated significantly higher levels of serum MMP-9, TIMP-1 and Galectin-3 and fecal MMP-9, TIMP-1 and calprotectin compared to controls (all p<0.05). Among fecal markers the best discriminators for UC patients were calprotectin and MMP-9, with the area under curve (AUC) of 1 (95%CI, 1), followed by TIMP-1 with AUC of 0.784 (95%CI, 0.601 to 0.967). The best serum marker for UC group was Galectin-3 with AUC of 0.895 (95%CI, 0.775 to 1), followed by TIMP-1 with AUC of 0.831 (95%CI, 0.675 to 0.987) and MMP-9 with AUC of 0.802 (95%CI, 0.645 to 0.96) compared to controls. No association between tested markers and clinical and endoscopic activity index, and CRP or ESR was found in UC group. However, significant inverse correlation between hemoglobin and serum MMP-9, and TIMP-1, and MMP-9 in feces was detected in UC patients. Additionally, in the same group, the serum level of TIMP-1 correlated with platelet and white blood count (p<0.05), the known inflammatory indicators.

Conclusion: The increased level of serum MMP-9, TIMP-1 and Galectin-3 and fecal MMP-9, TIMP-1 and calprotectin differentiate children with UC from controls. The best fecal markers for pediatric UC seemed to be calprotectin and MMP-9 and among serum markers Galectin-3 was superior to others. Further studies to evaluate the usefulness of these markers are required for larger group of UC patients.

Disclosure of interest: None Declare.
Patient perceptions of food-based dietary treatment of Crohn’s Disease; A survey of paediatric patients previously treated with exclusive enteral nutrition

Vaios Svolos¹, Konstantinos Gerasimidis¹, Vikki Garrick², Lee Curtis², Jacqueline Hay², Elaine Buchanan², Richard Russell², Richard Hansen²

¹Human Nutrition, School of Medicine, College of Mvls, University of Glasgow, Glasgow Royal Infirmary, Glasgow, United Kingdom
²Department of Paediatric Gastroenterology, Hepatology and Nutrition, Royal Hospital for Children, Glasgow, United Kingdom

Objectives and study: Exclusive Enteral Nutrition (EEN) is the primary treatment in active paediatric Crohn’s disease (CD) and there is emerging evidence that exclusion diets can treat or prevent disease flare ups (1-2). The aim of this questionnaire survey was to explore beliefs/issues around the use of EEN and acceptability of an alternative solid food diet (SFD) by paediatric CD patients and their parents/carers.

Methods: We retrospectively surveyed all the families of the paediatric patients who have been treated with EEN over one year by the IBD team at the Yorkhill Hospital. This was achieved by posting two copies of a questionnaire, which were both very similar, asking the parent/carer and the CD child/young person. A reminder was sent out two months later to encourage response. Questions explored participants’ demographic characteristics; opinion on how difficult EEN was and SFD would be; acceptability of an EEN course repeat - if needed; intention to participate in a future clinical trial assessing the therapeutic efficacy of a SFD on CD.

Results: Forty-one paediatric patients were identified and a total of 82 questionnaires were posted to them. Of these 58 (71% response) questionnaires were returned providing information on 29 CD children (median age, 13.3; interquartile range [IQR], 4.0 years), of which 20 (69%) were boys. The majority of them completed 8 weeks on EEN (n=23, 79%), while 55% had to use nasogastric tubing during the treatment course. Both patients and their carers rated (on a scale from 1-100) EEN course to be significantly more difficult when compared to an alternative SFD (Median, Patients: 62 vs 23, Carers: 50.5 vs 26.5, both p<0.03). Diet ratings by patients was strongly correlated to those of parents/carers (EEN: r=0.831, SFD: r=0.749, both p<0.001). Approximately two thirds of the patients and their carers (59%) were positive on completing another EEN course in a further relapse, however a high proportion of participants thought a SFD would be better than EEN (Patients: n=19, 66%, Carers: 21/72%). Participants reported that they would agree to participate in a trial comparing EEN with an alternative SFD in a high percentage (Patients: 52%, Carers: 66%). When they were given further explanation of a hypothetical randomised controlled trial, which would recruit only patients in need of EEN treatment, this percentage was further increased (Patients: 23/79%, Carers: 21/72%). Comments quoted by the participants included: "the liquid-only diet was very isolating at times for my child”; “I would like to try the solid food diet to avoid steroids in future”; “I think being on the other diet may make her feel more normal and part of the family”; and "I am delighted at the proposed solid food diet and we will do all that we can to help this work”.

Conclusion: This survey concluded that there is a positive attitude and perception on the use of a SFD, as an alternative to EEN, for the treatment of paediatric CD.


Disclosure of interest: None Declared
Objectives and study: To observe single nucleotide polymorphisms (SNPs) of vitamin D metabolism-related factors, vitamin D receptor (VDR) and vitamin D binding protein (DBP), in Crohn's disease (CD).

Methods: 121 patients with CD and 381 controls were enrolled. SNP (rs731236) in VDR gene and SNPs (rs4588, rs7401 and rs2282679) in DBP gene were typed in patients with CD and controls by gene sequencing.

Results: In our case-control cohort, no significant difference was observed on CD risk for any of the four SNPs (rs731236, rs4588, rs7401 and rs2282679) in vitamin D metabolism-related genes (P>0.05). For the three SNPs in DBP gene, gender stratification saw no significant difference in MAF in CD patients compared with healthy controls. However, a higher MAF was found for rs731236 in male CD patient than that in male controls (P<0.05). No association was investigated between CD susceptibility and the haplotypes of DBP gene (P>0.05).

Table: Associations between allele frequencies of VDR and DBP SNPs in cases and controls

<table>
<thead>
<tr>
<th>Genes</th>
<th>SNP</th>
<th>MAF Cases/ Controls</th>
<th>OR (95%CI) *</th>
<th>P*</th>
</tr>
</thead>
<tbody>
<tr>
<td>DBP</td>
<td>rs2282679</td>
<td>0.34/0.33</td>
<td>1.139 (0.836-1.551)</td>
<td>0.409</td>
</tr>
<tr>
<td></td>
<td>rs7401</td>
<td>0.26/0.25</td>
<td>1.057 (0.950-1.175)</td>
<td>0.308</td>
</tr>
<tr>
<td></td>
<td>rs4588</td>
<td>0.33/0.33</td>
<td>1.040 (0.839-1.289)</td>
<td>0.721</td>
</tr>
<tr>
<td>VDR</td>
<td>rs731236</td>
<td>0.05/0.05</td>
<td>0.925(0.782-1.095)</td>
<td>0.367</td>
</tr>
<tr>
<td></td>
<td>rs731236(male)</td>
<td>0.09/0.05</td>
<td>0.781(0.626-0.975)</td>
<td>0.029</td>
</tr>
<tr>
<td></td>
<td>rs731236(female)</td>
<td>0.06/0.06</td>
<td>1.228(0.905-1.666)</td>
<td>0.187</td>
</tr>
</tbody>
</table>

DBP, vitamin D binding protein; VDR, vitamin D receptor; SNP, single nucleotide polymorphism; MAF, minor allele frequency.

* All listed ORs and P values referred to the adjusted age and sex estimations.

Conclusion: Our study suggests that the four SNPs (rs731236, rs4588, rs7401 and rs2282679) in vitamin D metabolism-related genes may have no correlation with susceptibility of CD in Chinese Han population. SNP (rs731236) in VDR gene may play a role in the etiology of CD among affected males. However, our findings need to be confirmed in multi-center studies.

Disclosure of interest: None Declared.
Diagnostic Accuracy of Resonance Imaging Enterography, Capsule Endoscopy and Ileocolonoscopy in Children with Crohn’s Disease

Youyou Luo1, Jingan Lou1, Hong Zhao1, Kerong Peng1, Jindan Yu1, Youhong Fang1, Jie Chen1

1The Children’s Hospital, School of Medicine, Zhejiang University, Gastroenterology, Hangzhou, China

Objectives and study: To compare the diagnostic accuracy of resonance imaging enterography (MRE), capsule endoscopy (CE) and ileocolonoscopy in newly diagnosed pediatric Crohn’s Disease (CD).

Methods: We performed a retrospective study of a single-enter cohort. Data were retrieved from our inpatient databases between July 2007 and July 2015. Newly diagnosed CD patients who were received ileocolonoscopy and either of CE or MRE were included. All of the 3 procedures were done within 2 weeks. Suspected CD patients were excluded.

Results: Sixty-eight consecutive pediatric patients were included in the study. Out of these 68, 44 (64.7%) were male. The average age was 10, ranging from 1 to 17. Ileocolonoscopy was performed in all individuals. CE and MRE were conducted in 53 (77.9%) and 39 (57.4%) cases, respectively. Twenty-four (35.3%) subjects received all of the 3 procedures before CD was diagnosed. Patient characteristics are shown in Table 1. In ileocolonic CD group, no significant differences were found between the diagnostic yield of MRE and CE, which was 29.1%, 40.5%, respectively. Similar results were found in small bowel and colonic CD group. Interestingly, the diagnostic yield of the combination of CE and ileocolonoscopy in small bowel and colonic CD was significantly higher (97.3%) than that of CE (40.5%) or the combination of MRE and ileocolonoscopy (50.0%), (P<0.001). No significant differences were found in the diagnostic yield between either of the 3 procedures in ileocolonic diseases (P>0.05).

Table: Table 1 Patient Characteristics and disease location

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Ileocolonoscopy (n=68)</th>
<th>MRE (n=39)</th>
<th>CE (n=53)</th>
<th>Ileocolonoscopy+ MRE+CE (n=24)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean(SD), y</td>
<td>10(5)</td>
<td>8(5)</td>
<td>11(3)</td>
<td>10(4)</td>
</tr>
<tr>
<td>Male, n(%)</td>
<td>44(64.7%)</td>
<td>26(66.7%)</td>
<td>34(64.2%)</td>
<td>18(75.0%)</td>
</tr>
<tr>
<td>Small bowel and colonic disease, n(%)</td>
<td>42(61.8%)</td>
<td>24(61.5%)</td>
<td>37(69.8%)</td>
<td>19(79.2%)</td>
</tr>
<tr>
<td>Ileocolonic disease, n(%)</td>
<td>10(14.7%)</td>
<td>7(17.9%)</td>
<td>5(12.8%)</td>
<td>1(4.2%)</td>
</tr>
<tr>
<td>Isolated colonic disease, n(%)</td>
<td>12(17.6%)</td>
<td>6(15.4%)</td>
<td>7(13.2%)</td>
<td>1(4.2%)</td>
</tr>
<tr>
<td>Isolated small bowel CD, n(%)</td>
<td>4(5.9%)</td>
<td>2(5.1%)</td>
<td>4(7.5%)</td>
<td>3(12.5%)</td>
</tr>
</tbody>
</table>

MRE= magnetic resonance imaging enterography, CE=capsule endoscopy, SD=standard deviation
**Conclusion:** In newly diagnosed pediatric CD, the combination of CE and ileocolonoscopy has higher diagnostic accuracy than isolated CE or the combination of MRE and ileocolonoscopy. However, the results need confirmation in large-sample, multi-center studies.

**Disclosure of interest:** None Declared.
A novel exonic mutation inducing aberrant splicing in the IL10RA gene and resulting in infantile-onset inflammatory bowel disease

Yugo Takaki¹, Tadahiro Yanagi¹, Keisuke Eda¹, Tatsuki Mizuochi¹

¹Kurume University School of Medicine, Paediatrics, Kurume, Japan

Objectives and study: Although deleterious mutations in interleukin-10 and its receptor molecules cause severe infantile-onset inflammatory bowel disease, we know of no reports describing mutations affecting this signaling pathway in Japanese patients. Here we report a novel exonic mutation in the IL10RA gene that caused unique splicing aberrations in a Japanese patient with infantile-onset of inflammatory bowel disease in association with immune thrombocytopenic purpura and a transient clinical syndrome mimicking juvenile myelomonocytic leukemia.

Methods: Peripheral blood mononuclear cells were obtained from this patient and his parents. Direct sequence analysis of the IL10RA and IL10RB genes and reverse-transcription polymerase chain reaction amplifying the IL10RA gene were performed. Functional analysis of interleukin-10 receptor signaling was performed by flow cytometry.

Results: A Japanese boy, who was the first child of non-consanguineous healthy parents, developed bloody diarrhea, perianal fistula, and folliculitis in early infancy and was diagnosed with inflammatory bowel disease. He also developed immune thrombocytopenic purpura and transient features mimicking juvenile myelomonocytic leukemia. The patient failed to respond to various treatments, including elemental diet, salazosulfapyridine, metronidazole, corticosteroid, infliximab, and adalimumab. We identified a novel mutation (c.537G>A, p.T179T) in exon 4 of the IL10RA gene causing unique splicing aberrations (a 18-base deletion at the 3' end of exon 4 and a complete deletion of exon 4) and resulting in lack of signaling through the interleukin-10 receptor. At 21 months of age, the patient underwent allogeneic hematopoietic stem cell transplantation and achieved clinical remission.

Conclusion: We describe a novel exonic mutation in the IL10RA gene resulting in infantile-onset inflammatory bowel disease. This mutation might also be involved in his early-onset hematologic disorders. Physicians should be familiar with the clinical phenotype of IL-10 signaling defects in order to enable prompt diagnosis at an early age and referral for allogeneic hematopoietic stem cell transplantation.

Disclosure of interest: None Declared.
Diagnostic accuracy of faecal calprotectin in less than six-year-olds with gastrointestinal symptoms in a tertiary paediatric gastroenterology centre

Alexandra Zambrano Perez1, Aikaterini Kakotrichi1, Neil Shah1, Sara Sider1, Sibongile Chadokufa1, Bonita Huggett1, Fevronia Kiparissi1

1Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom

Objectives and study: The aim of this study was to describe the clinical features of less than 6 year olds, referred to Gastroenterology with either normal or raised values of faecal calprotectin (FC), their correlation with investigations and subsequent diagnoses.

Methods: We retrospectively reviewed demographics, working diagnoses, endoscopy findings and final diagnoses from clinical case notes and laboratory data in patients referred over a 2.5 year period. The high FC group was defined by those who had a FC value greater than 50 mg/kg (upper limit of normal). Descriptive analysis was performed using percentage, mean, minimum and maximum functions through STATA software version 14.

Results: From 1218 FC results collected, 363 (29.8%) were from children less than 6 years old. 35 samples were excluded due to technical laboratory issues, no follow-up or missing data. 328 reports were analysed. Mean age of presentation was 2.9 years (range 32 days to 5 years and 11 months), 149 (45.4%) samples were from females. 95 samples (28.8%) corresponded to follow-up samples on patients with very early onset inflammatory bowel disease (VEOIBD). 233 samples were from patients suspected of having inflammation of their gastrointestinal tract. 13 new cases (5.5%) were confirmed histologically as VEOIBD, of whom 2 had a normal FC value. 81/193 patients (41.9 %) underwent scopes in the high FC group and 31/135 patients (22.9%) in low FC group.

In the group with high FC (193 samples, 639 mean, range 51 to 7846) the most common diagnoses were VEOIBD follow-up, milk or food allergy, systemic immune conditions (i.e. LRBA deficiency, MHC class II deficiency) and post-transplant (bone marrow, heart, thymus, stem cell) related conditions. Other gastroenterological diagnoses seen when FC greater than 50 mg/kg were intestinal lymphangiectasia, autoimmune enteropathy, tufting enteropathy and colonic polyps. In the low FC group (135 samples, 22.4 mean, 0.01 to 50 range) the most common diagnoses were VEOIBD follow-up, milk or food allergy and functional disorders.

From all analysed samples, only 83 samples were from patients who had no comorbidity and were referred from secondary care centres, in contrast, 245 samples were obtained from patients with complex comorbidity seen in our centre (i.e. post-transplant, immunodeficiency, genetic, rheumatological conditions).

Conclusion: FC is now a test commonly used as a surrogate marker in assessing general gut inflammation. There is however a lack of a reliable cut off value and the value of 50 in paediatric gastrointestinal disease seems obsolete. A raised FC can be found in other non-IBD conditions for example food allergy or systemic inflammatory diseases; however a negative FC does not exclude inflammation, especially in patients with the diagnosis of VEOIBD. A clinical suspicion warrants further investigations even with normal FC levels.

Disclosure of interest: None Declared.
Epidemiology, clinical features and risk of recurrence of Clostridium difficile infection in children living in a low prevalence country

Andrea Lo Vecchio1, Maria Cristina Fedele1, Andrea Paonessa1, Laura Lancell2, Costantino De Giacomo3, Elena Borali3, Silvia Garazzino4, Susanna Esposito5, Alfredo Guarino1

1University of Naples Federico II, Department of Translational Medical Sciences - Section of Pediatrics, Naples, Italy
2Bambin Gesù Children's Hospital, Rome, Italy
3Niguarda Hospital Ca Granda, Milan, Italy
4University of Turin, Regina Margherita Children's Hospital, Pediatric Infectious Diseases Unit, Turin, Italy
5University of Milan - Fondazione Ircss Ca' Granda, Department of Pathophysiology and Transplantation, Milan, Italy

Objectives and study: Clostridium difficile infection (CDI) is increasingly found in children worldwide and considered an emerging threat particularly in USA and Western Europe. Limited epidemiological data are available in children living in southern Europe. A retrospective study was performed to investigate the epidemiology, clinical features, treatment and risk factors for recurrence in Italian children.

Methods: Data of children with community- and hospital-acquired CDI (CA- and HA-CDI) seen at 7 pediatric referral centers in Italy (Jan 2008-Dec 2013) were reviewed retrospectively. Annual infection rates/10,000 hospital admissions were calculated and compared in the 6-year study period. Logistic regression was used to investigate risk factors for CDI recurrence.

Results: 167 CDI episodes were recorded in 148 children (83 males, median age 55.3 months) with a cumulative infection rate of 2.25/10,000 admissions, with no significant change in the 6-year study period. The majority of children (60.8%) had CA-CDI. Children with HA-CDI (39.2%) had a longer duration of symptoms and hospitalization (p=0.003). A more frequent previous use of antibiotics was also found (p=0.0001). Among the 123 children who received treatment (83%), metronidazole was used in 70.7% of cases (87/123) and vancomycin in 29.3% (36/123), with similar success rates. Recurrence occurred in 16 children (10.8%), and 3 (2%) of them presented a further treatment failure. However, the use of metronidazole was associated with a 5-fold increase in the risk of recurrence, compared to vancomycin (OR 5.18, 95%CI 1.1–23.8, p=0.03). Short bowel syndrome was the only underlying condition associated with treatment failure (OR 5.29, 95%CI 1.17–23.8, p=0.03).

Conclusion: The incidence of pediatric CDI in Italy is low and substantially stable. In this setting there is a limited risk of recurrence. The latter is associated with oral metronidazole therapy and with short bowel syndrome.

Disclosure of interest: No conflict of interest to be declared.
Clinical evaluation of a synbiotic for children between 6 months and 2 years with acute viral diarrhea

Emilia García Menor¹, Fátima García Marín², Raquel Vecino López², Gloria Horcajo Martínez², María José de Ibarrondo Guerica-Echevarría⁶, Pedro Gómez González⁶, Jaime Moscoso del Prado⁷, Javier Suárez Almarza⁸, Concepción Nieto Magro⁹

¹Hospital del Sureste de Arganda del Rey, Madrid, Spain
²Policlínica Virgen del Mar, Madrid, Spain
³Hospital Universitario de Torrejón, Madrid, Spain
⁴Hospital Universitario de Torrejón, Madrid, Spain
⁵Clinica Santa Elena, Madrid, Spain
⁶Centro Médico del Val, Madrid, Spain
⁷Hospital Universitario Juan XXIII, Tarragona, Spain
⁸Itf Research Pharma S.L.U., Madrid, Spain

Objectives and study: Acute infectious gastroenteritis due to viruses accounts for most bouts of diarrhea in developed countries, with an incidence in European healthy children under 3 years of age of 0.5-2 episodes per child per year and it is associated with substantial health-care costs. Several studies have illustrated the efficacy of probiotics in the treatment of acute diarrhea however, it is well known that efficacy should be demonstrated with the specific strains, doses and formulations. The additional benefit of a synbiotic (Prodefen®) in the clinical management of acute viral diarrhea in children between 6 months and 2 years is studied. This synbiotic contains a combination of prebiotics (fructooligosaccharides) and 7 probiotic strains (L. casei PXN 37, L. rhamnosus PXN 54, S. thermophilus PXN 66, B. breve PXN 25, L. acidophilus PXN 35, B. infantis PXN 27, L. bulgaricus PXN 39) 1x10⁹ Colony Forming Units per sachet.

Methods: Multicenter, prospective, randomized and controlled study. Patients were randomized into two groups: one receiving supportive treatment based on diet and oral rehydration therapy (control group) and another one receiving, in addition, the synbiotic (Prodefen®), 1 sachet/day for 7 days (synbiotic group). After 7 days of treatment, the evolution of the diarrhea, tolerability and acceptance were evaluated.

Results: 50 children between 6 months and 2 years of age were recruited; 22 children that received the synbiotic and 19 controls successfully completed the study. Duration of diarrhea (median and interquartile range) was reduced by 2 days (3 [2-4] vs 5 [3-5] days, p=0.034) in the synbiotic group vs the control group. 73% of children that received the synbiotic vs 58% of controls and 96% of children that received synbiotic vs 68% of controls did not present with diarrhea after 4 (p=0.346) and 5 (p=0.036) days of treatment, respectively. Additionally, 59% of children that received the synbiotic vs 28% of controls were already recovered on the fifth day of treatment (p=0.035), defined as not presenting with diarrhea for two consecutive days. Significant differences in the perception of efficacy and evaluation of tolerability were observed in children receiving the synbiotic vs controls, as 77% and 28% of them found the treatment very or quite efficacious in the synbiotic and control groups, respectively and 64% and 27% of them tolerated very well the treatment in the synbiotic and control groups, respectively. 95% of parents of children receiving the synbiotic reported being very satisfied/satisfied with the treatment.

Conclusion: Overall, the results of this study indicate that the addition of the synbiotic (Prodefen®) is a well-tolerated and wellaccepted approach that provides an additional benefit to the standard supportive therapy in the management of acute viral diarrhea in young children.

Disclosure of interest: None Declared.
Hyperlipasemia in Rotavirus Infection: why?

Irene Rutigliano1, Maria Pastore1, Mario d’Altilia1, Salvatore Cringoli2, Anthea Bottoni2, Giuseppina D’Angelo2, Anna Pacilio2, Maria Pia Falcone2, Lucia Soldano3, Lorenza Chiossi2, Michele Pellegrino1, Pasquale Pio Maccarone1, Michele Carmine Sacco1

1Paediatrics, Ircss “Casa Sollievo Della Sofferenza”, San Giovanni Rotondo, Italy
2Paediatrics, University of Foggia, Foggia, Italy

Objectives and study: Acute gastroenteritis is one of the most important cause of morbidity and mortality in children. Among the responsible factors, rotaviruses are cause of severe acute diarrhoea in young children. Moreover, rotavirus infection is recognised as determinant of acute pancreatitis in children with acute gastroenteritis, but the pathogenesis is not well understood and the real incidence is not known. One possible cause could be pancreatic involvement for a direct invasion of parenchyma by the pathogen. Aim of our study: to investigate the presence of pancreatic hyperenzymemia in children affected by gastroenteritis, its relationship with clinical and laboratories findings and possible association with rotavirus infection.

Methods: We collected data of 274 children admitted to our Paediatric Unit with the diagnosis of acute gastroenteritis from January 2014 to August 2015. Collected data included: age, sex, anthropometric and clinical findings, laboratory and instrumental examination, duration of hospital stay, outcomes. Statistical Analysis was performed with IBM SPSS v.22.

Results: Mean age at hospital admission was 3.22±3.23 (range 0.06-15.88 Yrs), median age 2.06 yrs. Our population consisted of 140 males and 134 females (p=0.717), mean age 2.9±2.9 yrs and 3.5±3.6 yrs respectively (p=0.212). Stool examination was positive for: rotavirus antigen in 81 patients (GROUP A, 29.7%), adenovirus antigen in 16 patients (GROUP B, 5.9%), while Salmonella species was detected in 3 subjects (GROUP C, 1.1%). In 173 patients we did not recognised the etiological cause of gastroenteritis (GROUP D). Five patients (1.9% of overall population) had increased levels of plasmatic lipase (mean value 974±459 UI/L, laboratory cut off value 393 UI/L), they all presented rotavirus infection (p=0.010); while 3 children had mild hyperamylasemia (mean value 193±71 UI/L, laboratory cut off value 115 UI/L) all with no recognised cause of gastroenteritis. When we analysed the lipase levels in our population: children with rotavirus infection (group A) had statistically higher levels 119.5±250 UI/L (p=0.024) against 36.8±42 UI/L in Group B, 32.7±12.5 UI/L in Group C and 62.1±62.8 in Group D. No differences were recorded in duration of hospital stay between the groups (mean duration 4.2±2.5 days, p=0.880). Among laboratory findings, children of Group B had higher levels of uricemia (p<0.001) and alanine transaminase (p<0.024). No pancreatic alteration were found by ultrasonographic evaluation.

Conclusion: Our results confirm disturbance of pancreatic functionality by rotavirus infection. The pathogenic mechanism is not known, but it's important to define if these findings could be linked to virus replication and/or to the entity of dehydration. More studies are needed.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016
Assessing the colonic microbiome in children: Effects of sample site and bowel preparation

Naomi Black¹, Azelea Rushd², Kathleen Sim³, Alexander Shaw³, Paul Randell³, Simon Kroll³, Jenny Epstein⁴
¹Imperial College London, Medical Student, London, United Kingdom
²King's College London, Medical Student, London, United Kingdom
³Imperial College London, Department of Medicine, Section of Paediatrics, London, United Kingdom
⁴Chelsea and Westminster Hospital, Paediatric Gastroenterology, London, United Kingdom

Objectives and study: Despite the increasingly recognised importance of the gut microbiota in health and disease, and vast refinements in our ability to measure it, there is little consensus as to sample site, pathological interpretation or clinical extrapolation. Considering the invasiveness of a biopsy, a surrogate method of obtaining an accurate representation of the mucosa-associated colonic flora, such as a faecal sample or rectal swab may be more acceptable to patients. Furthermore, little is known about the short and long term effects of bowel cleansing on the colonic microbiota.

Our objectives are therefore:

1. To establish concordance or difference in the paediatric colonic microbiota as sampled in faeces, rectal mucosal biopsy and rectal swab.

2. To assess the effect of bowel preparation on the colonic microbiota.

Methods: We recruited 31 patients (7 months-18 years) undergoing a lower gastrointestinal endoscopy in our unit (February-May 2014). To provide a longitudinal view of the microbiota we collected 6 samples at 3 time points; pre-colonoscopy (faecal sample), colonoscopy (rectal biopsy, rectal swab, faecal sample) and post-colonoscopy (rectal swab, faecal sample). We collected the three samples at colonoscopy in 16 patients, successfully sequencing 14. Samples were split into three groups according to diagnosis, Crohn's Disease (CD), Ulcerative Colitis (UC) or Other. The samples underwent DNA extraction, PCR amplification of the V3-V5 regions of the 16S rRNA gene and amplicons were sequenced on the 454 platform.

Results: In a prepared bowel at colonoscopy (n = 14), paired faeces and biopsies were significantly similar (p < 0.001) in microbial diversity and abundance compared with paired biopsies and swabs. Faecal samples were significantly more similar (p < 0.001) to their paired biopsy than biopsies from different patients were to each other.

Faecal samples from an unprepared bowel (n = 8) were found to be significantly more similar (p = 0.03) to their paired biopsy than biopsies were to each other, although faecal samples at colonoscopy were significantly more similar still (p = 0.029). We found significant differences in the microbiota of CD patients that allowed differentiation of this disease state from others, for example a lower abundance of Clostridia in the biopsies (p = 0.021) and faecal colonoscopy samples (p = 0.012).

Microbial diversity in faeces was significantly lower during colonoscopy than in matched faecal samples both pre-bowel preparation (p = 0.03) and post-colonoscopy (p = 0.0005) (n=6). No significant change in diversity was seen in pre- and post-colonoscopy faecal samples suggesting that alterations in flora induced by bowel cleansing were transient, although some minor shifts in abundance at genus and phylum level were observed.

Conclusion: The similarity in bacterial diversity and composition between mucosal biopsies and faeces supports faecal sampling as a viable, non-invasive surrogate to biopsy. We conclude that the mucosa-associated microbiome can be accurately represented by faecal sample. Microbiota measurements shown in the biopsy, and therefore in the paired faecal samples, were able to segregate CD patients. Rectal swabs are not closely representative of the mucosa-associated colonic microbiome and are therefore unsuitable. Faecal microbiota at colonoscopy differs to pre-procedure, likely reflecting the effects of bowel cleansing, and these effects are largely transient.

Disclosure of interest: Non Declared
Interrater variability of Amsterdam Infant Stool Scale: a single center study

Katarzyna Wojtyniak¹, Piotr Dziechciarz¹, Andrea Horvath¹

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

Objectives and study: The Amsterdam Infant Stool Scale (AISS) is a visual descriptive scale used for assessing stool consistency, amount, and color in infants and toddlers who have not yet been toilet trained. The aim of this study was to evaluate interrater variability of stool assessment with the AISS between the patient’s parents and clinician both made in vivo and with physician stool photographic judgment.

Methods: Not toilet trained children (2-18 months) admitted to the pediatric tertiary center between September 2014 and February 2015 were enrolled in the study. The stool was assessed using the AISS independently at the same time by the parent and the physician (MD1) within the shortest possible time after the patient passed a stool. At the same time, 2 photos were taken with a smartphone camera, which were subsequently evaluated by another physician (MD2) who was unaware of the in vivo stool evaluation. The outcome measures were interrater variability of stool assessment with the AISS between the parent and MD1 in vivo and between the parent in vivo and MD2 photographic assessment.

Results: A total of 100 stools of 100 consecutive infants were analyzed. The study found excellent interrater variability, between the parent and MD1 who assessed stools in vivo, for: consistency (kappa 0.87%; 95% confidence interval [CI] 0.78-0.95) and color (kappa 0.81%; 95% CI:= 0.71-0.91), and good interrater variability for amount (kappa 0.79%; 95% CI 0.7-0.88). Photographic evaluation performed by the other clinician showed moderate interrater variability variability between the MD2 and parent in vivo evaluation for stool consistency (kappa 0.5%; 95% CI 0.36-0.64) and amount (kappa 0.44%; 95% CI 0.29-0.59) and fair interrater variability for color (kappa 0.33%; 95% CI 0.21-0.45).

Conclusion: Parental/clinician stool assessment with the AISS under in vivo conditions is better than photographic evaluation done by an experienced physician.

Disclosure of interest: None Declared.
GASTROENTEROLOGY: GI-infections

G-P-216

Oral microbiota is not a cause of basal increased levels of expired hydrogen

Kris Van de Maele¹, Bruno Hauser¹, Thierry Devreker¹, De Greef Elisabeth¹, Veereman Gigi¹, Yvan Vandenplas¹

¹Uz Brussel, Paediatrics, Brussels, Belgium

Objectives and study: A breath test is a simple, non-invasive, diagnostic technique. Besides hydrogen, expired methane may as well be measured as the microbiota of some patients does not produce hydrogen but methane. Some centers recommend tooth brushing or mouth desinfection prior to a lactose breath test considering that a high basal value of expired hydrogen may be caused by dental or oral microbiota. However, to the best of our knowledge, there are no data in literature for this hypothesis.

Methods. A carbohydrate-free toothpaste was selected. Twenty consecutive children (> 7 years) with an increased basal level of expired hydrogen (> 10 ppm) were proposed to brush their teeth assisted by a nurse. Then, a second measurement of the basal expired hydrogen was performed. The following 20 consecutive patients > 7 years with increased basal levels of expired hydrogen were proposed to rinse their mouth with 0.1% hexetidine. Also in these children, a second basal measurement was performed.

Results. Neither the toothpaste nor the hexetidine had any effect on the basal levels of expired hydrogen (Table 1).

<table>
<thead>
<tr>
<th>Toothpaste</th>
<th>H² expired mean, median (range)</th>
<th>CH⁴ expired mean, median (range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>26; 22 (12-82)</td>
<td>19; 19 (3-55)</td>
<td>10.8 (3-27)</td>
</tr>
<tr>
<td>Hexetidine</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Before</td>
<td>After</td>
<td>Before</td>
</tr>
<tr>
<td>24; 21 (13-78)</td>
<td>20; 21 (3-62)</td>
<td>11.8 (2-30)</td>
</tr>
</tbody>
</table>

Conclusion: The oral microbiota cannot be hypothesized to be a plausible cause of increased basal levels of expired hydrogen.

Disclosure of interest: None declared
Gut dysbiosis in children affected by autism spectrum disorder

Lorella Paparo

University of Naples "Federico II", Translational Medical Science, Naples, Italy

Objectives and study: Gut microbiota (GM) and its metabolites have remarkable effects on brain function and behavior. We aimed to evaluate GM composition and function (butyrate production) in children with autism spectrum disorder (ASD).

Methods: We enrolled 14 subjects affected by ASD (diagnosis according to DSM-5 diagnostic criteria) aged 2 to 6 years (10 males) and 15 healthy controls (9 males, matched by age and sex). Faecal levels analysis of butyrate was performed by gas-chromatography. The composition of GM was analysed by sequencing of the V3-V4 region of the bacterial 16S rDNA with the platform Illumina MiSeq. The sequences obtained were analyzed by the use of the pipeline Quantitative Insights Into Microbial Ecology (QIIME) and statistical programs Metastats and Galaxy platform-based LDA Effect Size analysis (Lefse).

Results: All children with ASD showed significant differences compared to healthy controls about type (unweighted UniFrac analysis) and abundance of species (weighted UniFrac analysis). Significant differences were observed at major bacterial phyla level (Actinobacteria, Bacteroidetes, Firmicutes and Proteobacteria). All children with ASD showed significantly higher levels of intestinal production of butyrate compared to healthy controls (+ 90%, p <0.05). CONCLUSIONS: GM of ASD children is characterized by a high rate of dysbiosis. These findings suggest a potential importance of GM as target for future strategies for ASD prevention and treatment.

Disclosure of interest: none declared.
Efficacy of an ORS enriched with L. reuteri DSM 17938 and zinc in infants with acute gastroenteritis: a double blind, placebo controlled trial

Maria Maragkoudaki¹, George Chouliaras¹, Antonia Moutafi², Athanasios Thomas³, Archodoula Orfanakou², Alexandra Papadopoulou¹

¹First Department of Paediatrics, University of Athens, Children's Hospital "Agia Sofia", Athens, Greece
²Paediatric Private Outpatient Clinics, Athens, Greece

Objectives and study: The efficacy of an ORS enriched with L. reuteri DSM 17938 and zinc in infants with acute gastroenteritis was assessed in a double blind, placebo controlled trial. Fifty-one infants (mean (SD) age 1.8 (0.7) years; 35 males) with acute gastroenteritis seen at private outpatient pediatric clinics were randomly assigned to receive during the diarrheal episode either ORS enriched with L. reuteri DSM 17938 and zinc (LR&Z ORS; N=28) or a commercial ORS of similar composition and osmolality without added probiotic and zinc (LR&Z ORS; N=23).

Methods: The stools volume and consistency according to Amsterdam stool scale⁴ during 48 hrs before recruitment were recorded while on the day of recruitment the patients underwent physical examination to assess dehydration and nutritional status. After recruitment, the parents recorded the daily number and consistency of the stools, the volume of consumed ORS, the presence of other symptoms, missed number of workdays for the parents or of days at day care/nursery for the child as well as hospital admissions during the study period. All of the above variables were compared between the two study groups. The severity of diarrhea was defined by a score taking into account the consistency and the volume of stools according to Amsterdam stool scale.

Results: All of the recruited patients were well nourished infants with mild (N=40) or moderate (N=11) dehydration according to Bailey scale (scores 1-2 and 3-4 respectively). Age, gender and weight for age were comparable between the two groups. The severity of diarrhea on day -1 was comparable in the LR&Z ORS and LR&Z ORS groups: mean (SD) score 21.5 (8.7) vs 22.9 (14.5); p=0.8. A significant reduction in the severity of diarrhea on day 2 compared to day -1 was observed in both groups (LR&Z ORS group: mean (SD) score 21.5 (8.7) vs 6.7 (5.0) respectively, p<0.001; LR&Z ORS group: mean (SD) score 22.9 (14.5) vs 8.6 (8.3), p<0.001). All of the outcomes showed a trend to be better in the LR&Z ORS arm without though reaching statistical significance in any of them: the proportion of children with diarrhea on day 2 (defined as at least 3 A3, A4, B3, or B4 bowel movements) in the LR&Z ORS vs LR&Z ORS groups were 10.7% vs 17.4% respectively, p=0.6; the overall diarrhea-severity score during the six-day period were mean (SD) score 28.0 (17.6) vs 33.8 (22.8) respectively; p=0.5; the number of days with watery stools (at least one A3 or A4 bowel movement) were 1.6 (0.7) vs 2.1 (1.2) respectively, p=0.3 while, the number of days with soft stools (at least one B3 or B4 bowel movement) were 4.0 (1.6) vs 4.5 (1.8) respectively, p=0.3; the number of lost work days were mean (SD) 1.1 (1.6) vs 1.4 (1.7) respectively, p=0.5 and the same was true for the day-care absences (mean (SD) 1.8 (2.4) vs 3.0 (1.9) respectively, p=0.15). The consumption of ORS during the 4 first hours was similar between the LR&Z ORS and the LR&Z ORS groups: mean (SD) milliliters 181 (116) vs 169 (108) respectively; p=0.5. No adverse effects were seen in either group.

Conclusion: ORS enriched with L. reuteri DSM 17938 and zinc is safe in infants with acute gastroenteritis but its effectiveness compared to conventional ORS needs to be tested in larger, adequately powered studies, in order to detect statistically significant differences.


Disclosures: Author and co-authors, Conflict with: Unrestricted grant Biogaia
Faecal calprotectin and eosinophil-derived neurotoxin in healthy children

Maria Roca\textsuperscript{1}, Ana Rodriguez Varela\textsuperscript{2}, Ana Armisen\textsuperscript{2}, Mª Jose Vaya\textsuperscript{2}, Paco Cano\textsuperscript{2}, Esther Donat\textsuperscript{3}, David Hervas\textsuperscript{4}, Carmen Ribes Koninckx\textsuperscript{3}

\textsuperscript{1}Instituto de Investigación Sanitaria La Fe, U. Enfermedad Celiaca e Inmunopatología Digestiva, Valencia, Spain
\textsuperscript{2}Centro de Salud Bétera, Bétera, Spain
\textsuperscript{3}La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
\textsuperscript{4}Instituto de Investigación Sanitaria La Fe, U. Bioestadística, València, Spain

Objectives and study: To investigate faecal calprotectin (fCP) and faecal eosinophil-derived neurotoxin (fEDN) levels in young healthy children and to determine their potential role as biological markers.

Methods: Prospective, multi-centre study including 98 healthy children, 0 to 16 years, from the general population. 98 faecal samples were collected in plastic containers, sent to the laboratory no later than 7 days after collection and stored at -20ºC until analysis. The extraction procedure was performed with the Faecal sample preparation kit (Roche Diagnostics). fCP and fEDN levels in the stool samples were measured by EliA Calprotectin 2 and an EDN research assay developed on the ImmunoCAP platform, respectively (Thermo Fisher Scientific).

Results: We found a statistically significant association for median fCP concentration values and age (p<0.001) and median fEDN concentration values and age (p<0.001). This association was stronger at younger ages and sharply decreased around 36 months of age. Moreover, for children up to 36 months, a large variability was found both for fCP and fEDN values, especially in the first month of life. No statistically significant association was found for gender, neither for fCP (p=0.46) nor for fEDN (p=0.43).

Breastfed babies aged up to 6 months showed overall higher fCP and fEDN values as compared to non-breastfed infants, but this difference was not statistically significant (p=0.55 and p=0.50).

Conclusion: The variability of fCP and fEDN for children up to 3 years of age justifies the need to establish different cut-off levels in this age range. It also suggests that the main utility of both markers could be intra-individual variation monitoring, allowing assessment of disease progression or response to therapeutic intervention. Beyond the age of 3 a unique cut off level can be used through childhood and also the lower variability could enable a better discrimination between true positive and true negative results.

Due to the extremely high variability of fCP and fEDN obtained in the first month of life, applicability at this age of any of the two markers in clinical practice as a diagnostic tool is debatable.

Disclosure of interest: "None Declared".
The influence of cefotaxime sodium on gut microbiota in neonate

Mizu Jiang¹, Huali Shao¹, Xiaoli Shu¹, Weirong Liu¹

¹Children’s Hospital, Zhejiang University School of Medicine, Hangzhou, China

**Objectives and study:** Our aim is to investigate the numbers of gut microbiota such as Bifidobacterium, Lactobacillus, Bacteroides, and Enterobacteriaceae with different ages of birth in neonatal period and the changes after intravenous treatment with cefotaxime sodium in newborn with infectious diseases.

**Methods:** 111 full-term newborns were enrolled in this study from August to December in 2013 in our Hospital. They were divided into two groups who treated with cefotaxime sodium intravenously lasting for 3 days or without any antibiotics. Stool specimens were collected during the hospitalization. The content of Bifidobacterium, Lactobacillus, Bacteroides, and Enterobacteriaceae in stool samples was detected by real-time PCR.

**Results:** The results showed that the number of Bifidobacteria was significantly increased with the increase of day age, and the number of Lactobacillus was increased, but relatively slowly, while the increasing of Enterobacteriaceae and Bacteroides was not obvious. In the group of 3 to 28 days age, the numbers of Bifidobacteria and Enterobacteriaceae were significantly decreased in patients with cefotaxime sodium than that without cefotaxime sodium (P<0.05), and there were no significant difference in the numbers of Lactobacillus and Bacteroidetes between the two groups (P>0.05).

**Conclusion:** The use of intravenous antibiotics in the neonatal period such as cefotaxime sodium can cause reduction of gut microbiota, such as Enterobacteriaceae and Bifidobacteria.
Anisakis: a new threat coming from the sea

Ramón Tormo¹, Hegoi Segurola¹, Guillermo Cardenas¹

¹Unidad de Gastroenterología Y Nutrición Via Augusta, Gastroenterología Y Nutrición, Barcelona, Spain

Objectives and study: In Mediterranean Diet we suggest eating fish regularly. Anisakis is a genus of nematodes of the superfamily ascaridoidea. Its organisms are found in the stomachs of marine animals and birds. Human infection occurs by ingestion of raw fish that contain larvae. The man becomes an occasional host to ingest larvae from fish. *Anisakis simplex* (AS) is a cause of allergic sensitization and potential occupational risk is suggested in fishermen and workers assigned to fish processing and sale. The prevalence of Anisakis in Spain varies according to studies and encrypted between 6-56%. The aim of our presentation is to describe the anisakis cases in 2015 (our paediatric consulting). To enumerate the list of the characteristic symptoms and to define prevention measures.

Methods: Descriptive study (2015). We checked the presence of the typical symptoms described of anisakiosis:
- Allergic symptoms (urticaria, edema, anaphylaxis);
- GI symptomatology: nausea, vomiting, abdominal pains

We determined *anisakis* RAST in all patients.

Results: 18 anisakiasis cases were detected: GI/allergic symptoms and *Anisakis Simplex*’s RAST > 0.35 U/l. Average age of 6 ± 8; Mean: 4.5±3years. Prick tests positive in 82% of them.

No food prevention measures (such as freezing) were taken.

Principal symptoms described: hives, rashes, abdominal pains. All patients had elevated IgE levels in blood. 80% of patients came from cities and towns from coast. Fresh fish consumption was high, mainly cod and tuna.

Conclusion: The high prevalence of anisakiasis in the Mediterranean coast, suggest the need of taking some preventive measures such eating frozen fish. The fish exclusion diet and oral antihistamines might be the best choice for the Anisakiosis treatment.

Disclosure of interest: Non Declared
Objectives and study: Early-life gut microbiota can influence the maturation of immune system and predisposition to several diseases in later years. Mode of delivery and feeding may influence the acquisition of gut microbiota. Toxigenic *Clostridium perfringens*, a subdominant but significant member of gut microbiota, is a widespread opportunistic pathogen linked with numerous diseases but the intestinal carriage of its toxin-types in infants remains underexplored. In these contexts, we aimed to examine the influence of mode of delivery and feeding on the composition of gut microbiota and fecal organic acids in 6-months-old infants, with a special focus on gut colonization of alpha-toxigenic and enterotoxigenic *C. perfringens*.

Methods: The study included healthy infants (*n* 124; M 70; F 54; Age: 161-178 days) enrolled at Gonohashi Obstetrics and Gynecology Hospital, Tokyo. Fecal samples (1 gm) were collected into fecal collection tube containing RNALater and an empty tube, and were stored at 4°C until nucleic acid extraction. *C. perfringens* was quantified by qPCR targeting α-toxin and enterotoxin genes. *Clostridium difficile*, and Bifidobacterial subgroups and species were enumerated by qPCR targeting 16S rRNA genes. Other bacterial groups, subgroups and genera were quantified by RT-qPCR.

Results: Alpha-toxigenic and enterotoxigenic *C. perfringens* were detected in 36% and 10% infants, respectively, with counts ranging from $10^3$-$10^8$ cells/g feces. Colonization rate of alpha-toxigenic *C. perfringens* was significantly higher in cesarean-born infants, as compared to vaginally-born infants. In contrast, the carriage of *Bacteroides fragilis* group and the concentration of fecal propionate was significantly lower in cesarean group. Enterotoxigenic *C. perfringens* was detected in 10% infants but remained undetected in exclusively breast-fed infants. Breast-fed infants were insignificantly less often colonized with *C. perfringens* and *C. difficile*, as compared to formula-fed or mix-fed infants.

Conclusion: These results indicate that mode of delivery and feeding can influence the neonatal microbiota composition and that healthy infants may also carry toxigenic *C. perfringens* at significant levels. Taken together, the findings are intriguing and suggest that cesarean-born and formula-fed infants are more likely to be colonized with toxigenic *C. perfringens*, as compared to vaginally-born and breast-fed infants. Further in-depth studies on its potential sources and clinical significance are clearly needed, as well as further investigation (which is already in-progress in the authors' laboratory) of its intestinal colonization at different stages of infancy and childhood so as to understand the factors affecting the acquisition of this opportunistic pathogen in the infant gut.

Disclosure of interest: “None Declared”.
Features of Intestinal Microbiota of Young Adults born by C-section

Ravinder Nagpal1, Kiyohito Ogata2, Hirokazu Tsuji2, Kazunori Matsuda3, Takuya Takahashi2, Koji Nomoto2, Yoshio Suzuki4, Satoru Nagata5, Yuichiro Yamashiro6

1Juntendo University Graduate School of Medicine, Probiotics Research Laboratory, Bunkyo-Ku, Japan
2Yakult Central Institute, Tokyo, Japan
3Yakult Honsha European Research Center for Microbiology, Ghent-Zwijnaarde, Belgium
4Juntendo University School of Health and Sports Sciences, Sports Science, Chiba, Japan
5Tokyo Women’s Medical University, School of Pediatrics Medicine, Tokyo, Japan
6Juntendo University Graduate School of Medicine, Probiotics Research Laboratory, Tokyo, Japan

Objectives and study: Intestinal microbiota development commences immediately after birth. The frequency of caesarean delivery is increasing worldwide. Caesarean-born infants may harbor a different microbiota as compared to vaginally-born infants, mainly due to evaded contact with maternal vaginal/fecal microbiota and an extended stay in the hospital. Such differences may influence whole-of-life health, but it is unclear how long-lasting these differences in the microbiota can be. In this context, we aimed to assess the intestinal microbiota of healthy Japanese young adults, profiled by the mode of delivery.

Methods: The study included healthy young adults (n 165; M 114; F 51; age: 18.8 ± 0.9 years; age range: 18-22 years) enrolled as students at Juntendo University Faculty of Health and Sports Sciences, Chiba. Fecal samples (=1.0 g) were collected into fecal collection tube containing RNAlater and an empty tube, and were stored at 4°C until nucleic acid extraction. Bacterial groups, subgroups and genera were quantified by RT-qPCR. C. perfringens was quantified by qPCR targeting α-toxin and enterotoxin genes. Written informed consent was obtained from subjects and the study was approved by the ethics committee of the university.

Results: Sixteen subjects had been delivered by C-section and 133 by vaginal delivery. We observed significantly higher detection rate of Bacteroides fragilis group and Lactobacillus sakei subgroup in vaginally-delivered subjects compared with caesarean-born subjects (p<0.05). The detection rate of fecal propionic acid was also significantly higher (p<0.05) in normally-delivered subjects compared to caesarean group. No differences were observed in the count or carriage rate of other fecal bacteria or organic acids.

Conclusion: These results might suggest that the differences in the composition of gut microbiota and intestinal environment, in particular the carriage of B. fragilis group, L. sakei subgroup and fecal propionic acid, possibly as a result of C-section may persist even beyond teenage. Further studies should endeavor to assess and validate these differences in different populations of different ages, as well as to decipher the association, if any, of these differences with any important aspect of host health and disease predisposition.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016
Development of the intestinal microbiota after short and long antibiotic treatment in late-preterm and term infants

Romy Zwittink1, Diny van Zoeren2, Rocio Martin3, Richard van Lingen2, Obbe Norbruis2, Liesbeth Groot Jebbink2, Ruurd van Elburg3, Ingrid Renes3, Clara Belzer1, Jan Knol1

1Wageningen University and Research Centre, Microbiology, Wageningen, Netherlands
2Isala Clinics, Paediatrics, Zwolle, Netherlands
3Nutricia Research, Utrecht, Netherlands

Objectives and study: Antibiotic treatment is common practice in the neonatal ward for prevention and treatment of sepsis, which is one of the leading causes of mortality and morbidity in preterm infants. The applied antibiotic strategies in neonatology led to decreased mortality and morbidity rates, however, there is a risk of impeding gut microbiota development and increasing antibiotic resistance. Antibiotic treatment during early colonisation of the gastrointestinal tract has shown to impede settlement of Bifidobacterium spp., allowing opportunistic pathogens to become dominant. Although, the effect of antibiotic treatment on microbiota development has been well recognised, not much attention has been paid to duration of treatment. Our aim is to study the effect of antibiotic treatment duration on intestinal microbiota development in preterm infants.

Methods: Faecal samples from fifteen (pre)term infants of 35±1 weeks gestation and 2871±260 gram birthweight (mean±SD), were collected during the first six postnatal weeks, including a sample before and after antibiotic treatment. The infants were stratified according to antibiotic treatment duration: no, short (<3 days) or long (>5 days) treatment with a combination of amoxicillin and ceftazidime during the first postnatal week. In total 96 faecal samples were analysed for their microbiota composition by sequencing of the 16S rRNA gene.

Results: The intestinal microbiota of infants receiving no antibiotics was dominated by Bifidobacterium, with average relative abundance of 45% in meconium increasing towards 73% at postnatal week six. Compared to infants receiving no antibiotics, the abundance of Bifidobacterium was significantly decreased immediately after treatment in infants exposed to short (p=0.016) or long (p=0.014) antibiotic treatment. Enterococcus became particularly abundant right after short and long treatment, with relative abundance of 63% and 59% respectively. Despite these disturbances, high abundance of Bifidobacterium was observed again at postnatal week six in infants receiving a short antibiotic course. Six weeks did not allow for potential restoration of Bifidobacterium levels in infants receiving a long antibiotic course. These findings were further confirmed by principal response curve analysis, showing divergent temporal microbiota development between infants receiving no, short or long antibiotic treatment (p=0.002). In addition, it showed that short treatment allowed for development towards a microbiota more similar to infants receiving no antibiotics, characterised by high abundance of Bifidobacterium.

Conclusion: Intestinal microbiota development in (pre)term infants is greatly affected by antibiotic treatment. However, short antibiotic treatment allowed for recovery of the intestinal microbiota within the first six postnatal weeks, while this was not observed after long antibiotic treatment. Restoration of microbiota composition, namely Bifidobacterium abundance, might have great impact on infant’s growth, immune development and clinical outcome. It would be advisable to take this into consideration when deciding about antibiotic treatment duration during the first postnatal week.

R. Martin, R. van Elburg, I. Renes, J. Knol: Conflict with: employee of Nutricia Research
**GASTROENTEROLOGY: GI-infections**

**G-P-226**

**elevated troponin levels in infants with acute gastroenteritis: is it ischemia or Rota associated carditis**

Sana Barakat¹, Rim Harfoush², Sherif Adel³

¹University of Alexandria, Faculty of Medicine, Pediatrics, Alexandria, Egypt
²Faculty of Medicine, University of Alexandria, Department of Microbiology, Alexandria, Egypt
³Faculty of Medicine, University of Alexandria, Pediatrics, Alexandria, Egypt

**Objectives and study** A large number of clinical case reports suggested that rotavirus could be found at extra-intestinal sites including the heart following infection and fatal rotavirus myocarditis has been recently reported in 2 children. We hypothesized that rotavirus may have a direct injurious effect on the myocardium of infants and this injury can be detected by the presence of cardiac troponin I (TnI).

**Methods:** Over 8 weeks period, 50 of 150 infants (5-18 months) with acute gastroenteritis were found to have human rotavirus (HRV) gastroenteritis with rotavirus antigenemia. Sera of 150 infants were analyzed for TnI. If TnI value was above the screening limit (0.05 ng/ml), electrocardiogram (ECG) and cardiac ultrasound were performed. Infants with primary conditions associated with elevated TnI were excluded.

**Results:** Thirty four infants (22.6%) had elevated TnI (0.06-2.5 ng/ml), 16 (47%) of them had HRV-GE (p=0.054). However, none of them had any sign of myocarditis or ischemia in their ECG or cardiac ultrasound scan and their TnI levels normalized within 24-72h after correction of dehydration. Infants less than 1 year, and those with dehydration, anemia or acidosis were more prone to have elevated cTnI (p=0.008, 0.009, 0.006, 0.001 respectively). Multivariate logistic regression analysis showed that severe dehydration and acidosis are still significantly associated with elevated TnI levels (adjusted OR, 95% CI = 22.9, 2.19-239 and 20.76, 6.15-70 respectively).

**Conclusion:** Our study is the first pediatric study to show that myocardial injury occurs in infants with gastroenteritis and this injury was precipitated by transient ischemia which may go unnoticed on the ECG. However, this injury is always self-limiting if the underlying perfusion disturbance is corrected.

**Disclosure of interest:**
"None Declared".
Practical approach to acute gastroenteritis in Austria: a nationwide survey on intravenous rehydration

Sebastian Bauchinger¹, Johannes Waldner¹, Evelyn Zöhrer¹, Almuthe Christine Hauer², Jörg Jahnel¹

¹Medical University Graz, Graz, Austria
²Medical University Graz, Department of Pediatrics and Adolescent Medicine, Graz, Austria

Objectives and study: Acute gastroenteritis (AGE) may lead to severe loss of fluid and electrolytes. Rehydration must be adequate why ESPGHAN publishes AGE recommendations. We sought to evaluate intravenous rehydration in everyday AGE management at Austrian paediatric hospitals.

Methods: A nationwide call for participation in autumn 2015 canvassed 13 children’s hospitals in Austria. An electronic survey comprised 15 questions regarding general information, the establishment of written standard operating procedures (SOPs), assessment of dehydration, laboratory parameters evaluated, admission criteria, fluids used for rehydration, supportive medication, assessment of success of therapy, and length of hospital stay after rehydration.

Results: Ten out of 13 hospitals (77%) had established written SOPs for AGE therapy. The bases of these SOPs were in 3 hospitals the recommendations of ESPGHAN; in 3 a combination of ESPGHAN recommendations and local clinical experience; in another 3, ESPGHAN recommendations and internally developed SOPs; and in the last 2 internally developed SOPs without contributions from ESPGHAN recommendations. All 13 hospitals assessed state of dehydration clinically (100%). Ten centres (77%) also used results of blood gas analysis (BGA) and 7 (54%) evaluated grade of dehydration by loss of body weight. All 13 hospitals assessed pH and electrolytes (92%, 12/13), followed by base excess (85%, 11/13). Further analytes mentioned were glucose (38%, 5/13), haematocrit (15%, 2/13), uric acid, osmolarity, bicarbonate, and anion gap (each 7.5%, 1/13). Criteria for admission to hospital were clinical condition (100%, 13/13), signs of shock (85%, 11/13), social or familial concerns (23%, 3/13), or abnormal BGA results (62%, 8/13); among laboratory-result criteria were abnormalities in electrolytes (100%, 13/13), pH (92%, 12/13), base excess (85%, 11/13), glucose (46%, 6/13), haematocrit (15%, 2/13), and uric acid, osmolarity, bicarbonate, and anion gap (7.5%, 1/13 respectively). In rehydration, fluid requirements were mostly expressed as millilitre per kilogram bodyweight per hour (ml/kg/h 85%, 11/13). One hospital expressed fluids required in millilitres per square metre of body surface per hour (ml/m²/h) and another adjusted calculations for patient age (each 7.5%, 1/13). The same largely held true during maintenance, although one hospital switched from ml/kg/h to ml/m²/h. For both phases the fluids given varied widely. Eight institutions (62%) used individually prepared solutions containing glucose and electrolytes as well as 6 different industrially produced solutions with sodium concentrations ranging from 45 to 154 mmol/l and glucose from 0 to 50 g/l. Every hospital assessed improvement clinically (100%, 13/13); 8/13 (62%) also used BGA for assessment. Hospital stays after completed rehydration lasted from 0 to 72 hours.

Conclusion: Although ESPGHAN provides AGE guidelines, approaches to diagnosis and therapy vary widely among Austrian children’s hospitals. The reasons for such parochialism are many-sided. Efforts toward unification around ESPGHAN-recommended standards in care of AGE including standardized compositions of infusions appear required in Austria and probably in other European countries.

Disclosure of interest: None Declared.
Gastric Functional Abnormalities in Children with Helicobacter Pylori Gastritis

Ahmed Megahed¹, Khaled Zalata², Ahmed Abdalla¹, Suzy Abd El-Mabood³

¹Monsoura University Children’s Hospital, Mansoura University, Pediatrics; Pediatric Gastroenterology, Hepatology and Nutrition, Mansoura, Egypt
²Mansoura University, Faculty of Medicine, Pathology, Mansoura, Egypt
³Monsoura University Children's Hospital, Mansoura University, Pediatrics, Mansoura, Egypt

Objectives and study: Worldwide H. pylori infection is highly prevalent, 70% of children in the developing world are infected usually before age of 10 years. A big list of H. pylori related organic diseases in children had been well described; however there are only very few reports on associated gastric functional abnormalities. The current study was conducted to quantify electrogastrographic (EGG) as well as gastric emptying (GE) time abnormalities in H. pylori infected children, and also to evaluate their possible relation to symptoms profile and histopathology severity.

Methods: A prospective non randomized observational study was conducted on 29 children (male/female = 12/17; age = 9.7±2.4 ys) with H. pylori gastritis evidenced by positive histopathology and rapid urease test; another group of 16 age and sex matched children were included as a control for GE & multichannel EGG testing. Clinico-epidemiologic data including 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: Based on the most bothersome symptom(s); Pain was the most bothersome symptom in 8 (28%) patients; pain and vomiting in 10 (34%) patients; pain and upper GI bleeding in 9 (31%) patients; and pain, vomiting and upper GI bleeding in the remaining 2 (7%) patients. The symptoms severity as measured on 5-points scale was reported as 3- moderate; 4- severe; 5- very severe in 6 (20.7%); 6 (20.7%); and 17 (58.6%) patients, respectively. While the symptoms frequency was reported as 2- ≤ 2 times /week: in 8(27.6%) patients; 3- ≥ 3 times /week, not daily: in 10(34.5%) patients; 4- daily, intermittent: in 5 (17.2%) patients; and 5- daily, almost continuous: in the remaining 6 (20.7%) patients.

Fourteen children reported gastric functional abnormalities, 10 with abnormal both EGG and GE test results; 2 with abnormal EGG; and another 2 children reported delayed GE. Gastric emptying test parameters significantly correlated with EGG parameters. Children with H. pylori had a significantly higher preprandial percentage EGG classification tachygastria; percentage EGG classification bradygastria; percentage EGG classification arrhythmia; and dominant frequency instability coefficient (DFIC) means, while the preprandial percentage EGG classification normogastria and average percentage slow wave coupling means were significantly lower as compared with controls. The same goes for postprandial findings with the exception that the difference in percentage EGG classification tachygastria mean from that of control did not reach significance. In addition the postprandial dominant power and EGG power change means were significantly lower than controls.

Children with H. pylori had significant slowing of GE than controls. Patients’ symptom profile, severity, frequency, histopathology topography and severity were not different among patients with functional abnormalities versus those without.

Conclusion: Children with H. pylori gastritis have a significant slowing of GE as well as gastric dysrhythmias 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.
Efficacy of Synbiotic, Probiotic, and Prebiotic Treatments for Irritable Bowel Syndrome in Children: a randomized controlled trial

Ahmet Basturk1, Reha Artan1, Aygen Yilmaz1

1Akdeniz University, Faculty of Medicine, Department of Pediatric Gastroenterology, Antalya, Turkey

Objectives and study: Dietary interventions involving non-starch polysaccharides and probiotics improve the symptoms of irritable bowel syndrome (IBS). Our study investigated the efficacy of synbiotic (Bifidobacterium lactis B94, inulin), probiotic (B. lactis B94), and prebiotic (inulin) treatment for IBS in a pediatric age group.

Methods: This study was randomized, double-blind, controlled, and prospective in design, and included 71 children between the ages of 4 and 16 years who were diagnosed with IBS according to the Rome III criteria. The first group received synbiotic treatment (5x10^9 colony forming units (CFU) of B. lactis B94 and 900 mg inulin), the second group received probiotic treatment (5x10^9 CFU B. lactis B94), and the third group received prebiotic treatment (900 mg inulin) twice daily for 4 weeks.

Results: The probiotic treatment improved belching–abdominal fullness (p<0.001, chi-square test), bloating after meals (p=0.016, chi-square test), and constipation (p=0.031, chi-square test); and the synbiotic treatment improved belching–abdominal fullness (p<0.001, chi-square test), bloating after meals (p=0.004, chi-square test), constipation (p=0.021, chi-square test), and mucus in the feces (p=0.021, chi-square test). The synbiotic group had a significantly higher percentage of patients with full recovery than did the prebiotic group (39.1% vs. 12.5%, p=0.036, chi-square test) (Table).

Table: Symptoms of IBS before and after 4 weeks of treatment, by study group. Values are numbers of patients with each complaint.

<table>
<thead>
<tr>
<th>Complaint</th>
<th>Prebiotic (n=24)</th>
<th>Probiotic (n=24)</th>
<th>Synbiotic (n=23)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before</td>
<td>After</td>
<td>p^a</td>
</tr>
<tr>
<td>Bloating after meals</td>
<td>12</td>
<td>12</td>
<td>1.000</td>
</tr>
<tr>
<td>Belching–abdominal fullness</td>
<td>13</td>
<td>11</td>
<td>0.250</td>
</tr>
<tr>
<td>Mucus in stool</td>
<td>8</td>
<td>7</td>
<td>1.000</td>
</tr>
<tr>
<td>Difficulty with defecation</td>
<td>15</td>
<td>12</td>
<td>0.250</td>
</tr>
<tr>
<td>Feeling of being unable to completely empty at bowel movements</td>
<td>14</td>
<td>10</td>
<td>0.125</td>
</tr>
<tr>
<td>Sudden urge to defecate</td>
<td>16</td>
<td>15</td>
<td>1.000</td>
</tr>
</tbody>
</table>

^a Chi-square test.

Conclusion: When compared to prebiotics, synbiotic and probiotic treatments provide greater improvements in the initial complaints. Additionally, when compared to the prebiotic group, there was a significantly higher number of patients with full recovery from IBS symptoms in the synbiotic group. At the same time the twice-a-day administration of synbiotics is suggested for the treatment of children with IBS.

Disclosure of interest: None Declared
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-P-230

**The systematic effect of infant formulas on stool consistency proven by longitudinal statistical models**

Alfonso Rodriguez-Herrera1, Thomas Ludwig2, Solphie Swinkels2, Hetty Bouritius2, Rocio P. Rubio3, Antonio Muñoz4, Massimo Agosti5, Gianluca Lista6, Luigi Tommaso Corvaglia7, Juan L. P. Navero8

1Instituto Hispalense de Pediatría, Unidad de Gastroenterología Y Nutrición, Sevilla, Spain
2Nutricia Research, Utrecht, Netherlands
3Hospital Quiron, Servicio de Pediatría, Barcelona, Spain
4Hospital Clínico Universitario San Cecilio, Department of Pediatrics, Granada, Spain
5Polo Universitario F. Del Ponte, Neonatologia e Terapia Intensiva Neonatale, Varese, Italy
6Ospedale Dei Bambini Vittore Buzzi, Terapia Intensiva Neonatale, Milan, Italy
7Hospital S. Orsola Malpighi, Intensive Therapy Unit, Bologna, Italy
8Hospital Universitario Reina Sofia, Jefe de Servicio de Pediatría, Cordoba, Spain

**Objectives and study:** Hard stools are an exception in breastfed infants, but have been reported to be more frequent and of relevant concern in infant formula (IF) fed infants. The probability of having a certain stool consistency (e.g. hard stools) in dependency of a specific IF was analysed by an advanced longitudinal statistical model, based on 23352 individual stool consistency observations.

**Methods:** After parent's autonomous decision to discontinue breastfeeding, healthy, term infants aged 0-28 days were randomized in a controlled, double-blind, multicenter, parallel-group, intervention study on gastrointestinal tolerance, growth, and safety (LIFE study, registration number NTR3455), to receive either IF which combined 30% of a specific fermented IF (FIF) with a specific mixture of short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides (scGOS/lcFOS, ratio 9:1, 0.8g/100ml; FIF+, n=95 infants), or infant formula without fermented formula and without scGOS/lcFOS (IF-, n=105 infants). Parents completed standardized diaries with daily entries on stool consistency until 17 weeks of age. Stool consistency was rated on a five point scale: watery, soft-pudding like, soft-formed, hard-formed, and dry hard pellets. The latter two categories were combined as hard stools. Data were analysed by longitudinal modelling of stool consistency as a nominal variable. The longitudinal model generated for the observation period continuous and daily probabilities and corresponding odds ratios (OR) for a specific stool consistency in relation to a specific IF.

**Results:** The probability to display a specific stool consistency was found to be formula dependent, and to change over the observation period. For example, over the entire observation period IF- fed infants had a probability between 0.06 and 0.21 to have hard stools, and a 3.6 to 12.5-fold OR to have hard stools as compared to FIF+ fed infants. Otherwise, FIF+ fed infants had a probability between 0.41 and 0.57 to have a soft-pudding like stool, and a 2.1 to 2.9-fold OR to have soft-pudding like stools as compared to IF- fed infants.

**Conclusion:** In summary, infants fed with FIF+, containing 30% fermented formula and scGOS/lcFOS, had a significantly higher probability of having soft stools, and a significantly lower probability of having hard stools than infants fed with IF-. The advanced longitudinal modelling approach enables to gather insights on effects on stool consistency of specific IF compositions with a high temporal resolution.

**Disclosure of interest:** Alfonso Rodriguez-Herrera, Rocio P. Rubio, Antonio Muñoz, Massimo Agosti, Gianluca Lista, Luigi T. Corvaglia, and Juan L. P. Navero, Conflict with: study support; Thomas Ludwig, Sophie Swinkels, and Hetty Bouritius, Conflict with: Employee of Nutricia Research
Accuracy of the Strobel and Modified Strobel formulae in pH catheter placement in children: A prospective cohort study

Amit Saha¹, Bim Bhaduri²

¹Kings College Hospital NHS Trust, Paediatric Hepatology, Gastroenterology and Nutrition, London, United Kingdom
²Maidstone and Tunbridge Wells Hospitals NHS Trust, Department of Paediatrics, Maidstone, United Kingdom

Objectives and study: Gastro-oesophageal reflux is a common, physiological and self limiting condition in infants. However early diagnosis and management is essential for prevention of complications. Oesophageal pH monitoring is the gold standard technique for the detection of acid gastro-oesophageal reflux episodes, and correct placement of the catheter is crucial for accuracy of the readings. The Strobel formula (0.252 × height in cm + 5) is frequently used as a guide to determine distance from the nostrils to the lower oesophageal sphincter(LES). However, a modified Strobel formula was introduced for more accuracy as follows: (1) infants <12 months (height in cm × 0.252 + 2); (2) older children >12 months (height in cm × 0.226 + 4.6)× 0.87. The aim of this study was to compare the accuracy of Strobel formula and modified Strobel formula in achieving correct placement of the catheter tip, in children more than 1 year of age.

Methods: A previous study on 15 infants less than 1 year of age showed that the modified Strobel formula was more accurate. We did a further prospective study with 14 children to determine the accuracy of these formulae in older children, more than 1 year age. Initial catheter length was calculated using the modified Strobel formula, and the actual catheter placement was adjusted and confirmed either by direct measurement of length at endoscopy and/or confirming its tip position between T8 and T10 level on chest X-ray.

Results: The 14 patients included in this study ranged in age from 1 year 2 months to 15 years (male n=8, female n=6), with a mean age of 7 years 7 months. The actual catheter tip position (as determined by direct vision at endoscopy or chest radiograph or both) was compared with the predicted position as determined by the above formulae, and their deviation from actual LES position was calculated. The mean deviation for the Strobel formula was +6.9(+ 2.8 to 11.0)cm, whereas the mean deviation for the modified Strobel formula was -0.99(-5.23 to + 3.61)cm. Therefore, our data shows that the Strobel formula overestimated the LES distance by an average of 6.9cm, whereas the modified Strobel underestimated it 0.99cm on average.
Conclusion: This study showed that the modified Strobel formula is more accurate than the Strobel formula in pH probe placement in children more than 1 year of age. Data from a similarly designed previous study had also shown it to be more accurate in infants less than 1 year of age. We recommend that the modified Strobel formula be used in all age groups of children for initial pH probe placement. However, in order to do a reliable pH study, we recommend that radiographic or endoscopic confirmation of the catheter tip position must still be considered when using any formula.

Disclosure of interest: None Declared.
Colonic manometry parameters can predict the outcome of the surgical ostomy formation in children with intractable constipation

Anna Rybak1, Efstratios Saliakellis3, Keith Lindley3, Licia Pensabene3, Francesco Valitutti4, Ylenia Perone3, Joseph Curry5, Simon Blackburn5, Nikhil Thapar3, Osvaldo Borrelli3

1The Great Ormond Street Hospital, Neurogastroenterology and Motility Division, London, United Kingdom
2Hellenic Police Medical Directorate, Paediatric Department, Thessaloniki, Greece
3Great Ormond Street Hospital, Neurogastroenterology and Motility Division, London, United Kingdom
4Sapienza University of Rome, Paediatric Gastroenterology and Liver Unit, Rome, Italy
5Great Ormond Street Hospital, General Surgery, London, United Kingdom

Objectives and study: Although colonic manometry is advocated as gold standard for assessing colonic neuromusculature in children with intractable chronic constipation, so far no specific biomarkers predicting the outcome post-surgical management have been identified. Therefore, we aimed to assess in children with intractable constipation whether any colonic manometry parameters could predict the outcome of the surgical ostomy formation.

Methods: A retrospective analysis of children with chronic constipation (CC) and chronic intestinal pseudoobstruction syndrome (CIPO), undergone high resolution colonic manometry completed prior surgery, was performed. Inclusion criteria were: 1. position of the manometry catheter in right to mid-transverse colon: 2. study protocol with at least one dose of bisacodyl given during procedure. Clinical symptoms (soiling, abdominal pain, presence of faecal mass or anal fissure, feeding intolerance, urinary symptoms, failure to thrive, dyspeptic symptoms) before and after surgical management were assessed, as well as need for another surgery. Colonic manometry data included: change in motility index (MI) before and after test meal, presence and characteristics of high amplitude propagated contractions (HAPCs) before and after the bisacodyl stimulation, low amplitude propagated contractions (LAPCs) and retrograde propagated contractions, and colorectal response. The data regarding type of performed surgery (antegrade colonic enema – ACE, ileostomy or colostomy) were included. T-test and chi-square test were used when appropriate. The adjusted effect of different variables on the outcome was assessed with logistic regression analysis.

Results: Of 67 children reviewed, 45 patients fulfilled inclusions criteria (CC n=42 and CIPO n=3; 25 girls; median age 7.7 years). Median age at first symptoms was 3 months (0-10 yrs). With regards to performed surgery, 17 patients had ACE, 17 had ileostomy and 11 had colostomy. There was a significant association amongst the outcome of the manometry and the choice of the initial surgical intervention (p=0.016 for neuropathy of the L and R colon and ileostomy formation). There was a significant improvement in reported symptoms post initial surgery (p<0.05). Because of persistent symptoms, subsequent surgery was required in 10 children. Three had an ACE formation, 2 had a colostomy and 3 ileostomy. There was no significant effect of the gender, age at onset, symptoms duration, colonic manometry outcome and initial surgical intervention on the need or the type of the subsequent surgical procedure.

Conclusion: The present study shows that in children with intractable chronic constipation colonic manometry may predict the clinical outcome of the surgical treatment, highlighting its role in the process of decision-making. Our data did not identify any predictors of unfavourable outcome. Further prospective data are needed to confirm our findings.

Disclosure of interest: None declared.
Efficiency and Immunologic Effects of Synbiotics in Children with Functional Abdominal Pain

Ayşegül Otuzbir¹, Tanju B. Özkaran¹, Taner Özgür¹, Ülkü Şahin¹, Derya Altay¹, Ferah Budak², Selçuk Kaya³

¹Uludağ University Faculty of Medicine, Pediatric Gastroenterology, Bursa, Turkey
²Uludağ University Faculty of Medicine, Bursa, Turkey
³İzmir Katip Çelebi University Faculty of Medicine, İzmir, Turkey

Objectives and study: Data about the treatment of FGDs associated with abdominal pain is limited; and there are few placebo controlled studies. Intestinal microbiota has important effects on maturation of gastrointestinal epithelia, formation of mucosal barrier, visceral hypersensitivity, intestinal immune response and motility; and considered to play a major role in pathogenesis of FGDs. Probiotics, prebiotics and synbiotics has substantial effects on intestinal microbiota and dysbiosis. Regarding the causes of functional abdominal pain and dyspepsia in children, we aim to investigate the efficacy of probiotics and synbiotics in treatment and their effects on levels of pro and anti-inflammatory cytokines in serum.

Methods: Patients presented with recurrent abdominal pain and diagnosed as functional abdominal pain and functional dyspepsia (Rome III Criteria) in Uludağ University Medical Faculty Pediatric Gastroenterology, Hepatology and Nutrition department between January 2015 and May 2015 are enrolled in the study. Study was designed and conducted as double blind and placebo controlled. Cases were divided into two groups as subject group (group 1, n=39) and control group (group 2, n=41) according to their time of admittance. Pain intensity and frequency, number of days of school without attendance, limitation of daily activities and serum levels of proinflammatory (TNF α, IFN γ) and anti-inflammatory (IL-10, TGF β, IL-13) cytokines were evaluated both at the beginning and at the end of the study. Treatment success (resolution of pain) and rate of reduction of complaints were also evaluated following the treatment. Associations between variables were evaluated using statistical program, ‘SPSS 16.0 for Windows’.

Results: Eighty patients with functional abdominal pain and dyspepsia were enrolled. Mean age was 11.48±3.86 (mean ±SD) years. Forty six of patients (%57.5) were girls and 34 (%42.5) were boys. We found no statistical difference in the presence of symptoms, pain intensity and frequency, location and duration of pain between groups. (p>0.05). Pre-treatment levels of serum IL-13, IL-10, IFN γ, TGF β, TNF α were similar (p>0.05). Complete resolution after 8 weeks of treatment was achieved in 25 patients (%58.1) in group 1 and 18 patients (%41.9) in group 2, difference was not statistically significant. (p>0.05). Rate of reduction in complaints was higher in group 1 (80.64±34.47) than group 2 (63.78±42.24); the difference was slightly significant (p=0.05). Post- treatment serum levels of IL-13, IL-10, IFN γ, TGF β, TNF α were similar between groups (p>0.05).

Conclusion: Pathophysiology of FGDs includes genetic, environmental, familial, psychosocial factors as well as gastrointestinal motility, impaired brain-gut axis, dysregulation of mucosal immunity, dysbiosis, dysfunction of mucus secretion and barrier formation. We tried to evaluate the efficacy and immunologic effects of probiotics in this complex disease group. We believe our study can lead to other studies investigating dose, duration and choice of probiotics in FGDs; and also their effect on cytokine levels.

Disclosure of interest: The authors have no competing interest.
Prevalence of small intestinal bacterial overgrowth in children with functional gastrointestinal disorders

Banu Bal Çermik¹, Ezgi Yalcin¹, Emel Torun¹, Selim Gokce¹

¹Bezmialem Vakif University, Istanbul, Turkey

Objectives and study: Small intestinal bacterial overgrowth (SIBO) is characterized by abnormally increased amounts of colonic type bacterial population in the small intestine. Clinical significance of SIBO is presence of chronic symptoms such as pain, bloating, diarrhea as in functional gastrointestinal disorders (FGID). The role of SIBO in functional disorders in children and adolescents is controversial. The aim of this study was to investigate prevalence of SIBO as assessed by lactulose H₂ breath test (LBT) in children with FGID.

Methods: Consecutive children diagnosed with FGID according to Rome III criteria were enrolled in this study. A questionnaire was administrated regarding abdominal pain, bloating and bowel movement disorders. All patients underwent a LBT to assess for SIBO. An abnormal LBT was defined as a basal H₂ excretion of ≥ 20 ppm or an increased H₂ excretion of >20 ppm before 90 min.

Results: One hundred twenty one patients children (56 boys; 46%) aged to 5 to 18 years were enrolled. Patients were diagnosed irritable bowel syndrome (n=20, 16,5%), functional dyspepsia (n=46, 38%) and functional abdominal pain (n=55, 45,5%) according to Rome III criteria). Prevalence of abnormal LBT result was 25% (n=31) in patient with FGID. SIBO prevalence was 25% (n=5) in irritable bowel syndrome, 19% (n=9) in functional dyspepsia and 31% (n=17) in functional abdominal pain. All of the patients diagnosed with SIBO were treated with non-absorbable antibiotics and showed improvement in clinical symptoms.

Conclusion: Small intestinal bacterial overgrowth is frequent in children with FGID. Placebo-controlled interventional studies are needed to determine if eradication of SIBO will lead to symptom improvement in these children.

Disclosure of interest: None Declared.
Intragastric pressure measurement during nutrient intake: a novel minimally invasive method to measure gastric accommodation in functional dyspepsia.

Carbone Florencia¹, Tack Jan¹, Hoffman Ilse²

¹University Hospitals Leuven, Gastroenterology, Leuven, Belgium
²University Hospitals Leuven, Pediatrics, Leuven, Belgium

Objectives and study: Functional dyspepsia (FD) in pediatrics is defined as the presence of upper abdominal symptoms in the absence of organic or metabolic disease likely to explain the symptoms. Impaired gastric accommodation (GA) is one of the main proposed pathophysiological mechanisms. The gastric barostat is the gold standard to measure GA. However, this procedure is very invasive and it might alter the normal gastric physiology. We proposed the measurement of intragastric pressure (IGP) during nutrient intake as a potential alternative for assessing GA. This technique uses a thin manometry (HRM) catheter that measures the IGP over the entire length of the stomach. The aim of this study is to introduce the HRM as new minimally invasive technique to measure GA and nutrient tolerance in children.

Methods: The HRM probe and a second infusion catheter were positioned in the stomach of the subjects. The IGP was measured before and during the intragastric infusion of a nutrient drink (300 Kcal, 60 ml per minute). The patients were asked to score their hunger, satiation and epigastric symptoms at 5-minute intervals. The experiment ended when the subjects scored maximal satiation at 1-minute intervals on a scale graded from 0–5 (1, threshold; 5, maximum satiety).

Results: 13 FD pediatric patients (92% female, 14.8 ± 0.8 years old, BMI: 19.5±0.8) and 12 healthy volunteers (HVs) (100% female, 22.2 ± 0.4 years old, BMI: 21.2 ± 0.3) were recruited. In both groups, intragastric infusion of nutrient drink induced a rapid drop in proximal stomach IGP. The average AUC change from baseline was -44.7±11.0 mmHg in patients and -48.4±24.1 mmHg in HVs. Patients tended to score maximal satiation at lower volumes compared HVs (433.9±64.2 ml and 600.0±67.6mL respectively, p=0.01). All FD patients and HVs tolerated the catheters and could finalize the study.

Conclusion: The IGP measurement during intragastric nutrient drink infusion is a promising method to assess GA accommodation and nutrient tolerance.

Disclosure of interest: None declared.
Is anorectal manometry useful in a gastroenterology pediatric unit?: our 10 years experience in a tertiary hospital

Mar Tolín Hernani1, César Sánchez Sánchez1, Guillermo Alvarez Calatayud1, Pablo Uriol2, Dario Martínez2, Belen González García3

1H. Materno Infantil. H.G.U. Gregorio Marañón, Pediatric Gastroenterology and Nutrition, Madrid, Spain
2Universidad Complutense, Facultad de Medicina, Madrid, Spain
3H. Materno Infantil. H.G.U. Gregorio Marañón, Nursing Department, Madrid, Spain

Introduction: Anorectal manometry can assess motor parameters of the anal sphincter, both at rest and simulated physiological conditions, specially in children diagnosed with constipation. This technique lets us know about anorectal continence, rectal sphincter function and sensitivity, and can be used for therapeutic purposes (biofeedback) and it lets us discriminate between organic or functional constipation.

Objectives: To analyze the results of anorectal manometry performed in children referred for constipation, abdominal distention, delayed meconium elimination, encopresis and incontinence to our Pediatric Gastroenterology Department in our hospital from January 2004 to November 2015.

Methods: Longitudinal retrospective study analyzing data from anorectal manometry performed from January 2004 to November 2015. We use perfused catheters and intrarectal balloon distension for stimulus. Manometric variables analyzed: resting sphincter pressure-pressure of internal anal sphincter (IAS), squeeze sphincter pressure- external anal sphincter (EAE), presence of recto-anal inhibitory reflex (RAIR), and critical volume capable of triggering sphincter response as well as the correlation between the data and final diagnosis by rectal biopsy in suspected cases of Hirschsprung disease. Statistical analysis was performed using SPSS 18.

Results: A total of 261 manometries performed. 93 girls and 168 boys with an average age of 51 months (range 0-180 months) were studied. Average annual manometries made were 21. In our study we found following data:
- Constipation (129 patients (49%), mean age 43 months): 51 (40%) were normal manometry and 74 (60%) showed high resting sphincter pressure. In all cases, except in one patient, RAIR was preserved, 19 cases needed higher balloon volumes to trigger it (> 50 ml).
- Abdominal distention (20 patients (7.7%), mean age 25 months): 15 (71%) normal manometry, 5 (23.8%) with hypertonic sphincter, without dilatation of rectal vault. RAIR was present in all of them.
- Delayed meconium elimination (42 patients (16.1%), mean age 7.5 months): 19 (50%) normal manometry, 10 (26%) sphincter hypertension and 11 patients (26.2%) preset studies compatible with Hirschsprung disease (absence of RAIR). Of these eleven patients, the disease was confirmed in ten of them by rectal biopsy. In our series, there are five patients in which RAIR was detected and who were later diagnosed with Hirschsprung's disease.
- Encopresis (37 patients (14%), mean age 92 months): 9 normal studies (24.3%) and 26 (70.3%) with hypertonic sphincter with increased basal tone and the high balloon volumes to get RAIR and high intensity voluntary contraction.
- Incontinence (34 patients (13%); mean age 145.8 months): 7 normal manometry (20.6%) and 20 (58.8%) with sphincter hypotonia and decreased voluntary contraction in almost half of patients.

Conclusions: The main indication of anorectal manometry in our series was constipation, detecting results similar to previous studies.
- This technique is essential in patients with delayed elimination of meconium as an initial screening of Hirschsprung's disease because it has a high specificity.
- It is also useful as a diagnostic and therapeutic tool for patients with constipation and/or incontinence (biofeedback), differentiating organic and functional constipation.

Disclosure of interest: None Declared.
How can we measure orocecal transit in critically ill children? Our hydrogen breath test lactulose experience

César Sánchez Sánchez¹, Jorge López², Mar Tolín Hernani¹, Guillermo Alvarez Calatayud¹, Sarah N. Fernandez², Jesús López-Herce²

¹H. Materno Infantil. H.G.U. Gregorio Marañón, Pediatric Gastroenterology and Nutrition, Madrid, Spain
²H. Materno Infantil. H.G.U. Gregorio Marañón, Pediatric Intensive Care, Madrid, Spain

Introduction: Orocecal transit time has been related with gastrointestinal motility disorders and can be measure by exhaled hydrogen after the administration of lactulose (lactulose e-H₂ test).

Objectives and study: The objectives of this study are to assess whether it is possible to carry out this test in critically ill children (spontaneous breathing and invasive mechanical ventilation) and to analyze if the results are consistent with clinical findings.

Patients and methods: Children admitted to the pediatric Intensive Care Unit (PICU) for more than three days were included in a prospective observational study performed. Those with gastrointestinal disease prior to admission were excluded. A modified technique to obtain eH₂ from the ventilator tubes were performed. Relationships between demographic and clinical data and lactulose e-H₂ test measurements were analyzed.

Results: Sixteen patients (37.5% boys) were included in this study. Median age was 19 months (5-86.5 m). Five patients (31.2%) were breathing spontaneously but lactulose e-H₂ test could not be performed. Eleven patients with invasive mechanical ventilation were studied and lactulose eH2 test was performed successfully in all of them. Seven patients (63.3 %) did not show an eH₂ peak during the 6 hour-study after lactulose intake. The other four, showed a median time from lactulose intake to a 10 ppm-eH₂ peak of 130 min (78.7 – 278.7 min). There were no differences in any of the variables between children with and without an eH₂ peak. Children with an eH₂ peak had intestinal movements earlier than those without one [6.5 (1.5-38.5) vs 44 (24-72) hours], although no significant differences were found. There were no side effects from lactulose intake or from the modified technique to obtain eH₂ from the ventilator tubes.

Conclusion: Although the designed adaption is useful for collecting breath samples, lactulose-eH₂ test is not useful for measuring OCTT in critically ill children because of difficulties at the high number of measurements that must be performed for a long period of time.

Disclosure of interest: None Declared.
Funding FEDER funds
Probiotics for the management of chronic constipation in children: A Cochrane systematic review

Morris Gordon¹, Chris Wallace², Joe Stone², Adrian Thomas³, Anthony Akobeng⁴

¹University of Central Lancashire, School of Medicine, Manchester, United Kingdom
²Blackpool Victoria Hospital, Blackpool, United Kingdom
³Royal Manchester Childrens Hospital, Manchester, United Kingdom
⁴Sidra Medical and Research Center, Sidra, Qatar

Objectives and study: Chronic constipation is one of the most common paediatric problems seen within primary, secondary and tertiary care. It is hypothesised that the use of probiotics might alter the growth of bacteria in the bowel, promote normal gut physiology and reduce constipation symptoms. Given the recent growth in published studies in this area it is necessary to produce a new and focused synthesis of this evidence by deploying a robust methodology to ensure that there can be a contemporaneous impact on clinical practice.

Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL and the Cochrane Inflammatory Bowel Disease and Functional Bowel Disorders Group Specialised Trial Register were searched (Inception – July 2015). Manufacturers of probiotics were contacted to identify unpublished trials. References of trials were also searched. Abstracts were considered for inclusion if full details to judge inclusion were offered or available from the authors. Randomised controlled trials (RCTs) were eligible for inclusion. Data extraction and assessment of methodological quality of included studies were independently performed by two authors. Analysis was completed in accordance with the intention to treat approach.

Results: The search yielded 1529 results, with 25 papers screened and one supplied in unpublished form. Seven placebo controlled studies (n = 496) met the inclusion criteria and were included in the review. All studies compared probiotics with placebo, but two gave all participants lactulose as concomitant therapy. The studies ranged in length from 3 to 12 weeks. The risk of bias was low for randomisation for five trials and moderate for two trials. Allocation concealment was low in one study and unclear in the others. All studies were double blinded, but one gave no details of how this was achieved. The risk of bias was low or unclear in all studies for incomplete outcome data and selective reporting. Meta-analysis of four studies (n=312, patients not on concomitant lactulose) found a statistical significant increase in the frequency of defecation using probiotics compared to placebo (MD 1.09; 95% CI 0.17 to 2.01). This result did not change on sensitivity analysis using a fixed effects model. Meta-analysis of these four studies found no statistical significant difference in adverse events between probiotics and placebo (OR 0.33; 95% CI 0.03 to 3.23).

Conclusion: The evidence from the published suggests superior efficacy of probiotics for chronic constipation in children when compared with placebo. There is no difference in adverse events, suggesting safety. The evidence base is of moderate quality and relatively small. Further research to investigate the long term impact of probiotic therapy on chronic constipation is suggested.

Disclosure of interest: “None Declared”. MG has received travel grants from various pharma companies for travel to scientific meetings. These companies have had no involvement with the planning, completion or write up of this or any other work.
Do Italian pediatricians apply the 2014 NASPGHAN-ESPGHAN guidelines for the diagnosis and management of Functional Constipation?

Cinzia Ciullo\textsuperscript{1}, Isabella Mezzina\textsuperscript{2}, D'Abramo Fulvio Salvatore\textsuperscript{3}, Massimiliano Praitano\textsuperscript{4}, Flavia Indrio\textsuperscript{5}, Marica Gentile\textsuperscript{6}, Ruggiero Francavilla\textsuperscript{7}, Fernanda Cristofori\textsuperscript{8}

\textsuperscript{1}Policlinico DI Bari-Giovanni XXIII Hospital, Bari, Italy
\textsuperscript{2}Università DI Bari, Italy, Dipartimento Interdisciplinare DI Medicina, Sezione DI Pediatria., Bari, Italy
\textsuperscript{3}Ospedale Giovanni XXIII, Bari, Italy
\textsuperscript{4}Policlinico Bari, Bari, Italy
\textsuperscript{5}Giovanni XXIII Hospital, Department of Pediatrics, Bari, Italy
\textsuperscript{6}Giovanni XXIII Hospital, Bari, Italy
\textsuperscript{7}University of Bari Aldo Moro/Department of Interdisciplinary Medicine, Bari, Italy
\textsuperscript{8}Ss. Annunziata Hospital/ Pediatric Department, Taranto, Italy

Objectives and study: In 2014 ESPGHAN and NASPGHAN have formulated guidelines for managing functional constipation (FC).

The purpose of this study is to examine how Italian paediatricians approach functional constipation and how closely their approaches adhere to the guidelines.

Methods: An anonymous multiple-choice questionnaire was developed and e-mail distributed to paediatricians (paediatric consultants (PC), paediatric general practitioners (PGP) and paediatric residents (PR)).

Results: A total of 189 responses were received (35% PC, 38% PGP, 27% PR). Of these, 63.0% reported being unfamiliar/slightly familiar with the guidelines(62.2% PC,62.7%PGP, 65.1%PR). Only 3% identified all Rome III criteria for the diagnosis of FC while 17% identified all the correct alarm signs/symptoms for organic causes of constipation. 64% of the responders didn’t know Bristol Stools Form scale.All responders based FC diagnosis on history and physical examination as suggested in guidelines, however 9.5% on laboratory investigation and 7.4% on imaging tests. The most common non pharmacological intervention used was toilet trainings (79.6%) followed by increased intake of liquids (70.7%) and fiber(61.9%). The most common initial interventions for constipation with faecal impaction included bowel cleafout (84.3%) followed bopolyethylene glycol (PEG) 1-1.5 g/kg/day (44.8%). PEG without electrolyteswas the most commonly prescribed maintenance medication(48.9%), followed by PEG with electrolytes(38%) and lactulose (34%).

Conclusion: Significant differences in knowledge and practice patterns exist regarding the approach to paediatric FC. Identification of knowledge gaps may be useful to develop educational materials to improve proper diagnosis and treatment of FC.

Disclosure of interest: no disclosure of interest.
Transverse rectal diameter and thickness of the anterior wall of the rectum in children with and without functional constipation

Daniela Pop¹, Otilia Fufezan², Simona Tătar¹, Dorin Farcău¹

¹University of Medicine and Pharmacy "Iuliu Hatieganu", Cluj-Napoca, Romania
²Clinical Emergency Hospital for Children, Cluj-Napoca, Romania

Objectives and study: Abdominal ultrasound is an investigation that may be used to objectify the severity of functional constipation in children. The aim of the study was to compare the values of the transverse rectal diameter and thickness of the anterior wall of the rectum in children with and without functional constipation, in different age groups.

Methods: The diagnosis of constipation was based on the Rome III criteria for functional constipation in children. We collected the clinical data using written questionnaires based on the Rome III criteria that were filled in by the parents, in both constipated children and children without constipation. The study took place between October 2014 and 30th November 2015. The transverse rectal diameter and the thickness of the anterior wall of the rectum were measured using transabdominal ultrasound.

Results: A total of 45 children entered the study. They were divided in 4 groups: Children between 0 and 4 years with normal intestinal transit (n=13, 7 boys), children between 0 and 4 years diagnosed with functional constipation (n=9, 4 boys), children between 4 and 16 years of age without constipation (n=11, 3 boys) and children with ages between 4 and 16 years diagnosed with functional constipation (n=12, 7 boys). The mean value of the transverse rectal diameter in children between 0 and 4 years of age was 21 mm in the group with normal defecation pattern and 33 mm in constipated children. The mean value of the thickness of the anterior wall of the rectum in the same age group was 1.75 mm and 2.4 mm for children with normal bowel movements and children with functional constipation, respectively. For the children with ages between 4 and 16 years the mean value of the transverse rectal diameter was 27 mm for children with normal defecation and 45 mm for children with constipation. We found mean values of the thickness of the anterior wall of the rectum in children between 4 and 16 years of 2.3 mm for children with normal bowel movements and 3.8 mm for children with functional constipation.

Conclusion: We found statistically significant differences between the values of the transverse rectal diameter or the thickness of the anterior wall of the rectum (as measured by abdominal ultrasound) in children with the symptoms of functional constipation as compared with children with normal defecation pattern.

Disclosure of interest: The authors have no conflict of interest to disclose.
GASTROENTEROLOGY: GI motility, GERD and functional GI disorders

G-P-241

Diagnosis and management of esophageal achalasia in children.

Dorota Jarzębicka¹, Joanna Sieczkowska¹, Jaroslaw Kierkus¹, Maciej Dadalski¹, Marek Woynarowski¹, Grzegorz Oracz¹

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Achalasia is a primary esophageal motility disorder. Clinical presentation may vary from mild symptoms to the patient’s starvation. Prompt differential diagnosis and early treatment warrants successful outcome in the majority of cases, but still passes a lot of time from the onset of symptoms to diagnosis. The main purpose of the study was to analyze the clinical presentations, diagnostic approach and assessment of treatment methods.

Methods: We performed the retrospective analysis of course disease, diagnostic methods and management in esophageal achalasia in children. Symptoms questionnaire was sent to all patients.

Results: Fifteen patients with achalasia diagnosed at the mean age of 11 years (range 4-16) were included to the study. Mean period of patient follow-up was 7.6 years (range 1-19). Mean age of symptoms onset was 8.6 years (range 1-14). Mean time from first symptoms to diagnosis was 2.5 years (range 0.5–9). All patients were treated with pneumatic dilatation (PD), and required 1-9 procedures of PD (mean 2). 2/15 patients had also 2 procedures of PD after surgical treatment. 13/15 patients (87%) undergo Heller’s myotomy (LHM). 2/15 patients without LHM were treated with PD and requires 3 and 1 procedure, respectively. Symptoms reported by patients before, after treatment and after follow-up period are presented in the Table. After treatment symptoms reported by patients were with significantly lower intensity.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Dysphagia</th>
<th>Vomiting</th>
<th>Chest pain</th>
<th>Heartburn</th>
<th>Cough</th>
<th>Weight loss</th>
<th>Slow eating</th>
<th>Choking</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before treatment</td>
<td>15</td>
<td>15</td>
<td>11</td>
<td>5</td>
<td>8</td>
<td>13</td>
<td>14</td>
<td>8</td>
</tr>
<tr>
<td>(Number of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After treatment</td>
<td>14</td>
<td>10</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>4</td>
<td>12</td>
<td>3</td>
</tr>
<tr>
<td>(Number of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>After follow-up</td>
<td>12</td>
<td>8</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>3</td>
<td>11</td>
<td>4</td>
</tr>
<tr>
<td>(Number of patients)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
**Conclusion:** Achalasia is a rare disease in childhood, with a long period from first symptoms to diagnosis. Endoscopic procedures followed by surgery are quite effective treatment option, however not guarantee relent of symptoms.

**Disclosure of interest:** None Declared.
Do children just grow out of Irritable Bowel Syndrome?

Eleonora Giannetti¹, Elisa Sciorio², Vincenzo Coppola², Marco Maglione¹, Erasmo Miele¹, Annamaria Staiano¹

¹Federico II University, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy
²Federico II University, Department of Translational Medical Sciences, Naples, Italy

Objectives and study: Irritable bowel syndrome (IBS), as defined by the Rome III criteria, includes weekly symptoms of abdominal pain/discomfort and changes in bowel patterns: constipation (C-IBS), diarrhea (D-IBS) or alternating C and D (A-IBS). Despite its high frequency in children, few data exist on its natural history.

We investigated the evolution of gastrointestinal symptoms over time in a cohort of IBS children, whose diagnosis was made before January 2014.

Methods: This is an observational, prospective, single-center study. We enrolled 83 IBS patients with a follow-up of at least 24 months from diagnosis. Once diagnosed, patients were prospectively followed at our tertiary care center and reassessed after 24 months. Both at diagnosis and after 24 months, patients and/or their parents were asked to complete the IBS symptoms questionnaire, and a score of stool consistency according to the Bristol Stool Form Scale was obtained. Moreover, we recorded which therapeutical strategy had been followed in each patient. At diagnosis, all children were reassured by oral and written instructions. Families were explained that IBS is a functional disorder with no organic cause and were educated to face episodes of abdominal pain by attempting to reduce patient’s anxiety.

Results: Eighty-three children with a diagnosis of IBS had been followed for at least 24 months (median age 11 yrs, range, 4-16.4 yrs; 53 males). At diagnosis, C-IBS was the most prevalent subtype, affecting 34 out of 83 children (41%). D-IBS and A-IBS were reported in 25 (30.1%) and 22 (26.5%) children, respectively. Diagnosis required no invasive investigations in most patients, and only 5 subjects (6%) underwent colonoscopy. Forty-seven (56.6%) patients received no medical treatment, whereas polyethylene glycol (PEG), probiotics and trimebutine were prescribed to 9 (10.8%), 24 (28.9%) and 3 (3.6%) subjects, respectively.

At 24 months of follow-up, 48 children (57.8%) reported resolution of symptoms, without significant differences between subtypes (C-IBS 43.7%, D-IBS 27%, A-IBS 29.2%, p=0.49). Of these 48 patients, 30 (62.5%) had been only reassured and 18 (37.5%) were prescribed medical treatment (p=0.26). Administered medications were PEG in 6 (33.4%, all belonging to the C-IBS subgroup), probiotics in 10 (55.5%) and trimebutine in 2 (11.1%) subjects.

Despite statistical significance was not achieved, the proportion of patients reporting resolution of symptoms was higher in the group receiving no medical treatment than in the group receiving probiotics (63.8% versus 41.6%, p=0.08).

Among C-IBS patients, the proportion of patients reporting resolution of symptoms was not significantly different between the group treated with PEG and the group receiving no therapy other than reassurance (67% and 40%, respectively, p=1).

Of the subjects still reporting symptoms at 24 months, 22 out of 35 (63%) belonged to the A-IBS subtype, whereas 7 (20%) and 6 (17%) reported D-IBS and C-IBS, respectively. In 14 cases (40%), changes in IBS subtype were reported (7 subjects from C-IBS to A-IBS, 6 from D-IBS to A-IBS, and 1 from A-IBS to C-IBS).

Conclusion: Children with IBS are likely to show spontaneous resolution of symptoms over a 24-month follow-up, regardless of subtypes. Treatment with probiotics, trimebutine or PEG was not associated with an increase in symptoms resolution.

Disclosure of interest: None Declared.
**Analysis of gastric and duodenal eosinophils in children with abdominal pain related functional gastrointestinal disorders according to ROME III criteria**

Eun Hye Lee¹, Hye Ran Yang², Hye Seung Lee³

¹Seoul National University Bundang Hospital, Pediatrics, Seongnam-Si, Gyeonggi-Do, Rep. of South Korea
²Seoul National University Bundang Hospital, Seoul National University College of Medicine, Pediatrics, Seongnam-Si, Gyeonggi-Do, Rep. of South Korea
³Seoul National University Bundang Hospital, Pathology, Seongnam-Si, Gyeonggi-Do, Rep. of South Korea

**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 implicated in the pathophysiology of AP-FGID in adults. The aim of this study was to evaluate the association of gastric and duodenal eosinophilia with pediatric AP-FGID.

**Methods:** In total, 105 pediatric patients with AP-FGID were recruited and classified into 4 subgroups based on the ROME III criteria. Eosinophil counts in the gastric and duodenal tissues of children with AP-FGID were compared to those from normal pathology references or those of children with Helicobacter pylori infection. Tissue eosinophil counts were also compared among the 4 subtypes of AP-FGID.

**Results:** Eosinophil counts in the gastric antrum and body were significantly higher in children with AP-FGID than normal reference values. Duodenal eosinophil counts were higher in children with AP-FGID, but not significantly when compared with normal reference values. There were no significant differences in eosinophil counts of the stomach or duodenum among the 4 subtypes of AP-FGID. Eosinophils counts in the gastric antrum and body were significantly higher in children with Helicobacter pylori infection than in those with AP-FGID. Duodenal eosinophilia was prominent in cases of Helicobacter pylori infection, but not statistically significant when compared with AP-FGID.

**Conclusion:** Our study revealed that gastric eosinophilia is associated with AP-FGID in children, regardless of the subtype of functional abdominal pain. This suggests some contribution of gastrointestinal eosinophils in the development of pediatric AP-FGID.

**Disclosure of interest:** None Declared.
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-P-244

**Combined multichannel intraluminal impedance-ph (MII-pH): a step forward towards reference values**

Fernanda Cristofori¹, Ruggiero Francavilla², Claudia Fontana³, Cinzia Ciullo⁴, Fulvio Moramarco³, Marica Gentile⁵, Antonietta Villirillo³, Martina Valenti⁶, Francesco Cresi⁶

¹Ss. Annunziata Hospital/ Pediatric Department, Taranto, Italy
²University of Bari Giovanni XXIII Hospital, Paediatrics, Bari, Italy
³Perrino Hospital, Pediatrics, Brindisi, Italy
⁴Policlinico DI Bari-Giovanni XXIII Hospital, Bari, Italy
⁵Giovanni XXIII Hospital, Bari, Italy
⁶Sant’Anna-Regina Margherita Hospital, Neonatology, Turin, Italy

**Objectives and study:** Multichannel intraluminal impedance (MII) monitoring is a test used in assessing gastroesophageal reflux (GER). Currently there is only one study on normal/reference values to identify children or infants with abnormal reflux. Study aim is to derive reference values for MII-pH parameters.

**Methods:** We evaluated MII tracings of patients referred for one or more GER symptoms where it wasn’t demonstrated a significant association symptom-reflux. We excluded tracings with durations <20 h, from patients who had reflux index (RI) >3%, positive association of GER with symptoms and from patients on anti-reflux medications.

**Results:** Study population consisted of 114 patients (69M; median age 3.3 months IQR 0.8–41.4): 34 neonates and 80 children. We identified an average of 53.3 (SD±27.8) reflux per patient: 45.8% (SD±23%) acids (AC) and 54.2% weakly acidic (WA); weakly alkaline reflux accounted for <0.1% of total reflux. The average duration of each reflux was 19.5 seconds (SD ±8.1 s). Mean WA reflux frequency was 2.02 episode/h (1.46–2.45 25–75 centile) in neonates and 1.06 episode/h (0.41–1.52) in children. Mean AC reflux frequency was 0.98 episode/h (0.59–1.14) in neonates and 1.16 episode/h (0.62–1.72) in children. We demonstrated the overall frequency of WA reflux decreases significantly in children, compared to both infants and neonates. Overall frequency of reflux decreases significantly during the fasting compared to the post-prandial period.

**Conclusion:** The analysis of traces of patients referred for GER symptoms and in which the disease was excluded (low RI, no temporal correlation of GER with symptoms) has resulted in a series of age related references values that can be used as a guide for reporting MII tests.

**Disclosure of interest:** None Declared.
Functional gastrointestinal disorders in children from low socioeconomic status and Helicobacter pylori infection

Francisca Jaime¹, Andrea Villagrán¹, Caroll Hernández¹, Marlene Ortiz¹, Paula Troncoso¹, Paul Harris¹

¹Pontificia Universidad Católica de Chile, Pediatric Gastroenterology and Nutrition, Santiago, Chile

Objectives and study: Most studies on functional gastrointestinal disorders (FGIDs) in children are based on data from the northern hemisphere. There is scarce literature on South American population, and even less on children from low socioeconomic status (SES) where Helicobacter pylori infection is endemic. The aim of this study is to determine the frequency of FGIDs in school children from low socioeconomic status, as well as to evaluate demographic factors associated and the relationship between these disorders and H. pylori infection.

Methods: Between October and December 2013, students from three public schools in Chile with low SES were included. Exclusion Criteria included use of antibiotics, proton pump inhibitors or histamine receptor inhibitors within the previous month. To evaluate the presence of FGIDs according to Rome III criteria, participants and/or their parents completed the Rome III Diagnostic Questionnaire for the Pediatric FGIDs in its Spanish version provided by The Rome Foundation and a survey that included: number of people living in the same house, educational level of the head of household, history of breastfeeding (in months), family history of gastric cancer and symptoms within the last three months: fever and weight loss. These symptoms were considered as warning signs, so those who presented them were excluded in the evaluation of FGIDs. In those participants who also accepted to do so, the presence or absence of H. pylori infection through ¹³C urea breath test (UBT) and ¹³C Infrared Spectrometer was determined, considering positive tests those with a delta over baseline ≥ 4‰. This project had approval of the Institutional Review Board (nº13-342) from the local University and complies with the Declaration of Helsinki.

Results: 506 children were included, 48% were male, with a median age of 15.7 years (range 7.1-19.6). In the overall sample, 190 students (37.5%) had alarm signs, and were excluded for the assessment of FGIDs. 20% of the sample (95% CI 16.7-23.7) met criteria for a FGIDs. The most frequent were: functional constipation 6.7%, aerophagia 6.3%, irritable bowel syndrome 4.9% and abdominal migraine 4.6%. Of those who met diagnostic criteria for any FGIDs, 29.7% met criteria for more than one. In multivariate analysis, variables associated with the presence of FGIDs were: educational level of the household head (primary or less) (adjusted OR 2.64, 95% CI: 1.50-4.66), family history of gastric cancer (yes) (adjusted OR 2.38, 95% CI: 1.21-4.69) and months of breastfeeding (adjusted OR 1.02, 95% CI: 1.004-1.049). Of these, 55.9% had a positive result (95% CI 50.7-60.9). In multivariate analysis, only the presence of abdominal pain (yes or no) was associated with increased likelihood of infection by H. pylori (OR 1.58, 95% CI 1.04-2.41) and not the presence of FGIDs in general and/or its subgroups.

Conclusion: FGIDs are common in low SES students. A low educational level of the household head was the most strongly associated risk factor to develop FGIDs. In this study, there was no relationship between the presence of H. pylori and FGIDs.

Disclosure of Interest: None declared. This study was supported by Proyecto Puente UC #15/2013 and Fondecyt #1130387.
Functional gastrointestinal disorders in Greek children: Prevalence and significant socioeconomic correlates

George Chouliaras1, Ilias Bouzios1, George Chrousos1, Vassiliki Gemou-Engesaeth1, Eleftheria Roma1

1University of Athens, Athens, Greece

Objectives and study: The functional gastrointestinal diseases (FGIDs) comprise a diverse group of disorders with no identifiable organic cause. They are one of the most common causes for seeking medical advice in childhood, resulting in high economic burden. The longstanding nature of these disorders generates significant anxiety and disrupts the everyday life of the affected families. In this large-scale, population-based study from Greece we studied the entire spectrum of FGIDs in children and adolescents and assessed the impact of socioeconomic geography on the distribution of FGIDs.

Methods: The study was conducted by the 1st Department of Pediatrics of the University of Athens, after obtaining approval by the authorities and written consent by the legal representatives of the participants. A total of 1588 children (6-18 years) were recruited from public schools. Collected data included the Greek official translation of the ROME-III questionnaire, which was used to diagnose the following FGIDs: functional dyspepsia, irritable bowel syndrome (IBS), abdominal migraine, functional abdominal pain (FAP), functional abdominal pain syndrome (syndromic FAP), functional constipation, non-retentive fecal incontinence (NRFI), aerophagia, rumination and cyclic vomiting syndrome (CVS). Socioeconomic data included: geographic region, gender, age, parental origin, parental educational level, family’s economic status, number of adults and children at home, parental presence at home, TV-exposure, report of bullying, presence of a person with a severe health problem at home and level of physical exercise. Statistical methodology included univariate and multivariate analyses (logistic regression models).

Results: The prevalence of any-FGID was 23.3%. In details: functional constipation 13.9%, abdominal migraine 5.6%, aerophagia 3.5%, IBS 3.0%, FAP 0.88%, NRFI 0.5%, rumination 0.5%, CVS 0.5%, functional dyspepsia 0.44% and syndromic FAP 0.44%. The results of the multivariate analysis are presented in Table 1. The prevalence of pain-related FGID was 9.3%. Girls were 2.4 times more likely to report a pain-related FGID (OR= 2.4, 95% ci: 1.6-3.5, p<0.001), bullying increased the likelihood of pain-related FGID by 90% (OR=1.9, 95% ci: 1.2-3.1, p=0.006) and children coming from families with a single adult had 1.4 times higher likelihood of pain-related FGID compared to two-adult families (OR=1.4, 95% ci: 1.1-3.3, p=0.023). In contrast, the presence of a person with a chronic health problem at home increased the probability of pain-related FGID by 2.1 times (OR=2.1, 95% ci: 1.3-3.6, p=0.004).

Table: Table 1. Logistic regression analysis on the probability of any-FGID

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Odds Ratio</th>
<th>95% ci</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical exercise (days per week)</td>
<td>none vs 4-7</td>
<td>1.43</td>
<td>0.016</td>
</tr>
<tr>
<td></td>
<td>1-7 vs 4-7</td>
<td>1.06-1.92</td>
<td></td>
</tr>
<tr>
<td>TV exposure (hours per day)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-3 vs 0-1</td>
<td>1.31</td>
<td>1.00-1.70</td>
<td>0.045</td>
</tr>
<tr>
<td>&gt;3 vs 0-1</td>
<td>2.14</td>
<td>1.30-3.52</td>
<td>0.003</td>
</tr>
<tr>
<td>Bullying</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>yes vs no</td>
<td>1.87</td>
<td>1.31-2.67</td>
<td>0.001</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>female vs male</td>
<td>1.29</td>
<td>1.01-1.66</td>
<td>0.040</td>
</tr>
<tr>
<td>Parental educational level</td>
<td>0.91</td>
<td>0.84-0.99</td>
<td>0.038</td>
</tr>
<tr>
<td>Number of children at home</td>
<td>1.17</td>
<td>1.03-1.33</td>
<td>0.015</td>
</tr>
<tr>
<td>Number of adults at home</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4 vs 2</td>
<td>2.00</td>
<td>1.19-2.37</td>
<td>0.009</td>
</tr>
<tr>
<td>1 vs 2</td>
<td>1.55</td>
<td>1.00-2.39</td>
<td>0.047</td>
</tr>
</tbody>
</table>
Conclusion: FGIDs are extremely common in the general pediatric population. Several socioeconomic factors, notably bullying, tv-exposure, physical exercise and the imbalance between the numbers of children and adults at home, significantly increase the probability of FGIDs in Greek children.

Disclosure of interest: No conflict of interest
Depression and Anxiety are Related to Various Functional Gastrointestinal Disorders in Adolescents

Munevver Bilgin1, 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: Functional gastrointestinal disorders (FGID) are related to depressive and anxiety disorders in adults. Although depression and anxiety prevalence are studied in individual FGID’s mainly IBS, their role in other FGIDs are largely unknown in early adolescence. In this study, we aimed to determine the prevalence of individual FGIDs in early adolescence by using Rome III questionnaire and tried to investigate their relationship to depression and anxiety.

Methods: Adolescents from 5th to 12th grade in two state schools were included. Half of the classrooms in each school were randomly selected and questionnaires containing previously validated Turkish versions of Rome III functional gastrointestinal disorders questionnaire, State-Trait Anxiety Inventory for Children and Children’s Depression Inventory were given alongside with survey for demographic data. WHO Anthro plus was used to determine body mass index z scores.

Results: Median age of adolescents was 13 years (range 10-18 yrs). 51.5% of the study population were female. According to the BMI, 5.4% and 7.3% of the study population were underweight and overweight respectively. Females had significantly higher scores in depression, and state and trait anxiety points with respect to males. Body mass index was not related to individual FGIDs. Prevalence of FGIDs and their relation to the depression and anxiety scores were given in Table 1.

Table 1: Prevalence of FGID’s and relation to depression and anxiety

<table>
<thead>
<tr>
<th>FGID</th>
<th>Prevalence</th>
<th>Depression</th>
<th>State Anxiety</th>
<th>Trait anxiety</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Scores, condition present vs absent</td>
<td></td>
<td></td>
</tr>
<tr>
<td>IBS</td>
<td>3.9%</td>
<td>19.40±8.13 vs. 12.54±7.17a</td>
<td>38.83±7.68 vs. 33.96±7.19a</td>
<td>42.97±7.40 vs. 36.35±7.80a</td>
</tr>
<tr>
<td>Abdominal migraine</td>
<td>6.2%</td>
<td>17.14±7.41 vs. 12.37±7.17a</td>
<td>37.90±8.63 vs. 33.68±7.06a</td>
<td>42.29±8.04 vs. 36.05±7.68a</td>
</tr>
<tr>
<td>Constipation</td>
<td>25.5%</td>
<td>15.28±7.39 vs. 11.65±6.97a</td>
<td>35.88±7.43 vs. 33.55±7.12a</td>
<td>39.28±7.71 vs. 35.95±7.62a</td>
</tr>
<tr>
<td>Non-retentive fecal incontinence</td>
<td>2.6%</td>
<td>16.38±7.53 vs. 12.56±7.28a</td>
<td>38.21±9.88 vs. 33.99±7.23c</td>
<td>41.00±9.83 vs. 36.52±7.79a</td>
</tr>
<tr>
<td>Aerophagia</td>
<td>5.8%</td>
<td>18.14±9.13 vs. 12.46±7.06a</td>
<td>38.15±8.80 vs. 33.95±7.12a</td>
<td>41.68±8.59 vs. 36.50±7.66a</td>
</tr>
</tbody>
</table>

*p<0.001, †p=0.01, ‡p=0.03, §p=0.04
Conclusion: Individual FGIDs were prevalent in adolescent school population. Depression and anxiety states were seem to be related to individual FGID’s in early adolescence. Therapies designed for FGIDs in this age group must take into account accompanying psychological disorders. Early childhood mental health support might have an important impact on adolescence FGIDs.

Disclosure of interest: Munever Bilgin: None declared, Gokhan Baysoy: None declared
The importance of combined 24-hour multichannel intraluminal impedance-pH monitoring for children with gastrointestinal symptoms suggesting gastroesophageal reflux disease

Iva Hojsak¹, Lana Ivković¹, Tena Trbojević¹, Zrinjka Mišak¹, Oleg Jadresin¹, Ivan Pavić², Sanja Kolacek³

¹Children's Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
²Children's Hospital Zagreb, Department of Pulmonology, Allergology and Immunology, Zagreb, Croatia
³Zagreb University Medical School, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia

Objectives and study: Gastroesophageal reflux disease (GERD) is common in pediatric patients, and 24-h multichannel intraluminal impedance (MII)-pH monitoring is considered a diagnostic method of choice; still MII-pH parameters in children are not standardized, and studies evaluating it are lacking. Therefore, the aim of this study is to determine the incidence of GERD in children who present with gastrointestinal (GI) symptoms suggestive of GERD evaluated by MII-pH and compare these results to results of pH-metry alone and endoscopy (macroscopic and pathohistological).

Methods: All children who underwent MII-pH monitoring due to GI symptoms suggestive for GERD from October 2013 to October 2015 in Children's Hospital Zagreb were retrospectively enrolled into the study. Inclusion criteria were GI symptoms suggestive for GERD (heartburn, epigastric pain, vomiting/regurgitation and back arching in infant) which lasted at least 4 weeks. Included parameters were age, gender, number of reflux episodes detected by pH-metry, number of reflux episodes (acidic, weakly acidic, non-acidic) detected by MII-pH and endoscopy finding if performed. Cohort was divided according to age to group 1: children < 1 years of age; group 2: 1 to < 9 years of age; and group 3: ≥ 9 years of age.

Results: Total of 133 patients met our inclusion criteria (73 female/60 male; mean age 9.2 years (0.19-18.0)). GERD was determined in 56/133 (42.1%) by MII-pH, and only in 21/133 patients (15.8%) by pH-metry alone. Difference in the number of reflux episodes between groups are presented in the Table 1. Endoscopy was performed in 77 (57.9%) children, and esophagitis was found in 32/77 (41.6%). Children with esophagitis had significantly higher number of total (mean 148.9 vs. 80.9; p<0.001), acidic (mean 28.1 vs. 21.5; p=0.02), weakly acidic (mean 86.9 vs. 47.1; p=0.009) and non-acidic reflux episodes (mean 33.9 vs. 14.6; p=0.02) detected by MII-pH, but not with pH-metry (reflux episodes: mean 42.8 vs. 34.1; p=0.07 and reflux index: 4.2% vs. 4.9%; p=0.1). Finding of esophagitis significantly correlated with the number of total reflux episodes (coef. 0.42, p<0.001), acidic (coef. 0.26, p=0.02), weakly acidic (coef. 0.3, p=0.008) and non-acidic (coef. 0.26, p=0.02) reflux episodes detected by MII-pH but not to reflux episodes detected by pH-metry alone (coef. 0.21, p=0.07).

Table:

<table>
<thead>
<tr>
<th>Group 1 (n=23)</th>
<th>Group 2 (n=33)</th>
<th>Group 3 (n=77)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of total reflux episodes</td>
<td>127.5 (30-239)</td>
<td>115.6 (4-306)</td>
<td>107.6 (1-395)</td>
</tr>
<tr>
<td>Number of acidic reflux episodes</td>
<td>28.7 (0-85)</td>
<td>24 (0-117)</td>
<td>22.4 (0-165)</td>
</tr>
<tr>
<td>Number of weakly acidic reflux episodes</td>
<td>82.2 (18-178)</td>
<td>67.7 (1-245)</td>
<td>63.2 (0-268)</td>
</tr>
<tr>
<td>Number of non-acidic reflux episodes</td>
<td>16.6 (0-57)</td>
<td>26.9 (0-152)</td>
<td>22 (1-131)</td>
</tr>
</tbody>
</table>
Table 1. Difference between the groups based on MII-pH finding; Kruskal–Wallis test; Post-hoc analysis: *Significant group 1 vs group 2 and group 1 vs group 3; ** Significant group 1 vs group 3.

**Conclusion:** Compared to pH-metry alone, pH-MII has a significantly higher probability of detection of GERD in all age groups. Based on our data pH-MII had strong correlation with endoscopically confirmed esophagitis. However, the number of children who underwent endoscopy was low in our study. Therefore, further studies are required.

**Disclosure of interest:** None Declared.
Probiotics for the management of functional abdominal pain in children: A Cochrane systematic review

Morris Gordon¹, Joe Stone², Adrian Thomas³, Anthony Akobeng⁴

¹University of Central Lancashire, School of Medicine, Manchester, United Kingdom
²Blackpool Victoria Hospital, Blackpool, United Kingdom
³Royal Manchester Childrens Hospital, Manchester, United Kingdom
⁴Sidra Medical and Research Center, Sidra, Qatar

Objectives and study: Functional abdominal pain is pain located in the abdomen that cannot be explained by any visible or detectable abnormality. It is hypothesised that the use of probiotics might alter the growth of bacteria in the bowel, promote normal gut physiology and reduce functional symptoms. Given the recent growth in published studies in this area it is necessary to produce a new and focussed synthesis of this evidence by deploying a robust methodology to ensure that there can be a contemporaneous impact on clinical practice.

Methods: The Cochrane Central Register of Controlled Trials, MEDLINE, EMBASE, CINAHL and Cochrane Inflammatory Bowel Disease & Functional Bowel Disorders Group Specialised Trial Register were searched (Inception – July 2015). Manufacturers of probiotics were contacted to identify unpublished trials. References of trials were also searched. Abstracts were considered for inclusion if full details to judge inclusion were offered or available from the authors. Randomised controlled trials (RCTs) that compared probiotics against placebo or any other intervention were eligible for inclusion. Data extraction and assessment of methodological quality of included studies were independently performed by two authors. Analysis was completed in accordance with the intention to treat approach.

Results: The search yielded 1672 results and nine placebo controlled studies (n = 701) met the inclusion criteria, two as abstracts and seven as published studies. Three studied Lactobacillus GG, three lactobacillus reuteri, one VSL#3, one bacillus coagulans and one bifidobacteria. The studies ranged in length from 4 to 16 weeks. The risk of bias was low for randomisation for seven trials and moderate for two trials. Allocation concealment was low in two studies and unclear in the others. All studies were double blinded, but only four gave details of how this was achieved. The risk of bias was low or unclear in all studies for incomplete outcome data and selective reporting. Meta-analysis of seven studies (n=541) found a statistical significant reduction in the severity of pain using probiotics compared to placebo (MD -0.32; 95% CI -0.38 to -0.25). Meta-analysis of four studies (n=440) found a statistical significant difference in patients reaching treatment success favouring probiotics compared to placebo (OR 1.80; 95% CI 1.20 to 2.69). Meta-analysis of five studies (n=385) found no statistical significant difference in adverse events between probiotics and placebo (OR 0.00; 95% CI -0.07 to 0.06).

Conclusion: The evidence from the published suggests superior efficacy of probiotics for functional abdominal pain in children when compared with placebo. There is no difference in adverse events, suggesting safety. The evidence base is of moderate quality and relatively small. Further research to investigate the long term impact of probiotic therapy is suggested.

Disclosure of interest: “None Declared”. MG has received travel grants from various pharma companies for travel to scientific meetings. These companies have had no involvement with the planning, completion or write up of this or any other work.
Endoscopic and histopathologic findings in patients with disphagia

Josefa Barrio Torres¹, Beatriz Martinez Escribano¹, Eugenia Oros Milián², Carmen María Hinojosa Mateo³, Miriam Herrera Arias³, Arantxa Vidal Esteban²

¹Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Fuenlabrada, Madrid, Spain
²Hospital Universitario de Fuenlabrada, Paediatric Gastroenterology Unit, Madrid, Spain
³Hospital Universitario de Fuenlabrada, Pediatric Gastroenterology Unit, Madrid, Spain

Objectives and study: The aim of the present study was to evaluate the endoscopic and histologic findings obtained in patients who consulted with dysphagia or food impaction in our medical center.

Methods: Retrospective data were collected from children under 16 years who underwent an upper endoscopy because of symptoms of dysphagia or food impaction. The recruitment period was January 2007 to December 2014. Epidemiological characteristics, endoscopic and histological findings were analyzed. Savary-Miller system was used for grading endoscopic esophagitis. The analysis of the data was carried out using the statistical program SPSS 22.0.

Results: A total of 864 endoscopic procedures were carried out in the period of time referred. 63 out of 864 patients were enrolled, of which 70% had dysphagia and 30% food impaction. Demographic data: 65.9% males, with a mean age of 9.5 years (2.9 DS). Esophageal endoscopic findings were: esophagitis grade I-II (Savary-Miller) in 37.8%, esophagitis grade III-IV or data suggestive of eosinophilic esophagitis (EoE) in 24.4% and herpetic esophagitis in 7.3%. Endoscopy was normal in 30.5%.

Histopathologic findings were: esophagitis in 53.7% (eosinophilic 30.5%, related to gastro-oesophageal reflux (GERD) 15.9% and herpetic 7.3%). 25 out of 63 had gastritis related to Helicobacter Pylori (HP) (40%) nearly half of them associated histological findings in esophagus (48%), mainly eosinophilic esophagitis (24%). There were no pathological findings in histopathologic exam in 45.1%. One of the patients with HP gastritis presented a lymphoma malt type and EoE. In addition, a patient without endoscopic pathological findings presented vellositary atrophy in duodenum and the diagnosed of celiac disease was made. There were only 6 patients who showed no macroscopic and histological pathologic findings.

Table: Endoscopic and histologic findings in patients with disphagia.

<table>
<thead>
<tr>
<th>Histopathologic Findings in esophagus</th>
<th>Histopathologic Findings</th>
<th>Gastritis HP</th>
<th>Other gastritis</th>
<th>Normal</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
<td>n %</td>
</tr>
<tr>
<td>GERD</td>
<td>4 30.8</td>
<td>3 23.1</td>
<td>6 46.2</td>
<td></td>
</tr>
<tr>
<td>EoE</td>
<td>6 24</td>
<td>6 24</td>
<td>13 52</td>
<td></td>
</tr>
<tr>
<td>EH</td>
<td>1 16.7</td>
<td>2 33.3</td>
<td>3 50</td>
<td></td>
</tr>
<tr>
<td>ulcer</td>
<td>1 100</td>
<td>0 0</td>
<td>0 0</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>13 35.1</td>
<td>8 21.6</td>
<td>16 43.2</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: - Most patients with dysphagia presented endoscopic pathological findings, however histopathological confirmation was obtained only in half of cases. - Although esophageal pathology is implicated in most cases of dysphagia, a high percentage of the patients had Helicobacter pylori gastritis, that in one case was associated with a lymphoma malt type.

Disclosure of interest: None Declared.
**GASTROENTEROLOGY: GI motility, GERD and functional GI disorders**

G-P-251

**Low impedance baseline values predict severe esophagitis.**

Judith Cohen Sabban¹, Gabriela Donato Bertoldi¹, Federico Ussher¹, Silvia Christensen¹, Maria Teresa Davila², Carlos Lifschitz¹, Marina Orsi¹

¹Hospital Italiano Buenos Aires, Buenos Aires, Argentina
²Hospital Garrahan, Buenos Aires, Argentina

**Objectives and study:** Multichannel intraluminal impedance (MII) and pH monitoring, are useful tools for esophageal function testing. Literature shows that esophageal intraluminal baseline impedance (BI) measurements could be a valuable indicator of esophageal mucosal integrity. Aim: To determine if esophageal BI values in children could be predictive of esophagitis.

**Methods:** MII tracings of children 3 to 17 yrs of age suspected of having gastroesophageal reflux (GER) and esophagitis, who had also undergone upper endoscopy with multiple esophageal biopsies, were reviewed. Esophageal histology was reported by two blinded independent pathologists unaware of the MII results. Mean BI was automatically calculated in the different MII channels (ch) by the specific software without removing any episode of increased/decreased BI. We plotted the BI results against the histological scores for each channel. Patients with eosinophilic esophagitis were excluded.

**Results:** Tracings of 87 children, 53 male, were evaluated. Mean age was 7.4 yrs: 45 had esophagitis. Mild esophagitis (ME) (Grade 1) was observed in 30 and 15 had moderate to severe esophagitis (SE) (Grade 2-3). Ten had grade 3 esophagitis. Looking at results in channel 6 of the MII, all 10 patients with grade 3 esophagitis had a BI lower than 900 Ohms/s (positive predictive value 100% and negative predictive value 100%), while none of those having a biopsy score of 0 to 2 had a mean BI below 2000 Ohm/s.

**Conclusion:** The evaluation of the BI measured in channel 6 gave us 100% prediction of grade 3 esophagitis. BI on channel 6 may be useful to predict severe esophageal mucosa inflammation and could potentially be used for follow up evaluation, rather than repeating an upper endoscopy.

**Disclosure of interest:** None Declared.
Excessive crying during infancy predisposes to behavioral problems in early childhood

Judith Zeevenhooven¹, Ninieck van Maasakker¹, Francoise de Bruin², Arine Vlieger³, Marc Benninga⁴, Monique L'Hoir⁵, Bregje van Sleuwen⁵

¹Emma Children's Hospital / Academic Medical Center (Amc), Pediatric Gastroenterology, Amsterdam, Netherlands
²Utrecht University, Faculty of Social and Behavioral Sciences, Utrecht, Netherlands
³St. Antonius Hospital, Department of Pediatrics, Nieuwegein, Netherlands
⁴Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
⁵Tno, Child Health, Leiden, Netherlands

Objectives and study: Excessive crying during infancy may predispose to the development of behavioral problems in early childhood. However, results from studies to date have not been unequivocal. Therefore the aim of our study was to assess whether excessive crying predisposes to the development of behavioral problems in the early years of life by using the Child Behavior Checklist (CBCL).

Methods: The study group consisted of 240 former excessively crying infants, as defined by the Wessel criteria, who were 0-3 months old when they participated in a RCT, conducted between February 2001-March 2003. In 2006, at the age of 3-5 years, their caregivers filled out the CBCL. The caregivers of 393 randomly selected children from the municipal registers of a Dutch province (aged 3-5 years at assessment, referred to as the normative sample), filled out the CBCL between December 2003-April 2005. Scores were obtained on the Internalizing Problems, Externalizing Problems and Total Problems scale of the CBCL and compared between the group of former excessively crying infants and the normative sample using Mann Whitney U-tests and Independent T-tests. The proportion of children scoring in the clinical range of the CBCL scales was compared between the two groups using Chi-square. Logistic regression was used to evaluate the effects of possible covariates.

Results: Baseline characteristics of the study cohort are displayed in Table 1. Former excessively crying infants scored significantly higher on the Internalizing scale of the CBCL than children of the normative sample (8.0 (IQR 4.0-14.0) vs 7.0 (IQR 3.0-11.0), p=0.015). The percentage of children scoring in the clinical range of the Internalizing scale and in the clinical range of the Total Problem scale was significantly higher in the group of former excessively crying infants compared to the Dutch norm group (29% vs 16%, p<0.001 and 20% vs 11%, p=0.001, respectively). Former excessively crying infants had an increased risk of scoring in the clinical range of the Internalizing Scale (OR=2.14; CI 1.40-3.27) and the Total Problem Scale (OR=2.43; CI 1.47-4.03) compared to the children of the normative sample, independent of age at time of assessment, gender, maternal educational level and ethnicity of both parents.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Former excessively crying infants (n=240)</th>
<th>Normative sample (n=393)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (months, median, IQR)</td>
<td>60.0 (55.0-65.0)</td>
<td>52.0 (44.0-62.0)</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Male (n,%),</td>
<td>124 (52%)</td>
<td>196 (50%)</td>
<td>0.661*</td>
</tr>
<tr>
<td>• Female (n,%),</td>
<td>116 (48%)</td>
<td>197 (50%)</td>
<td></td>
</tr>
<tr>
<td>Education mother</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>• Low (n,%), (no education/primary school/LBO¹/MAVO¹/VMBO¹)</td>
<td>43 (18%)</td>
<td>105 (27%)</td>
<td>0.015⁵</td>
</tr>
<tr>
<td>• Middle (n,%),</td>
<td>90 (38%)</td>
<td>148 (38%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>(MBO²/HAVO²/VWO²)</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Table 1. Baseline characteristics of the study subjects (n=633).

<table>
<thead>
<tr>
<th>Ethnicity parents</th>
<th>High (n,%: HBO²/University)</th>
<th>107 (45%)</th>
<th>138 (35%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dutch* (n,%:</td>
<td>205 (86%)</td>
<td>301 (77%)</td>
<td>0.005*</td>
</tr>
<tr>
<td>Non-Dutch (n,%:</td>
<td>34 (14%)</td>
<td>92 (23%)</td>
<td></td>
</tr>
</tbody>
</table>

1 pre-vocational secondary education; 2 secondary vocational education; 3 senior general secondary education; 4 pre-university secondary education; 5 higher professional education.

*One missing value
*Only if both parents are born in the Netherlands

**Conclusion:** Excessive crying in early infancy is associated with behavioral problems at preschool age. Therefore parents of former excessively crying infants may be helped by offering support in the early years of their child’s development.

**Disclosure of interest:** None Declared.
Treatment of functional gastrointestinal disorders with dietary exclusions in an adolescent population: Outcomes on “milk, egg, wheat and soya” (MEWS) free diet versus Low "Fermentable Oligo-Di-Mono and Di-saccharide (FODMAP) Diet exclusions

Katie Keetarut\textsuperscript{1}, Sara McCartney\textsuperscript{2}, Fevronia Kiparissi\textsuperscript{3}, Charles Murray\textsuperscript{2}

1University College London Hospital, Nutrition and Dietetics, London, United Kingdom
2University College London Hospital, Department of Gastroenterology, London, United Kingdom
3Great Ormond Street Hospital for Children Foundation Trust, Department of Gastroenterology, London, United Kingdom

Objectives and study: To assess the benefit of the low FODMAP (Fermentable Oligo-Di-Monosaccharides and Polyols) diet versus the “milk, egg, wheat and soya” (MEWS) free diet for symptom control in patients with functional gastrointestinal disorders and/or food allergy from over a 2 year period.

Methods: A total of 436 patients were seen during this time period for dietetic advice and the age range varied from 13-21 years old with 43 terms of diagnosis used. These included the broad categories of inflammatory bowel disease, food allergy, functional gastrointestinal disorders, congenital gut disorders, autoimmune disorders and oncology conditions. For functional gastrointestinal disorders/food allergy there were 14 terms used which varied from “Functional gut disorder” to “Irritable bowel syndrome” and also included patients with delayed gastric emptying. For patients with food allergy the terms “multiple food allergy” or eosinophilic oesophagitis or eosinophilic colitis were used.

A total of 40 patients with functional gastrointestinal disorders were referred for the MEWS or low FODMAP diet. The efficacy of the diet was measured using a symptom scale pre and post dietary intervention assessing if patients symptoms changed from nil/mild/moderate to significant. The results indicate whether the presenting predominant symptom e.g., bloating, constipation or abdominal pain improved following the dietary intervention.

Results: A total of 29 patients were seen for the “MEWS” free diet. These were 17 functional, 3 food allergy, 6 IBS, 2 eosinophilic oesophagitis, 1 oncology patient. The age ranged from 14 to 21 and average age at treatment was 16.6 years old with 11 males and 18 females.

13 patients were referred for the low FODMAP diet. The patients referred for the low FODMAP diet were 7 with a functional gut disorder, 5 Irritable Bowel Syndrome and 1 eosinophilic colitis. The age range was 14 to 19 years old with average age at treatment 16.3 years old. There were 6 males and 7 females.

The success rate of the MEWS diet measured by reported significant improvement in predominant presenting symptom was 14/29 (48.2%), moderate 4/29 (13.7%) mild 2/29 (6.9%) and 9/29 (31.2%) nil improvement. Overall combined improvement was 68.8%. For the low FODMAP diet 6/13 (46.1%) of patients reported a significant improvement in symptoms, 0/13 (0%) moderate, mild 2/13 (15.4%) and 5/13 (38.5%) had nil improvement. Overall combined improvement was 61.5%.

Conclusion: This review suggests that although there were larger referral rates for the MEWS diet both the MEWS and low FODMAP diet appear to be equally effective dietary approaches for treating patients with functional gut disorders and/or food allergy. Larger randomised controlled trials are needed to define dietary exclusions as treatment options for functional gastrointestinal disorders.

Disclosure of interest: None Declared
Could be the Reactive Gastropathy an Explanation for Functional Abdominal Pain?

Kinga Cristina Slavescu¹, Radu Razvan Slavescu², Alexandru Pirvan¹, Camelia Margescu³, Dan Gheban⁴

¹University of Medicine and Pharmacy "Iuliu Hatieganu", Mother and Child, Cluj-Napoca, Romania
²Technical University of Cluj-Napoca, Computer Science, Cluj-Napoca, Romania
³Children's Hospital, Cluj-Napoca, Romania
⁴University of Medicine and Pharmacy "Iuliu Hatieganu", Department of Pathology, Cluj-Napoca, Romania

Objectives and study: Childhood recurrent or chronic abdominal pain without evidence of infection, neoplasia or ulcerous disease and with insufficient criteria for other FGIDs could be defined, according to Rome III criteria, as functional abdominal pain. Previous studies associate reactive gastropathy with abdominal pain, but with no clear definition of the latter. In our study, we aimed to determine the prevalence of reactive gastropathy in children suffering from chronic/recurrent abdominal pain and to exclude, by using upper gastrointestinal endoscopy, other possible causes of abdominal pain (ulcers, GERD, H. pylori infection etc.).

Methods: 1499 children were evaluated, with age groups starting from toddlers to adolescents. They were divided into two groups: the first included children assessed for recurrent or chronic abdominal pain, in number of 474; the second group was investigated for other symptoms (vomiting, anemia, failure to thrive etc.).

Results: Reactive gastropathy was more frequent at children in the first group compared to those in the second group (58.65% and 41.85% respectively, RR=1.4, 95 % CI 1.26 to 1.56, p < 0.0001). 37.22% of the children in the first group had reflux esophagitis compared to 36.01% in the second group (p=0.67). 67.49% of children with abdominal pain had gastric mucosal lesions compared to 65.37% of children with no abdominal pain (p=0.45). 9.18% of children from the first group had duodenal lesions compared to 12.61% of children from the second group (p=0.07).

Conclusion: Reactive gastropathy may be a plausible explanation for functional abdominal pain. The frequency of gastric and duodenal mucosal lesions, and of the reflux esophagitis were similar in both groups and cannot be used to discriminate between children with and without chronic/recurrent abdominal pain.

Disclosure of interest: “None Declared”.
Primary Duodenogastric Reflux and Reactive Gastropathy – A Survey on Children in Romania

Kinga Cristina Slavescu¹, Radu Razvan Slavescu², Alexandru Pirvan¹, Costica Sarban³, Camelia Margescu³, Dan Gheban⁴

¹University of Medicine and Pharmacy “Iuliu Hatieganu”, Mother and Child, Cluj-Napoca, Romania
²Technical University of Cluj-Napoca, Computer Science, Cluj-Napoca, Romania
³Children’s Hospital, Second Pediatric Clinic, Cluj-Napoca, Romania
⁴University of Medicine and Pharmacy “Iuliu Hatieganu”, Department of Pathology, Cluj-Napoca, Romania

Objectives and study: Reactive gastropathy is the second most common diagnosis revealed by gastric biopsies, after H. pylori infection. Several studies regarding the primary duodenogastric reflux (DGR) were published, but only few of them describe the histological changes of the gastric mucosa in children with this disease. The aims of this survey were to evaluate the prevalence of reactive gastropathy in children in the studied group and to investigate the correlation between clinical symptoms and the endoscopic appearance. We also investigated the relation of primary DGR and reactive gastropathy and their association with other diseases (gastro-esophageal reflux disease or duodenitis).

Methods: A total of 3257 patients have been included (2058 females) with a median age of 13 (9-16) years. Regarding the endoscopic lesions reactive gastropathy were divided into erosive and non-erosive forms. Reactive gastropathy was defined according to Dixon description as a constellation of nonspecific elementary lesions such as foveolar hyperplasia, interfoveolar smooth muscle fibers, erosions, edema, and hyperemia, in the absence of significant inflammation.

Results: 1494 children had reactive gastropathy (45.9%) with a median age of 11 (7-16) years. Epigastric pain and recurrent abdominal pain were more common in children with reactive gastropathy compared to those with other types of gastritis (RR=1.25, CI95%=1.12 to 2.41, p<0.001, respectively RR=1.19, CI 95%=1.01 to 1.31, p=0.001). Erosive gastritis appears in 9.15% of patients with reactive gastropathy unlike in 5.53% of the children with other gastritis (RR=1.31, 95%CI=1.15 to 1.49, p=0.001). 475 cases (31.79%) were associated with duodeno-gastric biliary reflux and 54 of these patients also had H. pylori infection. 253 (16.93%) patients had gastric atrophy in biopsies taken from the antrum and 14 children (0.94%) had intestinal metaplasia. 36.81% of patients with reflux gastritis also had reflux oesophagitis comparing to 31.42% of patients with other types of gastritis (RR=1.17, CI95%=1.06 to 1.29, p=0.007).

Conclusion: The prevalence of reactive gastropathy in the studied group was relatively high. Abdominal pain (epigastric and recurrent) was significantly more frequent in children with reactive gastropathy compared to those with other types of gastritis. Endoscopic appearance of erosive lesions was related to reactive gastritis. One third of the cases of reactive gastropathy could be associated with duodeno-gastric biliary reflux. Varying degrees of esophagitis were significantly associated with reactive gastropathy.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 453
Letizia Zenzeri¹, Paolo Quitadamo², Annalisa Alessandrella², Erasmo Miele², Annamaria Staiano²

¹University of Perugia, Department of Pediatrics, Perugia, Italy
²Federico II University, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy

Objectives and study: Respiratory symptoms, such as chronic cough, hoarseness, and apnea, are possible atypical clinical pictures of gastro-esophageal reflux disease (GERD). However, a significant number of patients with GERD-related respiratory symptoms do not report improvement despite aggressive acid-suppressive therapy. Some of these refractory cases may be due to the recently appreciated entity of non-acid or weakly acidic reflux. The aim of our study is to assess the pH-impedance features of GER inducing airway symptoms, compared to GER inducing typical gastrointestinal (GI) symptoms.

Methods: We prospectively assessed pH-impedance parameters of infants, children and adolescents referred from January 2015 to November 2015 to the gastroenterology clinic of our Department for a diagnostic pH-impedance evaluation due to both GI or respiratory symptoms with no other underlying chronic disease. Patients diagnosed with GERD, based on the number and features of the detected reflux episodes or on the association between reflux episodes and symptoms, were enrolled in the study.

Results: Thirty patients (M/F: 15/15; mean age: 50.9 months; range: 2-163 months) among the 58 presenting with respiratory symptoms had a positive (>95%) symptom association probability index and were enrolled in the study group. Twenty-five/30 (83.3%) suffered from chronic cough, 3/30 (10%) from recurrent apneas and 2/30 (6.7%) from recurrent pneumonia. The comparison group consisted of 30 patients (M/F: 14/16; mean age: 66.9 months; range: 2-204 months), of which 10/30 (33.3%) showed regurgitation, 10/30 (33.3%) vomiting, 5/30 (16.7%) heartburn, 4/30 (13.3%) chest pain, and 1/30 (3.4%) dysphagia. The mean acid exposure index was 8.3% within the study group and 12.7% within the comparison group (p: 0.009). The mean number of reflux episodes was 62.4 among the study group and 75.7 among the comparison group (p: 0.258). Children with respiratory symptoms vs children with GI symptoms of GERD had a mean of 36.8 acid reflux episodes vs 49.4 (p: 0.089), a mean of 1.5 weakly acid reflux episodes vs 8.6 (p: 0.317), and a mean of 23.4 alkaline reflux episodes vs 17.7 (p: 0.128). Finally, the mean number of reflux episodes reaching the upper esophagus was 36.4 in the study group vs 43.4 in the comparison group (p: 0.170).

Conclusion: The main finding of this prospective, controlled study is that patients with GERD-related respiratory symptoms show a significantly lower esophageal acid exposure and a trend towards a lower number of acid reflux episodes compared to patients with GERD-related GI symptoms. This supports the hypothesis that respiratory symptoms are less related to acidity than GI symptoms. However, according to our preliminary data, the number of weakly acid and alkaline reflux episodes do not differ significantly between the 2 study groups. Moreover, we observed no difference in the number of reflux episodes with proximal extension.

Disclosure of interest: None Declared
Childhood functional constipation—change in behavioral difficulties based on treatment outcomes

Line Modin¹, Ida Skytte Jakobsen², Marianne Skytte Jakobsen³

¹Hc Andersen Childrens Hospital, University Hospital Odense, Pediatric Department, Odense, Denmark
²University College Lillebaelt, Odense, Denmark
³Hospital Lillebaelt, Department of Pediatrics, Kolding, Denmark

Objectives and study: To evaluate behavioral difficulties before and after conventional treatment according to treatment outcomes in children with functional constipation.

Methods: Children, aged 5 to 16 years, who fulfilled the Rome III criteria for functional constipation, were included. Medical history and physical examination were performed, followed by conventional treatment of FC, including laxative treatment. Parents completed the Strength and Difficulties Questionnaire at inclusion and at subsequent 6- and 12-month follow-up consultations. The five sub-scores were summed in a total difficulties score.

Results: Overall, 116 constipated children > 5 years of age were included, and 78.4% were successfully treated. The behavior score decreased between inclusion and 12 months in successfully treated boys (10.3 vs. 7.9; p<0.001) and girls (10.0 vs. 7.4; p=0.0001). There was no decrease in unsuccessfully treated children. Fecal incontinence was prominent in unsuccessfully treated boys [93.3% (14/15)] and girls [90.0% (9/10)]. The same result was observed when omitting children with fecal incontinence.

Unsuccessfully treated boys had significantly higher behavior score compared to successfully treated boys both at inclusion (13.2 vs 10.3; p=0.006) and after 12 months (11.4 vs. 7.9; p=0.02). Conversely, no difference was found between unsuccessfully treated girls and successfully treated girls at inclusion (10.5 vs. 10.0; p=0.77) or after 12 months (10.3 vs. 7.4; p=0.18).

Conclusion: Our findings indicate a positive impact of successful treatment on behavioral difficulties in constipated children both with and without fecal incontinence during conventional treatment of functional constipation. The importance of proactive detection and treatment of childhood functional constipation in a pediatric setting is underscored.

Disclosure of interest: None Declared.
The characteristic of gastroesophageal reflux disease in children with adenoid hypertrophy

Marcin Dziekiewicz¹, Renata Cudejko², Aleksandra Banaszkiewicz¹, Marcin Banasiuk¹, Andrzej Radzikowski³, Henryk Skarżyński², Piotr Albrecht¹

¹Medical University of Warsaw, Department of Pediatric Gastroenterology and Nutrition, Warsaw, Poland
²Institute of Physiology and Pathology of Hearing, Kajetany, Poland

Objectives and study: An increasing number of studies have indicated that gastroesophageal reflux disease (GERD) could be related to various extra-esophageal disorders. Recent studies suggested that in some cases it may be connected with adenoid hypertrophy (AH). The exact incidence of GERD in this population remains unknown, but according to pH-metric studies it may be as high as 65%. The aim of the study was to estimate the incidence of GERD among children with adenoid hypertrophy and characterize gastroesophageal reflux episodes (GERs).

Methods: This was a multicenter, prospective study of children with AH selected to surgical remove. The diagnosis of AH was made with flexible fiberoscopy by a single laryngologist. All children underwent 24 hour multichannel intraluminal pH impedance (MII-pH) study. The diagnosis of GERD was made with BioVIEW analysis software after manual review by single investigator.

Results: 33 consecutive patients (18 boys, median age 6.98) were enrolled into the study. GERD was diagnosed in 10/33 (30.3%) patients. A total of 1268 GERs were detected by MII-pH. 807 (63.3%) of them were acid, 434 (34.2%) - weakly acid and 27 (2.1%) - weakly alkaline. 517 (40.8%) GERs reached the proximal esophagus. None of the patients had typical GERD symptoms.

Conclusion: It was the first study characterizing reflux events in children with AH with a use of MII-pH. The frequency of GERD in this population appears to be lower previously raised. Although acid GERs were prevalent in children with AH, the number of weakly alkaline GERs was relatively high. It suggest that MII-pH might be a better method for diagnosing GERD in children with AH. Further studies are needed to confirm these results.

Disclosure of interest: None Declared
Frequency of gastroesophageal reflux disease and esophageal motility disorders in adolescents with anorexia nervosa

Katarzyna Weterle-Smolińska¹, Marcin Banasiuk², Marcin Dziekiewicz², Gabriela Jagielska¹, Aleksandra Banaszkiewicz², Tomasz Wolańczyk¹, Piotr Albrecht²

¹Medical University of Warsaw, Department of Child Psychiatry, Warsaw, Poland
²Medical University of Warsaw, Department of Pediatric Gastroenterology and Nutrition, Warsaw, Poland

Objectives and study: Symptoms of the gastrointestinal tract suggesting esophageal motility disorders (EMD) are one of the most common complaints reported by patients with anorexia nervosa (AN), especially in the initial period of realimentation. This issue is poorly understood. The frequency of gastroesophageal reflux disease (GERD) in AN is not known and, according to the few published studies EMD in this population are relatively common. They may impede the restoration of proper diet, if not detected early and treated. The aim of the study was to assess the frequency of GERD and EMD in adolescents with AN.

Methods: This was a multicenter, prospective study. At the same day enrolled patients underwent 24 hour multichannel intraluminal pH-impedance (MII-pH) monitoring and high resolution manometry (HRM). Results were analyzed with automatic analysis software and manual revised by single investigator.

Results: 24 consecutive female patients (median age 15.5) were enrolled into the study. MII-pH was performed in 23 of them. GERD was diagnosed in 4 (17.4%) patients. A total of 716 reflux episodes were detected. 263 (36.7%) of them were acid, 433 (60.5%) - weakly acid and 20 (2.8%) - weakly alkaline. HRM was performed in all patients. EMD were detected in 19 (79.2%) of them. In 11 (45.8%) patients ineffective esophageal motility was diagnosed. Moreover in 2 (8.3%) of them HRM revealed increased and in 6 (25%) other decreased median basal lower esophageal sphincter pressure. The most common reported symptoms were upper abdominal pain (16 patients), nausea (11), dysphagia (9) and heartburn (8).

Conclusion: The frequency of GERD among females suffering from AN is low. High prevalence of non-acid GER stresses the importance of MII-pH as a diagnostic method. EMD in AN patients are a very frequent phenomenon. However, it is crucial to assess the correlation between reported symptoms and abnormalities in diagnostic tests.

Disclosure of interest: None Declared
Magnesium Alginate plus Simethicone versus Lansoprazole in children with poorly controlled asthma: preliminary results

Marco Maglione¹, Eleonora Giannetti¹, Silvia Montella¹, Erasmo Miele¹, Francesca Santamaria¹, Annamaria Staiano¹
¹Federico II University, Department of Translational Medical Sciences, Section of Pediatrics, Naples, Italy

Objectives and study: Asymptomatic gastroesophageal reflux (GER) is common in children with asthma. When inadequately treated, GER may represent a relevant comorbidity, leading to poor asthma control, despite inhaled corticosteroid therapy. Recent evidence has shown that proton pump inhibitors, namely lansoprazole, are not effective in improving asthma symptoms or lung function, and are even associated with increased adverse events. Our aim was to assess the efficacy of magnesium alginate plus simethicone versus lansoprazole in reducing asthma symptoms and improving lung function in poorly controlled asthmatic children without overt GER.

Methods: Children with poorly controlled asthma were prospectively enrolled. Poor asthma control was defined as any one of the following: use of short-acting β2-agonists for asthma symptoms 2 or more times per week; nocturnal awakenings with asthma symptoms more than twice during the month before enrollment; 2 or more emergency department visits, unscheduled physician visits, oral steroids courses, or hospitalizations for asthma in the prior year. Subjects whose asthma therapy had been modified during the 8 weeks preceding enrollment, or those who were receiving anti-GER treatment were excluded. At enrollment (T0), all patients underwent spirometry and asthma control was assessed by means of the pediatric Asthma Control Test (pACT, higher score indicating better control). Patients were then randomized to receive either magnesium alginate plus simethicone at the dose of 10 ml three times a day (group 1), lansoprazole 15 or 30 mg/day (for a body weight <30 or >30 kg, respectively, group 2), or no anti-GER treatment (group 3) for 8 weeks. In all patients, ongoing asthma therapy was not modified. After 8 weeks (T1), asthma control was re-assessed by spirometry and pACT.

Results: Eighteen patients (median age, 9.9, range 6-13.6 years, 14 males) were recruited. No differences between groups were detected regarding passive smoke exposure, sensitization to inhalant allergens, and need for reliever medications during the study. Unlike groups 2 and 3, patients in group 1 showed an improvement in both FEV1 and pACT which approached statistical significance (Table).

<table>
<thead>
<tr>
<th></th>
<th>FEV1 (% predicted)</th>
<th>pACT</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T0</td>
<td>T1</td>
</tr>
<tr>
<td>Group 1 (n=7)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>104.4 (16.1)</td>
<td>110.8 (21.4)</td>
</tr>
<tr>
<td>Group 2 (n=5)</td>
<td>96.1 (14.9)</td>
<td>95.1 (8.6)</td>
</tr>
<tr>
<td>Group 3 (n=6)</td>
<td>95.6 (13.3)</td>
<td>98 (7.6)</td>
</tr>
</tbody>
</table>

Data are presented as mean values and standard deviations.

Conclusion: Despite no statistical significance was achieved due to the limited sample size, our preliminary results suggest that magnesium alginate plus simethicone may be of benefit when added to standard asthma therapy in children with poorly controlled asthma. The extension of the trial to a larger population is therefore needed to verify whether our results may be generalized.
Disclosure of interest: A. Staiano has participated as a clinical investigator, and/or advisory board member, and/or consultant, and/or speaker for D.M.G, Valeas, Angelini, Miltè, Danone, Nestlé, Sucampo, Menarini, Aboca.
Lactobacillus reuteri DSM 17938 for the management of functional abdominal pain (FAP) in children: a multicenter randomized controlled trial

Maria Maragkoudaki, George Chouliaras, Rok Orel, Andrea Horvath, Hania Szajewska, Alexandra Papadopoulou

First Department of Pediatrics, University of Athens, Children’s Hospital “Agia Sofia”, Athens, Greece
University Clinical Center, University of Ljubljana, Slovenia, Ljubljana, Slovenia
Department of Paediatrics, Medical University of Warsaw, Poland, Warsaw, Poland

Objectives and study: The efficacy of Lactobacillus reuteri DSM 17938 in children with functional abdominal pain (FAP) was assessed in a randomized, double blind, placebo controlled multicenter trial.

Methods: Fifty four consecutive children (mean±SD age 9.1±3.8 years; 25 males) with FAP diagnosed according to Rome III criteria in three centers (Athens, Ljubljana and Warsaw) were randomly assigned to receive a 4 week breakfast supplementation with 2 tablets of either L. reuteri DSM 17938 at a dose of 1x10^8 CFU/tablet (LR group; N=27; 14 males; mean age 9.2±4.3 years) or placebo (Placebo group; N=27; 16 males; mean age 9.0±4.2 years) indistinguishable in appearance and taste. The number of episodes of pain, its severity according to Wang Baker face scale, the interference with the child’s activities, the use of medication and the number of lost work days of the parents or school days of the children because of pain as well as the presence of other symptoms and their severity according to Gastrointestinal Symptom Rating Score (GSRS) were all recorded 2 weeks before and 8 weeks after recruitment.

Results: Both study groups were comparable at baseline with regards to age, gender, number of days with pain or episodes of pain, pain score, interference score, number of absences from school for children or lost work days for parents. Primary and secondary outcomes are presented in Table 1. Changes in each study group following the intervention are presented in Table 2.

Table 1. Primary and secondary outcomes

<table>
<thead>
<tr>
<th>Outcome</th>
<th>L reuteri (n=27)</th>
<th>Placebo (n=27)</th>
<th>MD or RR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of episodes of pain/day</td>
<td>0.8±1.2</td>
<td>1.0±1.4</td>
<td>0.19 (-0.54 to 0.92)</td>
</tr>
<tr>
<td>Score of pain/day</td>
<td>1.4±2.5</td>
<td>1.5±2.0</td>
<td>0.09 (-1.2 to 1.2)</td>
</tr>
<tr>
<td>Interference score/day</td>
<td>0.4±0.5</td>
<td>0.5±0.8</td>
<td>0.07 (-0.28 to 0.43)</td>
</tr>
<tr>
<td>Number of school absences/day</td>
<td>0.03±0.07</td>
<td>0.03±0.09</td>
<td>0.003 (-0.04 to 0.04)</td>
</tr>
<tr>
<td>Lost work days for parents/day</td>
<td>0.003±0.01</td>
<td>0.005±0.030</td>
<td>0.003 (-0.009 to 0.015)</td>
</tr>
<tr>
<td>Treatment success* at 2 wk</td>
<td>13/26</td>
<td>7/26</td>
<td>1.8 (0.91 to 3.8)</td>
</tr>
<tr>
<td>Treatment success* at 4 wk</td>
<td>19/27</td>
<td>14/24</td>
<td>1.2 (0.8 to 1.8)</td>
</tr>
</tbody>
</table>

*>50% reduction in pain score
Table 2. Changes within 4 weeks following the intervention compared to 2 weeks before

<table>
<thead>
<tr>
<th>Outcome</th>
<th>L reuteri (N=27)</th>
<th>P value</th>
<th>Placebo (N=27)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Episodes of pain/day</td>
<td>1.4±1.6 vs 0.8±1.2</td>
<td>&lt;0.001</td>
<td>1.3±1.5 vs 1.0±1.4</td>
<td>0.003</td>
</tr>
<tr>
<td>Score of pain/day</td>
<td>2.7±4.0 vs 1.4±2.5</td>
<td>&lt;0.001</td>
<td>2.5±3.3 vs 1.5±2.0</td>
<td>0.001</td>
</tr>
<tr>
<td>Interference score/day</td>
<td>1.0±1.6 vs 0.4±0.5</td>
<td>&lt;0.001</td>
<td>1.1±1.9 vs 0.5±0.8</td>
<td>0.001</td>
</tr>
<tr>
<td>Number of school absences/day</td>
<td>0.12±0.18 vs 0.03±0.07</td>
<td>0.003</td>
<td>0.06±0.13 vs 0.03±0.09</td>
<td>0.25</td>
</tr>
<tr>
<td>Number of lost work days for parents/day</td>
<td>0.06±0.13 vs 0.003±0.01</td>
<td>0.015</td>
<td>0.02±0.07 vs 0.005±0.30</td>
<td>0.15</td>
</tr>
</tbody>
</table>

**Conclusion:** *Lactobacillus reuteri* DSM 17938 is safe in children with FAP but its efficacy should be tested in larger, adequately powered studies in order to detect statistically significant differences.

**References**

**Disclosures:** Author and co-authors, Conflict with: Unrestricted grant from Biogaia
Efficacy and safety of gastrojejunal feeding tubes in children

Marta German¹, José Manuel Moreno¹, Carmen Gallego², M. Isabel Benavent³

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, Pediatric Surgery Unit, Madrid, Spain

Objectives and study: In some patients, requiring long-term enteral feeding, the use of a gastrostomy feeding is impossible because of severe gastro-oesophageal reflux (GER), delayed gastric emptying and/or antropyloric dysmotility. In these cases, enteral feeding through a gastrojejunal (GJ) tube could be an alternative to surgery or parenteral nutrition (PN). Our study aims to review our experience of GJ feeding over the last 2 years.


Results: Seven patients (5 girls, 2 boys) using GJ tubes were identified, with a total of 18 successful procedures documented (overall success rate of 94.7%). Fluoroscopic placement by interventional radiologist was the most frequent method of insertion (15) and 3 procedures were performed by a surgeon through a gastroduodenoscopy. The type of GJ tubes used during the study was Mic-Key transgastric jejunal (Kimberley Clark, USA). Patients presented with: cerebral hemorrhage (1), cerebral tumor (1), glutaric aciduria (1), Pierre Robin sequence (1), disseminated mycobacterium genavense infection with intestinal involvement (1) and esophagoeal atresia + tracheoesophageal fistula (2). Indications for jejunal feeding were severe GER (n=3) and gastroparesis (n=4). Six patients had a previous gastrostomy tube and two of them had Nissen fundoplication, with a median time between gastrostomy and GJ tube placement of 76.5 days (range 28-887). Before GJ tube placement, four patients received nutrition through a gastrostomy tube and three patients through a nasojejunal tube. At initial placement, the median age was 13 months (range 3-133) and the median weight was 12.76 kg (range 3.45-20). Patients had a median of 2 tubes placed per patient (range 1-6) during a follow-up of 10.8 months (range 2.4-25.6). The median lifetime of the tube was 71.5 days (range 9-486). The most common indications for replacement included internal balloon ruptures (4), broken tube component (4) and accidental dislodgement (4). In six episodes no complications were reported. At the end of the study, only one patient continued using GJ tube; five were transitioned back to gastrostomy or oral feeding, two of them (the patients with esophageal atresia) after a surgical intervention of Nissen fundoplication and other one after an endoscopic balloon dilatation of the pylorus. The remaining one required PN.

Conclusion: GJ tube is a good enteral access for effective and safe enteral nutrition in patients who do not tolerate intragastric feedings. Most common complications are about maintaining the device in place and the integrity of the GJ tube. No major complications were reported during the study.

Disclosure of interest: Non declared.
Infant colic is associated with low-grade systemic inflammation

Marko Kalliomäki¹, Anna Pärtty¹, Seppo Salminen², Erika Isolauri¹
¹University of Turku, Pediatrics, Turku, Finland
²University of Turku, Functional Foods Forum, Turku, Finland

Objectives and study: Prospective follow-up studies have found that children with abdominal-pain related functional gastrointestinal disorders, such as abdominal migraine and irritable bowel syndrome (IBS), have often suffered from colic-type crying. Altered gut microbiota, dysbiosis, has been demonstrated both in patients with colic and IBS. Since low-grade inflammation has been detected in IBS patients, our objective was to evaluate whether such an inflammation could be found also in infants with colic.

Methods: We used commercial ELISA-kits to measure the following immunological biomarkers in serum in 28 infants with colic and in 12 healthy matched controls: intestinal-fatty-acid-binding protein (ifabp), a marker of intestinal inflammation; chemokines monocyte chemotactic protein-1 (MCP-1), macrophage inflammatory protein1β (MIP-1β) and chemokine (C-X-C motiv) ligand 16 (CXCL16); cytokines interleukin 1β (IL-1β), IL-6, IL-8, IL-10, tumor necrosis factor α (TNF-α), interferon γ (IFN-γ); and zonulin, a marker of intestinal permeability. In addition, intestinal microbiota composition, evaluated by quantitative PCR, was correlated with the immunological biomarkers.

Results: Colic infants had increased levels of IL-8, MCP-1 and MIP-1β in serum as compared with healthy children. All the other immunological biomarkers were comparable between the groups (Table). Fecal numbers of Clostridium leptum correlated negatively with the pro-inflammatory markers MCP-1 (r=0.44, p=0.02), MIP-1β (r=0.43, p=0.02) and TNF-α (r=0.38, p=0.04). In addition, Clostridium coccoides correlated negatively with MCP-1 (r=0.43, p=0.02) and Bifidobacterium breve positively with CXCL16 (r=0.38, p=0.04), a bacterial scavenger receptor previously found to be increased in ulcerative colitis

Table: The mean (95%CI) serum levels of immunological biomarkers.

<table>
<thead>
<tr>
<th></th>
<th>i-fabp (pg/ml)</th>
<th>MCP-1 (pg/ml)</th>
<th>MIP-1 β (pg/ml)</th>
<th>CXCL16 (ng/ml)</th>
<th>IL-8 (pg/ml)</th>
<th>TNF-α (pg/ml)</th>
<th>Zonulin (ng/ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Colic</strong> (n=28)</td>
<td>1502 (1312-1692)</td>
<td>1461 (1242-1681)</td>
<td>99 (81-118)</td>
<td>3.3 (3.1-3.5)</td>
<td>17.5 (14.9-20.0)</td>
<td>26.7 (23.9-29.4)</td>
<td>20.9 (17.6-24.2)</td>
</tr>
<tr>
<td><strong>Healthy</strong> (n=12)</td>
<td>1716 (1284-2147)</td>
<td>971 (737-1205)</td>
<td>65 (51-79)</td>
<td>3.0 (2.6-3.4)</td>
<td>9.9 (6.6-13.3)</td>
<td>21.9 (18.7-25.1)</td>
<td>24.7 (15.0-34.5)</td>
</tr>
<tr>
<td><strong>p-value</strong></td>
<td>0.493</td>
<td>0.003</td>
<td>0.026</td>
<td>0.176</td>
<td>0.001</td>
<td>0.072</td>
<td>0.325</td>
</tr>
</tbody>
</table>
**Conclusion:** Infant colic is associated with low-grade systemic inflammation probably as a reflection of microbiota dysbiosis thus offering a possible explanation for therapeutic potential of certain probiotics in the condition.

**Disclosure of interest:** None declared.
Children’s GERD May Be Linked to Mothers’ Psychopathology

Oguzhan Zahmacioglu¹, Meltem Ugras², Oznur Kucuk², Hakan Aktalay³

¹Yeditepe University Medical Faculty, Child and Adolescent Psychiatry, Istanbul, Turkey
²Yeditepe University Medical Faculty, Pediatrics, Istanbul, Turkey
³Yeditepe University Medical Faculty, Psychiatry, Istanbul, Turkey

Objectives and study: Little but remarkable emphases have been laid on the relationship between Gastroesophageal Reflux Disease (GERD) and mother psychopathology. The studies have focused especially on the infancy period. In this study, the mothers of children belonging to a different age group (3-7 ages) were chosen, and obsessive-compulsive symptoms were reviewed for a change as well as depression and anxiety.

Methods: The study group is composed of mothers of 50 children diagnosed with GERD and mothers of 49 healthy children. The groups were matched according to age and educational status. The scales used in the study are Hospital Anxiety and Depression Scale and Maudsley Obsessive-Compulsive Inventory.

Results: Anxiety and depression scores of the mothers in the study group are significantly higher than those of the control group. There are also significant differences between the two groups in terms of feeding attitudes; however, no significant difference was found in the obsessive-compulsive symptoms.

Conclusion: These results should be assessed as important, external factors that affect the clinical process of a chronic disorder rather than being considered as a cause and effect relation. A distinctive increase in the risk of anxiety disorder and depression incidence in mothers in case of a chronic disorder like GERD needs to be considered important with regards to affecting both GERD’s course and the mother-child relationship in a negative way.

Disclosure of interest: “None Declared”.
High-resolution impedance manometry measurement of bolus flow time in pediatric achalasia

Maartje Singendonk1, Rachel Rosen2, Sam Nurko2, Nathalie Rommel3, Michiel van Wijk1, Marc Benninga4, Taher Omari5

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

Objectives and study: In achalasia, absent peristalsis and reduced esophagogastric junction (EGJ) relaxation and compliance underlie dysphagia symptoms. Flow across the EGJ is a function of mechanisms which transport swallowed bolus and flow resistance at the level of the EGJ. A novel high-resolution impedance manometry (HRIM) metric, the bolus flow time (BFT), has been developed to estimate the duration of EGJ opening and trans-EGJ bolus flow (Lin et al., 2014 & 2015). The aim of this study was to apply the BFT parameter to a cohort of children with dysphagia and/or gastro-esophageal reflux related symptoms, who underwent diagnostic HRIM and esophageal pressure topography based diagnosis of esophageal motor disorders using the Chicago Classification. We specifically compared children with normal esophageal motility with children diagnosed with achalasia.

Methods: HRIM recordings from 10 children who fulfilled the Chicago Classification (V3) criteria for achalasia (5M; 13.5 ± 2.3 yrs; BMI 19.0 ± 7.4) were compared with recordings of 10 children who had normal esophageal motility and no other evidence suggestive for achalasia based on clinical evaluation, endoscopy and/or timed barium swallow (6M; 12.7 ± 3.5 yrs; BMI 18.3 ± 8.3). All patients were studied in the semi-upright position and received a standardized protocol of 10 water swallows. HRIM tracings were analyzed using Manoview version 3.0 (Medtronic Inc). Bolus presence time across the EGJ (BPT) and the BFT were calculated according to the method of Lin et al. (2014) using Matlab-based analysis software.

Results: Eight patients were diagnosed with type II achalasia, one with type I and one with type III. Both BPT and BFT were significantly reduced in achalasia patients compared to children with normal esophageal motility (BPT 3.0 vs 5.6 p<0.001; BFT 0.9 vs 4.6, p<0.001). BFT was significantly shorter than BPT (achalasia difference -2.1 ± 0.2 s, p=0.001 and normal difference -1.0 ± 0.2 s, p<0.001). There was a significant correlation between BPT and BFT for children with normal motility (r=0.94, p=0.001), but not for achalasia patients (r=0.13, p=0.71).

Conclusion: In children with normal esophageal motility, bolus presence across the EGJ and bolus flow through the EGJ are correlated. This finding is consistent with synchronization of the mechanisms of esophageal bolus transport to the EGJ and esophageal emptying. The calculation of BPT and BFT may help determine when one or both of these mechanisms are aberrant. In the context of achalasia, this may help further quantify the degree of flow resistance at the EGJ for diagnosis as well as longitudinal objective assessment of therapeutic effects.

Disclosure of interest: Authors Nathalie Rommel and Taher Omari hold a patent on AIMplot methods. All other authors have no conflict of interests to declare.
Inter- and intraobserver reliability of the reflux finding score for infants (RFS-I) in flexible versus rigid laryngoscopy

Maartje Singendonk1, Bas Pullens2, Jan van Heteren1, Henriëtte de Gier2, Astrid König3, Hans Hoeve2, Marc van der Schroeff2, Carlijn Hoekstra3, Laura Veder2, Rachel van der Pol1, Marc Benninga4, Michiel van Wijk1

1Emma Children's Hospital/Amc, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
2Sophia Children's Hospital/Emc, Department of Otorhinolaryngology-Head and Neck Surgery, Rotterdam, Netherlands
3Academic Medical Center, Department of Otorhinolaryngology, Amsterdam, Netherlands
4Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: The Reflux Finding Score for Infants (RFS-I) was developed to assess signs of laryngopharyngeal reflux (LPR) in infants during laryngoscopy. Evaluation of the RFS-I using flexible laryngoscopy showed moderate interobserver reliability and highly variable intraobserver reliability. We hypothesized that examination of the infant larynx with rigid laryngoscopy would increase reliability. Aim of this study was to compare the reliability of the RFS-I for flexible versus rigid laryngoscopy.

Methods: We established a set of videos of consecutively performed flexible and rigid laryngoscopic examinations in infants. For this set, the RFS-I was scored twice by 4 otorhinolaryngologists, 2 otorhinolaryngology fellows, and 2 inexperienced observers. For categorical data, reliability was calculated using Cohen’s kappa and Fleiss’ kappa (κ; 2 and >2 observers respectively). For ordinal data the intraclass correlation coefficient (ICC) was used.

Results: The study set consisted of laryngoscopic videos of 30 infants (median age 7.5 (range 0-19.8) months; 17 male). Reasons for examination were: stridor (n=15), ALTE/apneas (n=7), follow-up of laryngeal abnormalities (n=6), aspiration (n=5), and other indications (n=7). Thirteen of the studied patients used anti-reflux medication and four patients were on asthma medication. Overall interobserver reliability of the RFS-I was moderate for both flexible (ICC=0.60, 95%Ci 0.44-0.76) and rigid (ICC=0.42, 95%Ci 0.26-0.62) laryngoscopy. There were no significant differences in reliability of overall RFS-I scores and individual RFS-I items for flexible versus rigid laryngoscopy. Intraobserver reliability of the total RFS-I score ranged from fair to excellent for both flexible (ICC=0.33-0.93) and rigid (ICC=0.39-0.86) laryngoscopy. Comparing RFS-I results for flexible versus rigid laryngoscopy per observer, reliability ranged from no to substantial (κ=0.16-0.63, mean κ=0.22) and the observed agreement was 0.08-0.35.

Conclusion: Reliability of the RFS-I was moderate and did not differ between flexible and rigid laryngoscopy. The RFS-I is not suitable to detect signs of LPR in infants or to guide treatment, neither with flexible, nor with rigid laryngoscopy.

Disclosure of interest: None of the authors have conflicts of interests to declare.
Effects of carob-bean gum thickened formulas on infants’ reflux, growth and tolerance indices

Miglena Georgieva1, Yannis Manios2, Niya Rasheva1, Ruzha Pancheva3, Elena Dimitrova1, Tatyana Draganova Stoeva1, Anne Schaafsma5

1Second Pediatric Clinic, University Hospital "st. Marine", Varna, Bulgaria
2Harokopio University, Nutrition and Dietetics, Athens, Greece
3Department of Hygiene, Medical University, Varna, Bulgaria
4Department of Pediatrics, University Hospital "Lozenetz", Sofia, Bulgaria
5Frieslandcampina, Amersfoort, Netherlands

Objectives and study: Gastro-esophageal reflux (GER) is commonly observed among infants, both breastfed and non-breastfed, making a peak at three months of age. Although most cases recover spontaneously within the first 6-12 months of life, symptoms can be relieved in non-breast fed infants by using carob bean gum (CBG) fortified formulae. Both hot and cold soluble CBGs are available for this purpose, although cold soluble might be preferred since it is easier to prepare and lowers the risk of offering milk that might be too hot. Low CBG dose is also preferred since at higher dose stool may become very thin. This study examined the effects of 0.45 g/100 ml of cold versus hot soluble CBG and of a lower concentration of 0.33 g/100 ml of cold soluble CBG on infants’ reflux, growth and tolerance indices.

Methods: Fifty-six eligible infants (1-6 months old) were randomly allocated to receive for two weeks a formula with either 0.33g/100ml (Formula A) or 0.45g/100ml (Formula B) of cold soluble CBG galactomannans respectively, or a third formula with 0.45g/100ml of hot soluble CBG galactomannans (Formula C). At baseline and follow-up, data were obtained on 24h esophageal pH monitoring, anthropometric (body weight and length) and tolerance indices (colics, defecations). From the eligible infants, 47 were included in an intention-to-treat analysis to examine the effects of the trial on esophageal 24h pH monitoring, growth and tolerance indices.

Results: Regarding 24h pH monitoring indices, significant decreases from baseline to follow-up were observed in the “Boix Ochoa Score” (an esophageal acid exposure index ), in the number of visible refluxes and in all symptoms related indices due to acid reflux only for infants provided with Formula A. In addition, the significant decreases observed in two symptoms related pH monitoring indices (i.e. “Symptom index for reflux” and “Percentage of all reflux”) for infants provided with Formula A were also found to differentiate significantly compared to the changes in the other two groups (P=0.048 and P=0.014 respectively). Concerning changes in anthropometric indices, body weight significantly increased among infants provided with Formulas A and C, but not for infants provided with Formula B. Regarding tolerance indices, the numbers of total and diarrheic defecations increased significantly only in infants provided with Formula B and these changes were significantly higher compared to the decreases observed in infants fed with Formulas A and C (P=0.003 and P=0.015 respectively). Lastly the number of colics significantly decreased in all infants, irrespective of the tested formula.

Conclusion: The formula containing low concentration (0.33g/100 ml) of cold soluble CBG (Formula A) was most effective in reducing certain pH-monitoring indices of uncomplicated GER, increased body weight and was well-tolerated by infants. Furthermore, significant body weight gains were observed for infants fed with Formula A and Formula C (i.e. 0.45g/100 ml of hot soluble galactomannans). On the other hand in infants fed with Formula B (i.e. 0.45g/100 ml of cold soluble galactomannans) an increased number of diarrheic and total defecations was observed, probably explaining the non-significant body weight gain in this group.

Disclosure of interest: M. Georgieva, N. Rasheva, R. Pancheva, E. Dimitrova, T. Draganova Stoeva: “None Declared”, A. Schaafsma is employed for FrieslandCampina and Y. Manios worked as a consultant for FrieslandCampina to monitor the study.
**Development of a core outcome set for infant colic**

Nina Steutel¹, Marc Benninga¹, Miranda Langendam², Judith Korterink¹, Flavia Indrio³, Hania Szajewska⁴, Merit Tabbers¹

¹Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Academic Medical Center, Department of Clinical Epidemiology, Bioinformatics and Biostatistics, Amsterdam, Netherlands
³Giovanni XXIII Hospital, Department of Pediatrics, Bari, Italy
⁴University of Warsaw, Pediatrics, Warsaw, Poland

**Objectives and study:** Infant colic (IC) is a common functional gastrointestinal disorder with a worldwide prevalence of 5 – 25%. This self-limiting disorder can have negative long-term consequences. Its etiology remains unknown, resulting in a wide variety in interventions and use of heterogeneous outcomes across therapeutic trials. To facilitate and improve evidence synthesis, development of a core outcome set (COS) is necessary.

**Methods:** The Delphi technique was used to collect opinions of relevant stakeholders: 133 health care professionals (HCPs) were approached at pediatric conferences and 55 parents of infants with IC were approached at pediatric outpatient clinics. All were asked to list up to 5 outcomes they considered to be relevant in the treatment of IC. Outcomes mentioned by ≥ 10% of participants were forwarded to a shortlist. Outcomes on this shortlist were rated and prioritized by HCPs and parents. Treatment outcomes with the highest scores were included in the COS.

**Results:** In total, 86% of invited stakeholders contributed to the development of the final COS. Duration of crying, reduced family stress, sleeping time of infant, quality of life (of the family), infant discomfort and reduced hospital admission/duration were rated as most important outcomes in IC.

**Conclusion:** This is the first COS that has been developed for IC. Researchers are encouraged to use this COS when setting up a new clinical trial on IC. It should serve as a minimum of outcomes to be measured and reported. This will benefit evidence synthesis, by enhancing homogeneity of outcomes, and enable evaluation of effectiveness in therapeutic trials of IC.

**Disclosure of interest:** None Declared.
Lactobacillus reuteri in the treatment of functional abdominal pain in children – randomized, double-blind, placebo-controlled study

Oleg Jadresin1, Iva Hojsak2, Zrinjka Misak2, Alemka Jaklin Kekez3, Tena Trbojevic2, Lana Ivkovic2, Sanja Kolacek2

1Children’s Hospital Zagreb, Referral Center Pediatric Gastroenterology and Nutrition, Zagreb, Croatia
2Children’s Hospital Zagreb, Paediatric Gastroenterology and Nutrition, Zagreb, Croatia
3Center for Paediatric Medicine Helena, Zagreb, Croatia

Objectives and study: Beneficial therapeutic effect of probiotics has been reported in children with the irritable bowel syndrome (IBS) but not consistently in other functional abdominal pain-related disorders. The aim of this study was to investigate the effect of Lactobacillus (L.) reuteri DSM 17938 in the treatment of functional abdominal pain (FAP) and IBS in children.

Methods: Children (age 4-18 years) referred to paediatric gastroenterologist at Children’s Hospital Zagreb from May 2012 to December 2014, diagnosed as FAP or IBS, were randomized to receive L. reuteri DSM 17938 10^8 CFU daily or placebo. The study was a prospective, randomized, double-blind, placebo-controlled parallel study. Symptoms were evaluated using Wong-Baker FACES pain rating scale for pain and Bristol scale for stool shape and consistence.

Results: Data were analyzed for 55 children (26 in the intervention group and 29 in the placebo group). Children in the intervention group had significantly more days without pain (median 89.5 vs. 51 days, p=0.029). Abdominal pain was less severe in children taking probiotics during the 2nd month (p<0.05) and 4th month (p<0.01). The two groups did not differ in the duration of abdominal pain, stool type or absence from school. Both groups experienced significant reduction in the severity of abdominal pain from 1st to 4th month, with the reduction more prominent in the intervention group (p<0.001 vs. p=0.004).

Conclusion: Administration of L. reuteri DSM 17938 was associated with a reduction of the intensity of pain and significantly more days without pain in children with FAP and IBS.

Disclosure of interest: Both preparations, active and placebo, were supplied by probiotic strain producer Biogaia, Stockholm, Sweden. BioGaia had no involvement in the design, implementation, analysis and interpretation of the data.
Long-term outcome of neonates with suspected Hirschsprung’s disease but normal rectal biopsy

Oren Ledder¹, Daniel Graph², Oleg Kharenko², Jacob Waxman², Tanya Frankel², Dan Turner³
¹Shaare Zedek Medical Center, Pediatric Gastroenterology, Jerusalem, Israel
²Shaare Zedek Medical Center, Jerusalem, Israel
³Shaare Zedek Medical Center, Genius Group, Jerusalem, Israel

Objectives and study: Hirschsprung’s disease (HD) is a congenital disorder in which ganglion cells are absent in the colon, causing constipation and, in severe cases, life-threatening toxic megacolon. The aganglionosis starts at the anus and progresses proximally to a varying degree. HD must always be considered in neonates presenting with delayed passage of meconium or very early onset constipation. Definitive diagnosis is made by rectal biopsy. Occasionally ganglia are identified but are deemed atypical in number or phenotype. The clinical significance of these findings is unknown. We aimed to assess the long-term outcomes of neonates in whom HD was suspected clinically, yet excluded by rectal biopsy.

Methods: Single-center, double cohort, comparative study. Neonates in whom suspected HD was excluded by rectal biopsy, were age and gender-matched with healthy controls born on the same day. A survey relating to clinical outcomes, stooling patterns and other gastrointestinal-related conditions was sent to parents. Pathology slides were re-reported by an experienced histopathologist blinded to the clinical data.

Results: A total of 51 neonates were included [25 case, 26 control; 41% male, median follow-up 4.25 years (IQR 2.7-6.9)]. Nine (36%) of the case group required prolonged laxative use for constipation during the first year of life compared with 0 (0%) of controls (P<0.001). This difference was maintained at the end of follow-up with 5 (20%) vs 0(0%) respectively (p=0.02). Case neonates were significantly more likely to be hospitalized or be diagnosed with a chronic gastrointestinal-related condition than controls (33% vs 12%, p=0.01; and 19% vs 8%, p=0.04 respectively). Biopsies with normal and atypical (small and/or immature ganglions) histology were compared and no significant differences were noted in any clinical outcome.

Table: Clinical manifestations during the first year of life

<table>
<thead>
<tr>
<th>Manifestation</th>
<th>Entire cohort (n=51)</th>
<th>Control group (n=26)</th>
<th>Study group (n=25)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Constipation</td>
<td>18 (35%)</td>
<td>0 (0%)</td>
<td>18 (72%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Laxative Use</td>
<td>9 (18%)</td>
<td>0 (0%)</td>
<td>9 (36%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Vomiting</td>
<td>13 (26%)</td>
<td>0 (0%)</td>
<td>13 (52%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Reflux</td>
<td>4 (8%)</td>
<td>0 (0%)</td>
<td>4 (16%)</td>
<td>0.051</td>
</tr>
<tr>
<td>Abdominal Distention</td>
<td>17 (33%)</td>
<td>1 (4%)</td>
<td>16 (64%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Abdominal Pain</td>
<td>14 (28%)</td>
<td>0 (0%)</td>
<td>14 (56%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Increased Effort of defecation</td>
<td>16 (31%)</td>
<td>1 (4%)</td>
<td>15 (60%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>Use of Anal Stimulants</td>
<td>18 (35%)</td>
<td>1 (4%)</td>
<td>17 (68%)</td>
<td>p&lt;0.001</td>
</tr>
<tr>
<td>------------------------</td>
<td>----------</td>
<td>--------</td>
<td>----------</td>
<td>---------</td>
</tr>
<tr>
<td>Irritability</td>
<td>23 (45%)</td>
<td>4 (15%)</td>
<td>19 (76%)</td>
<td>p&lt;0.001</td>
</tr>
</tbody>
</table>

**Conclusion:** Neonatal constipation is associated with long term gastrointestinal related disorders and should be considered clinically significant even when the diagnosis of HD is excluded. Neonates with early onset abnormal stooling patterns should be monitored with adequate pediatrician or pediatric gastroenterologist follow-up.

**Disclosure of interest:** “None Declared”. 
The colo-anal reflex is mediated via an extrinsic neural pathway

Palittiya Sintusek¹, Keith Lindley², Nikhil Thapar², Anna Rybak², Osvaldo Borrelli³

¹Great Ormond Street Hospital for Children NHS Foundation Trust, London, United Kingdom
²Great Ormond Street Hospital for Children NHS Foundation Trust, Pediatric Gastromotility, London, United Kingdom
³Great Ormond Street Hospital for Children NHS Foundation Trust, Neurogastroenterology and Motility Division, London, United Kingdom

Objectives and study: Colo-anal reflex is defined as internal anal sphincter (IAS) relaxation in association with high amplitude propagating contractions (HAPC). In contrast the rectoanal inhibitory reflex (RAIR) is the transient relaxation of IAS response to rectal dilatation. RAIR is considered to be neuronal in origin and plays vital pathological role in Hirschsprung’s disease while few data support the pathophysiology of colo-anal reflex. The colo-anal reflex is thought to be neurally mediated neural pathways are poorly defined. Our aim was to measure the RAIR and colo-anal reflex in children who had undergone segmental distal bowel resection.

Methods: We retrospectively reviewed motility investigations (anorectal manometry and colonic manometry) performed in 3 constipated children who had previously undergone a Hartmann’s procedure +/- pullthrough.

Results: All 3 cases demonstrate persistence of the the coloanal reflex when the myenteric plexus has been disrupted with a colostomy. This suggests that the reflex is mediated either via the extrinsic nerves or through non-neural mechanisms. Case 2, had undergone a Duhamel procedure for Hirschprung’s disease but had a preserved colo-anal reflex despite the rectum being aganglionic. RAIR was absent in keeping with disruption of the myenteric plexus. This finding supports the notion that the extrinsic nerves might control colo-anal reflex.

Table:

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age (year)</th>
<th>Underlying condition</th>
<th>Surgical operation</th>
<th>Rectal suction biopsy</th>
<th>High resolution anorectal manometry</th>
<th>High resolution colonic manometry</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Resting pressure (mm Hg)</td>
<td>RAIR</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Position of catheter</td>
<td>HAPC s</td>
</tr>
<tr>
<td>1</td>
<td>Male</td>
<td>9.2</td>
<td>Distal colonic dysmotility</td>
<td>- Hartmann’s procedure</td>
<td>Ganglionic</td>
<td>50-70</td>
<td>Present</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>Presen t</td>
<td>Catheter 2: via rectum</td>
</tr>
<tr>
<td>2</td>
<td>Male</td>
<td>9.4</td>
<td>Hirschsprung’s disease</td>
<td>Duhamel procedure. Subsequent</td>
<td>Ganglionic</td>
<td>45</td>
<td>Absent</td>
</tr>
</tbody>
</table>
Conclusion: This study supports the notion that colo-anal reflex is mediated via extrinsic neural pathways and not via the myenteric plexus. We suggest that with the increasing use of high resolution colonic manometry catheters, it is likely that documentation of the presence of colo-anal reflex will become an important part of the manometric assessment protocol to confirm integrity of the spinal nerves. Further studies are necessary to extend the knowledge of the physiological processes involved in the colo-anal reflex.

Disclosure of interest: None Declared.
Utility of antroduodenal manometry in predicting response to prokinetics children with upper gastrointestinal symptoms

Raquel Plácido Paías¹, Aldo Recinos², Leonel Rodríguez³

¹Hospital de Mérida, Mérida, Spain
²Lincoln Medical Center, New York, United States
³Boston Children’s Hospital, Co-Director Colorectal Center, Boston, United States

Objectives and study: Evaluate the utility of the antroduodenal manometry (ADM) in predicting therapeutic response to prokinetics in children with upper gastrointestinal (UGI) symptoms.

Methods: Retrospective study including children referred to the Motility and Functional Gastrointestinal Disorders in Boston for evaluation of UGI symptoms (nausea, early satiety, vomiting and abdominal pain) undergoing an ADM study. Response to 4 prokinetic agents (erythromycin, cyproheptadine, cisapride and metoclopramide) was classified as successful (those with symptom resolution or response that did not require further therapies/interventions) or failure (lack of response or partial response with requirement of other therapies/interventions). Response was also classified as initial (response to first prokinetic medication given after ADM was performed) or final (response to all prokinetic medications received after ADM). ADM study included fasting (presence of migrating motor complex or MMC), post-prandial response and response to challenges with erythromycin (for antrum) and octreotide (for intestine), divided in antrum and duodenum.

Results: A total of 127 children were included, mean/median age were 9.9/8.8, respectively and 58% were female. We found no association between overall ADM diagnosis and prokinetic response. We did not observe an association between response to prokinetics and the findings of the ADM in the antrum. We did observe an association between the presence of MMC in the intestine during fasting and the initial and final response to prokinetic agents as well as with the intestinal post-prandial and the initial response to prokinetic agents.

<table>
<thead>
<tr>
<th>Prokinetic Response</th>
<th>Fasting</th>
<th>Postprandial</th>
<th>Erythromycin</th>
<th>Octreotide</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antrum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Initial Response</td>
<td>(p=0,056)</td>
<td>(p=0,124)</td>
<td>(p=0,117)</td>
<td>N/A</td>
</tr>
<tr>
<td>- Final Response</td>
<td>(p=0,420)</td>
<td>(p=0,628)</td>
<td>(p=0,275)</td>
<td>N/A</td>
</tr>
<tr>
<td>Intestine</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- Initial Response</td>
<td>(p=0,004)</td>
<td>(p=0,004)</td>
<td>N/A</td>
<td>(p=0,228)</td>
</tr>
<tr>
<td>- Final Response</td>
<td>(p=0,034)</td>
<td>(p=0,109)</td>
<td>N/A</td>
<td>(p=0,396)</td>
</tr>
</tbody>
</table>

*Statistical significance when p value <0.05

Table: You can include one table here. Your table can contain a maximum number of 10 columns and a maximum number of 10 rows. Please note that the table may significantly reduce the number of available characters. If you do not want to include a table, please delete this section in your document.

Conclusion: Although we found no association between the overall results of the ADM and the response to prokinetics we did observe a significant association between the presence of MMC in the intestine during fasting and the intestinal postprandial response with the response to prokinetics. Despite the knowledge that prokinetics agents effect is located in the antrum, it seems that the
presence of normal fasting function is more important to predict outcomes. The presence of the MMC may be useful to predict a successful response to prokinetic agents.

Disclosure of interest: "None Declared".
GASTROENTEROLOGY: GI motility, GERD and functional GI disorders

G-P-273

Hydrogen breath testing in children: A retrospective audit of practice in a tertiary paediatric unit.

Rashad Hasanov1, David Rawat2, Daniel Sifrim3, Qasim Aziz2, Sarah Allen2

1 Queen Mary’s University, London, United Kingdom
2 The Royal London Hospital, Paediatric Gastroenterology, London, United Kingdom
3 Queen Mary University of London, Wingate Institute of Neurogastroenterology, London, United Kingdom

Objectives and study: Hydrogen breath testing (HBT) is a non-invasive, sensitive test used to detect small intestinal bacterial overgrowth (SIBO) and intolerance or malabsorption of certain carbohydrates i.e. lactose, fructose, sucrose. SIBO may be a common cause of irritable bowel syndrome (IBS). It is associated with a range of common paediatric gastrointestinal symptoms including abdominal pain, bloating, diarrhoea and constipation. Despite this there is a lack of consensus regarding the methodology and interpretation of results for HBT. The objective of this study was to evaluate the current protocol for HBT in a tertiary paediatric gastroenterology unit by retrospectively reviewing our current practice.

Methodology: Patients suspected of having SIBO or carbohydrate malabsorption (based on clinical symptoms) by paediatric gastroenterologists at a tertiary gastroenterology unity were recruited. Bedfont Gastro+ Gastrolyzer device was used for HBT measurement using a standard, departmental protocol. Data of medical comorbidities, clinical presentation, symptom reportage during testing, results and clinical outcomes were recorded and analysed. 123 paediatric patients (M: F 54:80), median age 11 years (range 2 to 21) were included in the study. Data was collected over a 28 month period from January 2013 to April 2015.

Results: In total 134 hydrogen breath tests were analysed (Lactulose n=93; lactose n=33; fructose n=5; sucrose n=3). 63/134 (47%) of HBT were positive, of which follow-up data was available for 56 patients. 63.1% with a diagnosis of SIBO had a complete improvement of symptoms and 15.7% had a partial improvement. 5.2% had a deterioration in symptoms and 5.2% patients relapsed following antibiotic treatment. 9 patients (6.7%) reported symptoms of discomfort or related GI symptoms during SIBO or lactose HBT. Abdominal pain (n=88) was the main presenting symptoms as indication for HBT, followed by constipation with bloating (n=47), chronic diarrhoea (n= 39). 83% patients with a positive result for carbohydrate intolerance / malabsorption had complete resolution of symptoms following referral to a dietician and adherence to an elimination diet.

Conclusion: HBT is a useful, differential investigation for children presenting with functional and chronic gastrointestinal disorders. Two thirds of selected patients in a tertiary paediatric gastroenterology unit had a clinical improvement following treatment after a positive result using HBT. As yet there is no documented consensus for the indications, methodology and analysis of HBT in the paediatric population. Further studies are required to validate the investigation protocol for HBT and the treatment for SIBO.

Disclosure of interest: None Declared.
Gastroesophageal reflux symptoms in healthy infants measured by the Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R): a cross-sectional study

Romy Koning¹, Maartje Singendonk¹, Marije Smits¹, Marc Benninga², Michiel van Wijk¹

¹Emma Children's Hospital/Amc, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands
²Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Symptoms related to gastroesophageal reflux (GER) are nonspecific, occur frequently in healthy infants and diminish with age. Nevertheless, they remain the cornerstone in diagnosing gastroesophageal reflux disease (GERD). The Infant Gastroesophageal Reflux Questionnaire Revised (I-GERQ-R) is available to objectively score and evaluate GER related symptoms, but has not been validated to differentiate GERD infants from other symptomatic, but non-GERD infants. This could partially be due to the lack of established reference values for symptoms in specific age groups. Our aim was therefore to measure the presence of GER related symptoms in healthy infants in different age groups, using the I-GERQ-R.

Methods: We performed a cross-sectional survey in healthy children aged 0-24 months during their regular check-ups at well-baby clinics. Caregivers completed the I-GERQ-R (total score 0-42, cut-off value suggestive for GERD ≥16) and information regarding growth and nutrition was noted. Data are presented as median (p5-p95 or IQR). Spearman's correlation coefficient (rs) was calculated to explore age-related trends. Grouped data were compared using Kruskal-Wallis one-way ANOVA on ranks.

Results: 164 consecutive infants (52.5% male) aged 6.3 (IQR 2.3-11.2) months were included. Five infants (3.0%) had an I-GERQ-R score ≥16, one of these infants had also received a diagnosis of GERD by a healthcare professional. Median I-GERQ-R score for all infants was 5.0 (p5-p95: 0.0-13.8). I-GERQ-R scores significantly decreased with age (rs= -0.641, p<0.001; table 1). A similar trend was seen for clustered symptoms regarding regurgitation and colic associated symptoms only. No significant differences were found in I-GERQ-R scores between solely breastfed and solely formula-fed infants (p=0.68).

Table:

<table>
<thead>
<tr>
<th>Median scores (p5-p95)</th>
<th>0-1 months (n=12)</th>
<th>1-2 months (n=22)</th>
<th>2-4 months (n=22)</th>
<th>4-6 months (n=21)</th>
<th>6-12 months (n=52)</th>
<th>12-18 months (n=21)</th>
<th>18-24 months (n=21)</th>
<th>TOTAL (n=164)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I-GERQ-R (0-42)</td>
<td>9.50 (4.0-18.9)</td>
<td>9.00 (2.15-21.10)</td>
<td>7.00 (0.15-12.85)</td>
<td>6.00 (1.0-13.5)</td>
<td>4.00 (0.0-9.35)</td>
<td>1.50 (0.0-4.9)</td>
<td>1.00 (0.0-6.2)</td>
<td>5.00 (0.0-13.8)</td>
</tr>
</tbody>
</table>

Conclusion: Symptoms of gastroesophageal reflux measured by the I-GERQ-R decreased with age in the first 24 months of life in healthy infants. These findings implicate that age dependent reference values are needed for future diagnostic tests for GERD. Infants experience the same GER related symptoms when solely formula fed compared to when solely breastfed.

Disclosure of interest: None declared.
An Importance of Magnesium Deficiency in the Formation of Vegetative Disadaptation in Children and Adolescents with Digestive Tract Pathology

Serhii Potapenko1, Liudmyla Boiarska1

1Zaporizhzhia State Medical University, Department of Children Deseasees, Zaporizhzhia, Ukraine

Objectives and study: The level of absorption disorder depends on the depth and reversibility of damage over the whole length of digestive tube. Pathology development of the digestive system runs the gamut from minimal, reversible, functional disorders to organic pathological changes. Vegetative disadaptation of the organism plays an important role during the development of functional and organic digestive organs disorders. As a result, detection of the magnesium deficiency and its influence on vegetative disadaptation progression can help to correct damages in early stages and to decrease frequency of chronization of digestive tract disorders in children. Determination of frequency of magnesium deficiency occurrence and its influence on the vegetative disadaptation development in children and adolescents with digestive tract pathology.

Methods: 48 children at the ages from 7 to 17 years with complaints of sickliness, stomachache, dyspeptic symptoms were under the care. History taking, physical examination, fiberoptic esophagogastroduodenoscopy were carried out. Patients were divided into two groups: the first group – 28 children with organic digestive system disorders, the second one – 20 children with functional digestive system disorders. In both groups serum and intracellular concentration of Mg, Holter monitoring of ECG were carried out.

Results: In 43% of children serous and intracellular magnesium indices were lowered, what speaks for magnesium deficit. 18,7% of children had normal indices of serous magnesium and lowered intracellular magnesium indices, i.e. magnesium hypoelementosis came around. There was no evidence of magnesium deficiency in 67,8% of patients in the first group. 25,1% of children had characters of magnesium hypoelementosis. Deficit of magnesium was diagnosed in 7,1% of cases. Examination of patients from the second group has demonstrated normal indices of magnesium more frequently (90%, p ≤0,001), but magnesium hypoelementosis more rarely (10%, p ≤0,05), then in children from the first group and magnesium deficit was not detected. Correlation relationships between time-line analysis of heart rate variability (mRR, SDNNi, RMSSD, pNN50) and serous and intracellular magnesium content were analyzed. It was detected direct, strong correlation line between lowering of intracellular magnesium level and lowered indices of HRV time-line analysis in children from the first group (pNN50 and intracellular magnesium (r=0,85; t≥3), SDNNi, intracellular magnesium (r=0,8; t≥3) and absence of correlation in patients from the second group.

Conclusion:

1. Among children and adolescents with digestive tract pathology, 4,3% patients with magnesium deficit characters were educed.
2. Characters of hypoelementosis were detected in 18,7% cases, what demonstrates great prevalence of latent magnesium deficiency and the necessity to study its intracellular content.
3. In children from the 1st group indices of both intracellular (p≤0,05) and extracellular (p≤0,001) magnesium are much lower than in children from the 2nd group, what demonstrates mutual influence of organic digestive tract pathology and magnesium deficit on the development and severity of pathologies.
4. Direct and strong correlation line between intracellular magnesium level lowering and lowered indices of HRV time-line analysis in the 1st group and correlation absence in the 2nd group.

Disclosure of interest: None Declared.
Neonatal programming of functional gastrointestinal disorders in infants

Silvia Salvatore¹, Enzo Dattoli¹, Dario Dillilo², Licia Pensabene³, Mariella Baldassarre⁴, Lucia Morando⁴, Valentina Mancini⁵, Valentina Talarico⁶, Loredana Bellantuomo⁷, GianVincenzo Zuccotti⁸, Massimo Agosti⁹

¹University of Insubria, Varese, Italy
²Ospedale Buzzi, University of Milan, Pediatrics, Milan, Italy
³University of Catanzaro, Pediatrics, Catanzaro, Italy
⁴University of Bari, Neonatology Unit, Bari, Italy
⁵Pediatrìa, Parma, Italy
⁶Pediatrics, Catanzaro, Italy
⁷University of Bari, Bari, Italy
⁸Ospedale Buzzi, University of Milan, Milan, Italy
⁹Neonatal Department, Varese, Italy

Objectives and study: Functional gastrointestinal disorders (FGIDs) are common in infants, represent a frequent condition of parental distress and pediatric referral. To date, predisposing or protective factors for FGIDs still need to be clarified but could be crucial to identify preventive strategies. The aim of this study was to assess the influence of different neonatal factors on the incidence of FGIDs in the first months of life.

Methods: This is a prospective multicenter study including preterm and at term newborns consecutively enrolled at birth and followed up till one year of age. Exclusion criteria were represented by: malformations, (any kind of) surgery, neurological, immune, metabolic, cardiac or renal diseases or incomplete follow-up. FGIDs were classified according to Rome II criteria and assessed through a standardized interview by a dedicated physician at each hospital. Data were collected using a specific form at 1, 3, 6, and 12 months. Gestational age, mode of delivery, feeding pattern, antibiotic administration in neonatal period, and duration of hospitalization at birth were considered.

Statistical analysis was performed by JMP program (version 11) using chi square test and multivariate analysis.

Results: 1152 newborns (gestational age 163-297 days, 337 preterm, 29%, and 815, 71%, at term newborns) were recruited and completed the study. Preliminary analysis showed an overall significantly (p<0.0001) higher incidence of FGIDs during the first year of life in preterm compared to at term newborns, and particularly of regurgitation (47% vs. 39%, p =0.019) and colic (60% vs. 45%, p<0.001). Overall FGIDs were significantly (p=0.001) more reported in infants born with caesarean section (OR 1.7) or given antibiotics in the first week of life (OR 2.1), or with a long hospitalization at birth (OR 1.9). Regurgitation was also more frequent (p<0.001) in infants who had a longer (>7 days) hospitalization at birth. Colic was significantly associated with preterm delivery, low birth weight, neonatal antibiotics, duration of hospitalization and formula feeding.

Conclusion: Preterm delivery and neonatal use of antibiotic are associated with an increased incidence of FGIDs in the first months of life. Caesarean section, formula feeding and longer hospital staying at birth may represent additional risk factors determining the higher prevalence of FGIDs in preterm compared to at term newborns and need to be further analyzed.

Disclosure of interest: None Declared.
Transanal irrigation in the treatment of children with intractable constipation

Sophie Kuizenga-Wessel¹, Ilan Koppen¹, Heleen Voogt¹, Marc Benninga²

¹Emma Children's Hospital / Amc, Pediatric Gastroenterology, Amsterdam, Netherlands
²Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Transanal colonic irrigation (TAI) has been shown effective in the management of children with defecation disorders due to organic causes. However, data on the effectiveness of TAI in children with functional constipation (FC) are scarce. Aim of this study was to assess the treatment efficacy and parental satisfaction in pediatric patients treated with TAI.

Methods: Cross-sectional survey study among parents of children (age 0-18 years) treated with TAI (Peristeen®) for either organic or functional constipation. FC had been diagnosed based on the Rome III criteria. Anonymous questionnaires were sent out to parents via mail, these consisted of 25 self-developed, multiple-choice questions regarding the use of TAI, current gastrointestinal symptoms, concomitant medication use, school absence, hospitalizations and parental satisfaction.

Results: Out of 121 invited families, 91 (75%) returned the questionnaire. The majority of children had FC (74%), other diagnoses included anorectal malformations (12%) and Hirschsprung’s disease (4%). In total, 92% of patients suffered from fecal incontinence prior to treatment. Out of all children who still used TAI at the time of survey (n=68), fecal incontinence had resolved completely in 35%, 15% experienced occasional episodes of fecal incontinence (<1 episode per week) and the remaining 50% still suffered from episodes of fecal incontinence regularly (≥1 time per week). A total of 40 children (44%) experienced pain during rectal irrigation, especially during insertion of the catheter, inflating the balloon or during irrigation. Overall, 90% of the parents was satisfied with the result of transanal irrigation and 70% reported that they would continue using transanal irrigation for the treatment of their child’s symptoms.

Conclusion: TAI is an effective treatment for children with either organic or functional constipation with a high parental satisfaction.

Disclosure of interest: M.A. Benninga has worked as a consultant for Shire, Sucampo, Astra Zeneca and Danone. The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed. Other authors: “none declared”.
Reporting on outcome measures of functional constipation in children

Sophie Kuizenga-Wessel¹, Sascha Heckert¹, Willemijn Tros¹, Faridi Van Etten-Lamaludin¹, Marc Benninga², Merit Tabbers²

¹Emma Children's Hospital / Amc, Pediatric Gastroenterology, Amsterdam, Netherlands
²Academic Medical Center / Emma Children's Hospital, Department of Pediatric Gastroenterology and Nutrition, Amsterdam, Netherlands

Objectives and study: Standardized outcome measures provide a basis for comparing outcomes of different clinical trials. Consequently, they can serve as the foundation for determining which therapeutic interventions are most effective. The aim of this study is to systematically assess how definitions and outcome measures are defined in therapeutic randomized controlled trials (RCTs) of children with functional constipation (FC).

Methods: Pubmed, EMBASE, and Cochrane databases were searched. Studies were included if it was a (systematic review of) therapeutic RCT, concerning children 1-18 years old with FC, a definition of FC was provided, and if they were written in English. The Delphi list was used for quality assessment.

Results: A total of 4092 articles were found but only 45 studies fulfilled our inclusion criteria. In these 45 trials, 22 different definitions of FC were used (17 studies used the Rome III criteria), 27 different interventions were investigated and 29 different definitions of treatment success were used. A total of 30 RCTs (57%) reported primary outcomes of which treatment success was the most frequently used. Most trials (80%) used parental diaries of which only 2 RCTs stated that their instrument was validated. Twenty-four trials (53%) were of good methodological quality.

Conclusion: Inconsistency and heterogeneity exist in definitions and outcome measures used in RCTs on childhood FC. Standard definitions, outcome measures and also validated instruments are needed. We recommend the development of a minimum core outcome set for clinical research in children with FC in order to make comparison possible between the effects of different therapeutic interventions across studies. As next step, we will involve health care professionals and care givers in the development of COS.

Disclosure of interest: “None declared”.

Vol. 62, Supplement 1, May 2016
Surgical management of children with functional constipation: What are we doing and are we doing it right?

Sophie Kuizenga-Wessel1, Ilan Koppen1, Peter Lu2, Marc Benninga3, Carlo Di Lorenzo2, Victoria Lane4, Marc A. Levitt5, Richard Wood5, Desalegn Yacob2

1Emma Children's Hospital / Amc, Pediatric Gastroenterology, 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
4Nationwide Children's Hospital, Center for Colorectal and Pelvic Reconstruction, Columbus, United States
5Nationwide Children's Hospital, Pediatric Surgery, Columbus, United States

Objectives and study: Surgical decision-making in children with intractable functional constipation (FC) is a challenge faced by pediatric gastroenterologists and pediatric surgeons worldwide. Currently, there are no guidelines for the surgical management of children with intractable FC. The development of advanced manometry techniques has enabled better characterization of motility disorders, but there are no clear recommendations for its use in surgical decision-making. We want to evaluate the diagnostic and surgical approach towards pediatric patients with intractable FC among physicians working in pediatric surgery and pediatric gastroenterology.

Methods: A self-developed survey was administered to physicians attending the 2015 Pediatric Colorectal, Motility and Pelvic Reconstruction Conference, held simultaneously in Columbus, Ohio, USA and Nijmegen, the Netherlands.

Results: 74 physicians (16 countries) filled out the questionnaire; 55 from pediatric surgery (29 faculty members, 23 fellows, 3 residents) and 19 from pediatric gastroenterology (13 faculty members, 5 fellows, 1 private practice). Anorectal manometry (AMAN) was used routinely by 20% of responders while 50% used it occasionally. Colonic manometry (CM) was used routinely by 11% and occasionally by 27%. Responders who used AMAN (n=52) utilized this to rule out Hirschsprung's disease (65%), to diagnose anal achalasia (58%), to detect dyssynergia (56%), to assess sphincter integrity (50%) and for guidance of pelvic floor surgery decision-making (27%). Out of all physicians utilizing AMAN, 52% would consider anal sphincter botulinum toxin injections for anal achalasia and 21% would use it to treat dyssynergia. Out of 28 responders who used CM, 61% employed it to differentiate neuropathic from myopathic dysmotility, 57% to guide surgical decision-making, 54% to differentiate organic from functional pathology and 36% to assess disease severity. Case-based survey questions on patients with intractable FC and specific manometry findings resulted in a variety of surgical approaches among the 28 responders (16 faculty, 11 fellows and 1 resident) who reported using both AMAN and CM (Table 1).

Conclusion: Surgical decision-making for children with intractable FC differs among physicians and medical centers. In specialized centers, AMAN and CM are often used to guide surgical decision-making. However, since there are no guidelines, the application and interpretation of manometry varies among physicians, resulting in various surgical approaches. There is a need for clinical guidelines regarding the role of AMAN and CM in surgical decision-making in children with intractable FC.

Disclosure of interest: “None Declared”.
GASTROENTEROLOGY: GI motility, GERD and functional GI disorders

G-P-280

Gastric emptying and myoelectrical activity in children with Esophageal atresia-tracheoesophageal fistula

Angela Le¹, Sara Hulbert², Taher Omari³, Usha Krishnan²

¹University of New South Wales, School of Women’s and Children’s Health, Sydney, Australia
²Sydney Children’s Hospital, Pediatric Gastroenterology, Sydney, Australia
³Flinders University, School of Medicine, Bedford Park, Australia

Objectives and study: The aim of this study was to determine gastric emptying and myoelectrical activity in children with repaired oesophageal atresia and tracheoesophageal fistula (EA-TEF). The secondary aim was correlation of the results of gastric emptying and myoelectrical activity with symptoms in this cohort.

Methods: Prospective study in children with EA-TEF where gastric myoelectrical activity and gastric emptying were studied using surface electrogastrography (EGG) and ¹³C-octanoic acid breath test (OBT) respectively. The studies were conducted over a four hour period and involved a liquid test meal after a period of fasting. Where applicable, prokinetics were ceased a week prior to the study. EGG results were considered abnormal if there was < 75% of waves in 2-4cpm during post prandial period and/or post-prandial to fasting power ratio < 1 (Bentur et al., 2006). Gastric emptying parameters including gastric emptying half time (T1/2), maximal excretion time, (Tmax), lag phase before emptying starts (Tlag), gastric emptying coefficient (GEC) were defined as normal/abnormal by matching with historical age and sex matched control data. The validated PedsQL gastrointestinal symptoms questionnaire was completed by each parent and also by child if >5 years. Correlations between EGG and OBT parameters was determined. Relationships between EGG and OBT parameters and PedsQL symptom scores, demographic factors (age, type of EA-TEF), surgical history (gastrostomy and fundoplication), previous strictures needing dilatations, use of anti-reflux medications, results of investigations for gastroesophageal reflux disease (endoscopy and impedance (MII-pH) study) was also explored.

Results: Eight orally fed patients were included (see Table 1). The majority (75%) of participants showed abnormal gastric myoelectrical activity in EGG and 50% had delayed gastric emptying in OBT. There was significant correlation between abnormal gastric myoelectrical activity in EGG (postprandial to fasting power ratio) and gastric emptying coefficient (GEC) in OBT, (p = 0.03). No significant correlations were seen between any of the other EGG and OBT parameters. There was no significant correlation between EGG or gastric emptying results and parent or child reported PedsQL gastrointestinal symptom scores. There was also no significant correlation between age of patient, type of EA-TEF, history of gastrostomy, fundoplication, strictures needing dilatations, use of anti-reflux medications, abnormal endoscopy and impedance results, and EGG or OBT results.
Table:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Male</th>
<th>1</th>
<th>12.5%</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Female</td>
<td>7</td>
<td>87.5%</td>
</tr>
<tr>
<td>Age (mean years)</td>
<td>4.0425</td>
<td>(0.25 – 8)</td>
<td></td>
</tr>
<tr>
<td>Birth weight (mean g)</td>
<td>2706.67</td>
<td>(2090 – 4210)</td>
<td></td>
</tr>
<tr>
<td>Type of EA</td>
<td>A</td>
<td>1</td>
<td>12.5%</td>
</tr>
<tr>
<td></td>
<td>C</td>
<td>7</td>
<td>87.5%</td>
</tr>
<tr>
<td>Anti-reflux medications use</td>
<td>6</td>
<td>75%</td>
<td></td>
</tr>
<tr>
<td>Fundoplication</td>
<td>3</td>
<td>37.5%</td>
<td></td>
</tr>
<tr>
<td>Gastrostomy (closed)</td>
<td>3</td>
<td>37.5%</td>
<td></td>
</tr>
<tr>
<td>Strictures</td>
<td>4</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Endoscopy results</td>
<td>7</td>
<td>87.5%</td>
<td></td>
</tr>
<tr>
<td>Performed</td>
<td>1</td>
<td>14.3%</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>6</td>
<td>85.7%</td>
<td></td>
</tr>
<tr>
<td>Impedance results</td>
<td>4</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Performed</td>
<td>0</td>
<td>0%</td>
<td></td>
</tr>
<tr>
<td>Normal</td>
<td>4</td>
<td>100%</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** In this pilot study, abnormal gastric myoelectrical activity and delayed gastric emptying were prevalent in children with EA-TEF. Whilst there was significant correlation between objective measures of gastric function as determined by EGG and OBT, measures of abnormal gastric function did not significantly correlate with subjectively reported gastrointestinal symptoms.

**Disclosure of interest:** None Declared.
Prevalence of Gastrointestinal functional disorders in a cohort of children affected by type II and III Spinal Muscular Atrophy

Valentina Giorgio¹, Roberta D’Aniello², Anna Galimberti¹, Debora Panico², Alessandra Ciliberti², Silvia Marcanio², Daniela Leone³, Marika Pane³

¹Fondazione Policlinico Gemelli, University of Sacred Heart of Rome, Pediatric Department, Rome, Italy
²Fondazione Policlinico Gemelli, Rome, Italy
³Fondazione Policlinico Gemelli, Centro Clinico Nemo, Rome, Italy

Objectives and study: Spinal Muscular Atrophy (SMA) are genetic disorders that occur with different degrees of severity in paediatric age. The spectrum of neuromuscular symptoms is wide and variable, frequently including gastrointestinal (GI) disorders such as dysphagia, constipation and malnutrition. SMA types II and III have nowadays are less linked to GI disorders, and are characterized by a longer life expectation than SMA type I. Little is known about functional GI disease prevalence in this subgroup of patients. The aim of this study was to evaluate the prevalence of functional GI disorders in a cohort of children affected by SMA types II and III.

Methods: A questionnaire was administered to parents to investigate caloric intake, type of food preparation, presence of cough during meal, vomiting, regurgitation, and chronic constipation. To evaluate bowel habits we used the Bristol Stool Chart.

Results: The study included 22 patients, 14 males, age range 2-20 years (median age 4.7 years), affected by SMA type II and III. Data obtained from questionnaire are reported in table 1 (Table 1). Concerning food preparation, 91% of the studied population can manage solid foods. None reported cough or other respiratory problems during meals. The evaluation of GI symptoms showed in 13% of patients symptoms suggestive of gastroesophageal reflux, and in 45.5 % chronic constipation needing medically assisted defecation (polietilenglicole was effective in all constipated children). 36.3% of children evacuates hard or impacted stool (type 1 and 2 of the Bristol Scale).

Table:

<table>
<thead>
<tr>
<th>Type of food preparation</th>
<th>LIQUID /</th>
<th>SEMI SOLID</th>
<th>SOLID</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vomiting/regurgitation</td>
<td>YES 13%</td>
<td>NO 87%</td>
<td></td>
</tr>
<tr>
<td>Cough or other respiratory problems during meal</td>
<td>/</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Constipation</td>
<td>YES 45.5%</td>
<td>NO 55.5%</td>
<td>NO 87%</td>
</tr>
</tbody>
</table>

Conclusion: Constipation is prevalent in children affected by SMA types II and III. Polietilenglicole should be offered to this group of children to improve defecation despite low grade of active motility. Further studies on larger series are needed to clarify GI prevalence in SMA children, and to assess the appropriate polietilenglicole dosage in constipated once..

Disclosure of interest: None declared.
Effects of postnatal overfeeding and ω3PUFAs diet on hepatic ACC in rats

Nan Zhou¹, Yanyan Dai¹, Fan Yang¹, Dongqing Xia¹, Cuiting Min¹, Xiaonan Li²

¹Departments of Child Health Care, Nanjing Medical University, Nanjing Children’s Hospital, Nanjing, China, Nanjing, China
²Departments of Child Health Care, Nanjing Medical University, Nanjing Children’s Hospital, Nanjing, China, Institute of Pediatric Research, Nanjing Medical University, Nanjing, China, Nanjing, China

Objectives and study: Early life nutrition is important in the regulation of metabolism in adulthood. The present study aimed to evaluate the effects of postnatal overfeeding and polyunsaturated fatty acid diet given after weaning on the expression of lipid synthesis associated enzyme acetyl-coa carboxylase (ACC) and its transcription factors (SREBP-1c) in adulthood, and clarify the mechanism of hepatic lipid metabolism in the early nutrition programming.

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. After weaning (P21), the two groups were given standard chow or fish oil diet enriched with polyunsaturated fatty acids until postnatal week 13 (W13). Four groups were NL, SL, NL-FO, SL-FO. In vitro study, HepG2 cells were induced by oleate (OA) and then stimulated by EPA for 24h, or HepG2 cells were blocked with SREBP-1c siRNA firstly, then repeated previous steps. The mRNA expression of ACC, SREBP-1c was determined by real-time qPCR, and the enzyme activity of ACC was determined by isotopic assay.

Results: The weight gain, dyslipidemia and greater liver mass gain and hepatic triglyceride accumulation were higher in SLs than those of NLs at W3(P<0.05) and W13 (P<0.05) due to the postnatal overfeeding. Moreover, the postnatal overfeeding could increase the levels of ACC and SREBP-1c mRNA expression from W3 to W13(P<0.05). Compared to standard diet, fish oil diet in SLs not only reduced weight gain, improved serum lipid levels and hepatic triglyceride accumulation, but also reduced the level of ACC and SREBP-1c mRNA expression at W13 (P<0.05). In vitro, Intracellular lipid droplets was increased in HepG2 cells induced by OA (P<0.05), according with ACC, SREBP-1c mRNA expression up-regulated. In contrary, intracellular lipid droplets was reduced (P<0.05) and the mRNA expression of ACC, SREBP-1c was down-regulated in HepG2 cells stimulated with EPA (P<0.05). Moreover, SREBP-1c siRNA inhibited the effect of OA on HepG2 cells and consistently reduce ACC mRNA and activity when combined with EPA (P<0.05).

Conclusion: Postnatal overfeeding promoted the development programming of ACC, and fish oil diet could reduce ACC expression through down regulating SREBP-1c, which could improve hepatocyte lipid accumulation and provide a scientific basis for prevention and treatment of children non-alcoholic fatty disease.

Disclosure of interest: None Declared.
Liver transplantation for young people with biliary atresia and academic outcome of long-term survivors

Vandana Jain¹, Mark Davenport², Anil Dhawan¹, Dino Hadzic¹, Nigel Heaton³, Marianne Samyn¹

¹King's College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom
²King's College Hospital, Department of Paediatric Surgery, London, United Kingdom
³King's College Hospital, Institute of Liver Studies, London, United Kingdom

Objectives and study: Approximately 50% of BA patients are reported to survive into adulthood with their native liver, however, the progressive nature of the illness leads to complications as cholangitis and portal hypertension +/- variceal bleeding necessitating liver transplantation (LT) in adulthood. The optimal timing for LT remains a matter of debate but with adult listing criteria based on prognostic models, longer waiting times and living related donation a less likely option, young people (YP) requiring LT face different challenges compared to their younger peers. The aim of this study was to review the indications, listing criteria and outcome post LT for a cohort of YP with BA.

Methods: A retrospective review, single centre review was carried out on BA patients post Kasai portoenterostomy who required listing for LT > 11 yrs.

Results: 36 YP (16 M) had LT between 1991-2014 at a median age of 16.6 yrs (range 11.2-27.2). Median age at listing was 14.7 yrs (range 10.3-26.7) and median time on the waiting list 6.5 mths (range 0.3-79.7). The most common indications for listing were recurrent cholangitis (31%), synthetic failure (20%) and acute variceal bleeding (15%). Laboratory data and prognostic models did not change from time of listing to LT (table). Five (3 female) required admission to intensive care unit (ICU) at the time of listing (cholangitis (n=3), variceal bleeding (n=2)). MELD score > 12 (72% at listing and LT) and UKELD score > 49 (88% at listing and 92% at LT), used as minimal listing criteria for adults in the UK, were not associated with death or ICU admission. Patient survival after 1, 5 and 10 yr was 97%, 88% and 88% respectively. 4 had re-LT. 89% are alive after median follow up of 7.9 yrs (range 0.2-22.7). Admission to ICU at listing was associated with death (p<0.01) and re-LT (p=0.027). Patients aged >18 yrs (n=10) at listing, spent longer on the waiting list (med 10 vs 6 mths, p=0.01) and were more likely to be admitted to ICU (5 vs 1, p<0.01) with no difference in survival, re-LT, laboratory data or prognostic models. Serum bilirubin levels of > 100 micromol/l at LT were associated with death (4/16 vs 1/20, p=0.045) but not with ICU admission or re-LT. When comparing educational and professional outcome of 22 with a matched group of 14, transplanted at median age of 1.2 yrs (range 0.6-10.9), those transplanted at a younger age were more likely to have completed higher education and/or be in employment at follow up (100% vs 77%, p=0.054) with no difference in graft function or re-LT.

Table:

<table>
<thead>
<tr>
<th>N=36</th>
<th>Listing</th>
<th>LT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>16.2 (11.7-26.7)</td>
<td>16.6 (12.3-27.2)</td>
</tr>
<tr>
<td>INR</td>
<td>1.23 (0.93-2.63)</td>
<td>1.31 (0.81-2.64)</td>
</tr>
<tr>
<td>Serum bilirubin (micromol/l)</td>
<td>58 (17-368)</td>
<td>78 (22-801)</td>
</tr>
<tr>
<td>Sodium (micromol/l)</td>
<td>139 (124-143)</td>
<td>138 (127-145)</td>
</tr>
<tr>
<td>Albumin (g/l)</td>
<td>34 (21-45)</td>
<td>34 (22-46)</td>
</tr>
<tr>
<td></td>
<td>LT</td>
<td>&lt;18 yrs</td>
</tr>
<tr>
<td>------------------</td>
<td>------</td>
<td>--------</td>
</tr>
<tr>
<td>GGT (IU/l)</td>
<td>142</td>
<td>129</td>
</tr>
<tr>
<td>(10-560)</td>
<td>(17-564)</td>
<td></td>
</tr>
<tr>
<td>AST (IU/l)</td>
<td>102</td>
<td>112</td>
</tr>
<tr>
<td>(20-317)</td>
<td>(43-657)</td>
<td></td>
</tr>
<tr>
<td>Platelets (10⁹/l)</td>
<td>57</td>
<td>53</td>
</tr>
<tr>
<td>(20-283)</td>
<td>(23-257)</td>
<td></td>
</tr>
<tr>
<td>MELD</td>
<td>14</td>
<td>16</td>
</tr>
<tr>
<td>(3-29)</td>
<td>(7-33)</td>
<td></td>
</tr>
<tr>
<td>UKELD</td>
<td>52</td>
<td>54</td>
</tr>
<tr>
<td>(47-65)</td>
<td>(48-71)</td>
<td></td>
</tr>
<tr>
<td>PELD</td>
<td>3</td>
<td>5</td>
</tr>
<tr>
<td>(-8-28)</td>
<td>(-13-27)</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Patient and graft survival for LT in YP with BA is excellent however patients listed >18 yrs waited longer and were more likely to be admitted to ICU, which was associated with poor outcome. Prognostic listing models were not useful in this age group. Educational and professional outcome was poorer for YP compared to those with LT at a younger age and further research into neuro-cognitive function in this group is required to establish ‘optimal timing’ for LT in YP with BA.

**Disclosure of interest:** “None Declared”.
Serum autoantibodies are associated with chronic hepatitis and graft fibrosis after pediatric liver transplantation

Jeremy Rajanayagam1, Wolfram Haller2, Dominique Debray3, Henkjan Verkade4, Valérie McLin5, Helen Evans6, Etienne Sokal7, Ekkehard Sturm8, Vladimir COUSIN9, Varma Sharat10, Xavier Stephenne10, Steffen Hartleif12, Deirdre Kelly13

1Birmingham Children's Hospital, The Liver Unit, Birmingham, United Kingdom
2Birmingham Children's Hospital, Liver Unit, Birmingham, United Kingdom
3Necker Hospital, Department of Hepatology and Gastroenterology, Paris, France
4Dept of Paediatrics, University of Groningen, University Medical Center Groningen, Groningen, Netherlands
5University Hospitals Geneva, Pediatrics, Geneva, Switzerland
6Starship Children's Hospital, Department of Paediatric Gastroenterology, Auckland, New Zealand
7Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium
8Childrens Hospital University of Tuebingen, Pediatric Gastroenterology, Tuebingen, Germany
9Geneva University Hospital, Pediatric, Geneva, Switzerland
10Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
12Universitätsklinikum Tübingen, Tübingen, Germany
13The Liver Unit, Birmingham, United Kingdom

Objectives and study: Chronic hepatitis (CH) and fibrosis are frequent features of protocol liver biopsies after pediatric liver transplantation (LT). Previously reported associations with positive autoantibodies (AuAb) and abnormal immunoglobulins (Ig) suggest immunologic mechanisms of graft injury. Objective: To evaluate the role of AuAbs and Igs in the etiology of CH and fibrosis.

Methods: International, multicenter, retrospective analysis of pediatric LT recipients with 5 and/or 10yr protocol liver biopsies (normal aminotransaminases), paired serum AuAbs (ANA, SMA titre>1:40) and Ig levels, excluding those with pre-LT autoimmune liver disease, or other causes of graft injury.

Results: 467 children, from 7 centres underwent LT between 1985-2010, predominantly for biliary atresia (n=274), metabolic disease (n=58), other cholestatic disorders (n=53), acute liver failure (n=44), cryptogenic cirrhosis (n=20) and malignancy (n=7). CH was seen in 119/279 (43%) biopsies at 5yrs, and 121/229 (53%) biopsies at 10yrs. Fibrosis was present in 163/301 (54%) at 5yrs (of which 36% were mild, 12% moderate and 6% severe) and 178/226 (79%) at 10yrs (mild=45.6%, moderate=20.4%, and severe=12.8%). Children positive vs negative for AuAbs were more likely to exhibit not only CH (5yrs: 59% vs 34%, p<0.001; 10yrs: 79% vs 42%, p<0.001) but also fibrosis (5yrs: 71% vs 44%, p<0.001; 10yrs: 90% vs 76%, p=0.018). Presence of autoantibodies was not significantly associated with gender (p=0.672) or donor graft type (living-related vs deceased, p=0.111). Median IgG and IgM levels were within normal range, but significantly higher in children with CH (p=0.016, p=0.003) and fibrosis (p=0.024, p=0.015) at 5yrs. Only the association between IgM and fibrosis remained significant at 10yrs (p=0.007). Children whose maintenance immunosuppression included steroids were significantly less likely to have CH compared to those without steroids (5yrs: 22% vs 56%, p<0.001; 10yrs: 38% vs 80%, p<0.001). Similarly, fibrosis was significantly less likely at 5yrs (42% vs 61%, p=0.002), but not 10yrs (82% vs 73% p=0.124). In those who did not receive steroids, there was no significant difference in inflammation and fibrosis between Tacrolimus and Cyclosporin at 5yrs (both p=1.000) or 10yrs (p=0.277, and p=1.000). Important factors that were not associated with chronic hepatitis and fibrosis, included age, gender, deceased or living-related donor and graft-type (whole, split or reduced).

Conclusion: CH and fibrosis become increasingly prevalent after pediatric LT and are strongly associated with AuAbs. Steroids may mitigate CH but may not prevent fibrosis long-term.

Disclosure of interest: None Declared
Pediatric CLIF-SOFA score is the best predictor of 28-day mortality in children with decompensated chronic liver disease

Rishi Bolia¹, Anshu Srivastava¹, Surender Yachha¹, Ujjal Poddar¹

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

Objectives and study: A sub-set of patients with decompensated chronic liver disease (DCLD) have a rapid downhill course and high short term mortality often due to extra-hepatic organ failure. (1) Timely identification helps in prognostication and planning of therapy. We evaluated the 28 days mortality, predictors of outcome and role of Child Pugh (CP), Pediatric End- stage Liver Disease (PELD) and chronic liver failure sequential organ failure assessment (CLIF-SOFA) score in predicting short term outcome in DCLD children.

Methods: Children with DCLD were enrolled prospectively from Mar 2013 to Dec 2014. Clinical, laboratory details and outcome (mortality, improved) at 28days after enrollment were recorded. Organ failure (OF) at admission was identified and defined as per the International pediatric sepsis consensus conference guidelines (2). The CLIF – SOFA (1) score was modified for application in children (Table) and labeled as pediatric CLIF-SOFA (p CLIF SOFA).

Results: 110 children (74 boys, age 96 (4 – 204) months) were enrolled. Autoimmune liver disease (n-22, 20%) was the common most etiology followed by Wilson’s disease (n=19, 17.1%) and Budd Chiari syndrome (n=18, 16.3%). Most common mode of decompensation was ascites (102, 92.7%) followed by hepatic encephalopathy (44, 43.1%) and gastrointestinal bleeding (18, 16.3%). At 28 days, 37 (33.6%) patients died. On comparison of survivors (n=73) with non-survivors (n=37), the risk factors for mortality were a higher INR [4.04 ± 3.00 vs. 2.28 ± 1.65; p = 0.00] and bilirubin [17.34 ± 10.53 vs. 8.7 ± 8.63; p = 0.00], lower albumin [2.37 ± 0.49 vs. 2.72 ± 0.77.; p = 0.01] and sodium [129.2 ± 7.6 vs. 133.6 ± 6.5; p = 0.004] and presence of OF [35/37 vs. 47/73; p = 0.0004]. 7.1% (2/28) children with no OF, 8.5% (3/35) with a single OF, 36.8% (7/19) with two OF and 92.5% (25/27) with three or more OF had a poor outcome. Respiratory failure had the worst individual outcome with a 95.4% (21/22) mortality. pCLIF SOFA [16 (9 – 22) vs. 9(5-15) p = 0.001], CP [11 (9 – 15) vs. 10 (8 – 14), p = 0.02] and PELD [22.2(7.5 – 45.3) vs. 15.3(4.5 -23.9), p = 0.03] scores at admission were higher in non-survivors as compared to survivors. pCLIF SOFA score fared the best with an AUC (area under curve) of 0.977. The AUC for CP and PELD were 0.815 and 0.741 respectively. A p CLIF-SOFA score of ≥11 derived by ROC curve predicted 28 –day mortality with a sensitivity of 94.9% and specificity of 91.5%.
Table:

<table>
<thead>
<tr>
<th></th>
<th>0</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Respiratory</td>
<td>&gt;400</td>
<td>&lt;400</td>
<td>&lt;300</td>
<td>&lt;200</td>
<td>&lt;100</td>
</tr>
<tr>
<td>(PaO²/FIO²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Or</td>
<td>&gt;512</td>
<td>&gt;357 &amp; ≤ 512</td>
<td>&gt;214 &amp; ≤ 357</td>
<td>&gt;89 &amp; ≤ 214</td>
<td>≤ 89</td>
</tr>
<tr>
<td>(SpO²/FIO²)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurologic</td>
<td>No HE</td>
<td>1</td>
<td>2</td>
<td>3</td>
<td>4</td>
</tr>
<tr>
<td>(Grade of HE)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Circulatory</td>
<td>No hypotension</td>
<td>Systolic BP</td>
<td>Dopamine &lt;5</td>
<td>Dopamine &gt;5</td>
<td>Dopamine &gt;15</td>
</tr>
<tr>
<td></td>
<td></td>
<td>&lt;5th %</td>
<td>μg /kg/min</td>
<td>μg /kg/min</td>
<td>μg /kg/min</td>
</tr>
<tr>
<td></td>
<td></td>
<td>for age</td>
<td>or epinephrine ≤0.1 μg/kg/min or norepinephrine ≤0.1 μg/kg/min</td>
<td>or epinephrine &gt;0.1 μg/kg/min or norepinephrine &gt;0.1 μg/kg/min</td>
<td></td>
</tr>
<tr>
<td>Hematological</td>
<td>≤1.1</td>
<td>&gt;1.1 to &lt; 1.25</td>
<td>≥1.25 to &lt;1.5</td>
<td>≥1.5 to &lt;2.5</td>
<td>≥2.5</td>
</tr>
<tr>
<td>(INR)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Renal</td>
<td>Normal for</td>
<td>&gt;1 &amp; ≤2 times upper limit of normal for age</td>
<td>&gt;2 to ≤3 times upper limit of normal for age</td>
<td>&gt;3 times upper limit of normal for age</td>
<td>use of renal replacement therapy</td>
</tr>
<tr>
<td>(serum creatinine)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Liver</td>
<td>&lt;1.2</td>
<td>≥1.2 to &lt;2</td>
<td>≥2 to &lt;6</td>
<td>≥6 to &lt;12</td>
<td>≥12</td>
</tr>
<tr>
<td>(serum bilirubin)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** One third of children with DCLD have a poor short term outcome. The pCLIF-SOFA is the best predictor of 28 day mortality and a score of ≥ 11 has a sensitivity of 94.9% and specificity of 91.5% in predicting 28 days mortality.

**Reference:**

**Disclosure of interest:** None Declared
Chronic liver disease in young people; what has mental health got to do with it?

Anna Hames¹, Faith Matcham², Deepak Joshi¹, Marianne Samyn³

¹King's College Hospital, Institute of Liver Studies, London, United Kingdom
²King's College London, Institute of Psychiatry, Psychology and Neuroscience, London, United Kingdom
³King’s College Hospital, Paediatric Liver GI and Nutrition Service, London, United Kingdom

Objectives and study: Young people (YP) with chronic illness have higher rates of mental health problems than the general population. Psychosocial complexity has been associated with non-adherence and poorer health outcomes. This study aimed to describe the prevalence of anxiety and depression in YP with LT, autoimmune liver disease (AILD) and other chronic liver diseases; identify the factors YP attribute their distress to; and whether anxiety and depression are related to YP’s beliefs about their illness and treatment.

Methods: An electronically-administered questionnaire battery was given routinely to YP attending a liver transition clinic. Prevalence rates were described for depression and suicidal ideation (Patient Health Questionnaire-9), anxiety (Generalised Anxiety Disorder Scale-7), factors contributing to distress (adapted Distress Thermometer), and illness beliefs (Brief Illness Perception Questionnaire). Further analyses were conducted between disease groups, comparing YP with LT (n=51), AILD (n=69), and other liver diseases (n=67).

Results: 187 out of 232 patients attending clinic participated (81% response rate, mean age 18 yrs, range 15-23, 53% female). 17.7% of YP screened positive for anxiety or depression. 9.7% reported probable major depressive disorder, with 2.2% reporting suicidal ideation. 14.5% had probable anxiety disorder, with 5.4% reporting severe anxiety symptoms. These are higher than the estimated prevalence rates of anxiety/depression in the general adolescent population of around 6%. There were no significant differences between disease groups. Patients most frequently attributed their distress to fatigue (42.3%), money (30.8%), worry (30.2%), problems at work/school (29.1%), low self-esteem (27.5%) and sleep difficulties (27.5%).

Higher levels of depression and anxiety were significantly associated with increased perceptions of illness consequences (depression r=0.37; anxiety r=0.44), identity (depression r=0.40; anxiety r=0.49), concern (depression r=0.38; anxiety r=0.45), emotional response (depression r=0.50; anxiety r=0.53) and reduced perceived personal control (depression r=0.17; anxiety r=0.17). See table for factor descriptions. Neither anxiety nor depression were associated with perceived understanding of illness or treatment control.

Table: Brief Illness Perception Questionnaire items

<table>
<thead>
<tr>
<th>Consequences</th>
<th>How much does your illness affect your life?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Timeline</td>
<td>How long do you think your illness will continue?</td>
</tr>
<tr>
<td>Personal Control</td>
<td>How much control do you feel you have over your illness?</td>
</tr>
<tr>
<td>Treatment Control</td>
<td>How much do you think your treatment can help your illness?</td>
</tr>
<tr>
<td>Identity</td>
<td>How much do you experience symptoms from your illness?</td>
</tr>
<tr>
<td>Concern</td>
<td>How concerned are you about your illness?</td>
</tr>
</tbody>
</table>
### Understanding
<table>
<thead>
<tr>
<th>Understanding</th>
<th>How well do you feel you understand your illness?</th>
</tr>
</thead>
</table>

### Emotional response
<table>
<thead>
<tr>
<th>Emotional response</th>
<th>How much does your illness affect you emotionally?</th>
</tr>
</thead>
</table>

**Conclusion:** YP with LT, AILD and other chronic liver disease had elevated rates of depression and anxiety (17.7%) as compared with the general adolescent population. Depression and anxiety were significantly correlated with YP’s beliefs about their illness, problems with fatigue and practical stressors, but not with their perceived understanding of their condition or beliefs about treatment. Holistic care should be provided routinely for this age group, which should include mental health screening and interventions for illness beliefs.

**Disclosure of interest:** None declared
**Long-term outcome of juvenile autoimmune liver disease: what has changed since 1997?**

Angelo Di Giorgio¹, Nedim Hadzic¹, Anil Dhawan¹, Diego Vergani², Giorgina Mieli-Vergani¹, Marianne Samyn¹

¹King’s College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom
²King’s College Hospital, Institute of Liver Studies, London, United Kingdom

**Objectives and study:** Juvenile autoimmune liver disease (AILD) is a rare progressive inflammatory liver disease characterized by specific histological and serological features in the absence of a known aetiology. It comprises autoimmune hepatitis (AIH) and autoimmune sclerosing cholangitis overlap syndrome (ASC), the latter characterized by the presence of a cholangiopathy on imaging and/or histology. Following our 1997 report on a 20-year experience in paediatric AIH, we aimed to review the long-term outcome of patients diagnosed with AILD over the following decade.

**Methods:** Retrospective analysis of clinical and biochemical data of all patients diagnosed with AILD between 2000 and 2004. Patients are classified as AIH and ASC and further sub-classified as type 1 (ANA/anti-SMA+); type 2 (anti-LKM1/LC1+); and exclusively anti-SLA+.

**Results:** 91 children (male 45) were diagnosed with AILD at a median age of 12.4 yrs (range 1.0-17.7). Sixty (66%) had AIH (27 male) (type 1: 77%, type 2: 18%, anti-SLA+: 5%). Thirty-one (34%) had ASC (20 male) (type 1: 90%, type 2: 3%); 2 (7%), treated for inflammatory bowel disease (IBD) at time of presentation to our centre, were autoantibody negative. Laboratory results in table. IBD was diagnosed in 29/91 (32%) and other autoimmune diseases in 17/93 (19%). ASC was more frequently associated with IBD (77% vs 8% in AIH p<0.01). Type 2 AIH was associated with younger age (5.4 vs 13.2 yrs, p<0.05) and lower IgG levels (16.8 vs 26.4 g/l, p<0.05) at diagnosis, compared to other types of AIH. After a median follow up of 11.8 y (0.3-16.8), all patients are alive. Ten patients (12%), 5 with AIH and 5 with ASC required liver transplantation (LT) at a median age of 18.9 yrs (3.5-25.0 yrs) and a median time of 5.4 yrs (0.03-12.9 yrs) post diagnosis. LT was associated with higher INR (p<0.05) and lower serum albumin (p<0.01) at diagnosis. Patient and graft survival is 100% at a median time of 8.1 yrs (2.4-14.6) post LT. 2 developed recurrence of ASC with stable graft function at last follow up. For the remainder, treatment was stopped in 14 (17.5%: 12 AIH type 1, 1 AIH type 2, 1 ASC), 13 are on prednisolone (P) alone, 29 on P/azathioprine, 10 on P/MMF, 6 on azathioprine alone, 8 on other treatments. AST levels are normal (<35 IU/l) in 63% and < 2xULN in 90%. During the study period an average of 12 AIH cases/year were diagnosed (18.2 AILD cases/year) a marked increase compared to our previous report of 3.3/year.

**Table:**

<table>
<thead>
<tr>
<th>Demographic and Laboratory features (median) at diagnosis</th>
<th>Total 91 pts</th>
<th>AIH 60 pts</th>
<th>ASC 31 pts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at Diagnosis (years)</td>
<td>12.4 (1.0-17.7)</td>
<td>12.2 (1-17.1)</td>
<td>13.2 (8.4-17.7)</td>
</tr>
<tr>
<td>IBD (N/%)</td>
<td>29 (2)</td>
<td>5 (8)</td>
<td>24 (77)</td>
</tr>
<tr>
<td>AST (U/L)</td>
<td>279 (12-2725)</td>
<td>547(14-2725)</td>
<td>84(12-434)</td>
</tr>
<tr>
<td>GGT (U/L)</td>
<td>97 (3-790)</td>
<td>83(3-790)</td>
<td>140(9-541)</td>
</tr>
<tr>
<td>Total bilirubin (µmol/L)</td>
<td>27(3-425)</td>
<td>62(3-425)</td>
<td>10(5-88)</td>
</tr>
<tr>
<td>INR</td>
<td>1.0 (0.8-4.1)</td>
<td>1.1(0.8-4.1)</td>
<td>1.0(0.9-1.1)</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>40 (20-50)</td>
<td>38(20-49)</td>
<td>42 (29-50)</td>
</tr>
<tr>
<td>Platelets (10³/l)</td>
<td>256 (32-627)</td>
<td>198 (32-613)</td>
<td>359 (46-627)</td>
</tr>
<tr>
<td>IgG (g/L)</td>
<td>19.1 (5.2-89.5)</td>
<td>23.1 (5.2-89.5)</td>
<td>17.3(6.1-44.4)</td>
</tr>
</tbody>
</table>
Conclusion: Long-term outcome in a cohort of 91 patients with AILD is excellent with 17.5% of patients off immunosuppressive treatment and AST levels <2xULN in 90%. LT requirement in 12% was associated with synthetic failure at diagnosis. IBD was more common in ASC but also diagnosed in 8% of AIH. Over the last two decades the survival of juvenile AILD has improved; interestingly its incidence has increased 4-fold.

Disclosure of interest: “None Declared”.
Diagnosis of monogenetic metabolic hepatopathies in children by next generation sequencing

Amelie Stalke¹, Ulrich Baumann², Thomas Illig³, Britta Skawran⁴, Brigitte Schlegelberger⁴, Nils von Neuhoff⁴, Eva-Doreen Pfister²

¹Hannover Medical School, Paediatric Gastroenterology and Hepatology; Institute of Human Genetics, Hannover, Germany
²Hannover Medical School, Paediatric Gastroenterology and Hepatology, Hannover, Germany
³Hannover Medical School, Hannover Unified Biobank, Hannover, Germany
⁴Hannover Medical School, Institute of Human Genetics, Hannover, Germany

Objectives and study: As neonatal cholestasis is a common infant problem with more than 50 possible differential diagnoses, fast and comprehensive, cost effective and ideally non-invasive diagnosis is desirable to initiate timely therapy to improve patient outcome. Also for other hepatopathies, especially those manifesting in acute liver failure, quick diagnosis is important, as they could constitute contraindication to liver transplantation or can be treated with specific curative therapies. We developed a next generation sequencing (NGS) panel of 21 genes associated with acute and chronic hepatopathies. The panel includes familial progressive intrahepatic cholestasis syndromes, Niemann–Pick disease type C, Alagille syndrome, congenital bile acid synthesis defects, Crigler-Najjar Syndrome, Wilson disease, mitochondrial DNA depletion syndromes, Deoxyguanosine kinase deficiency, Hereditary fructose intolerance and Transaldolase deficiency.

Methods: DNA was extracted from 1-2 mL EDTA peripheral blood samples of 131 patients with hepatopathy (age: 8-18 years; 63 female, 68 male; 23 of them with already genetically proven hepatopathies for validation purposes) after obtaining informed consent of the patients and/or their parents. A TruSeq Custom Amplicon (TSCA) panel of 21 genes related to paediatric or juvenile hepatopathies was used for targeted resequencing on the MiSeq sequencing device (Illumina). Data analysis was performed using Sequence Pilot 4.1 2 software (JSI medical systems GmbH). Interpretation of variants was done with the help of Alamut Visual (Interactive Biosoftware, Rouen, France).

Results: For validating the method, samples of 23 patients with already genetically proven hepatopathies were measured by NGS and blindly analyzed. All NGS results were identical with the previous findings.

In 21 out of 108 patients without previous positive genetic findings we could detect disease related or likely disease related variants with the help of the NGS panel. The related diseases include 2x Wilson disease, 9x Alagille syndrome, 4x familial progressive intrahepatic cholestasis, 5x Crigler-Najjar syndrome and 1x congenital bile acid synthesis defect.

Conclusion: Our NGS based analysis of 21 genes represents a fast and comprehensive tool to diagnose genetically determined paediatric hepatopathies. As a result, next to shortening the hospital stay by reduction of examinations and reduced patient’s burden because of smaller required blood volumes, fast and specific initiation of therapy enables a better prognosis.

Up to now more than 100 genes related to paediatric hepatopathies are known. Therefore we aim to perform our future NGS analyses by whole exome sequencing, which also allows us to include genes in our analysis whose relevance for the disease pattern was newly discovered.

Disclosure of interest: None Declared
Clinical, histopathological and molecular genetics of children with inborn errors of bile acid synthesis and liver disease: results from an eight years prospective study

Abdulrahman Al-Hussaini¹, Bader Alsaleem¹, Khurram Lone¹

¹King Fahad Medical City, Children's Specialized Hospital, Riyadh, Saudi Arabia

Objectives and study: Bile acid synthesis errors (BASE) are rare inherited causes of pediatric liver disease. Early diagnosis of BASE is important because, if untreated, these conditions may be fatal. The objectives of our study were to screen infants and children with cholestasis or unexplained liver disease for BASE, study the clinical, laboratory, histopathologic, and molecular characteristics of BASE, and examine the effect of oral bile acid therapy.

Methods: From 2007 to 2014, we prospectively screened infants and children presenting with cholestasis (Conjugated bilirubin > 34 µmol/l), liver cirrhosis, liver failure (INR ≥ 2 unresponsive to vitamin K) of unknown etiology for BASE. Serum bile acid was obtained from all included patients. Urine specimen was obtained from all but was sent for analysis by Gas Chromatography–Mass Spectrometry if serum bile acid level was normal or low, or if etiology of liver disease was not identified after extensive work up. Cases of BASE were then initiated on oral cholic acid therapy with periodic follow-up of the biochemical and histopathologic response. Genomic DNA was sequenced for HSD3B7 or AKR1D1 genes mutations.

Results: Over the study period, we evaluated 952 patients; 450 were infantile cholestasis. Twelve cases of BASE were diagnosed: 9 presented with infantile cholestasis (2%, 6 males), an 8-year old boy presented with cirrhosis, and 2 eighteen months old boys presented with hepatomegaly and rickets. Nine were caused by 3ß-hydroxy-D5-C27-steroid dehydrogenase deficiency [two novel HSD3B7 homozygous missense mutations], 2 were caused by D4-3-oxo-steroid 5ß-reductase deficiency [one novel AKR1D1 homozygous missense mutation], and one case of zellweger syndrome. With cholic acid therapy, the clinical, biochemical, and histopathologic response were excellent in 9 patients with their native liver without the need for liver transplantation. Liver failure developed in 2 infants despite initiation of cholic acid therapy; one died and the other had successful liver transplantation. One more infant had excellent response to oral cholic acid but died due to cardiomyopathy.

Conclusion: BASE are rare but treatable causes of severe pediatric liver disease in Saudi Arabia. Therefore, they are important targets for screening in children with liver disease.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016
Mitochondrial nuclear gene mutations in aetiology of acute liver failure of infancy

Nik Nazimah Nik Mahmood1, Emma Blakely2, Robert Taylor2, Aydan Kansu3, Figen Özcay4, Chioma Nwекe5, Anil Dhawan5, Patrick McKiernan6, Ulrich Baumann7, Nedim Hadzic1
1King's College Hospital, Paediatric Liver Unit, London, United Kingdom
2Institute of Neuroscience, Newcastle University, Welcome Trust Centre for Mitochondrial Research, Newcastle, United Kingdom
3Ankara University Hospital, Paediatric Gastroenterology, Ankara, Turkey
4 Başkent University Hospital , Paediatric Gastroenterology, Ankara, Turkey
5King's College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom
6Birmingham Children's Hospital, Paediatric Liver Unit, Birmingham , United Kingdom
7Medizinische Hochschule Hannover, Paediatric Liver Unit, Hannover, Germany

Objectives and study: In a considerable proportion of young children with acute liver failure (ALF) its aetiology remains unexplained. In recent years autosomal recessive mutations in at least 5 nuclear genes implicated in disorders of mitochondrial DNA maintenance have been associated with ALF.

We investigated the prevalence of identifiable nuclear gene mutations in young children presenting with indeterminate ALF (iALF).

Methods: We undertook a retrospective multicentre study. Stored blood or DNA samples from children with iALF (age <2 years) were obtained from five European liver centres. All samples were screened for the pathogenic variants in the following mitochondrial genes: POLG, MPV17, DGUOK, TINKLE (PEO1) and TRMU, using a combination of targeted next-generation sequencing ((Ampliseq capture) and Sanger sequencing. Clinical data were collected using a questionnaire.

Results: A total of 34 (20M, 58.8%) patients were enrolled, with a median age at presentation of 9 months (range, 0-22). Standard criteria for diagnosis of ALF were used. Patients from one of the centres (n=7) were selected from their liver transplant (LT) program and all had LT. Patients from the other 4 liver centres were selected on the basis of available consented stored blood samples.

At presentation 27 (79%) had jaundice, 9 (26%) pale stools and 11 (32%) hypoglycaemia. Five (15%) children had fever. Ascites, splenomegaly and encephalopathy each were reported in 6 (18%) patients. One (pt A) had consanguineous parents and family history of recurrent ALF (RALF) (sister). Median serum bilirubin was 252 micromol/L (normal <20) (n=32), median serum lactate 2.5 micromol/L (normal <2) (n=11), median INR 4.2 (range, 2-9.32) (n=22).

Twenty patients (58.8%) received emergency LT. Re-LT was performed in 3 patients (15%); one child had 3 LTs and six episodes of rejection, one had the second LT following uncontrolled graft rejection, while one developed CMV viraemia post-LT associated with haemorrhagic hepatic infarction. Six patients (17.6%) died at median 1 month post-LT (range, 1-12). Of the 28 survivors, one was lost to follow up at 12 month. Median follow up for 27 patients was 98 m (range, 23-327) after the initial presentation. All who did not receive LT, except pt A, recovered with no further episodes of ALF.

During follow up one child (pt A), had RALF 22 and 35 months after the initial presentation. She had evidence of chronic liver disease on the liver biopsy 3 years post initial presentation, did not have LT and remains alive and well after 80 months. She had soft facial dysmorphism and lumbar lordosis. Among others, 2 had mild learning difficulties and 3 seizures (pt A had both). Three children had head MRI, all reported normal except in pt A (cerebral atrophy). Overall clinical picture of pt A remains suspicious of a mitochondriopathy.

Our analysis did not identify any known or likely pathogenic variants in the five nuclear-mitochondrial genes. Additional genetic analysis is being undertaken to look for other genetic causes of ALF. Overall 82% survival (70% in LT cohort) and 15% re-LT rates are comparable to other causes of ALF.

Conclusion: We could not demonstrate pathogenic variants in the five nuclear-mitochondrial genes in our series of ethnically mixed young children with iALF. The standard clinical criteria for LT in ALF
remain valid, although with the improved clinical availability these genetic tests may become a part of the acute clinical work up.

Disclosure of interest: This study was funded by ESPGHAN.
Neonatal livers may avoid the instant blood mediated inflammatory response and are an excellent source of cell for hepatocyte transplantation

Charlotte Lee¹, Sharon Lehec¹, Ragai Mitty¹, Shirin Khorsandi¹, Celine Filippi¹, Raquel Fernandez Dacosta¹, Anil Dhawan², Emer Fitzpatrick²

¹Institute of Liver Studies, King’s College London, London, United Kingdom
²Paediatric Liver, GI and Nutrition Centre, King's College Hospital, London, United Kingdom

Objectives and study: Hepatocyte transplantation is a promising alternative to orthotopic liver transplantation (OLT) for children with liver-based metabolic disease and acute liver failure. A major hurdle to its success is early cell loss (up to 70% of hepatocytes) due to the instant blood mediated inflammatory response (IBMIR). Neonatal livers are generally not used for OLT in view of their low weight and small vessel size however may be an excellent source of good quality hepatocytes for transplantation purposes. In addition, they may also potentially be less immunogenic and thus may not elicit the IBMIR to the same extent as adult-liver derived hepatocytes. We set out to compare the viability, function and immunogenicity of neonatal and adult hepatocytes.

Methods: Neonatal hepatocytes were isolated as described by Dhawan et al 2012. Cell viability was assessed using an MTT assay and hepatocyte function was determined with albumin and urea immunoassays. A Chandler loop model using heparin-coated PVC tubing was incubated at 37°C and rotated at 24rpm to mimic portal vein blood flow. This was used to compare neonatal and adult hepatocyte immunogenicity when cells were in contact with ABO-matched blood. Samples were taken at 0, 15 and 30 min following perfusion and full blood count measured on a haematology analyser. Plasma was stored at -80°C and later analysed for cytokine expression using a Cytokine Panel Randox Array Chip.

Results: Neonatal hepatocytes had a high viability upon isolation 86% ± 3.7 (n=3). Hepatocytes were cultured in collagen coated 96 well plates overnight and MTT assays revealed neonatal hepatocytes had a significantly higher viability than hepatocytes isolated from adult livers (OD: mean ± SEM; 0.99 ±0.24 (n=3) Vs 0.34 ± 0.077 (n=6), P<0.05). Neonatal hepatocytes secreted significantly higher albumin concentrations than adult hepatocytes one day post plating (1028 ng/ml ±573 (n=3) Vs 139.7 ng/ml (n=6) P<0.05). There was no significant difference in urea production (3.2ng/ml ± 0.61 Vs 6.8 ng/ml ± 3.5), most likely due to lack of mitochondrial function. The Chandler loop model showed adult hepatocytes elicited a significant drop in platelet count compared to the control (55.5 x10⁹ cell/L ± 12.5 Vs 178.8 x10⁹ cell/L ± 17.6 n=6 P<0.001). Neonatal hepatocytes did not cause a drop in platelet count compared to the control (165 x10⁹ cell/L). Cytokine expression in plasma from the loop was analysed in one neonatal dataset. This showed adult hepatocytes (N=3) had higher concentrations of the pro-inflammatory cytokines IL-6, IL-1α, IL-1RA and VEGF and lower concentrations of the anti-inflammatory cytokine IL-10 than plasma containing neonatal hepatocytes.

Conclusion: Hepatocytes isolated from neonatal livers have very high viability and albumin production. Initial results suggest neonatal hepatocytes do not activate the immune response compared to adult hepatocytes. Neonatal hepatocytes may engraft more successfully and function at a higher rate, improving the clinical efficacy of hepatocyte transplantation.

Disclosure of interest: None declared
Defective plasma membrane targeting of p.I661T-ATP8B1, associated with familial intrahepatic cholestasis, can be rescued in vitro by CFTR correctors

Wendy van der Woerd¹, Catharina Wichers², Anna Vestergaard³, Jens Peter Andersen³, Coen Paulusma⁴, Roderick Houwen¹, Stan van de Graaf⁴

¹Wilhelmina Children’s Hospital, University Medical Centre Utrecht, Department of Pediatric Gastroenterology, Utrecht, Netherlands
²University Medical Center Utrecht, Department of Molecular Cancer Research, Section of Metabolic Diseases, Utrecht, Netherlands
³Aarhus University, Department of Biomedicine, Aarhus, Denmark
⁴Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, Netherlands

Objectives and study: ATP8B1 deficiency is an autosomal recessive liver disease caused by mutations in the ATP8B1 gene. Clinical symptoms range from intermittent (benign recurrent intrahepatic cholestasis; BRIC) to progressive intrahepatic cholestasis (progressive familial intrahepatic cholestasis; PFIC). Current therapeutic options for the more severe phenotype (PFIC) are insufficient. For this group of patients, the development of targeted compounds for mutation-specific therapy might be a promising new strategy. ATP8B1 mutation p.I661T, the most frequent mutation in European patients, results in protein misfolding and impaired targeting to the plasma membrane. Similarly, mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene, associated with cystic fibrosis, impair protein folding and trafficking. The aim of this study was to investigate whether compounds that rescue CFTR F508del trafficking are also capable of improving p.I661T-ATP8B1 plasma membrane expression.

Methods: Effect of CFTR corrector compounds on plasma membrane expression of p.I661T-ATP8B1 was evaluated by cell surface biotinylation and immunofluorescence.

Results: The clinically-approved compounds, 4-phenylbutyric acid (4-PBA), suberoylanilide hydroxamic acid (SAHA) and N-butyldeoxynojirimycin (NB-DNJ) improved p.I661T-ATP8B1 plasma membrane targeting. The pre-clinical CFTR correctors C4, C5, C13 and C17 also significantly increased plasma membrane expression of p.I661T-ATP8B1. SAHA and compound C17 upregulated ATP8B1 transcription. p.I661T-ATP8B1 was partly targeted to the canalicular membrane in polarized cells, which became more evident upon treatment with SAHA and/or C4. Combination therapy of SAHA and compound C4 resulted in an additional improvement of ATP8B1 cell surface abundance.

Conclusion: This study shows that several compounds, previously identified as CFTR correctors, improve expression of p.I661T-ATP8B1 at the plasma membrane in vitro. Hence, these compounds may be suitable to be part of a future therapy for ATP8B1 deficiency as well as other genetic disorders associated with protein misfolding.

Disclosure of interest: None Declared
Evaluation of Exchangeable copper and Relative Exchangeable Copper in ATP7b-md mice

Sophie Heissat¹, Muriel Bost², Valerie Hervieu³, Anne Sophie Brunet⁴, Olivier Guillaud⁴, Elisabeth Mintz⁵, Alain Lachaux⁶

¹Hopital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology, Lyon, France
²Edouard Herriot Hospital, Trace Element Analysis Laboratory, Biochemistry and Molecular Biology, Lyon, France
³Edouard Herriot Hospital, Department of Pathology, Lyon, France
⁴Hopital Femme Mère Enfant, Reference Centre for Wilson Disease, Lyon, France
⁵Cea, Laboratory of Chemistry and Biology of Metals, Grenoble, France
⁶Hopital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology; Reference Centre for Wilson Disease, Lyon, France

Objectives and study: Wilson's disease (WD) is an autosomal recessive disease caused by mutations in the ATP7B gene responsible for a toxic accumulation of copper, mainly in the liver and central nervous system. The diagnosis of WD is based on a combination of clinical and biological findings. Phenotypic heterogeneity may challenge the diagnostic confirmation. Exchangeable copper (CuEXC) and its derived Relative Exchangeable Copper (REC, ratio CuEXC/total serum copper, %) have recently been proposed as reliable diagnostic markers in WD. The aim of our study was to validate these new markers in ATP7B-md mice, an animal model of WD.

Methods: ATP7B-md (group a) and wild type mice (WT, group b) were bred and investigated in the same conditions. The animals were classified by subgroup based on age at sacrifice (group 1a and 1b = 6 weeks, 2a and 2b = 20 weeks, 3a and 3b = 40 weeks, 4a and 4b = 50 weeks). The following plasma data were compared between groups: liver function tests, serum copper (Cu), CuEXC, and REC. Histological analysis of the liver and intrahepatic copper (CuIH) determination were also performed.

One group of ATP7B-md mice received a treatment with D-penicillamine from week 40 to sacrifice, at week 50 (Group 5).

Results: 141 ATP7B-md mice and 117 WT mice were included in the study. No mice died before the scheduled sacrifice. In the WT groups, histological analysis was constantly normal and the values of Cu, CuIH, and CuEXC remained stable over time. Histological analysis of ATP7B-md mice showed a progressive development of chronic liver injury (group 1a: isolated moderate inflammation (48%), group 4a: inflammatory fibrosis (100%) with cirrhosis (65%)). The Cu, CuIH, and CuEXC varied over time with maximum values at week 20 for CuIH and at week 40 for the CuEXC and Cu. In each subgroup, CuIH and CuEXC were significantly higher in ATP7B-md mice as compared to WT mice (p <0.005). The REC was also significantly higher in ATP7B-md mice (mean, 37.9 vs. 11.2%, p <0.001). A threshold value of 20% for the REC provided diagnostic sensitivity and specificity of 100%, regardless of age, sex, or the use of a treatment (group 4a: 34.9% vs. group 5: 33%). Copper chelator significantly reduced liver fibrosis (p=0.03) and Cu (p=0.028) and decreased the CuIH (p=0.29) and the CuEXC (p=0.175).

Conclusion: This study confirms the mouse model ATP7B-md as a reliable animal model of chronic liver disease by copper overload. Relative exchangeable copper is a sensitive and specific diagnostic marker in this model. Further studies are needed to confirm that CuEXC is a good biomarker to monitor the evolution of mouse WD, particularly when copper chelators are used.

Disclosure of interest: None Declared.

Diana Kamińska, Marcin Krawczyk, Wojciech Jańczyk, Frank Lammert, Magdalena Pawikowska, Małgorzata Podłaska, Maciej Pronicki, Piotr Socha

1Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology and Nutritional Disorders, Warsaw, Poland
2Saarl and University Medical Center, Saarland University, Department of Medicine II, Homburg, Germany
3Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
4Saarl University Medical Center, Saarland University, Department of Medicine II, Homburg, Germany
5The Children’s Memorial Health Institute, Department of Pathology, Warsaw, Poland
6The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Wilson’s disease (WD) is a rare liver disease driven by mutations in the ATP7B gene. Presence of genetic modifiers of WD has for long been suspected, however no common polymorphism affecting progression of this condition in pediatric patients has been detected so far. In our previous studies (Krawczyk/Lammert J Hepatol 2011, Krawczyk/Arslanow Liver Int in press) we demonstrated that two prosteatotic genetic variants, i.e. PNPLA3 p.I148M and TM6SF2 p.E167K, are associated with increased liver injury in adults with chronic liver diseases. Here we investigate these two variants as potential modifiers of hepatic steatosis and fibrosis in a large cohort of pediatric WD.

Methods: In total we recruited 78 children (boys 50%, age 9.1±4.5 years) with WD. In all patients liver function tests were measured before the start of therapy. Genotyping of the TM6SF2 rs58542926 and PNPLA3 rs738409 polymorphisms was performed using TaqMan assays with fluorescent detection. Liver biopsy was performed in 59 children. Steatosis and fibrosis were quantified by a pathologists blinded to the genotyping results. Steatosis and fibrosis were assessed according to the modified Kleiner scoring system used for NAFLD. Association test were calculated in contingency tables, continuous variables were compared using Mann-Whitney or Anova tests.

Results: Among biopsied individuals 57% had steatosis grade I and 20% presented with steatosis grade II. Fibrosis grade 2–4 was present in 74% of patients, whereas only 5% had no fibrosis at liver biopsy. The genotype frequencies of the TM6SF2 p.E167K (i.e. [EE] = 64, [EK] = 13, [KK] = 2) and PNPLA3 p.I148M (i.e. [CC] = 52, [CG] = 21, [GG] = 6) polymorphism neither differed from the frequencies deposited in the Entrez database for Caucasian cohorts (P > 0.05) nor deviated from HWE (all P > 0.05). Presence of the TM6SF2 minor allele was associated with increased risk of developing fibrosis grade ≥2 (OR=9.43, 95% CI 0.51-171.41, P=0.04). Indeed all carriers of this allele had fibrosis grade ≥2 at biopsy. On the other hand, this variant did not increase the steatosis risk (P>0.05). We did not detect any association between PNPLA3 genotype and fibrosis or steatosis (all P>0.05) and neither the PNPLA3 nor TM6SF2 genotypes affected serum ALT (P=0.12 and P=0.07, respectively) or AST (P=0.64 and P=0.89, respectively) activities. The results could be affected by some confounding factors like age at diagnosis.

Conclusion: Our results suggest the TM6SF2 p.E167K polymorphism might modulate liver injury in children with WD. Since fibrosis seems to be a frequent trait in pediatric Wilson, testing of the TM6SF2 variant might help to detect patients bearing increased risk of rapid progression of liver disease.

Disclosure of interest: “None Declared”.
**HEPATOLOGY: Transplantation**

H-O-016

**C3d DSA with high MFI is associated with a higher rate of graft loss in a pediatric cohort of LT patients**

Eduardo Couchonnal¹, Christine Rivet², Stéphanie Ducreux³, Jérôme Dumortier¹, Alexis Bosch¹, Christine Chambon-Augoyard¹, Olivier Boillot⁴, Rémi Dubois⁴, Anne Sophie Brunet⁵, Alain Lachaux⁶, Valérie Dubois³, Olivier Guillaud⁵

¹Hôpital Edouard Herriot, Unité de Transplantation Hépatique, Lyon, France
²Hôpital Femme Mère Enfant, Service D'hépatologie-Gastroentérologie et Nutrition Pédiatriques, Bron, France
³Etablissement Français du Sang, Laboratoire D'histocompatibilité, Lyon, France
⁴Hôpital Femme Mère Enfant, Chirurgie Uro-Génitale, Viscérale, Thoracique, Néonatale et Transplantation, Bron, France
⁵Hôpital Femme Mère Enfant, Reference Centre for Wilson Disease, Lyon, France
⁶Hôpital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology; Reference Centre for Wilson Disease, Lyon, France

**Objectives and study:** The incidence and the clinical impact of DSAs developed after liver transplantation remain controversial and have not been extensively studied, especially in pediatric populations.

**Methods:** This cross-sectional study included 100 nonconsecutive patients who underwent a first LT in childhood (<18 years old at LT) and alive one year or more after LT. Anti HLA immunization study was performed using Luminex Single Ag tests (Immucor) with classical anti-IgG conjugate and new anti-C3d conjugate.

**Results:** Forty five percent of the patients were male with a median age at LT of 4.6 years. The main indication for LT was biliary atresia (52%). The median time after LT for DSA assessment was 7.8 years (range 1 month – 21 years). Twenty-four patients (24%) developed de novo DSA after LT with a prevalence for DSA of 8%, 28%, 33%, 50% respectively 0-5 yrs, 5-10 yrs, 10-15 yrs and >15 yrs post LT. De novo DSA were mainly class II (23/24) with a mean MFI of 9.731 ± 5.489 and 18 (79.2%) were C3d-binding DSA.

In univariate analysis, combined liver-kidney transplantation and initial immunosuppression (use of FK, MMF, antiIL2R) were associated with a lower rate of DSA, whereas history of fulminant hepatitis and time elapsed since LT were associated with a higher rate of DSA. Multivariate analysis disclosed that time elapsed since LT (p<0.001) and history of fulminant hepatitis (p=0.041) remained statistically significant.

Liver function tests (at time of DSA assessment) were not different in groups with or without DSA. Patient survival and graft survival were similar between groups, however patients with C3d-positive DSA MFI >10000 had a significant poorer long-term graft survival (p=0.027).

**Conclusion:** in our pediatric cohort of LT, prevalence of DSA is high and increases regularly with time. C3d positive-DSA with high MFI are associated with a higher rate of graft loss.

**Disclosure of interest:** None Declared
Evaluating risk of esophageal variceal bleed in children with cirrhosis and waitlisted for liver transplantation

Xavier Stephenne1, Bonnet Nicolas1, Varma Sharat1, Thibault Helleputte2, Francis Veyckemans3, Francoise Smets4, Eeckhoudt Stephane5, Hermans Cedric5, Etienne Sokal6

1Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
2Dnalytics, Louvain-La-Neuve, Belgium
3Ucl, Department of Anesthesiology, Brussels, Belgium
4Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Brussels, Belgium
5Université Catholique de Louvain, Brussels, Belgium
6Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Objectives and study: Children with cirrhosis and waitlisted for liver transplant are prone to bleeding from ruptured esophageal varices; for which presence of grade 2-3 varices and red signs are known risk factors. The involvement of hemostasis remains controversial at the moment because of the rebalanced state of coagulation during cirrhosis.

Methods: Prospective observational study was designed, including children with portal hypertension and decompensated cirrhosis. Portal hypertension assessment was done by ultrasound, endoscopy and hemostasis evaluation with dynamic parameters of thromboelastometry (ROTEM®), platelet function with Multiplate®, in addition to conventional tests. The clinical end point was occurrence of upper gastrointestinal bleeding. Above mentioned parameters were compared between children with and without bleeding using univariate statistical methods. Additionally an earlier developed predictive model for risk of variceal bleeding was applied and validated on the prospective cohort, which comprises of presence of grade 2-3 varices and/or red spots on the upper endoscopy and fibrinogen <150 mg/dl.

Results: Twenty children were enrolled (18 biliary atresia patients, median age 9 months (4-129)), six had upper gastrointestinal bleed during the pre-transplant period. Waiting time before transplantation, presence and severity of oesophageal varices, levels of factor V (49% (34-65) vs 70(40-108)), INR (1.8 (1.3-2.8) vs. 1.5 (1.0-2.0)) or platelets count (104 10^3/µl (45-330) vs 219 (60-424)) were not statistically different between the two groups. Significant differences were observed in fibrinogen levels (109 mg/dl (69-227) vs 257 (126-392), p <0.05), ADP dependent platelet aggregation (103 AU/min (89-176) versus 368 (126-781), p <0.05), the thrombin dependent platelet aggregation (265 AU/min (160-291) vs 558 (288-989), p <0.05) and clotting time (64 sec (57-72) vs 52 (39-68), p <0.05) of EXTEM analysis. The bleeding risk model was tested in this prospective cohort and predictive performance of bleeding risk (accuracy) was 85.18% (sensibility 90.5%, specificity 66.7%, NPV 90.5%, PPV 66.7%).

Conclusion: We demonstrate involvement of hemostasis in bleeding risk of esophageal varices. A low fibrinogen levels seems to be risk factor of bleeding tendency in patients with decompensated cirrhosis, which suggests the potential benefit of prophylactic treatment with fibrinogen in high risk cases. Multiplate® analysis should also help us in the future to determine the risk of bleeding esophageal varices in children with decompensated cirrhosis and would be further integrated into our predictive model.

Disclosure of interest: “None Declared”.
**HEPATOLOGY: General Hepatology**

**H-O-018**

**Clinico-pathological features of liver disease following paediatric bone marrow transplantation**

Natalia Maximova¹, Lorenza Matarazzo², Aurelio Sonzogni³, Lorenzo D’Antiga⁴

¹Hospital Burlo Garofolo, Onco-Haematology and Bone Marrow Transplantation Unit, Trieste, Italy
²University of Trieste, Paediatrics, Trieste, Italy
³Hospital Papa Giovanni XXIII, Liver and Transplant Pathology, Bergamo, Italy
⁴Hospital Papa Giovanni XXIII, Paediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy

**Objectives:** The knowledge on clinico-pathological features of liver injury following paediatric bone marrow transplantation (BMT), including liver graft versus host disease (L-GVHD), is scarce. Previous studies showed that the main target of hepatic damage is the biliary tract. We aimed to describe the features of bile duct injury in a cohort of children who consecutively underwent BMT for haematological disorders, and correlate them to clinical signs of liver disease.

**Methods:** From 2013 to 2015 protocol biopsies were scheduled for every child listed for BMT at our haematono- oncology unit. All patients showing significant clinical and/or histological liver disease were scheduled for follow up biopsies. Histology samples were reviewed and scored according to a previously reported semi-quantitative system¹, and compared with liver function tests (ALT, GGT, bilirubin, serum bile acid). Features of bile duct disease (ductular proliferation, biliary metaplasia, bile duct atrophy and ductopenia) were also reported separately. Ductopenia (bile duct to portal tract ratio <0.5) was evaluated on cytokeratin 7 stained histology slices. Overt L-GVHD was diagnosed when clinical cholestatic disease and histology consistent with GVHD were present, after exclusion of other causes.

**Results:** 50 BMTs in 44 patients (28 males, mean age 9.3 years) were carried out in the study period; overall 97 liver biopsies were performed and 89 were available for review; 45 patients had one, 30 had two, 15 had three and 5 had 4 liver biopsies taken following BMT. The mean L-GVHD score was 6.3, 5.8, 5.6 and 4.6 at the respective number of serial biopsies taken during the follow up. Bile duct proliferation was diagnosed in 81/89 (91%), metaplasia in 33/89 (37%), atrophy in 72/89 (81%). Ductopenia was diagnosed in 83/89 samples (93%), and was persisting in 11/27, worsening in 16/27 pts who had a second biopsy. Ductopenia, bile duct proliferation and atrophy were the main features in all patients who had three or four follow up biopsies, whereas metaplasia tended to disappear. Over a mean follow up of 1.4 years (SD ±0.7), 16 patients (32%) developed overt L-GVHD, 9 died of systemic complications and 7 are alive, 4 of whom with liver disease. All the other patients, at the last follow up, have normal liver tests.

**Conclusion:** Ductopenia is found in almost all children undergoing a liver biopsy following BMT, is persisting and often accompanied by ductular proliferation and atrophy. The clinico-pathological correlation, though, reveal that only a minority of such patients develops a clinical liver disease which, when fully expressed, is associated with a poor prognosis.

¹Quaglia et al. Histopathology 2007;50:727–738

**Disclosure of interest:** None declared
Prevalence and prognosis of patients with autoimmune liver disease in a population based childhood-onset inflammatory bowel disease cohort from northern Stockholm County

Petter Malmborg1, Maja Ideström1, Jan Björk2, Annika Bergquist3, Henrik Arne1l, Björn Fischler4, Eva Beijer4, Antal Nemeth4, Hans Hildebrand1, Thomas Casswall4

1 Astrid Lindgren Children's Hospital, Karolinska University Hospital, Department of Women's and Children's Health, Karolinska Institutet, Stockholm, Sweden
2 Karolinska University Hospital, Department of Medicine-Solna, Karolinska Institutet, Stockholm, Sweden
3 Karolinska University Hospital, Department of Medicine -Huddinge, Karolinska Institutet, Stockholm, Sweden
4 Astrid Lindgren Children's Hospital, Karolinska University Hospital, Department of Clinical Science, Intervention and Technology, Karolinska Institutet, Stockholm, Sweden

Objectives and study: Childhood-onset inflammatory bowel disease (IBD) is recognized as a distinct disease phenotype [1]. Some population based studies report that extra-intestinal manifestations seem to occur more frequently in patients with childhood-onset IBD [2]. Autoimmune liver disease (AILD) in patients with adult-onset IBD is associated with substantial intestinal and hepatic morbidity and mortality [3]. Here we report the prevalence and prognosis of patients with AILD in a general population-based childhood-onset IBD cohort.

Methods: Medical records of all 280 patients diagnosed in the period 1990-2007 with childhood-onset IBD (<16 years) in northern Stockholm County were followed until 2011 (median follow-up time 8.8 years (1.0-20.8)). All patients were categorized according to the Paris paediatric IBD-classification.

During the study period 22 patients were diagnosed with AILD (primary sclerosing cholangitis (n=19), autoimmune hepatitis (n=1), autoimmune sclerosing cholangitis (n=2)) in consistency with upgraded diagnostic recommendations [4]. The IBD-AILD patients were examined with ERCP or MRCP (n=21), liver biopsy (n=19) and auto-antibody tests (n=21). In the sub-cohort the median age at IBD diagnosis was 12.2 years (4.1-15.7) and at AILD diagnosis 14.2 years (6.2-27.3). The IBD-AILD patients were followed for a median time of 6.9 years (1.6-15.6) after AILD diagnosis.

The prevalence of AILD in the IBD cohort over time and the cumulative risk of complicated liver disease (defined as signs of portal hypertension or obstructive cholangitis [4]) in the IBD-AILD sub-cohort were estimated using the Kaplan-Meier method.

Results: The prevalence of AILD in the childhood-onset IBD cohort at was 5% (95% CI 3%-9%) at 5 years and 7% (95% CI 5-11%) at 10 years after IBD diagnosis.

All IBD-AILD patients presented with an extensive colitis. Eleven of the patients were diagnosed with ulcerative colitis (E3 (n=2), E4 (n=8)) and 12 with Crohn’s disease (L2 (n=11), L3 (n=1)). None of the IBD-AILD patients presented with or developed intestinal or perianal complication during the study period. One patient with IBD-AILD was colectomised during the study period.

The cumulative risk of complicated liver disease in the IBD-AILD sub-cohort was 14% (95% CI 4%-36%) at 5 years after AILD diagnosis. No IBD-AILD patient underwent liver transplantation during the study period.

None of the IBD-AILD patients developed liver- or colorectal cancer and no patient in the sub-cohort died during the study period.

Conclusion: This is one of the first studies that provides an estimate of the risk of AILD over time in a population based childhood-onset IBD cohort. The IBD phenotype of childhood-onset patients with AILD seems to be characterized by extensive but uncomplicated colitis. Childhood-onset IBD patients with concomitant AILD seem to have a relatively low early intestinal- and hepatic morbidity and mortality.
Disclosure of interest: None Declared.

Successful identification of high risk young people with biliary atresia using the Mayo PSC risk score

Deepak Joshi1, John O’Grady1, Michael Heneghan1, Nigel Heaton1, Mark Davenport2, Dino Hadzic3, Anil Dhawan3, Marianne Samyn3

1King’s College Hospital, Institute of Liver Studies, London, United Kingdom
2King’s College Hospital, Department of Paediatric Surgery, London, United Kingdom
3King’s College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom

Objectives and study: Biliary atresia (BA) is a progressive inflammatory cholangiopathy of unknown aetiology presenting in infancy. It is the leading indication for liver transplantation (LT) if the Kasai portoenterostomy is unsuccessful. In young adults (YA) surviving with their native liver complications as cholangitis and portal hypertension with variceal bleeding are common and an indication for LT.

Methods: Distinct similarities exist between BA patients and patients with primary sclerosing cholangitis. We therefore, hypothesized that the adult Mayo PSC risk score (MPSCrs) calculated at the age of 18 years could help identify high-risk YA with BA who were at risk of hepatic decompensation or require liver transplantation (LT). Patients were divided into group 1 (low risk, MPSCrs <0) and group 2 (intermediate/high risk, MPSCrs >0) using the MPSCrs. Endpoints included hepatic decompensation or LT assessment or LT (HD/LT).

Results: 107 (51% female) BA patients (> 18 years) were identified. Median follow up was 60 months (range 18-204). At 18 years of age: 94% had a heterogeneous liver architecture, 68% splenomegaly (median spleen size 16cm, range 8-27cm) and 80% signs of portal hypertension. Only 6 patients had suffered a variceal bleed prior to the age of 18 years. Median MELD, UKELD and CPS were 8 (6-18), 45 (43-55) and 5 (5-9) respectively. 21 (20%) patients were in Group 2. Overall survival was excellent (94% at 10 years). Cumulative risk for the HD/LT was 7%, 18% and 47% at 1, 5 and 10 years. 29 patients (27%) fulfilled the primary endpoint (median time 24 months, 12-144). 22 patients underwent LT assessment, 14 were successfully transplanted, 4 are active on the waiting list. 4 patients were assessed but then subsequently declined for LT. The spleen size and MPSCrs were significantly higher in those that fulfilled the endpoints (p<0.0001). Group 2 were more likely to meet HD/LT compared to Group 1 (72% vs 15%, p<0.0001) and within a shorter period of time (24 months vs 72 months, p=0.05). AUROC analysis identified the MPSCrs to be a significant predictor of requiring HD/LT (0.87, 0.77-0.96, p<0.0001).

Conclusion: The MPSCrs calculated at 18 years of age can help identify high-risk young adults with BA. Patients with an intermediate or high risk MPSCrs require closer surveillance and consideration for LT. Further studies are required to validate our preliminary observations.

Disclosure of interest: “None Declared”.
**HEPATOLOGY: General Hepatology**

H-O-021

**DEFI-ALPHA Cohort: phenotype of liver disease in children with alpha-1 antitrypsin deficiency in France**

Mathias Ruiz¹, Gottrand Frederic², Dabadie Alain³, Jacquemin Emmanuel⁴, Lamireau Thierry⁵, Broue Pierre⁶, Borderon Corinne⁷, Bonneton Marjorie⁸, Jobert Agathe⁹, Billiemaz Kareen¹⁰, GFHGNP members of¹¹, Joly Philippe¹², Lacaille Florence¹³, Lachaux Alain¹⁴

¹Children's Hospital of Lyon, Department of Pediatric Gastroenterology Hepatology and Nutrition, Bron, France
²Chu Lille, France
³Chu Rennes, France
⁴Chu Bicêtre, Paris, France
⁵Chu Bordeaux, France
⁶Chu Toulouse, France
⁷Chu Clermont Ferrand, France
⁸Chu Nancy, France
⁹Chu Nantes, France
¹⁰Chu St Etienne, France
¹¹Chu, All Cities, France
¹²Hospital Edouard Herriot, Laboratory of Molecular Biology, Lyon, France
¹³Hospital Necker Sick Children, Pediatric Hepatology and Gastroenterology, Paris, France
¹⁴Children's Hospital of Lyon, Department of Pediatric Gastroenterology Hepatology and Nutrition, Lyon, France

**Objectives and study:** The DEFI-ALPHA Cohort includes the French children with alpha-1 antitrypsin deficiency (AATD). The main objective is to find prognostic factors linked to liver complications. Secondary objectives are the description of natural history, recommendations for management and follow-up, and the study of candidate genes, for polymorphisms related to liver complications (PHRC Polygen).

**Methods:** It is a multicenter study, retrospective, and prospective from 2008, including all children with AATD born in France from 1989. The inclusion criterion is AAT less than 0.8 g/L whatever the phenotype. The following factors are recorded: sex, consanguinity, intrauterine growth restriction (IUGR), age at diagnosis, mode of diagnosis (neonatal cholestasis, abnormal liver tests, familial screening), AAT blood level, phenotype, ursodeoxycholic acid (UDCA) therapy, medical history, presence of portal hypertension (PHT), liver transplantation.

**Results:** In December 2015, 146 patients had been included, from 17 centres, with a sex ratio of 1.92 (96 boys). Mean age at last follow-up was 12.4 years. At diagnosis, mean age was 1.6 year, 56% had neonatal cholestasis, and 67% abnormal liver tests (ALT or GGT more than 100 UI/L). Diagnosis was made before 2 months in 53%; before 1 year in 65%. Mean level of AAT was 0.41 g/L. The phenotype was ZZ in 79%, with a mean AAT level of 0.30 g/L. It was SZ in 9%, MZ in 5%, SS in 2%, and other in 5%. UDCA therapy was introduced in 68%. AATD was found in siblings in 39%. Mean follow-up was 3.9 years (1 month - 6 years). 22 children (15%) developed PHT at a mean age of 2 years (1 month - 4 years). The diagnosis had been made before the age of two months in 52%, with neonatal cholestasis in 60%. The phenotype was ZZ in 15, SZ in 3, MMalton in 1 (3 still unknown). Only one did not receive UDCA. Fifteen children received a liver transplant, at a mean age of 6.3 years (range 2-15). One child died at 3 years of age of infection.

**Conclusion:** AATD is responsible for severe liver disease in 15 % of children in this cohort. The presence of cirrhosis and PHT in non-ZZ patients with low levels of AAT highlights the possible severity of other phenotypes such as SZ or MMalton. The genetic study will hopefully further help to find genetic factors involved in liver complications. Two complementary strategies are ongoing: the Sanger sequencing of candidate genes and the whole exome sequencing of siblings presenting with
the same ZZ genotype but experiencing markedly different clinical outcomes. Both strategies focus on genes implied in the degradation of misfolded proteins by the endoplasmic-reticulum-associated protein degradation pathway.

Disclosure of interest: The cohort was funded by LFB Laboratory.
Early onset LAL deficiency mimicking haemophagocytic lymphohistiocytosis

Maja Klaudel-Dreszler1, Agnieszka Bakula1, Ewa Orlowska1, Anna Tylki-Szymańska2, Agnieszka Ługowska3, E. Y. Zakharova4, Aldona Wierzbicka5, Piotr Socha6

1Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutritional Disorders and Paediatrics, Warsaw, Poland
2Children's Memorial Health Institute, Department of Paediatrics, Nutrition and Metabolic Disorders, Warsaw, Poland
3Institute of Psychiatry and Neurology, Department of Genetics, Warsaw, Poland
4Russian Academy of Medical Sciences, National Research Centre for Medical Genetics, Mocsow, Russian Federation
5Children's Memorial Health Institute, Warsaw, Poland
6The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Early onset LAL deficiency (EOLALD), also referred to as Wolman’s disease, represents an inborn error of metabolism caused by complete loss of lysosomal acid lipase (LAL) activity that presents in early infancy with hepatosplenomegaly, vomiting, diarrhea, subsequently leading to cholestatic jaundice, liver insufficiency and death. Most patients present with calcification of the adrenal glands. Haemophagocytic lymphohistiocytosis (HLH) is a life-threatening condition, caused by congenital or acquired defects of cellular cytotoxicity, manifesting with fever, hepatosplenomegaly, duo- or pancytopenia, coagulopathy, hyperferritinemia and cholestasis. Both diseases have poor prognosis. There are few case reports on infants with EOLALD who developed symptoms suggesting HLH.

Methods: We present a 4-month old-girl with progressive hepatosplenomegaly, jaundice, failure to thrive and vomiting. Bone marrow biopsy, immunologic screening towards HLH, ultrasound of abdomen, LAL activity in DBS screening (dry blood spot) and LIPA gene sequencing were tested in the girl.

Results: The infant presented with huge hepatosplenomegaly, anaemia (Hb 7.1 g/dl), thrombocytopaenia (67 K/μl), severe coagulopathy (INR 8.33, PT 82 s, fibrinogen 1.2 g/l), elevated activity of ALT 230 U/l, AST 460 U/l, GGTP 350 U/l and LDH 3300 U/l, hyperbilirubinaemia with predominance of direct bilirubin (increasing from 6.5 to 55 mg/dl), hyperferritinaemia (21600 ng/ml), hypertriglyceridaemia (360 mg/dl), hypercholesterolaemia (185 mg/dl) and haemophagocytosis found in myelogram. She fulfilled 5 out of 8 diagnostic criteria of HLH so she received dexamethasone and cyclosporine A, according to HLH-2004 protocol, with no improvement. Because of progressive disease, with the suspicion of acute liver failure due to HLH she was admitted to our department. We achieved partial correction of coagulopathy after an intravenous dose of vitamin K. Ultrasound of abdomen revealed calcification of the adrenal glands that suggested EOLALD. LAL activity measured in DBS screening was extremely low. Cytotoxic activity of T lymphocytes and NK cells was normal; she had normal sCD25 and perforin expression. Immunological diagnostics helped to exclude HLH. We stopped immunosuppressive treatment. The girl died at the age of 6 months due to cardio-respiratory insufficiency in the course of liver failure. Molecular analysis of the LIPA gene identified two pathological mutations in heterozygous status: c.509C>A(p.S103R)/c.796>T(p.G266X).

Conclusion:
1. Infants presenting symptoms of HLH should be tested for acid lipase deficiency (DBS screening is currently available)
2. EOLALD and HLH share some clinical symptoms and laboratory findings that may lead to diagnostic and therapeutic mistakes.

Disclosure of interest: None declared.
Brain MRI and Spectroscopy in the diagnosis of early neurological involvement in Wilson’s disease in children

Hatem Hussein1, Hosam F. Elsaadany2, Ashgan A. Elghobashy2, Hadeel Abdelrahman2, Mohamed A. Talaat3, Ayman F. Zeid2

1Zagazig Faculty of Medicine, Pediatrics, Zagazig, Egypt
2Zagazig Faculty of Medicine, Zagazig, Egypt

Objectives and study: Wilson’s disease is an inherited disorder of copper metabolism characterized by accumulation of copper in the liver, brain, kidneys and other tissues resulting in hepatic and neuropsychiatric features. Magnetic resonance imaging (MRI) helps in the diagnosis of neuropsychiatric Wilson’s disease. The literature regarding MR spectroscopy (MRS) in Wilson’s disease is limited. The aim of this work was to evaluate the validity of brain MRI and spectroscopy in early detection of central nervous system abnormalities in children with Wilson’s disease.

Methods: A case-control study was carried out at the Gastroenterology unit, Pediatric department and the Radiology department, at Zagazig University Hospitals, Zagazig, Egypt between March 2011 and March 2014 after IRB approval. Twenty-six patients with Wilson’s disease and 26 healthy volunteers were included. Detailed history taking; complete physical examination including anthropometry, regional examination, full abdominal examination and neurological assessment were done. Routine laboratory investigations included CBC, CRP, ESR, reticulocytic count, complete liver function tests, abdominal ultrasound, Immunoglobulin electrophoresis and kidney function tests. Specific investigations included serum ceruloplasmin level, copper concentration in 24-hour urine collection, copper concentration in 24 hour-urine collection with D-penicillamine challenge test, autoantibodies panel (ANA, ASMA and ALKMA). Slit lamp examination for Kayser-Fleischer ring and percutaneous liver biopsy looking for consistent liver histology (fatty changes or glycogenated nuclei). MRI and MRS were done for all patients.

Results: Eight patients showed abnormal magnetic resonance imaging in the form of bilateral increased signal intensity in the basal ganglia in T1-weighted axial MR images. Compared with control subjects, patients with WD had a highly significant decrease in N-acetyl aspartate, choline and creatine values (p<0.001) and significantly decreased N-acetyl aspartate/choline, N-acetyl aspartate/creatine and choline/creatine ratios (p<0.05) of right basal ganglia. Patients complicated with liver cell failure had a highly significant decrease in N-acetyl aspartate (p<0.001) and Significant decrease of choline, creatine values, N-acetyl aspartate/choline, N-acetyl aspartate/creatine and choline/creatine ratios (p<0.05) than patients without complications

Conclusion: MRI abnormalities were detected in eight patients out of 26 (30.7%) while MRS showed decrease of N–acetyl aspartate, Choline, Creatinine, N-acetyl aspartate/choline, N-acetyl aspartate/creatine and choline/creatine in all patients. MRS in patients diagnosed as a Wilson’s disease detects early neurological changes even with normal MR imaging.

Disclosure of interest: “None Declared”.
What coagulation parameters define a safe liver biopsy in children?

Winita Hardikar¹, Judy Matta¹, Rishi Bolia¹, Rohan Malik²

¹Royal Children's Hospital, Gastroenterology, Parkville, Australia
²All India Institute of Medical Sciences, Paediatrics, New Delhi, India

Objectives and study: There are no evidence based guidelines regarding the management of coagulopathy in children undergoing a liver biopsy as per a recent international survey involving centers in Europe, North America and Australia [1]. We aimed to determine coagulation parameters associated with a safe liver biopsy, taking into account preoperative coagulation studies, the liver biopsy method and the operator.

Methods: A retrospective review of all children who underwent a percutaneous liver biopsy at our institution between January 2005 and June 2015 was performed. The demographics, indications, comorbidities, approach, operator, laboratory data, pre-procedural blood product transfusion history, complications, and outcomes were recorded.

Results: 626 biopsies were performed on 497 patients (250 males and 247 females) with a mean age of 6 years (age range, 2 months-19.3 years). The indications for the biopsy were abnormal liver enzymes (n=283, 45.2%), abnormal liver enzymes post liver transplant (n=163, 26%), neonatal cholestasis (n= 77 12.3%), liver lesion (n= 55, 8.8%), mitochondrial disease (n= 41, 6.5%), splenomegaly (n=5, 0.8%) and as a part of a work up for small bowel transplant (n=22, 0.3%). The procedure was performed either by an interventional radiologist (ultrasound guided +/- plugged tract, n=498, 79.6%) or a pediatric gastroenterologist (ultrasound assisted, no plug, n=128, 20.4%).

Complications occurred in 28 (4.47%) of the biopsies. Bleeding complications were seen in 22 (3.5%), and comprised of subscapular hematoma (n= 14, 2.2%), haemobilia (n= 2, 0.3%), ooze from the skin site (n=3, 0.4 %) and intraperitoneal bleed (n=3, 0.5%). Other complications included sepsis (n=1, 0.2%) and systemic inflammatory response syndrome (n= 5, 0.8%).

Patients who received either fresh frozen plasma or platelet infusion prior to the procedure (n=75) were excluded from further analysis. In the remaining biopsies (n = 551), no bleeding – related complications occurred at a cut–off of INR ≤1.7 and platelet count of ≥39,000 /mm³.

If the proposed cut-offs in the ESPGHAN 2015 position paper (2) are used, platelet count and INR did not predict the risk of bleeding (Table). The use of a gel foam plug however significantly decreased the risk of bleeding.
Table:

<table>
<thead>
<tr>
<th></th>
<th>Bleeding (n = 18)</th>
<th>No Bleeding (n = 533)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Plts &lt; 60,000/mm³</td>
<td>0</td>
<td>6</td>
<td>1.0</td>
</tr>
<tr>
<td>Plts &gt; 60,000/mm³</td>
<td>18</td>
<td>527</td>
<td></td>
</tr>
<tr>
<td>INR ≥ 1.5</td>
<td>0</td>
<td>5</td>
<td>1.0</td>
</tr>
<tr>
<td>INR &lt;1.5</td>
<td>18</td>
<td>528</td>
<td></td>
</tr>
<tr>
<td>Radiologist</td>
<td>5</td>
<td>426</td>
<td>0.00</td>
</tr>
<tr>
<td>Gastroenterologist</td>
<td>13</td>
<td>107</td>
<td></td>
</tr>
<tr>
<td>Gel Foam Plug</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>4</td>
<td>399</td>
<td>0.00</td>
</tr>
<tr>
<td>No</td>
<td>14</td>
<td>134</td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Routinely used coagulation parameters are not reliable in predicting risk of bleeding after a liver biopsy in children. Instead risk may be related to the operator and mechanical issues. The effect of coagulation support requires further study.

**References**


**Disclosure of interest:** None declared
Reference values for exchangeable copper and rec, new promising biomarkers for diagnosis and treatment-monitoring of Wilson disease

Anne Sophie Brunet1, Mustapha Moulsma2, Alexandre Teyssier2, Olivier Guillaud1, Emmanuel Broussolle2, Laurence Lion-François1, Alain Lachaux4, Muriel Bost4

1Hôpital Femme Mère Enfant, Reference Centre for Wilson Disease, Lyon, France
2Edouard Herriot Hospital, Trace Element Analysis Laboratory, Biochemistry and Molecular Biology, Lyon, France
3Hôpital Pierre Wertheimer, Reference Centre for Wilson Disease, Lyon, France
4Hôpital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology; Reference Centre for Wilson Disease, Lyon, France

Objectives and study: Wilson disease (WD) diagnosis can be challenging and is based on several clinical and biological features. REC [ratio CuEXC / Total serum copper (CuT)] calculation and measuring of the serum exchangeable copper (CuEXC) seem to be promising tools for diagnosis and treatment-monitoring of WD respectively (1,2). In the present study, the reference values for CuEXC and REC were evaluated in different age groups covering the whole life range.

Methods: CuEXC concentration and REC calculation were determined in 146 healthy children (57 between 0 et 6 years old et 89 between 6 and 18 years old) and in 120 adult blood-donors (53 females and 67 males). The age distribution within these groups ranged from 22 months to 18 years (mean age = 9.5 years) and from 18 to 68 years (mean age = 44 years). The CuEXC and CuT determination were performed by Electrothermal Atomic Absorption Spectrometry with Zeeman background correction and Inductively Coupled Plasma Optical Emission Spectrometry respectively. Statistical analyses were carried out with XLStat and R softwares. The check for normal distribution was performed with the Kolmogoroff-Smirnoff test. Group differences were identified with ANOVA with PLSD Fisher post-hoc test (p<0.05).

Results: The adult serum reference values were ranged between 38.3 and 92.5 µg/L (0.60 – 1.46 µmol/L) (IC 95%) for CuEXC and between 2.61 and 9.31 % (IC 95%) for REC. In the child and adolescent group, the serum reference values were ranged between 23.6 and 63.5 µg/L (0.37 – 1.00 µmol/L) for CuEXC and between 1.41 and 6.99 % (IC 95%) for REC. CuEXC levels and REC values exhibited a significant age-dependant increase (between group 0 – 6 years and group 6 – 18 years, p<0.0001). No correlation between CuEXC concentration and sex could be shown.

Conclusion: Reference ranges are established for six different age groups (266 healthy subjects). The present study is an important pre-requisite for using CuEXC and REC in diagnosis and monitoring of clinical treatment of WD.

Disclosure of interest: “None Declared”.

NK cells phenotype as a risk marker of posttransplant lymphoproliferative disease in liver transplanted children

Francoise Smets¹, Breda Ugo¹, Stephenne Xavier¹, Saussoy Pascale², Sokal Etienne¹

¹Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Brussels, Belgium
²Ucl, Cliniques Universitaires Saint-Luc, Irec, Clinical Laboratory, Brussels, Belgium

Objectives and study: Post-transplantation lymphoproliferative disease (PTLD) is a serious complication in liver transplanted children, most often related to Epstein-Barr virus (EBV) infection. The monitoring of EBV viral load by PCR is the easiest method to identify children at risk of PTLD. However, a high viral load has a low specificity after pediatric liver transplantation. The role of NK cells in the control of EBV primary infection is increasingly recognized and a modification of their phenotype and function was demonstrated in thoracic transplanted children developing PTLD.

Methods: Between August 2013 and July 2015, we prospectively analyzed the rate of total NK cells and the proportion of their subpopulations by flow cytometry in 29 liver transplanted children who were naïve for EBV before transplantation. In this population, we also measured the expression of 3 membrane receptors of NK cells: NKG2D, NKp46 and PD-1.

Results: Five patients (17.2%) developed PTLD within one year post transplantation (median 84 days, range 83-109 days). In those children, in the first trimester after transplant, we identified an increased proportion of total NK cells (CD3-CD56±, 13.52% vs 9.05%, p=0.0011) and CD3-CD56dimCD16+ cells (63.08% vs 43.18%, p=0.0011) and a reduced proportion of CD3-CD56bright cells (5.26% vs 10.42%, p=0.0033). In this context, a test based on a rate of CD3-CD56± cells ≥ 12.5% and a rate of CD3-CD56dimCD16+ cells ≥ 63% would offer a positive and a negative predictive value of 100% to detect children at risk of PTLD. This increased or decreased NK cells proportions were also observed in correlation with the EBV load (negative, low, high or PTLD), although not significant (p=0.05-0.089). There were no differences of the NK membrane receptors expression between patients with or without PTLD.

Conclusion: The phenotypic analysis of NK cells by flow cytometry could be an easy and useful tool to monitor pediatric liver transplant recipients in order to quickly identify children at risk of PTLD.

Disclosure of interest: None Declared
Similarities and differences in allocation policies for pediatric liver transplantation across the world

Björn Fischler1, Ulrich Baumann2, Daniel D'Agostino3, Lorenzo D'Antiga4, Antal Dezsofi5, Dominique Debray6, Helen Evans7, Esteban Frauca8, Nedim Hadzic9, Loreto Hierro10, Jörg Jahnel11, Jerome Loveland12, Valérie McLin13, Vicky Lee Ng14, Valerio Nobili15, Joanna Pawłowska16, Francoise Smets17, Henkjan Verkade18, Evelyn Hsu19, Simon Horslen19, John Bucuvalas20

1Dept. of Pediatrics, Karolinska University Hospital, Clintec, Stockholm, Sweden
2Medizinische Hochschule Hannover, Paediatric Liver Unit, Hannover, Germany
3Gastroenterology-Hepatology Division Liver and Intestinal Transplantation Unit Department of Pediatrics Hospital Italiano, Buenos Aires, Argentina
4Hospital Papa Giovanni XXIII, Paediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy
5First Dept of Paediatrics, Semmelweis University, Budapest, Hungary
6Hepatology Unit, Hôpital Necker-Aphp, Paris, France
7Starship Children’s Hospital, Department of Paediatric Gastroenterology, Auckland, New Zealand
8Paediatric Hepatology and Liver Transplantation Unit. Hospital Universitario Infantil La Paz, Madrid, Spain
9H. La Paz, Pediatric Hepatology, Madrid, Spain
10Medical University Graz, Graz, Austria
11Transplant Unit Wits Donald Gordon Medical Centre University of the Witwatersrand, Johannesburg, South Africa
12University Hospitals Geneva, Pediatrics, Geneva, Switzerland
13The Hospital for Sick Children, Toronto, Canada
14Hepatometabolic Unit, Bambino Gesu Children’s Hospital, Rome, Italy
15The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
16Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Brussels, Belgium
17Dept of Paediatrics, University of Groningen, University Medical Center Groningen, Groningen, Netherlands
18Seattle Children's Hospital, Seattle, United States
19Cincinnati Childrens Hospital, Cincinatti, United States

Objectives and study: At the ESPGHAN monothematic conference on pediatric liver transplantation (LT) in 2013 some interesting preliminary differences in national organ allocation policies were noted. Since few data are available on the topic, in the present study we aimed to further investigate these policies in a larger number of countries.

Methods: A survey on national policies on organ allocation for pediatric LT was prepared by ESPGHAN hepatology committee in collaboration with SPLIT (Studies of Pediatric Liver Transplantation) and sent to pediatric hepatologists in 18 countries worldwide. National data were mostly obtained from centrally based registers.

Results: Replies were obtained from 12 countries (Table) from five of the world continents. Overall donation rate varied between 9 and 35 per million inhabitants. The number of pediatric liver transplantations was similar around 5-9 per million inhabitants below 18 years of age for 9 of the 11 respondents. In the youngest children (<2 years of age) mortality on the waiting list (WL) varied between 0 and 20%. In the same age group, there were large differences in the ratio of living donor (LD) LT to deceased donor (DD) LT as well as in the ratio of split liver segments to whole liver.
### Table:

<table>
<thead>
<tr>
<th>Country</th>
<th>Donation rate (per million inhabitants)</th>
<th>Pediatric LT per million inhabitants &lt; 18 years</th>
<th>Mortality on waiting list children &lt; 2 years (%)</th>
<th>Ratio of LDLT to DDLT children &lt; 2 years</th>
<th>Ratio of split livers to whole livers children &lt;2 years</th>
</tr>
</thead>
<tbody>
<tr>
<td>Argentina</td>
<td>13.0</td>
<td>5.6</td>
<td>17</td>
<td>1.1 : 1</td>
<td>1 : 2.2</td>
</tr>
<tr>
<td>Belgium</td>
<td>33.2</td>
<td>16.5 (70% foreign patients)</td>
<td>2.6</td>
<td>4.5 : 1</td>
<td>1 : 7</td>
</tr>
<tr>
<td>Canada</td>
<td>15.5</td>
<td>6.7</td>
<td>NA</td>
<td>2.3 : 1</td>
<td>1.3 : 1</td>
</tr>
<tr>
<td>France</td>
<td>25</td>
<td>5.7</td>
<td>4.1</td>
<td>1 : 10</td>
<td>2.2 : 1</td>
</tr>
<tr>
<td>Italy</td>
<td>21.8</td>
<td>6.6</td>
<td>0</td>
<td>0 : 284</td>
<td>8.5 : 1</td>
</tr>
<tr>
<td>Netherlands</td>
<td>16.1</td>
<td>5.4</td>
<td>12</td>
<td>0.7 : 1</td>
<td>NA</td>
</tr>
<tr>
<td>New Zealand</td>
<td>9</td>
<td>9.0</td>
<td>9</td>
<td>1.04 : 1</td>
<td>8 : 1</td>
</tr>
<tr>
<td>Poland</td>
<td>15.4</td>
<td>6.2</td>
<td>0</td>
<td>10 :1</td>
<td>1 : 100</td>
</tr>
<tr>
<td>Spain</td>
<td>35.1</td>
<td>7.0</td>
<td>8</td>
<td>2.4 : 1</td>
<td>1 : 6</td>
</tr>
<tr>
<td>South Africa</td>
<td>NA</td>
<td>0.9</td>
<td>20</td>
<td>1:1</td>
<td>10 : 1</td>
</tr>
<tr>
<td>Switzerland</td>
<td>14.6</td>
<td>6.3</td>
<td>0</td>
<td>0:4</td>
<td>1.1 : 1</td>
</tr>
<tr>
<td>USA</td>
<td>26.4</td>
<td>7.7</td>
<td>~5/100 WL years</td>
<td>1.4.8</td>
<td>1 : 2.9</td>
</tr>
</tbody>
</table>

LT=Liver transplantation; LD=Living donor; DD=Deceased donor; WL=Waiting list; NA=Not available

**Conclusion:**

1. The number of LT performed per inhabitants in the pediatric age group was remarkably stable across nations.
2. Countries with a high ratio of LDLT versus DDLT often had a low ratio of split livers to whole livers and vice versa.
3. The waiting list mortality could presumably be lowered either by increasing the number of LDLT or the number of split LT.

**Disclosure of interest:**
None Declared
The histological quantification of alpha-smooth muscle actin predicts future graft fibrosis in pediatric liver transplant recipients

Sharat Varma¹, Xavier Stephenne², Mina Komuta³, Caroline Bouzin⁴, Jérome Ambroise⁵, Francoise Smets⁶, Raymond Reding⁷, Etienne Sokal⁸

¹Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium
²Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
³Clinique Universitaire St Luc, Pathology, Brussels, Belgium
⁴University Catholique de Lovain, Brussels, Belgium
⁵Université Catholique de Louvain, Center for Applied Molecular Technologies, Bruxelles, Belgium
⁶Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Brussels, Belgium
⁷Clinique Universitaire St Luc, Pediatric Liver Transplantation and Surgery, Brussels, Belgium
⁸Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Objectives and study: To evaluate the significance of alpha-smooth muscle actin (ASMA) expression on liver biopsy specimens as a predictor of future graft fibrosis in pediatric liver transplant (LT) recipients.

Background: Activated hepatic stellate cells (HSCs) express cytoplasmic alpha-smooth muscle actin (ASMA), while subsequently secreting collagen that causes liver fibrosis. As this stellate cell activation precedes the collagen deposition, we hypothesized that quantifying ASMA could predict the severity of subsequent liver fibrosis.

Patients and methods:

Patients: Stable pediatric LT recipients having received transplant in 2006-20012 were included, all with two protocol biopsies less than two years apart and the first over 1 year post-LT. Patients with biliary or vascular complications, autoimmune hepatitis, hepatitis B or C infection, re-transplantation or inadequate biopsy size were excluded from analysis.

Methods: The Metavir and liver allograft fibrosis scores (LAFSc) were used for fibrosis assessment. Automated staining for ASMA was performed, followed by digital quantification of ASMA positive area percentage. Any fibrosis on initial biopsy specimens was labelled “current fibrosis”, then as “prospective fibrosis” on following specimens. Change between “current” and “prospective” fibrosis score was termed “prospective change in fibrosis”. Bile duct proliferation, lobular inflammation, and portal tract infiltration were also evaluated.

Results: In total, 32 biopsy specimens from 18 patients were stained for ASMA, and 56 assessed for fibrosis. There was a significant association between ASMA positive area percentage on initial biopsy and “prospective change in fibrosis” using Metavir (p value = 0.02), cumulative LAFSc (p value = 0.02), and portal LAFSc (p value = 0.01) values. Area under (AU) receiver operating characteristic (AUROC) curve analysis indicated an ASMA positive area percentage >1.05 predicted increased fibrosis on the next biopsy (60.0% sensitivity, 90.0% specificity).

Conclusion: ASMA quantification on biopsy specimens in liver transplant recipients predicts the future course of fibrosis, especially portal fibrosis.

Disclosure of interest: All authors - “None Declared".
Objectives and study: Auto-immune hemolytic anemia (AIHA) is a rare condition occurring after solid organ transplantation. The incidence of which is not known. The aim of this retrospective study was to analyze a single center cohort in order to identify potential risk factors.

Methods: Donor, recipient and surgical parameters were collected from the records of 96 children having received a liver transplant (LT) between the years 2000-2013. AIHA was defined as acute anemia with positive direct Coombs. Using AIHA as the outcome, univariate data's were compared by Fischer’s exact test and by Mann-Whitney test. Analyses were performed using PRISM 6 software (Graph PAD Software). A p-value of 0.05 was considered as significant. Early AIHA was defined as AIHA occurring during the first 3 months after LT and late AIHA as AIHA occurring more than 3 months after LT.

Results: Seven (7/96) patients with AIHA were identified (Table 1). All patients received a primary immunosuppressive protocol consisting of tacrolimus, basiliximab and corticosteroids for three months. Patients with early AIHA were treated by corticosteroids or immunoglobulins. All patients with late AIHA (4/4) were refractory to this treatment but later responded to rituximab.

Development of AIHA was significantly (p= 0.04) associated with biliary atresia (BA) and young age at LT (p= 0.04). The use of IGL1 preservation solution seemed also to favor the development of AIHA (p=0.05). Viral infections occurring more than 3 months after transplantation were also associated with development of late AIHA (p=0.01). Patients at high risk of CMV infection (defined as positive donor and negative recipient serology at LT) were also at higher risk of developing AIHA (p=0.035). Likewise, there was a significant association between the onset of AIHA and CMV primary infection during first year post LT (P=0.03).
**Conclusion**: The incidence of AIHA following pediatric LT was 7% in this cohort. There were two distinct clinical phenotypes: early and late. They differed in two ways: differential response to treatment and probable viral triggers in the late presentation. These findings should encourage clinicians to look for AIHA, especially among younger recipients, who may be more vulnerable to viral infections. The association between AIHA and the use of the IGL-1 preservation solution needs to be investigated further since this is a novel finding. It seems that CMV infection, known to be an important cause of morbidity early post LT may also contribute to AIHA, adding credence to the importance of primary prophylaxis. Therefore, it can be argued that others viruses should be sought and considered among potential culprits.

**Disclosure of interest**: None Declared.

---

**Table 1**: Description of 7 cases of AIHA occurring before one year after transplantation. * At transplant BA= Biliary Atresia. AIHA: Auto-immune hemolytic anemia

<table>
<thead>
<tr>
<th>Primary diagnosis</th>
<th>Age * (months)</th>
<th>AIHA onset (time after transplant)</th>
<th>Direct Coombs test</th>
<th>Red blood cell antibody</th>
<th>Infectious trigger</th>
<th>Preservative Solution</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>EARLY AIHA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>13</td>
<td>9 days</td>
<td>++</td>
<td>Anti A1 (Allo or Auto)</td>
<td>no</td>
<td>UW</td>
</tr>
<tr>
<td>BA</td>
<td>5</td>
<td>9 days</td>
<td>+</td>
<td>Not searched</td>
<td>Laryngitis</td>
<td>UW</td>
</tr>
<tr>
<td>Alpha 1 anti-trypsin deficiency</td>
<td>119</td>
<td>9 days</td>
<td>+++</td>
<td>Not searched</td>
<td>no</td>
<td>IGL 1</td>
</tr>
<tr>
<td><strong>LATE AIHA</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>BA</td>
<td>8</td>
<td>10 months</td>
<td>++++</td>
<td>Warm IgG Auto - AntiC</td>
<td>CMV Primary Infection</td>
<td>UW</td>
</tr>
<tr>
<td>BA</td>
<td>8</td>
<td>11 months</td>
<td>+++</td>
<td>Warm IgG and IgM Auto - Antibodies</td>
<td>Viral gastro-enteritis</td>
<td>IGL1</td>
</tr>
<tr>
<td>BA</td>
<td>7</td>
<td>7 months</td>
<td>+++</td>
<td>Warm IgG and IgM Cold agglutinins Auto - Antibodies</td>
<td>Viral gastro-enteritis</td>
<td>UW</td>
</tr>
<tr>
<td>BA</td>
<td>12</td>
<td>8 months</td>
<td>+++</td>
<td>Warm IgG Auto – Anti-e</td>
<td>Clostridium enteritis</td>
<td>IGL1</td>
</tr>
</tbody>
</table>
Long Term Outcome of Biliary Atresia into Adult Life

Javaid Sadiq¹, Aditi Kumar², Hifsa Sohail¹, Carla Lloyd¹, James Ferguson², Khalid Sharif¹, Darius F. Mirza², Gideon Hirschfield³, Deirdre Kelly⁴

¹Birmingham Children’s Hospital, Liver Unit, Birmingham, United Kingdom
²Queen Elizabeth University Hospital, Liver Unit, Birmingham, United Kingdom
³University of Birmingham, Birmingham, United States
⁴The Liver Unit, Birmingham, United Kingdom

Objectives and study: Biliary Atresia (BA) is the single commonest cause of neonatal cholestasis leading to cirrhosis, portal hypertension and liver failure and is the main indication for pediatric liver transplant (LT). The objective of this study was to evaluate the long-term outcome of children with BA transitioning to adult services with their native liver or after LT and outcome before or after centralization of BA services.

Methods: Records of patients of BA managed over a period of 34 years (1980–2014) at a single institution were retrospectively reviewed. Patients with more than 10 years of follow-up were included in the study. Data collection included demographics, age at Kasai Portoenterostomy (KPE), associated malformations, survival with native liver or post-LT, mortality, current education/work/marital/family status.

Results: 493 BA patients were managed during this period (260 F & 233 M). Median age at kasis was 53 days (range: 7-183 days). 92% had isolated BA while 8% had BA polysplenia malformation syndrome. 332 patients were included in this study (1980–2004). 11 patients were lost to follow-up. Median patient survival is 17.3 yrs (0.32-34.6) & median survival with native liver is 2.25 yrs (0.07-34.6).

53 patients (16.5%) died in pediatric care; 26 with their native livers & 27 after LT. 135 patients (50.3%) are still in pediatric care (Group A). 57 are surviving with their native liver (A1) while 78 children have been transplanted (A2). 7 patients are awaiting transplant in Group A1. 133 (49.6%) patients were transferred to adult services (Group B); 49 with native livers (B1) and 84 after LT (B2). 28 patients in group B1 had portal hypertension (PH): 20 treated with beta blockers, esophageal banding or shunts. 9 patients transferred to adult services with native liver (B1) subsequently required LT & 7 are listed for LT due to decompensated liver disease. 6 patients in group B2 required retransplant. After transfer to adult care, 3 patients in Group B1 died (one due to ruptured splenic aneurysm & 2 due to decompensated liver disease) while 5 patients in Group B2 died from post-transplant lymphoproliferative disorders (PTLD), Hepatopulmonary syndrome, ruptured psoas cyst and bleeding & chronic rejection. Out of 268 patients in this series, majority participated in normal school education while 32 (12%) required special needs support. 29 transferred went to university, 18 obtained non-vocational qualifications and 33 joined various training courses.

Conclusion: Improved medical and surgical management have improved the outcome and quality of life for patients with BA, allowing them to live into adult life, complete their education & function as useful members of the society.

Disclosure of interest: None
Mortality of young biliary atresia patients listed for liver transplantation: results from the Eurotransplant registry

Hubert van der Doef¹, Patrick van Rheenen², Marieke van Rosmalen³, Xavier Rogiers³, Henk-Jan Verkade¹

¹University Medical Center Groningen, Groningen Transplant Center, Dept. Pediatrics, Groningen, Netherlands
²University Medical Center Groningen, Pediatric Gastroenterology and Nutrition, Groningen, Netherlands
³Eurotransplant, Leiden, Netherlands

Objectives and study: Liver transplantation has become the standard treatment for children with biliary atresia (BA) who develop end stage liver disease despite Kasai portoenterostomy. Up to 50% of BA patients need a liver transplantation before the age of 5 years. The prognosis after transplantation has steadily improved, but the overall prognosis of BA patients is also determined by pre-transplant mortality. The primary objectives of this study were to assess the magnitude of waiting list mortality and to identify possible risk factors.

Methods: We retrospectively studied 642 patients with BA, listed before their fifth birthday for liver transplantation in the Eurotransplant region between 2001 and 2014, and with a waiting list duration of < 1 year. In a subcohort of 365 children (84% from the period 2007-2014) we evaluated the association of pre-transplant variables [dichotomous variables: age at listing (</> 0.5 years), gender, MELD score (</> 20) and renal replacement therapy; continuous variables: albumin, bilirubin, creatinin, and international normalized ratio (INR)] with waiting list mortality by Cox regression analysis.

Results: Waiting list mortality was 4.5%, 7.5% and 8.4%, at 3, 6 and 12 months after listing for liver transplantation, respectively. By far the majority of children who died were listed before the age of 1 year (51/54 = 94%). Age at listing below 0.5 years [n=169, P<0.001, hazard ratio (HR) 4.9, 95% confidence interval (CI) 2.1-11.5] and MELD score above 20 [n=131, P<0.001, HR 8.8, 95% CI 3.8-20.5] were independently associated with waiting list mortality. Other pre-transplant variables were not significantly associated. In the subcohort of 365 children, 48 patients (13.2%) had both risk factors (age<0.5 yr and MELD>20), which coincided with waiting list mortality of 23% already at 6 months. This subgroup accounted for 39% (11/28) of all pre-transplant mortality.

Conclusion: In the Eurotransplant region waiting list mortality of BA patients below 5 years is 8.4%. Waiting list mortality of young BA patients is an important contributor to overall prognosis of these patients. Identification of risk factors could be helpful in optimizing the allocation of donor organs.

Disclosure of interest: None Declared.
Long-term follow up of childhood autoimmune liver disease: the importance of resolving nomenclature

Jeremy Rajanayagam1, James Ferguson2, Ye Htun Oo3, David Adams4, Deirdre Kelly5, Gideon Hirschfield6
1Birmingham Children's Hospital, The Liver Unit, Birmingham, United Kingdom
2Queen Elizabeth Hospital, Birmingham, United Kingdom
3Uhb NHS Foundation Trust & University of Birmingham, Liver Unit, Birmingham, United Kingdom
4University of Birmingham, Birmingham, United Kingdom
5The Liver Unit, Birmingham, United Kingdom
6University of Birmingham, Birmingham, United States

Objectives and study: The nomenclature and long-term outcomes for patients with autoimmune liver diseases transitioned to adult practice lacks consensus. Objective: To study the nature and progression of childhood onset autoimmune liver disease in patients transitioned from pediatric to adult liver care.

Methods: Clinical review of transitioned patients with standard definitions of AIH and PSC was performed. AISC was defined as cholangiographic and/or histologic evidence of biliary involvement, clinical features of autoimmunity (increased IgG, and positive autoantibodies), and histological findings of AIH. The term AIH-PSC overlap was used for concomitant occurrence of clinical, biochemical, serological and/or histological features of PSC and AIH.

Results: 73 children with pediatric autoimmune liver disease were transitioned over a median follow-up of 13 years (IQR 8-16 years). At presentation, 52 were diagnosed with AIH (38F), 4 with PSC (1F), 17 with AISC (8F) (Table1). IBD occurred in 4% of AIH, 25% of PSC and 65% of AISC at diagnosis with liver disease. Median IAIHG score at diagnosis was 19 (IQR 17-21), 4 (IQR 3.5-5) and 12 (IQR 10-14) for AIH, PSC and AISC, respectively. Children with AIH & AISC were treated with corticosteroids and azathioprine, with ursodeoxycholic acid added in AISC. 10/52 (19%) patients initially presenting as AIH had phenotypic progression by last adult review: 6 (11.5%) developed an overlap syndrome whilst 4 (7.6%) had clinically dominant PSC. 8/17 (47%) AISC patients retained an adult overlap phenotype, but 9 (53%) had clinically dominant PSC. Those presenting as childhood PSC (n=4) remained phenotypically as PSC in adulthood. Thus by last review in adult care the clinical diagnoses were AIH n=42, PSC n=17 and Overlap AIH/PSC n=14. IBD occurred in 5% of AIH, 65% of PSC and 64% of Overlap.

Table: Characteristics of children with AIH, PSC and AISC at diagnosis

<table>
<thead>
<tr>
<th></th>
<th>AIH N=52</th>
<th>PSC N=4</th>
<th>AISC N=17</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13</td>
<td>13.8</td>
<td>12.7</td>
</tr>
<tr>
<td>IQR</td>
<td>10.7-14.3</td>
<td>11.3-15.3</td>
<td>9.9-13.4</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>470</td>
<td>122</td>
<td>103</td>
</tr>
<tr>
<td>IQR</td>
<td>230-751</td>
<td>95-139</td>
<td>60-378</td>
</tr>
<tr>
<td>GGT (IU/L)</td>
<td>130</td>
<td>332</td>
<td>259</td>
</tr>
<tr>
<td>IQR</td>
<td>77-198</td>
<td>189-385</td>
<td>168-370</td>
</tr>
<tr>
<td>IgG (g/L)</td>
<td>30</td>
<td>15</td>
<td>20</td>
</tr>
<tr>
<td>IQR</td>
<td>21-44</td>
<td>13-29</td>
<td>15-26</td>
</tr>
</tbody>
</table>

Conclusion: The nomenclature of autoimmune liver disease remains inadequate and in need of consensus. Of young adult PSC patients, half presented with an AISC phenotype, and of young adult AIH-PSC overlap, nearly half presented as AIH. Evaluating whether immunosuppressive therapy in childhood prevents ultimate disease progression remains an important goal for prospective studies.

Disclosure of interest: None Declared

Vol. 62, Supplement 1, May 2016
Adenosine kinase deficiency is a new cause of infantile cholestasis with a severe neurological phenotype

Christian Staufner¹, Henk J. Blom², Georg Friedrich Hoffmann³, Stefan Kölker⁴

¹University Hospital Heidelberg, Department of General Pediatrics, Heidelberg, Germany
²University Hospital Freiburg, Center for Pediatrics and Adolescent Medicine, Freiburg, Germany
³Universitätsklinikum Heidelberg, Department of General Pediatrics, Heidelberg, Germany
⁴Zentrum für Kinder- und Jugendmedizin, Universitätsklinikum Heidelberg, Department of General Pediatrics, Heidelberg, Germany

Objectives and study: Adenosine kinase deficiency (ADK deficiency) is a recently described inborn error at the cross-road of methionine and adenosine metabolism comprising mainly hepatic and neurological impairment and dysmorphism. Disruption of ADK is a known cause of neonatal hepatic steatosis in the murine model.

Methods: Clinical and biochemical data of all known patients (n=20) from eleven families with ADK deficiency were analysed, including liver biopsies.

Results: One of the main clinical symptoms is moderate to severe liver dysfunction with neonatal onset. Liver dysfunction typically presents as severe cholestasis within the first year of life and can lead to liver failure. It ameliorates with increasing age. Liver biopsies show a pattern characterized by pronounced microvesicular steatosis. Besides the hepatic phenotype, all patients have dysmorphism (especially frontal bossing), muscular hypotonia and global developmental retardation and most have recurrent hypoglycemia due to hyperinsulinism and develop epilepsy. Major biochemical findings are intermittent hypermethioninemia, increased S-adenosylmethionine and S-adenosylhomocysteine in plasma and increased adenosine in urine. Therapeutic trials with a methionine restricted diet indicate a beneficial effect on the hepatic phenotype and on biochemical parameters.

Conclusion: ADK deficiency is a new cause of severe but often transient infantile cholestasis and manifests with muscular hypotonia, developmental retardation and frontal bossing. It should be added to the list of metabolic differential diagnosis of infantile cholestasis. Methionine-restricted diet can be considered as therapeutic option.

Disclosure of interest: None declared.
Hepatic sinusoidal obstruction syndrome due to herbal ingestion in South African children - A 7 year review

Lesley Hendricks¹, Albertha Jacomina Terblanche¹, Anell Meyer¹

¹University of Pretoria, Department of Pediatric Gastroenterology and Hepatology, Pretoria, South Africa

Objectives and study: Herbal remedies containing pyrrolizidine alkaloids is known to cause hepatic sinusoidal obstruction syndrome in South African children. The aim of this study was to characterize 23 paediatric patients diagnosed with hepatic sinusoidal obstruction syndrome due to herbal ingestion and to document the complications and long term outcome of these patients.

Methods: A single centre cohort of patients over 7 years (2008 – 2015) was identified, and the patient data were collected by a retrospective examination of medical records. Long term outcome and progression of disease were documented.

Results: Twenty three children were identified with hepatic sinusoidal syndrome due to herbal ingestion. All patients were diagnosed based on clinical features of painful hepatomegaly, jaundice and ascites, duplex Doppler ultrasonography and liver histology. Nine patients had cholestatic jaundice at presentation. Three patients had reversal of their symptoms. Sixteen patients developed chronic liver disease but no one required liver transplantation.

Conclusion: Patients with hepatic sinusoidal obstruction syndrome usually present with severe ascites and life threatening upper gastro-intestinal hemorrhage. This study is limited by a short observation period and small numbers but would suggest that most patients will develop chronic liver disease.

Disclosure of interest: None Declared
Effect of sebelipase alfa on survival and liver function in infants with rapidly progressive lysosomal acid lipase deficiency: 2-year follow-up data

Simon A. Jones¹, Anais Brassier², Joanne Hughes³, Dominique Plantaz⁴, Roshni Vara⁵, Catherine Breen⁶, J. Jay Gargus⁷, Sachin Marulkar⁸, Mark Friedman⁸, Vassili Valayannopoulos⁹

¹Manchester Centre for Genomic Medicine, St Mary’s Hospital, Central Manchester Foundation Trust, University of Manchester, Manchester, United Kingdom
²Hôpital Necker-Enfants Malades and Imagine Institute, Paris, France
³The Children’s University Hospital, Dublin, Ireland
⁴Evelina Children’s Hospital, London, United Kingdom
⁵Hôpital Couple Enfant Chu Grenoble, Grenoble, France
⁶Manchester Centre for Genomic Medicine, Central Manchester Foundation Trust, University of Manchester, United Kingdom
⁷University of California, Irvine, United States
⁸Alexion Pharmaceuticals, Inc., Lexington, MA, United States
⁹Hôpital Necker-Enfants Malades and Imagine Institute, Paris, France

Objectives and study: Sebelipase alfa (SA) prolongs survival in infants with Lysosomal Acid Lipase Deficiency (LAL-D), compared with historical controls.

Methods: Two-year survival data are presented here from an ongoing phase 2/3 study of SA in infants with LAL-D, providing insight into extent of survival, and details of weight, functional development and hematological effects over extended duration.

Results: All 9 patients enrolled had significant liver dysfunction at baseline; 8 had early growth failure. Median (range) age at SA treatment initiation was 3.0 (1.1-5.8) months. As of 26-July-2015, 5 subjects remain on study and have survived beyond age 2 years (range, 2 years 5 months-4 years 7 months) with a mean time in the trial of 33.8 months, and all 5 continue to receive SA. The oldest subject has been receiving SA for 4 years 3 mos. Surviving patients demonstrate improvements in median percent change (range) for serum alanine aminotransferase -45.59% (-68.46% to 80.00%), aspartate aminotransferase -39.36% (-65.33% to -4.26%), hemoglobin 29.79% (4.21 to 61.11%), albumin 11.84% (3.81% to 73.68%), median weight percentile from 3.59% baseline to 35.09%, and improvement in gastrointestinal symptoms and reduction in hepatosplenomegaly. Median percent change (range) in platelets was 0.39% (-10.59 to 97.69%). At the most recent assessments (Week 74-218) of the Denver II developmental screening test, 4/5 ongoing subjects scored normal, with one subject suspect. One patient experienced treatment-related serious AEs (tachycardia, pallor, chills, and pyrexia) that resolved; no patient discontinued treatment because of tolerability or infusion reactions. Of 7 patients tested, 4 had detectable anti-drug antibody titers; 2 of whom developed neutralizing antibodies; all 4 continue treatment.

Conclusion: In conclusion, SA is associated with a substantial survival benefit, a favorable safety profile, and now improvement in disease activity parameters sustained over prolonged treatment in infants with LAL-D can be demonstrated. The majority of patients demonstrated normal development.

Disclosure of interest: S.A. Jones, Grants and travel support: Synageva BioPharma (now Alexion Pharmaceuticals, Inc.); A. Brassier, None Declared; J. Hughes, None Declared; D. Plantaz, None Declared; R. Vara, None Declared; C. Breen, None Declared; J.J. Gargus, Contracted research: Synageva BioPharma (now Alexion Pharmaceuticals, Inc.); Sachin Marulkar (Alexion Pharmaceuticals, Inc.); Mark Friedman (Alexion Pharmaceuticals, Inc.); V. Valayannopoulos, Consulting fees: Shire, Principal investigator fees, educational grants and speaker’s fees: Synageva BioPharma (now Alexion Pharmaceuticals, Inc.)
A new prediction tool of portal hypertension in cirrhotic children

Peter Witters¹, Dominic Hughes¹, Mark Davenport¹, Anil Dhawan¹, Tassos Grammatikopoulos¹
¹Paediatric Liver, GI & Nutrition Centre, King’s College Hospital, London, United Kingdom

Objectives and study: Variceal bleeding due to portal hypertension can be a devastating complication in cirrhotic children. Currently there is no consensus in the prophylactic management and selection criteria of children undergoing surveillance upper gastrointestinal endoscopy (OGD). We derive a new prediction model of clinically significant varices (CSV) and validate it in a separate cohort.

Methods: All cirrhotic children presenting in our centre with suspected portal hypertension or gastrointestinal (GI) bleeding, undergoing a first OGD between January 2005-December 2012, were included. A validation cohort from 2013-2015 was obtained. Clinical, biochemical and radiological data were collected. Equivalent adult spleen size (EASS) was calculated based on previously reported normal spleen size values. To derive a new prediction score Pearson’s bivariate correlation was performed with subsequent logistic regression.

Results: Data on 124(67M) treatment-naïve patients were collected of whom 50% had biliary atresia. Mean age was 8.81 ± 5.60 years. 35(28%) presented with GI bleeding and overall 79(64%) were in CSV+ve group. Mean values in CSV+ve vs. CSV-ve group are shown in the table. Previously published predictions rules had, at optimal cut-off, a sensitivity and specificity of 76% and 59% (clinical prediction rule (CPR)), 60% and 55%(AST-to-platelet ratio index), 80% and 59%(varices prediction rule), respectively. Logistic regression yielded a new prediction score King’s Variceal Prediction Score (K-VaPS)=[3 x albumin (g/L)]-[2 x EASS (cm)]. K-VaPS had a favourable AUROC of 0.772 (0.677-0.867) compared to CPR 0.732(0.632-0.832). At optimal cut-off of 76 it yielded a sensitivity and specificity of 72% and 73% with a positive and negative predictive value of 82% and 60%, respectively.

The validation cohort consisted of 24(15M) treatment-naïve patients who underwent a first OGD. Mean age was 8.7 ± 5.46 years. In the validation group AUROC was 0.818 (0.654-0.995) with sensitivity and specificity of 78% and 73%, respectively.

Table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CSV+ve</th>
<th>CSV-ve</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Haemoglobin (mg/dL)</td>
<td>10.58</td>
<td>11.62</td>
<td>0.008</td>
</tr>
<tr>
<td>Platelet count (x10⁹/ml)</td>
<td>111</td>
<td>167</td>
<td>0.001</td>
</tr>
<tr>
<td>White cell count (x10³/ml)</td>
<td>5.3</td>
<td>6.9</td>
<td>0.019</td>
</tr>
<tr>
<td>INR</td>
<td>1.22</td>
<td>1.13</td>
<td>0.004</td>
</tr>
<tr>
<td>Bilirubin (mg/dL)</td>
<td>53.33</td>
<td>28.22</td>
<td>0.014</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>37</td>
<td>41</td>
<td>0.0001</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>121</td>
<td>104</td>
<td>0.815</td>
</tr>
<tr>
<td>Spleen size (cm)</td>
<td>16.41</td>
<td>14.49</td>
<td>0.073</td>
</tr>
<tr>
<td>Spleen size (z-score)</td>
<td>9.1</td>
<td>6.35</td>
<td>0.009</td>
</tr>
<tr>
<td>EASS (cm)</td>
<td>23.21</td>
<td>19.3</td>
<td>0.003</td>
</tr>
</tbody>
</table>
Conclusion: K-VaPS is a prediction tool derived from the currently largest cohort of cirrhotic children. It is an easily applicable and useful tool in the selection of CSV+ve children in risk of GI bleeding who will benefit from a prophylactic endoscopy.

Disclosure of interest: None Declared
Acute variceal bleeding (AVB) in children causes significant morbidity: a 15 year retrospective study

Marta Carneiro de Moura¹, Shiyi Chen², Binita M Kamath¹, Vicky L Ng¹, Simon C Ling¹

¹Hospital for Sick Children, Division of Gastroenterology, Hepatology and Nutrition, Department of Pediatrics, University of Toronto, Toronto, Canada
²Hospital for Sick Children, Clinical Research Services, Toronto, Canada

Objectives and study: Acute variceal bleeding (AVB) is a severe complication of portal hypertension in children. Because death from the first bleed is unusual, the need for primary prophylaxis of AVB in children is unclear. There is limited knowledge regarding morbidity associated with pediatric AVB and we therefore aimed to describe this morbidity and to identify contributing factors.

Methods: Retrospective study of AVB episodes between May 2000- May 2015. AVB requiring volume support and/or red cell transfusion were included if endoscopy was undertaken to confirm presence of varices. Clinical, laboratory, ultrasound and endoscopic data were extracted from review of medical charts. Generalized estimating equation was used to examine the association between outcomes and variables of interest. Both univariate and multi-variable regressions were performed. P<0.01 was considered significant, accounting for multiple comparisons.

Results: We included 70 episodes of AVB in 57 children (median age 6 y (0.5-17y), 52% female). 47 (67%) episodes were the patient's first AVB. 33 (58%) patients had cirrhotic portal hypertension, 17 (30%) had portal vein thrombosis, 6 (11%) Caroli disease/Congenital Hepatic Fibrosis and 1 Nodular Regenerative Hyperplasia. Median admission values for platelets 79 (7-407), total bilirubin 14 (1-503) µmol/l, PELD score (n=53) -1.4 (-6.7 to +4.5) and MELD score (n=13) 9 (6-19). Management included octreotide in 62 (89%) and antibiotics within 24h in 38 (54%). Endoscopy was performed at a median 35 h after admission (range 3-288h) and showed grade I varices in 7 (10%), grade II in 7 (10%), grade III in 33 (47%) and grade IV in 21 (30%) (2 patients unknown grade). Endoscopic therapy was performed in 55 (79%) (band ligation 38 (54%), sclerotherapy 17 (24%)). Post-AVB morbidity occurred in 35 (50%) of all AVB and 31 (54%) of first AVB admissions, including infection 21(30%), development or worsening encephalopathy 5 (7%), new onset or worsening ascites 24 (34%), respiratory complications 17 (24%) and acute kidney injury 4 (6%). Failure to control bleeding occurred in 4 (6%), re-bleed in 8 (11%, at a median of 17 days) and ICU admission in 14 (20%). Two patients died following their first bleed (4% of first bleeds) and 1 underwent liver transplant within 6 weeks of the AVB. Median length of hospital stay was 7 days (2-220). Incidence of morbidity did not change between eras 2000-04, 2005-09 and 2010-15. By univariate analysis, factors associated with post-AVB morbidity were: PELD (p=0.005), total bilirubin (p=0.006) and use of antibiotics (p=0.007), but not cause of portal hypertension (cirrhotic vs non-cirrhotic). By multiple regression, PELD was associated with onset or worsening ascites (OR=1.2, 95% CI 1.08-1.36, p=0.001) and total bilirubin was associated with higher risk of respiratory complications (OR=1.02, 95% CI 1.01-1.04, p=0.007).

Conclusion: Significant morbidity including ICU admission is common after AVB in children, but death from the first bleed is rare. Overall morbidity rates are similar in cirrhotic and non-cirrhotic portal hypertensive children and have not changed over 15 years. PELD score and total bilirubin are associated with higher risk of ascites and respiratory complications, respectively. Studies are now needed to identify interventions to reduce post-AVB morbidity.

Disclosure of interest: None Declared.
“Atypical” bile acids are typical in the newborn infant

Evelyn Zöhrer, Katharina Meinel, Günter Fauler, Jörg Jahnel

1Medical University Graz, Graz, Austria
2Medical University Graz, Clinical Institute of Medical and Chemical Laboratory Diagnostics, Graz, Austria

Objectives and study: Serum levels of the typical human bile acids (BA), cholic acid and chenodeoxycholic acid, are low in the first days of life and then increase, reaching a peak at age 6-24 months. They then decline until age 11 years, when constant values are reached. Atypical BA have been neglected in pediatrics. We hypothesized that newborn infants include a high percentage of the atypical BA: alpha, beta, gamma and omega-muricholic acid - all C-6 hydroxylated BA - and tracked evolution of these BA values with aging in normal children.

Methods: In 54 healthy children and adolescents (0 – 19 years) concentrations of C-6 hydroxylated BA and BA composition in the serum were determined using high-performance liquid chromatography high-resolution mass spectrometry. Individuals were classified by ages into five groups: 0 – 5 months, 6 – 24 months, 3 – 5 years, 6 – 11 years, and >11 years.

Results: C-6 hydroxylated BA values were highest in young infants (0-5 months; 4.5 ± 1.9 µmol/L; 45% of total BA, 10.0 ± 3.3 µmol/L). These were significantly higher than those in all other age groups (p≤0.05). C-6 hydroxylated BA levels were markedly decreased in children from 6-24 months of age, at 0.6 ± 0.4 µmol/L; 11% of total BA, 6.8 ± 3.4 µmol/L, and remained continuously low thereafter (3-5 years, 6-11 years, and >11 years, all 0.3 ± 0.2 µmol/L; 5%, 7% and 10% of total BA, 5.9 ± 3.4 µmol/L, 4.2 ± 2.8 µmol/L and 3.0 ± 1.0 µmol/L, respectively). In patients younger than 11 years, C-6 hydroxylated BA were mainly unconjugated; however, after 11 years C-6 hydroxylated BA were primarily conjugated with glycine, as seen in healthy adults. Omega-muricholic acid and the FXR antagonist tauro-alpha-muricholic acid were the predominant C-6 hydroxylated BA species in neonates.

Conclusion: These are the first reference values for “atypical” BA in healthy children. Such BA are high in young infants and are replaced by adulthood-typical BA with increasing age. We speculate that these shifts reflect maturation of the enterobiome; ontogenic changes in BA metabolism independent of such maturation also may play a part. We propose that “atypical” BA are not atypical in early infancy. The physiological and pathological importance of these BA awaits elucidation.

Disclosure of interest: None Declared.
HEPATOLOGY: Basic Science

H-eP-002

Nuclear localization of hepatitis B virus cccDNA, X protein and epigenetic modifications and their relevance for chronification and carcinogenesis

Kai Hensel1, Franziska Cantner1, Claudia Hagedorn2, Stefan Wirth1, Hans Lipps2, Jan Postberg1

1Witten/Herdecke University - Helios Medical Center, Pediatrics - Center for Clinical and Translational Research, Wuppertal, Germany
2Witten/Herdecke University, Center for Biomedical Education and Research, Witten, Germany

Objectives and study: Hepatitis B virus (HBV) associated cirrhosis and hepatocellular carcinogenesis significantly account to cancer mortality worldwide. In a chronically infected hepatocyte the HBV DNA is located episomal as a covalently closed circular DNA (cccDNA). HBV integration events into the host genome are a potential pathomechanism for hepatocellular carcinogenesis that is probably influenced by HBV X protein (HBx) induced epigenetic modifications. However, spatiotemporal localization of the episomal cccDNA, HBx and their potential interactions with the host genome remain to be understood. Aim of this study was to analyze whether episomal cccDNA are associated with specific chromosomal loci and whether cccDNA location has relevance for subsequent host genomic integration events.

Methods: We utilized circularized chromosome conformation capture (4C) technology followed by high throughput sequencing analysis to identify spatiotemporal interactions of cccDNA and host genomes in HBV infected HepaRG cells. Furthermore, we transfected full length HBx and several truncated HBx sequences, performed subsequent ChIP for selected posttranslational histone modifications (PTM) and analyzed transcriptomics.

Results: 4c analyses revealed specific nuclear localization patterns of HBV cccDNA and HBx that were associated with activating chromatin marks and heavily transcribed loci. Strikingly, repressive chromatin-associated PTMs showed a profoundly different localization pattern.

Conclusion: Our data give rise to a novel concept indicating that other than previously suggested HBV genomic sequences seem to be associated with functionally active chromatin regions rather than with specific genes and proteins. This might contribute to both chronification and HBV-related hepatocellular carcinogenesis and may provide a new concept regarding virus-host interaction.

Disclosure of interest: None declared.
**HEPATOLOGY: Basic Science**

H-eP-003

Vertical transmission of hepatitis C is not influenced by IL28B genotype in children

Afrodite Psaros Einberg¹, Anton Lutckii², Ann-Sofi Du Berg³, Jessica Nyström², Erwin Brenndörfer², Lars Frelin², Matti Sällberg², Björn Fischler⁴

¹Karolinska University Hospital, Clin Tec, Dep. of Pediatrics, Stockholm, Sweden  
²Karolinska Institutet, Dep. of Laboratory Medicine, Stockholm, Sweden  
³Örebro University, Department of Infectious Diseases, Örebro, Sweden  
⁴Dept. of Pediatrics, Karolinska University Hospital, Clin Tec, Stockholm, Sweden

**Objectives and study:** Single genetic nucleotide polymorphism (rs12979860) near the gene for IL28B on chromosome 19, which encodes the type III interferon IFN-λ3, has been shown in numerous studies to be of importance for treatment outcome and frequency of spontaneous clearance in patients with hepatitis C virus (HCV) infection. Most studies have been carried out in adults. One pediatric study has shown an association between spontaneous clearance of HCV genotype 1 and IL28B genotype C/C in vertically infected children, but could not show any association between the risk of vertical transmission and IL28B genotype in the child. The aim of this study was to investigate if IL28B polymorphism in children and/or their mothers play a role in vertical transmission of HCV.

**Methods:** Plasma samples from three different centers in Sweden and Russia, including 59 infected women, 69 uninfected children born to infected mothers, and 47 children with known vertically transmitted HCV infection, were analyzed for IL28B polymorphism and classified by the IL28B genotype (C/C, C/T and T/T) as well as by viral genotype. Groups were compared to determine if there was an association between IL28B genotype, viral genotype and the risk of vertical HCV transmission.

**Results:** The proportion of children with genotype C/C was the same in the vertically infected and the exposed but uninfected children (36 %, 17/47 and 38 %, 26/69 respectively). When looking at children exposed to HCV genotype 1 exclusively, the proportion of children with C/C genotype was 30 % (8/27) in the vertically infected group and 46 % (13/28) in the exposed but uninfected group (p = 0.3, Fischer exact test). There was no association between the mothers IL28b genotype and the risk of vertical transmission.

**Conclusion:** There is no significant association between IL28B genotype in children or mothers and the risk of vertical HCV transmission, regardless of viral genotype.

**Disclosure of interest:** None declared.
Serum Zinc levels discriminate “indeterminate” acute liver failure from “Wilson disease” acute liver failure

Palittiya Sintusek¹, Anil Dhawan¹
¹King’s College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom

Objectives and study: Wilson disease (WD) is a rare autosomal recessive disorder of copper metabolism. Combined clinical and laboratory findings are needed for early diagnosis. There is the hypothesis suggested that low serum Zinc (Zn) is related to phenotypic severity of WD. Indeed, alkaline phosphatase (ALP), a Zn-containing metallo-enzymes that reflects the real Zn deficiency is relatively low in WD patients might support this presumption. However, few studies underscore the role of these biomarkers in WD pathogenesis and severity. Our study was aimed to observe the values of serum Zn and other basic biomarkers in acute liver failure (ALF) of indeterminate cause and WD.

Methods: Retrospective data was reviewed from children with WD (n=30) and indeterminate ALF (n=9) at King’s college hospital in 2005 - 2015. WD patients were diagnosed by King’s protocol and 23 patients were confirmed by genetic analysis. WD is classified into WD-ALF and WD non-ALF. The values of serum Zn, copper, ceruloplasmin(CP) and liver function tests were collected.

Results: Our study demonstrates, a significantly lower level of serum Zn and corrected Zn in WD-ALF compare to WD non-ALF and ALF of indeterminate cause.

Table:

<table>
<thead>
<tr>
<th>Parameters</th>
<th>WD non-ALF (n = 20)</th>
<th>WD-ALF (n = 10)</th>
<th>Indeterminate ALF (n = 9)</th>
<th>Normal value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (year)</td>
<td>10.9 (3.8-15.2)</td>
<td>13.1 (7.8-16.0)</td>
<td>7.6 (1.0-12.2)*</td>
<td>-</td>
</tr>
<tr>
<td>Female : male (%female)</td>
<td>11 : 9 (55)</td>
<td>3 : 7 (30)</td>
<td>1 : 8 (11%)</td>
<td>-</td>
</tr>
<tr>
<td>Zn (μmol/L)</td>
<td>12.6 (6.1-22.2)*</td>
<td>5.95 (4.1-8.3)</td>
<td>9.8 (7.0-12.1)*</td>
<td>Depend on albumin</td>
</tr>
<tr>
<td>Corrected Zn (μmol/L)</td>
<td>12.5 (6.0-20.2)*</td>
<td>7.9 (5.6-11.6)</td>
<td>11.4 (7.6-17.8)*</td>
<td>&gt;11</td>
</tr>
<tr>
<td>Copper (μmol/L)</td>
<td>2.28 (0.9-14.6)*</td>
<td>12.9 (4.5-26.8)</td>
<td>18.1 (11.4-36.7)*</td>
<td>12-25</td>
</tr>
<tr>
<td>Free copper (μmol/L)</td>
<td>2.22 (0.0-6.62)*</td>
<td>6.54 (3.08-21.14)</td>
<td>6.41 (3.38-23.48)</td>
<td>1.6-2.4</td>
</tr>
<tr>
<td>TB (μmol/L)</td>
<td>10 (4-73)*</td>
<td>81 (33-625)</td>
<td>282 (48-448)*</td>
<td>3-20</td>
</tr>
<tr>
<td>AST (IU/L)</td>
<td>110 (20-385)</td>
<td>136 (83-403)</td>
<td>2778 (2039-6637)*</td>
<td>7-36</td>
</tr>
<tr>
<td>ALT (IU/L)</td>
<td>133 (14-511)</td>
<td>57.5 (16-185)</td>
<td>2744 (1816-2857)*</td>
<td>5-55</td>
</tr>
<tr>
<td>Albumin (g/L)</td>
<td>44 (22-50)*</td>
<td>22 (19-35)</td>
<td>36 (25-41)*</td>
<td>35-50</td>
</tr>
<tr>
<td>INR (ratio)</td>
<td>1.06 (0.91-1.68)*</td>
<td>2.26 (1.66-4.04)</td>
<td>2.01 (1.69-4.24)</td>
<td>0.9-1.2</td>
</tr>
<tr>
<td>ALP (IU/L)</td>
<td>286 (65-915)</td>
<td>115 (19-1120)</td>
<td>345 (159-758)</td>
<td>Depend on age</td>
</tr>
</tbody>
</table>

Depend on albumin

Depend on age
<table>
<thead>
<tr>
<th>CP (g/L)</th>
<th>Value = Median (range), *P&lt;0.05 vs WD-ALF</th>
</tr>
</thead>
<tbody>
<tr>
<td>0.05 (0.01-0.19)</td>
<td>0.12 (0.03-0.7)</td>
</tr>
</tbody>
</table>

Conclusion: The present study showed that the dramatic aberrance of serum Zn in WD-ALF can discriminate WD-ALF from indeterminate ALF.

Disclosure of interest: "None Declared".
HEPATOLOGY: Transplantation

H-eP-005

Effect of demographic characteristics and underlying disease on cellular markers of immunity at time of liver transplantation - an analysis within the ChilSFree study

Tamara Drenk1, Imeke Goldschmidt2, Christine Falk3, Dominique Debray4, Lorenzo d’Antiga5, Valerie McLin6, Loreto Hierro7, Patrick McKiernan8, Joanna Pawlowska9, Ulrich Baumann2, Rafael Mikolajczyk1, André Karch1

1Helmholtz Centre for Infection Research, Research Group Epidemiological and Statistical Methods (Esme), Brunswick, Germany
2Hannover Medical School, Division of Pediatric Gastroenterology and Hepatology, Children’s Hospital, Hanover, Germany
3Hannover Medical School, Institute of Transplant Immunology, Integrated Research and Treatment Center of Transplantation IFB-Tx, Hanover, Germany
4Hôpital Necker-Enfants Malades, Paris, France
5Hospital Papa Giovanni XXIII, Bergamo, Italy
6Serv. Spécialités Pédiatriques, Geneva, Switzerland
7Hospital Infantil Universitario La Paz, Madrid, Spain
8Birmingham Children’s Hospital, Birmingham, United Kingdom
9The Children’s Memorial Health Institute, Warszawa, Poland

Objectives and study: Despite a continuous improvement of survival rates, liver transplantation (LTx) during childhood remains a challenge due to high graft rejection rates and the scarcity of donor organs. While there is no good prognostic model available for graft rejection yet, markers of cellular immunity have been proposed as potential biomarkers for graft rejection after LTx. However, it is still poorly understood how these cellular immune markers are related to baseline characteristics of LTx patients like age, sex, and underlying disease. It was, thus, the aim of this analysis to investigate if age, sex, and cause of LTx are associated with immune cell subpopulation counts at the time of LTx in a large multicenter cohort study (ChilSFree).

Methods: ChilSFree is a European multicenter cohort study investigating the longitudinal patterns of immune response after pediatric LTx. It combines demographic, laboratory and therapy information with immune cell numbers per µl whole blood as assessed by TrucountTM FACS analysis. For the current project, 134 pediatric LTx patients from seven European centers were included. Immune cell counts at time of LTx were logarithmized due to skewed distributions and then compared between predefined groups (sex, underlying diagnosis) using t-tests, ANOVAs, and Tukey Post-hoc tests. The association of immune cell counts at time of LTx and patients’ age was assessed using a fractional polynomial approach.

Results: The majority of studied cellular markers showed strong evidence for a linear (CD3+T, CD4+T cells all p<0.05) or loglinear (monocytes, CD5616 NK cells all p<0.05) decrease with increasing age, while there were no clear age patterns for granulocytes, CD8+CD56 T, CD4+CD56+, and CD4+CD8+ T cells. Sex did not affect any of the immune cell subpopulations. Patients with underlying liver cirrhosis at point of LTx had lower numbers of most lymphocyte subpopulation (CD3+T, CD4+T, CD8+T all p<0.05), while monocytes and granulocytes were not affected. Immuno-suppressive therapy before LTx was associated with higher numbers of granulocytes (p=0.001); numbers of lymphocyte subpopulations of those immuno-suppressed individuals did not differ from those with no prior immuno-suppressive therapy. There were no systematic differences in immune cell numbers between patients with elevated bilirubin at time of LTx and those without.

Conclusion: Patient’s age and underlying cause of LTx need to be taken into account when studying the development of cellular immunity after LTx. The ChilSFree study provides for the first time age-specific and diagnosis-specific reference ranges for immune cell counts for pediatric patients undergoing LTx which can be used as a reference in future studies.

Disclosure of interest: None Declared.
HEPATOLOGY: Transplantation

H-eP-006

Risk factors and impact of viremia on liver transplant outcomes in children undergoing preemptive therapy for Cytomegalovirus

Emanuele Nicastro¹, Paola Stroppa¹, Valeria Casotti¹, Sara Giovannozzi¹, Anna Paola Callegaro², Claudio Farina², Alessandra Tebaldi³, Michele Colledan⁴, Lorenzo D’Antiga¹

¹Hospital Papa Giovanni XXIII, Paediatric Hepatology, Gastroenterology and Transplantation, Bergamo, Italy
²Hospital Papa Giovanni XXIII Bergamo, Microbiology and Virology, Bergamo, Italy
³Hospital Papa Giovanni XXIII Bergamo, Infectious Diseases, Bergamo, Italy
⁴Hospital Papa Giovanni XXIII Bergamo, Surgery, Bergamo, Italy

Objectives and study: Most paediatric liver transplant (LT) centres use prophylaxis over preemptive therapy (PET) for Cytomegalovirus (CMV) without evidence of benefit. PET consists in treating CMV infection to avoid disease and possible indirect virus-induced graft injury. The rationale for prophylaxis is that viremia could worsen LT outcomes. We aimed at investigating possible impact of CMV viremia and risk factors for its development in a cohort of LT patients managed with PET.

Methods: The clinical records of LT children (2008-2014) were reviewed. Retransplants, combined transplants, liver tumors, immune deficiencies and follow up < 200 days were exclusion criteria. Children with CMV-DNA above 100000 copies/ml were treated with iv ganciclovir 10 mg/kg/day for at least two weeks and until two negative results.

Results: One hundred children (50 F, mean age 2.3 ± 2.9 years) were included in the analysis. Sixty-one of them developed CMV viremia and 19 required treatment. Only 3 patients developed CMV disease, and none of them died from CMV. The donor(D)+/recipient(R)- serostatus resulted the only independent risk factor for the development of viremia at multivariate analysis [OR: 17.23 (95%CI: 1.88-157.87) vs Dany/R+; \( P = 0.012 \)]. None of the putative indirect effects of CMV were associated to CMV infection (acute rejection, EBV infection, sepsis, PTLD). Namely, viremia did not have impact on graft dysfunction, loss and death at 3 and 5 years after LT. Children with and without CMV viremia had similar proportion of acute rejection at 200 days post-LT (\( P = 0.655 \)), as well as of graft dysfunction (\( P = 0.362 \)), biliary complications (\( P = 0.449 \)) and vascular complications (\( P = 0.421 \)) at 3 years post-LT as demonstrated by Log-rank curve comparison.

Conclusion: D+/R- serostatus is associated with higher risk of CMV viremia in paediatric LT recipients. PET is safe and effective in controlling CMV disease and related morbidity and mortality. CMV viremia per se does not worsen the LT outcomes in children, therefore PET should be preferred to prophylaxis in this setting.

Disclosure of interest: None Declared
Psychosocial outcome after paediatric liver transplantation

Katrin Mayer¹, Ulrich Baumann², Eva Pfister³

¹Medizinische Hochschule Hannover, Paediatric Gastroenterology and Hepatology, Hannover, Germany
²Medizinische Hochschule Hannover, Paediatric Liver Unit, Hannover, Germany
³Paediatric Gastroenterology and Hepatology, Hannover, Germany

Objectives and study: We aimed to investigate psychosocial outcome and quality of life in our single centre cohort of patients long term after liver transplantation (LT). The focus of our project was on day to day life-style management, career development and family planning.

Methods: A questionnaire was designed by a multi-disciplinary group and given priority over standardised tools such as SF36 in order to capture day to day routines and transition to adult care. The patients were asked to respond without external support. Included in the survey were all consecutive patients after LT above the age of 13 with a post-transplant follow up of more than 4 years. 98 patients had died and 58 patients were lost to follow up. Exclusion criteria was mental disability (n=1). Clinical data was compared to the electronic patient records. Data analysis was executed using IBM SPSS Statistics 23 for Windows.

Results: All together 365 patients met inclusion criteria of whom 98 patients had died (27%) and 58 patients were lost to follow up. 82 patients (female: 42.7%, male: 57.3%) aged 13-41 years responded to the survey (40.2%). Seven patients with acute liver failure and 92% (n=75) with chronic liver damage (biliary atresia (n=33, 40%), primary sclerosing cholangitis (n=5), cystic fibrosis (n=5) and other (n=32)) underwent LT at the median age of six years. 71 patients received a transplant from a deceased donor. With an adherence rate of 33.3% (n=26) all but two patients were immunosuppressed (calcineurin inhibitor agents (n=70, 85%), mycophenolic acid (n=36, 44%), oral steroids (n=17, 21%). Graft rejections appeared in 53.7% (n=44), 11 patients were re-transplanted (13.4%). Linear growth impairment was observed in 16% (n=13), underweight in 22% (n=18) and overweight in 13% (n=11).

Most patients had a detailed knowledge about their medical history. Mainly without problems 53 patients had transitioned to adult care. 83% (n=68) valued their current health status as “(very) good”, 14 patients reported physical limitations. Alcohol abstinence was reported in 73% (n=60). 67 patients (82%) experienced their current daily life without health-related fears and 78% felt sufficiently informed about medical issues (n=64). Five patients had at least one child of their own (6.1%). 22 patients (<21 years) were still in education, the rest (n=60, 73%) graduated from school mostly working full-time (n=21).

Conclusion: Our data suggests excellent clinical and psychosocial outcome after LT. Unlike other studies our findings display psychological stability, despite some limitations and challenges patients experience a good emotional quality of life after paediatric LT. A high non-adherence rate remains the major problem amongst young people.

Disclosure of interest: None Declared.
HHV-6 virus in children undergoing clinically-indicated liver biopsy following liver transplantation.

Ino Kanavaki1, Manuel Schibler2, Anne-Laure Rougemont3, Barbara Wildhaber4, Laetitia-Marie Petit1, Valerie McLin1

1Geneva University Hospitals, Gastroenterology Unit, Department of Children and Adolescents, Geneva, Switzerland
2Geneva University Hospitals, Laboratory of Virology, Geneva, Switzerland
3Geneva University Hospitals, Division of Clinical Pathology, Geneva, Switzerland
4Geneva University Hospitals, Division of Pediatric Surgery, Geneva, Switzerland

Objectives and study: Human herpesvirus 6 (HHV-6) is a human ubiquitous DNA virus with emerging clinical significance. Almost all infants are infected in their first year and 90% of adults are seropositive. After primary infection, HHV-6 remains latent in the nuclei of the hepatocytes but also in the nuclei of epithelial cells in the intrahepatic bile ducts. Immunosuppression can lead to asymptomatic or symptomatic viral reactivation, something which can be observed in 40-50% of patients following solid organ or bone marrow transplantation. In adult liver transplant recipients there is evidence that HHV-6 reactivation may be associated with late graft failure or rejection. HHV-6 co-infection with CMV or HCV has also been shown to result in more invasive CMV, HCV or opportunistic infections due to the immunomodulatory properties of HHV6.

The aim of our retrospective study was to examine whether the presence of HHV-6 DNA in clinically-indicated liver biopsies (LB) of pediatric liver transplant (pLT) recipients was associated with histological findings and pre-transplant serology.

Methods: We included all patients having undergone clinically indicated LB for abnormal liver tests between January 2011 and November 2015. Patient charts were reviewed for clinical data, histological findings, and semi-quantitative HHV-6-specific real-time PCR results in blood and tissue samples.

Results: 24 patients underwent 39 liver biopsies. HHV-6 PCR was positive in 58% (23/39) in the liver. Peripheral blood PCRs were obtained in 32 cases and only 2/32 were positive. Patient age at biopsy ranged from 1 to 18 years (median of 5 years). Pre-transplant serology was obtained in 18 patients, and 60% (11/18) of patients tested positive. No correlation was observed between pre-transplant serology and PCR results in the liver tissue (p=0.7). There was no correlation between the presence of HHV-6 in the liver and acute cellular rejection (p=0.7), fibrosis (p=0.7) or hepatitis (p=0.6). There were no cases of co-infection.

Conclusion: In a subset of patients with clinically indicated LB, the presence of HHV6 DNA is frequent, but there is no clear association between the presence of HHV6 in liver tissue and histology. Positive pre-transplant serology is not protective for post-transplant seroconversion or reactivation. To our knowledge studies concerning the role of HHV-6 in pediatric liver transplantation are rare. Further studies are required to understand the role of HHV6 in pLT.

Disclosure of interest: None Declared
Effect of treatment with ganciclovir and of pretransplant serologic status on EBV viremia after pediatric liver transplantation

Anniken Østensen¹, Truls Sanengen¹, Ellen Kristine Holter², Pål-Dag Line³, Runar Almaas¹

¹Oslo University Hospital, Department of Paediatrics, Oslo, Norway  
²Oslo University Hospital, Department of Microbiology, Oslo, Norway  
³Oslo University Hospital, Section for Transplantation Surgery, Department of Transplantation Medicine, Oslo, Norway

Objectives and study: EBV viremia is common after paediatric liver transplantation, and appears as a primary infection or as a reactivation. Data concerning efficacy of ganciclovir are scarce. The aim of this study was to retrospectively evaluate risk factors for EBV viremia and assess the effect of ganciclovir on duration of EBV viremia.

Methods: We retrospectively reviewed all paediatric patients who underwent orthotopic liver transplantation at Oslo University Hospital, Norway, from October 2002 until December 2014, and had a minimum follow up after transplantation of >1 year (n=61). Data are given as median (25-75 percentile) or as relative risk (95% confidence interval). Informed consent was obtained from parents and/or children.

Results: Thirty-eight patients out of 61 (62%) developed EBV viremia after transplantation at a median of 92 (37-194) days after transplantation. 87% of these had a primary EBV infection and 13% had EBV reactivation. Patients without EBV seroconversion prior to transplantation had a significantly higher risk for developing viremia after transplantation than patients with EBV seroconversion (relative risk 2.7(1.3-5.9), p=0.0005). Twenty-two out of 38 patients with viremia were treated with ganciclovir for a median of 22 (21-38) days. At 8 weeks after start of viremia 4 out of 15 treated with ganciclovir and 3 out of 14 not treated with ganciclovir (p=1.00) had reduced number of EBV copies measured by PCR in blood. After 6 months 6 out of 20 treated with ganciclovir and 3 out of 11 untreated had reduced virus load (p=1.00). At 12 months 6 out of 19 treated and 6 out of 14 untreated had reduced EBV load compared to start of viremia (p=0.72). Twelve months after start of viremia 14 out of 19 treated with ganciclovir and 9 out of 14 untreated still had detectable EBV virus in blood (relative risk 1.1(0.7-1.8), p=0.71). Correction for age at viremia, tacrolimus concentration in blood at start of viremia, or at 4 weeks after start of viremia, did not reveal any differences between patients treated with ganciclovir and not, with respect to reduction in virus load at 8 weeks.

Conclusion: Children without seroconversion prior to transplantation were at higher risk of EBV viremia after transplantation than seroconverted patients. Ganciclovir did not change the proportion of patients with reduction in EBV load at 8 weeks, 6 months and 12 months after transplantation.

Disclosure of interest: None Declared
**Histopathological evaluation of the native liver in propionic acidaemia**

Napat Angkathunyakul¹, Roshni Vara², Nedim Hadzic³, Maesha Deheragoda¹

¹King's College Hospital, Institute of Liver Studies, London, United Kingdom
²Evelina Children’s Hospital, London, United Kingdom
³King's College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom

**Objectives and study:** Propionic acidaemia (PA) is a rare autosomal recessive metabolic disorder, caused by deficiency of the mitochondrial enzyme propionyl-CoA carboxylase. Orthotopic liver transplantation (OLT) may be indicated in cases with frequent metabolic decompensation. Auxiliary liver transplantation (ALT) has been reported to provide similar clinical and biochemical outcomes in PA. There is currently no consensus on the optimum time at which OLT/ALT should be undertaken. The histopathological features of PA in the explanted liver are not widely reported in the literature, limiting understanding of native liver appearances in cases where ALT is undertaken. The aim of our study was to evaluate the histopathological features of the native liver in PA and to determine whether fibrosis stage is related to length of time prior to OLT/ALT.

**Methods:** Native liver biopsies (N=2) and explants (N=13) from patients with propionic acidaemia were evaluated by two independent liver histopathologists for the presence of fibrosis, steatosis, siderosis and metallothionein deposits. Fibrosis was staged from F0 to F4 using the Metavir system.

**Results:** 15 specimens (native liver needle biopsy = 2, explants arising from ALT = 4 and explants arising from OLT = 9) from 14 patients (Male = 9; median age = 35, range 9-84, months) were available for assessment. All complete hepatectomy specimens had an increased liver mass, exceeding the normal range expected for body mass. The most common histopathologic feature was hepatocyte clarification (N=12; 80%) either in the entire lobule or focally with centrilobular predilection and periportal sparing. Nine (60%) and eight (53.33%) specimens revealed the presence of excess stainable iron and copper-associated protein (CAP) in the periportal hepatocytes, respectively. Mild, predominantly macrovesicular steatosis was seen in six cases (40%) with a non-zonal distribution. There was no significant hepatitis or confluent/spotty necrosis. Four cases (26.67%) revealed F2 stage fibrosis. One case demonstrated F3 stage fibrosis. No correlation was found between the stage of fibrosis and the age of the patient pre-transplant (Spearman’s correlation coefficient, r = -0.256; p = 0.357).

**Conclusion:** The characteristic histological features of the native liver in PA are hepatocyte clarification and the presence of haemosiderin and CAP in the periportal hepatocytes in the absence of significant inflammation or hepatocellular necrosis. Significant fibrosis was present in a minority of patients and did not appear to be associated with age at transplant. These histological findings provide support for ALT as a treatment modality, given the minor morphological features in the native liver, and do not suggest an optimal age at which transplantation should be undertaken.

**Disclosure of interest:** None Declared
**Allograft inflammation and fibrosis among maintenance pediatric liver transplant recipients – genetic predisposition and antibodies, connecting the missing links**

Sharat Varma¹, Dominique Latinne², Mina Komuta³, Ambroise Jerome⁴, Francoise Smets⁵, Raymond Reding⁶, Xavier Stephenne⁷, Etienne Sokal⁸

¹Université Catholique de Louvain, Pediatric Hepatology and Cell Therapy, Bruxelles, Belgium
²Cliniques Universitaires Saint-Luc, Brussels, Belgium
³Clinique Universitaire St Luc, Pathology, Brussels, Belgium
⁴University Catholique de Louvain, Brussels, Belgium
⁵Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Brussels, Belgium
⁶Clinique Universitaire St Luc, Pediatric Liver Transplantation and Surgery, Brussels, Belgium
⁷Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
⁸Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

**Objectives and study:** To determine impact of HLA allo-antibodies, non-HLA auto-antibodies and HLA-DRB1 genotype amongst stable, long term pediatric liver transplantation (LT) recipients; on allograft health.

**Patients and Methods:**

**Patients:** Stable LT recipients transplanted in 2006-2012 and with >2 protocol biopsies were included. Autoimmune hepatitis, hepatitis B or C infection as indication of LT; ABOi graft, biliary or vascular complications post LT, re-transplantation were exclusion criteria.

**Methods** Data were collected at 1-month pre-LT and simultaneous to last protocol biopsy. HLA, ANA, SMA, LKM antibodies, HLA-DRB1 genotype of recipients and histological aspects of biopsy, were collected. Histological parameters including rejection, bile duct proliferation, lobular inflammation, and portal tract infiltration were assessed while fibrosis was evaluated using Metavir and liver allograft fibrosis scoring (LAFSc).

**Results:** 15 of 89 included children had class-II DSA post LT. Class-II DSA was associated with allograft fibrosis using Metavir and LAFSc–score (p <0.01), specifically portal fibrosis (p<0.01). Class-II DSA, non-HLA auto-antibodies were associated with portal inflammation (p <0.01) and showed additive effects. Recipient HLA-DRB1*03 or 04 genotype was associated with portal fibrosis (p <0.05) and showed additive effect with class-II DSA.

**Conclusion:** Class-II DSA, non-HLA auto-antibodies, HLA-DRB1 genotype of recipient are important factors for long term allograft health and have additive effect.

**Disclosure of interest:** For all authors: “None declared”.

Cardiovascular risk factors after pediatric liver transplantation

Piotr Czubkowski¹, Jolanta Antoniewicz², Aldona Wierzbicka³, Piotr Socha⁴, Joanna Pawłowska⁴

¹The Children's Memorial Health Institute, Warsaw, Poland
²The Children's Memorial Health Institute, Department of Nephrology, Kidney Transplantation and Arterial Hypertension, 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 Pediatrics, Warsaw, Poland

Objectives and study: Adult liver transplant recipients present with increased risk of cardiovascular (CV) events, but there is no evidence in children. Diabetes, arterial hypertension, renal dysfunction and lipid disturbances may result from long-term immunosuppression. The aim of this study was to assess the risk of CV complications after pediatric liver transplantation (LTx).

Methods: We prospectively analyzed 69 patients at the median age of 14.3 years (range 10.2-17.8) and at least 5 years (range 5-16) after LTx. We assessed blood pressure, carotid intima-media thickness (cIMT), relative wall thickness (RWT), left ventricular mass index (LVMI), aortal pulse wave velocity (PWV), lipids including apolipoproteins (apoA1, apoB, ApoE), lipoprotein(a)-Lp(a) and markers of oxidative injury: glutathione (GSH), glutathione peroxidase (GPx), atherosclerosis markers: asymmetric dimethylarginine (ADMA) and oxidized-LDL (oxyLDL). All values were normalized for age and expressed as SDS values. Laboratory results were compared with age-matched healthy control group, n=60, median age 13.7 (10.4-18.0).

Results: All patients presented with normal BP (< 95th percentile). BMI Z-score 90th percentile was exceeded in 11 patients (16%). cIMT was normal in all patients according to age percentiles, mean 0.38±0.02; mean RWT was 0.32±0.02, abnormal in 8 (11.5%) and LVMI-S was 28.0±5.8 abnormal in 5 (7%) patients. Mean PWV was 4.75 ± 0.75 and 4 (5.7%) patients showed PWV values >95 percentile. Cholesterol 153.2±37 mg/dl, triglycerides 81.7±30 mg/dl, HDL 50.4±12 mg/dl and LDL 85±32 mg/dl were normal in the study group. Apolipoproteins differed between the study group and control: ApoE 10.3±3.1 vs 16.9±2.5 g/l (p<0.01), ApoB 0.66 g/l ±0.21 vs 0.78 ± 0.20 (p<0.01), ApoAI 1.41±0.22 vs 1.29±0.30 (p<0.01) and Lp(a) 16.0 ±6.3 vs 12.0 ±11.6 mg/ dl (p=0.02). Oxidative stress markers showed decreased GSH 719±28 vs 787±26 mol/ml (p<0.01), increased: ADMA 0.58±0.11 vs 0.31±0.15 mol/l (p<0.01) and oxyLDL 229±64 vs. 116±28 mU/ml (p<0.01).

Conclusion: Patients after pediatric LTx present with higher risk of cardiovascular issues, however the risk of atherosclerosis is not significantly increased. Cardiac follow-up is mandatory, especially in adolescents before transition to adult care.

Disclosure of interest: Authors declare no conflict of interests
Liver Disease In Pediatric Patients With Ataxia Telangiectasia: A Novel Report

Alexander Krauthammer¹, Michalle Soudack¹, Avishay Lahad¹, Ifat Sarouk¹, Raz Somech², Gali Heimer¹, Bruria Ben-Zeev², Andreea Nissenkorn²

¹Edmond & Lily Safra Children's Hospital, Tel-Hashomer, Ramat Gan, Israel
²Edmond & Lily Safra Children's Hospital, Tel-Hashomer, and Sackler Faculty of Medicine, Tel Aviv University, Tel-Aviv, Ramat Gan, Israel

Objectives and study: Ataxia telangiectasia (A-T) is a rare genetic multiorgan disease. Although gastrointestinal involvement is known, hepatic involvement in A-T has not been investigated. We aimed to study the hepatic involvement in a large cohort of A-T patients.

Methods: A retrospective review of patients, followed from January 1986 to January 2015 at a National A-T Center. Clinical data including demographic, genetic, laboratory, nutritional, radiographic and histological data, were retrieved.

Results: Fifty three patients, 27 (49%) males, aged 14.6±5.2 years (range 5.9-26.1 years), were included. Twenty three patients (43.4%), age 9.9±5.1 years, had consistently abnormal liver enzymes. The mean enzyme levels were: ALT 76.8±73.8 IU/l, AST 70±50 IU/l, AP 331±134 IU/l, and GGT 114.7±8 IU/l. Evaluation of other etiology of liver disease was negative. Ultrasonography revealed fatty liver in 9 of them (39%). Liver biopsy was performed in 2 patients, revealing mild – moderate steatosis in both, and fibrosis in one patient. Progression to advanced liver disease occurred in 2/23 (9%) patients within 2-5 years. Dyslipidemia was significantly associated with abnormal liver enzymes: 3/30 (10%) of patients without vs. 10/23 (45.5%) of patients with abnormal liver enzymes, respectively (p<0.05, Fisher exact test). No correlation was found between hepatic involvement and HbA1C, gender, presence of malignancy or type of mutation.

Conclusion: Abnormal liver enzymes and fatty liver are common in A-T patients, and may progress to advanced liver disease at a young age. These findings are novel, and implicate that A-T patients with abnormal liver enzymes should be evaluated for the presence of liver disease.

Disclosure of interest: None Declared
Very good response to hepatitis B virus vaccine in patients on treatment for latent tuberculosis

Björn Fischler¹, Ulrika Melin-Orre¹, Charlotte Buxbaum¹

¹Dept. of Pediatrics, Karolinska University Hospital, Clintec, Stockholm, Sweden

Objectives and study:
Universal hepatitis B virus (HBV) vaccination has been recommended globally for more than two decades. However, some affluent low endemic countries in Northern Europe have not yet introduced universal vaccination and vaccinate only risk groups. On the other hand, vaccination rates in less affluent and conflict ridden areas of intermediate to high endemicity are suboptimal. Newly arrived immigrants to Sweden are screened for HBV infection as well as for tuberculosis (TB). Children and adolescents with symptomatic as well as asymptomatic, latent TB are offered prophylactic treatment. Our aim was to prospectively investigate if non-infected, non-immunized patients can be successfully vaccinated against HBV while receiving treatment for latent TB.

Methods:
All patients attended the outpatient pediatric TB clinic covering the Southern part of Stockholm County, Sweden. Latent TB in newly arrived asymptomatic immigrants was defined by any of the following criteria:
1. Positive tuberculin skin test (TST) and origin from a high incidence region.
2. Positive TST in non-BCG-immunized individuals regardless of origin exposed to TB.
3. Positive TST and positive interferon-gamma release assay in screening or in BCG-immunized individuals found in contact investigation.

Treatment with either isoniazid (INH) for 6-9 months or the combination of INH and rifampicin (RIF) for 3 months was given to patients with latent TB. Liver function tests were checked regularly and INH treatment was stopped and exchanged for RIF in patients with elevated transaminases of more than 5 times the upper limit of normal value. Patients lacking seroprotection against hepatitis B were offered monovalent vaccine (Engerix®) 10 microgram/ml at 0, 1, and 6 months (for children below 10 years of age), 20 microgram/ml at 0 and 6 months (11-15 years) and at 0, 1, and 6 months (16-18 years). Anti-HBs was analysed 1 month after the last dose. Serum levels of 25-OH-vitamin D were checked before starting the vaccination.

Results:
A total of 35 patients (21 girls, median age 14.8 years, range 7.3-17.5 years) were given HBV vaccination while on treatment for latent TB. The geographic area of origin was Africa in 21, Asia in 12, and South America in 2 patients, respectively. Two patients had to stop INH due to elevated transaminases, but could subsequently be treated with RIF. At follow-up, 34 out of 35 (97%) had protective levels of anti-HBs, i.e. at or above 10 IU/ml. Of these, 19 had anti-HBs >1000 IU/ml, 11 had anti-HBs of 100-1000 IU/ml, and 4 had anti-HBs of 10-100 IU/ml. The single patient who had anti-HBs of 8 IU/ml was given one extra dose of vaccine, after which the anti-HBs level rose to 69 IU/ml. The serum level of 25-OH-vitamin D was measured in 24 out of the 35 patients and was low in all of them, i.e. 14 had levels <30 nmol/l, 9 had 30-50 nmol/l, and 1 had 50-75 nmol/l. No correlation could be detected between 25-OH-vitamin D and anti-HBs levels.

Conclusion:
1. Ongoing treatment for latent TB at an outpatient clinic offers a good opportunity to vaccinate unprotected patients at risk for HBV infection.
2. The response to the vaccine is very good, this despite the possible immunological importance of latent TB as well as that of low vitamin D levels.
3. The described schedule may be further useful for the currently rising number of potentially unprotected refugees migrating to countries in Northern Europe where universal HBV vaccination has not yet been implemented.

Disclosure of interest: None Declared
Poor long-term results of internal biliary diversion in patients with PFIC

Antal Nemeth¹, Björn Fischler², Jan F. Svensson³, Henrik Arnell⁴, Karin Littmann⁵, Ruth Bolier⁶, Gösta Eggertsen⁵

¹Karolinska University Hospital, Alb Childrens’ Hospital, Pediatric Gastroenterology, Hepatology & Nutrition, Stockholm, Sweden
²Dept. of Pediatrics, Karolinska University Hospital, Clintec, Stockholm, Sweden
³Karolinska University Hospital, Alb Childrens’ Hospital, Pediatric Surgery, Se-171 76 Stockholm, Sweden
⁴Karolinska University Hospital, Alb Childrens’hospital, Pediatric Gastroenterology, Hepatology & Nutrition, Se-141 86 Stockholm, Sweden
⁵Karolinska University Hospital, Dept of Clinical Chemistry, Se-141 86 Stockholm, Sweden
⁶Univ of Amsterdam, Tytgat Inst for Liver & Intest Research, Dept of Gastroenterology, Nl-1100 Dd Amsterdam, Netherlands

Objectives and study: External biliary diversion (EBD) has most often a good effect on the cholestasis in patients with progressive familial intrahepatic cholestasis (PFIC) but the late psychosocial consequences are often serious. For these patients an internal diversion (ID) can offer a good cosmetic solution. The medical outcome, though, is still uncertain.

Methods: In 4 of our PFIC patients (labelled A-D, Table) the diversion was internalized. Three received a partial diversion (Bustorff-Silva J, 2007), and one a total hepatico-jejuno-colostomy. Three patients were homozygous for the 890G>A (ABCB11) mutation, in patient A no mutation was detected. In this patient serum levels of bilirubin, alkaline phosphatase, serum fasting bile acids, a marker of bile acid synthesis, 7-OH-cholestanon (“C-4”) and autotaxin, a putative marker of pruritus were repeatedly measured after the internal diversion procedure.

Results: Previously, in all four patients excellent or good long-term results were achieved with the external diversion (see Table). The conversion into biliary diversion with internal conduit from the gallbladder (or from the liver in patient D) to the ascending colon gave good cosmetic solution, important for young adult patients with PFIC. However, the initial good results of the operation were difficult to maintain. The initial biliary diarrheas were easy to handle but partial or complete cholestasis and pruritus soon reappeared. During the relapse the biochemical markers of cholestasis were discordant. In three patients within a few years the cholestasis also lead to hepatocellular failure necessitating liver transplantation. The only patient left with native liver has also a low-grade cholestasis. In patient A serum levels of autotaxin correlated with the degree of pruritus, in accordance with recent results in other cholestatic children (KremerAE, 2015).

Table: Outcome of diversions

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age at EBD</th>
<th>Outcome</th>
<th>Age at ID</th>
<th>Outcome 12 mo**</th>
<th>Outcome 24 mo**</th>
<th>Outcome 48 mo**</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>M</td>
<td>11 mo</td>
<td>2</td>
<td>11 y</td>
<td>D,B,B.ac, P</td>
<td>Tx</td>
<td></td>
</tr>
<tr>
<td>B</td>
<td>F</td>
<td>18 mo</td>
<td>2</td>
<td>20 y</td>
<td>P.B.ac</td>
<td>P.B.ac</td>
<td>P,B.ac</td>
</tr>
<tr>
<td>C</td>
<td>F</td>
<td>13 mo</td>
<td>3</td>
<td>21 y</td>
<td>P.B.ac, LF</td>
<td>Tx</td>
<td></td>
</tr>
<tr>
<td>D</td>
<td>F</td>
<td>36 mo</td>
<td>3</td>
<td>22 y</td>
<td>P.B.ac</td>
<td>P,B.ac</td>
<td>LF</td>
</tr>
</tbody>
</table>

*: Outcome of PEBD: 2=Good:1-2 relapses/year, 3=excellent, <1 relapse/year

**: Outcome of ID: B: elevated s-bilirubin, B.ac: elevated s bile acids, D: diarrhea, LF: liver failure, P: Pruritus, Tx: transplantation

Conclusion: 1) In PFIC patients the psychosocial consequences of EBD can be reversed with ID and this makes it tempting to offer this solution to unhappy young adults 2) However, after initial success, the underlying disease may return also in patients who previously responded to EBD with decades of
stable liver function with few relapses. This might cause hepatic decompensation. 3) For the time being there are no reliable markers to help the preoperative prediction of the outcome of the ID. 4) Further follow-up of cholestatic markers, bile acid metabolism and candidate markers of pruritus will help to understand the underlying dynamics.

Disclosure of interest: None declared
Biliary Atresia Splenic Malformation may not be indicative of bad prognosis?

Naved Alizai¹, Sanjay Rajwal¹, Suzanne Davison¹, Patricia McClean²

¹Paediatric Liver Unit, Leeds General Infirmary, Leeds, United Kingdom
²Leeds Teaching Hospitals NHS Trust, Department of Paediatric Hepatology, Leeds, United Kingdom

Objectives and study: Biliary Atresia Splenic Malformation syndrome (BASM) is characterised by congenital anomalies (polysplenia, malrotation, situs inversus, interrupted inferior vena cava, preduodenal portal vein etc) occurring in association with Biliary Atresia (BA). Past studies suggested that infants with BASM have a worse prognosis than those with isolated BA, with fewer achieving resolution of jaundice after Kasai Portointerostomy (KP). Objective of the present study was to determine the jaundice clearance rate post KP in infants with BASM.

Methods: All infants undergoing KP between Aug 2006 - Jul 2015 performed by a single surgeon were included in the study. All infants received adjuvant therapy consisting of: oral dexamethasone 0.3mg/kg twice daily for 5 days, 0.2 mg/kg twice daily for 5 days, 0.1 mg/kg twice daily for 5 days, beginning on postoperative day 5 (along with ranitidine). In addition to steroids, oral ursodeoxycholic and phenobarbitone were given until 1yr of age. All children received intravenous antibiotics postoperatively for 5 days then prophylactic antibiotics for another 4 weeks.

Results: 104 infants who underwent KP were identified of whom 16 (15%) had BASM. Median age at Kasai was 32d (11-90) in those with BASM compared to 50d (14-144) in those without. Overall, clearance of jaundice (serum bilirubin < 20 µmol/L) was achieved in 73/104 ((70%). Of those with BASM, 75% (12/16) cleared jaundice compared to 69% (61/88) in those without. All 12 children with BASM who cleared jaundice remain well with native liver at median follow up of 2.6y (0.5 - 7). Of the remaining 4 children with BASM who did not clear jaundice: 2 had liver transplant (alive and well) and 2 died (1 waiting for liver transplant, 1 sepsis).

Conclusion: Seventy five percent of children with BASM cleared jaundice. The prognosis for BASM may not be as poor as has been depicted in the past. Success may be partly because of earlier age at KP and adjuvant therapy.

Disclosure of interest: "None Declared".
Pediatric hepatocellular adenoma: benign hepatic tumors that may transform

Isabelle Scheers¹, Xavier Stephenne², Francoise Smets³, Mina Komuta⁴, Raymond Reding⁵, Christine Sempoux⁶, Etienne Sokal¹

¹Clinique Universitaire St Luc, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium
²Cliniques Universitaires St Luc, Pediatric Gastroenterology and Hepatology, Brussels, Belgium
³Ucl, Cliniques Universitaires Saint-Luc, Irec, Pediatrics, Brussels, Belgium
⁴Clinique Universitaire St Luc, Pathology, Brussels, Belgium
⁵Clinique Universitaire St Luc, Pediatric Liver Transplantation and Surgery, Brussels, Belgium
⁶Centre Hospitalier Universitaire Vaudois, Pathology, Lausanne, Switzerland

Objectives and study: Hepatocellular adenoma (HCA) is a benign tumor occurring in a non cirrhotic liver. HCA may be symptomatic due to hemorrhage, compression or malignant transformation; however, the tumor is mostly found incidentally. In children, HCA develops in patients with underlying diseases such as MODY3, portosystemic shunt, glycogenosis or sexual hormone imbalance. In adults, HCA can be subclassified according to their immunophenotype and genotype. However exceptionally described, HCA might complicate with malignant transformation. Risk factors for transformation are poorly understood in pediatrics. We aimed to investigate the immunophenotype and natural evolution of HCA in pediatric patients. We further searched predictors of malignant transformation according to tumor immunophenotype. Finally, we assessed the usefulness of alpha-fetoprotein and imaging techniques in early diagnosis of HCC.

Methods: Our retrospective, single center study included 13 children with HCA. Clinical, biochemical, imaging and histologic characteristics were reviewed on admittance and during follow-up.

Results: Thirteen patients were followed for HCA of whom 2 girls and 11 boys. Seven had multiple lesions. Eight HCA were discovered during routine ultrasound follow-up of the underlying liver disease, 4 by chance and 1 had an enlarged liver on physical examination. All patients presenting HCA had an underlying risk factor for developing adenomas: 1 was diagnosed with MODY3, 4 with glycogenosis, 7 with portosystemic shunts or intrahepatic vascular anomalies and 1 had McCune Albright. HCA could be categorized into 4 distinct groups after immunophenotyping: inflammatory (n=1), beta-catenin mutated (B-HCA, n=2), HNF1alpha mutated (n=4) and unclassified adenoma (n=1); three of the tumors had a combined inflammatory and B-HCA phenotype. HCA transformed in hepatocellular carcinoma (HCC) in three patients, at a mean age of 19 years (range 11-24 years). All these patients had a B-HCA immunophenotype and only one of them had a high alpha-fetoprotein. Ultrasound was poorly sensitive to early diagnose HCC. Contrast enhanced MRI was the most accurate imaging modality to distinguish HCA from HCC.

Conclusion: HCA in children could be classified according to immunophenotype and may transform. Children with beta-catenin mutated HCA are the most at risk to evolve to hepatocellular carcinoma. Contrast MRI imaging is recommended to follow-up HCA as it is the most sensitive technique, and neither alpha-fetoprotein and ultrasound are sufficiently accurate to formally rule out HCC.

Disclosure of interest: “None Declared”.

* CS and ES contributed equally to this work
Non-adherence in young people with autoimmune liver disease: it's about more than not taking medications

Marianne Samyn¹, Faith Matcham², Isobel Makin¹, Deepak Joshi³, Anna Hames³

¹ King’s College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom
² King’s College London, Institute of Psychiatry, Psychology and Neuroscience, London, United Kingdom
³ King’s College Hospital, Institute of Liver Studies, London, United Kingdom

Objectives and study: Non-adherence (NA) to treatment is common in young people (YP) with chronic conditions and associated with poor outcome. Measuring adherence is difficult and often subjective, relying on self-report and clinicians’ observation. Mental health problems can contribute to NA, are more common in people with chronic health conditions yet under-identified. As part of our multidisciplinary adolescent liver clinic, patients are invited to take part in IMPARTS, a means of integrating mental health screening with the clinic appointment. In addition to a standardised depression and anxiety questionnaire, the electronic screening includes an adherence tool and an adapted distress thermometer (DT) (table). Autoimmune liver disease (AILD) is a chronic liver condition often presenting during adolescence and managed with immunosuppressive medications. Qualitatively the team have noticed that these YP struggle with adjusting to their condition and have elevated rates of NA. The aim of the study was to describe the results of the IMPARTS screening, demographics and biochemistry data in a cohort of YP with AILD.

Methods: Patients attending the liver adolescent clinic were invited to complete the IMPARTS questionnaires between November 2013- September 2015. Demographics and blood results for patient with AILD were obtained retrospectively from the clinical records.

Results: During the study period 187/232 (81%) YP attending clinic completed IMPARTS. 69 (31 M) had AILD, diagnosed at a median age of 12.4 y (range 4-16) with a median disease duration of 5.3 yrs (range 0.6-20). All but 2 patients took a median of 5 medications a day (range 1-9). 77% were on maintenance prednisolone (5 mg od) with median values for liver function tests within normal range. Anxiety +/- depression was recorded in 12 (17.4%), and 74% reported worries on the DT (median 5, range 0-10). Overall self-reported adherence was 91% and >80% in 71%. YP with abnormal AST (>35 IU/l) at screening were found to take more medications (5 vs 4, p=0.036), not on maintenance prednisolone dose (54% vs 97%, p<0.01), had a higher score on DT (6 vs 2, p=0.01) and reported taking their medications more regularly in the weeks before coming to clinic (62% vs 30%, p=0.02). Females reported higher scores on DT (5 vs 1, p=0.017). Males were more likely to disclose intentional NA (14% vs 0%, p=0.02).

Table:

<table>
<thead>
<tr>
<th>%</th>
<th>Total n=69</th>
<th>AST&lt;35 IU/l n=33</th>
<th>AST 35&gt;IU/l n=29</th>
<th>Female n=38</th>
<th>Male n=31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall adherence</td>
<td>91</td>
<td>91</td>
<td>90</td>
<td>91</td>
<td>91</td>
</tr>
<tr>
<td>Punctuality</td>
<td>79</td>
<td>80</td>
<td>79</td>
<td>79</td>
<td>74</td>
</tr>
<tr>
<td>I have a routine</td>
<td>70</td>
<td>73</td>
<td>61</td>
<td>72</td>
<td>68</td>
</tr>
<tr>
<td>for taking my</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>medications</td>
<td>43</td>
<td>30</td>
<td>62</td>
<td>51</td>
<td>32</td>
</tr>
<tr>
<td>I take my</td>
<td>63</td>
<td>67</td>
<td>65</td>
<td>66</td>
<td>61</td>
</tr>
<tr>
<td>medications more</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>regularly in the</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>weeks before</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>coming to clinic</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>I sometimes forget</td>
<td>63</td>
<td>67</td>
<td>65</td>
<td>66</td>
<td>61</td>
</tr>
</tbody>
</table>
I find it more difficult to take my medications regularly when my routines change

<table>
<thead>
<tr>
<th></th>
<th>57</th>
<th>50</th>
<th>65</th>
<th>60</th>
<th>50</th>
</tr>
</thead>
</table>

I sometimes remember my medication but chose not to take it.

|                                      | 6  | 7  | 8  | 0# | 14#|

There can be good things about not taking my medications

|                                      | 5  | 3  | 8  | 3  | 7  |

**Conclusion:** 29% of YP with AILD self-reported being non-adherent with medication, with anxiety +/- depression reported in 17%. Abnormal liver function tests, in 53%, were associated with medication load, poorer disease control, more psychological distress and a different pattern of adherence. Overall, females reported more worry and males disclosed more intentional NA. Integrating mental health and adherence screening in a clinic setting is acceptable to YP and can help health professionals to identify barriers to NA and manage them accordingly.

**Disclosure of interest:**
“None Declared”. 
Gut microbiota composition and metabolism in infants with biliary atresia after hepatopancreaticoenterostomy compared to healthy controls

Ewa Orłowska¹, Piotr Czubkowski¹, Katarzyna Śliżewska², Elżbieta Klewicka², Ilona Motyl², Zdzisława Libudzisz², Piotr Socha¹

¹The Children's Memorial Health Institute, Gastroenterology, Hepatology, Nutritional Disorders and Pediatrics, Warsaw, Poland
²Lodz University of Technology, Lodz, Poland

Objectives and study: Children with biliary atresia after hepatopancreaticoenterostomy receive antibiotic prophylaxis to prevent ascending cholangitis related to bacterial infection from the intestine, ursodeoxycholic acid as a cholangiolytic and nutritional support. All these factors can significantly contribute to microbiota composition.

We aimed at quantitative assessment of the gut microbiota composition and metabolism in infants with biliary atresia after hepatopancreaticoenterostomy in comparison with healthy controls.

Methods: 30 children with biliary atresia (13 girls and 17 boys) aged <4 months after hepatopancreaticoenterostomy and 24 healthy aged matched infants (11 girls and 13 boys) were included into the study. Quantitative assessment of the gut microbiota composition was performed through the analysis of the presence and participation of specific intestinal bacteria by growing methods from stool samples with the use of non-selective (differential) and selective growth media (Lactobacillus sp., Bifidobacterium sp., Bacteroides sp., Clostridium sp., Enterobacteriaceae, Enterococcus sp.). Short-chain fatty acids (acetic, butyric, propionic) as well as lactic acid were measured in stool samples.

All the patients received standard non-invasive medical treatment in the form of antibiotic therapy, vitamin supplementation and ursodeoxycholic acid (UDCA).

Results: The microbiological analysis of the stool revealed a significant increase in the number of Enterococcus bacteria compared to controls (2.0 x 10⁹ CFU vs. 0.086 x 10⁹ CFU) but there were no differences in Lactobacillus sp., Bifidobacterium sp., Bacteroides sp., Clostridium sp., Enterobacteriaceae.

We also found a significant difference in the concentration of short-chain fatty acids (SCFA) in the stool of the healthy infants and the ones suffering from the bile duct obstruction: lower concentration of lactic and acetic acids (1.2 mg/g of stool vs. 1.01 mg/g of stool), butyric acid (0.37 vs. 0.22) and propionic acid (0.23 vs. 0.18), in children suffering from the bile duct obstruction.

Conclusion: The results showed differences in microbiota composition and bacterial metabolism in infants with biliary atresia. Significant disturbances of bacterial metabolism expressed by decreased concentration of lactic and acetic, butyric and propionic acids may affect clinical outcome and could possibly contribute to adverse reactions like ascending cholangitis or malnutrition.

Disclosure of interest: None Declared.
Prophylactic endoscopic therapy in children with portal hypertension

Harry Sutton1, Mark Davenport1, Alastair Baker1, Anil Dhawan1, Tassos Grammatikopoulos1

1King’s College Hospital, Paediatric Liver, Gi & Nutrition Centre, London, United Kingdom

Objectives and study: Gastrointestinal (GI) variceal bleeding can be a life-threatening complication of portal hypertension (PHT). Due to limited clinical studies in children with PHT, current treatment options for GI varices are based on practices adopted in adults. To evaluate the safety and efficacy of primary prophylactic endoscopic band ligation (EVL) and sclerotherapy (EST), for the prevention of variceal haemorrhage in children with PHT of various aetiologies.

Methods: Children with hypersplenism admitted for first surveillance upper GI endoscopy between 2012-2015 with splenomegaly and platelet count (PLT) <150x10⁶/L comprised the study groups. Clinical and biochemical data were collected and the efficacy and safety of prophylactic therapy versus non-treatment were compared.

Results: 79 patients (43M) median age 8 years (IQR 7) were included. Patients were categorized based on the aetiology of their PHT into group 1 biliary atresia (37%), group 2 portal vein thrombosis (26%) and group 3 other liver disease (37%) including congenital hepatic fibrosis, Wilson's disease, cystic fibrosis, autoimmune hepatitis and α-1-antitrypsin deficiency. Variceal grading was recorded as per UK national guidelines. Prophylactic treatment was administered during a surveillance endoscopy at least once in 17 (59%), 16 (76%) and 25 (86%) patients from groups 1, 2 and 3, respectively with the remaining patients receiving no treatment. The prophylactic treatment subgroup showed variceal grade improvement in 13 (76%), 14 (88%) and 20 (80%) patients, no change in 1 (6%), 1 (6%) and 3 (12%) and worsening of varices in 3 (18%), 1 (6%) and 2 (8%), in groups 1, 2 and 3, respectively. In the non-treatment subgroup spontaneous improvement of varices was recorded in only 3 (25%) patients in group 1, no change in 4 (33%), 3 (60%) and 2 (50%) and worsening of varices in 5 (42%), 2 (40%) and 2 (50%), in groups 1, 2 and 3, respectively.

<table>
<thead>
<tr>
<th>[normal values]</th>
<th>Treatment</th>
<th>Non-treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Group 1</td>
<td>Group 2</td>
</tr>
<tr>
<td>Clinical Prediction</td>
<td>106.7</td>
<td>107.4</td>
</tr>
<tr>
<td>Rule</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Risk Score</td>
<td>4.96</td>
<td>4.71</td>
</tr>
<tr>
<td>Albumin(g/L) [35-45]</td>
<td>39</td>
<td>39</td>
</tr>
<tr>
<td>Bilirubin (mg/dL) [3-20]</td>
<td>17.4</td>
<td>15.8</td>
</tr>
<tr>
<td>PLT(x10⁹/L)[150-450]</td>
<td>104</td>
<td>107</td>
</tr>
<tr>
<td>Haemoglobin (g/L) [115-155]</td>
<td>111.5</td>
<td>114.6</td>
</tr>
<tr>
<td>INR [0.9-1.2]</td>
<td>1.25</td>
<td>1.24</td>
</tr>
</tbody>
</table>

Table: Mean values of non-invasive, biochemical and haematological parameters at time of 1st endoscopy. No significant difference was found between treatment and non-treatment subgroups in CPR (p=0.5), RS (p=0.9), albumin (p=0.7), bilirubin (p=0.8), PLT (p=0.5), Hb (p=0.5) or INR (p=0.9). Seven (8%) patients in the prophylactic treatment group suffered a single GI bleed. No other
complications were recorded in either group. Four patients, from the treatment group, had a MesoRex bypass placed during the study period.

**Conclusion:** Prophylactic treatment of GI varices results in an overall reduction of varices and GI bleeds without significant complications. Children with PTH could benefit from surveillance endoscopy programs with prophylactic treatment in the form of EVL or EST as it has been shown to be both safe and effective.

**Disclosure of interest:** None Declared
Semiquantitative evaluation of liver histology in children with Wilson's disease

Magdalena Naorniakowska¹, Maciej Pronicki², Diana Kamińska¹, Wiesława Grajkowska³, Małgorzata Podlaska¹, Wojciech Jańczyk¹, Dariusz Lebensztejn³, Piotr Socha⁴

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology and Nutritional Disorders, Warsaw, Poland
²The Children’s Memorial Health Institute, Department of Pathology, Warsaw, Poland
³Medical University of Bialystok, Department of Pediatrics, Gastroenterology and Allergology, Bialystok, Poland
⁴The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Liver histology was reported in a few cohorts of children with Wilson’s disease but was not analyzed in detail semiquantitatively in relation to clinical course, liver function tests and biochemical diagnostic tests. In our study we aimed at semiquantitative detailed evaluation of liver histology in children with Wilson’s disease.

Methods: We analyzed retrospectively liver histology, biochemical and clinical descriptions of 63 children with Wilson’s disease aged 10 ± 4 years. Liver histology was described semiquantitatively according to the modified Kleiner scoring system used for NAFLD (Non-alcoholic fatty liver disease) where micro- and macrovesicular steatosis was evaluated separately (score 0-3). Other parameters included: portal inflammation (0-3), lobular inflammation (0-3), fibrosis (0-4), cholestasis (0-3). The associations were tested with Spearman R test, the frequencies with Fisher-Freeman-Halton exact test.

Results: In our cohort the patients presented with variable fibrosis (grade 3-4 in 22 patients), lobular inflammation (grade 2-3 in 8 pts), portal inflammation (grade 2-3 in 8 pts), cholestasis (in 7) and microvesicular (grade 1 in 37, 2-3 in 13) and macrovesicular steatosis (grade 1 in 27, 2-3 in 24). 8 patients had features of liver insufficiency (INR > 1.5).
We found a significant association between portal and lobular inflammation (R=0.44), macro- and microvesicular steatosis (R=0.33) as well as portal inflammation and fibrosis (R=0.37) which clearly corresponds with pathological mechanisms of liver injury.
Alanine aminotransferase (ALT) correlated significantly only with lobular inflammation (R=0.35) and microvesicular steatosis (R=0.31) and aspartate aminotransferase (AST) was significantly related to lobular inflammation (R=0.28), fibrosis (R=0.27) and cholestasis (R=0.28).
Bilirubin was only correlated with cholestasis on liver biopsy (R=0.32).
INR correlated only with fibrosis (R=0.38) and cholestasis (R=0.32). Still, liver insufficiency was associated with advanced fibrosis (in 7 pts) and steatosis.
Increased steatosis was inversely related with copper liver content (R=-0.45), which indicates possible underestimation and risk of falsely negative results of liver copper in considerably steatotic livers.
Ceruloplasmin was not related to histological findings but urinary copper excretion correlated with periportal (R=0.57) and lobular inflammation (R=0.5).

Conclusion: Micro- and macrovesicular liver steatosis are relatively common features of Wilson’s disease in childhood. Liver insufficiency is strictly related to severe liver fibrosis and liver function tests correspond with histological findings in Wilson’s disease. Lobular, in contrast to portal inflammation results in higher AST/ALT level probably as a result of more direct intraparenchymal hepatocellular damage. Periportal inflammation is related to advancing severity of fibrosis.
Biochemical diagnostic tests are affected by histopathological liver changes - urinary copper excretion increases with severity of inflammation and liver copper content decreases with increasing steatosis, which should be considered when concluding the results.

Disclosure of interest: None Declared
Hepatokines in children with nonalcoholic fatty liver disease

Marta Flisiak-Jackiewicz1, Eugeniusz Tarasów2, Małgorzata Wojtkowska3, Dariusz Marek Lebensztejn1

1Dept. of Pediatrics, Gastroenterology & Allergology, Medical University of Bialystok, Poland
2Dept. of Radiology, Medical University of Bialystok, Poland
3Dept. of Radiology, University Children Hospital, Bialystok, Poland

Objectives and study: Hepatokines are proteins produced by the liver involved in regulating glucose and lipids metabolism. Nonalcoholic fatty liver disease (NAFLD) is strongly associated with visceral obesity, insulin resistance and dyslipidemia, therefore NAFLD is regarded as a hepatic manifestation of the metabolic syndrome. However, the role of hepatokines in NAFLD is not clear. The aim of the study was to evaluate serum concentration of selected hepatokines: fibroblast growth-21 (FGF-21), selenoprotein P1 (SeP1) and sex hormone-binding globulin (SHBG) in obese children with NAFLD.

Methods: The study comprised 86 obese children (median age – 12 years) with the initially suspected liver disease (hepatomegaly and/or increased ALT activity and/or liver steatosis in ultrasound). Viral hepatitis (HCV, HBV), autoimmune (AIH) and selected metabolic liver diseases (Wilson’s disease, alfa-1-antitrypsin deficiency, cystic fibrosis) were excluded. Serum levels of FGF-21, SeP1 and SHBG were determined by ELISA in all patients. The degree of liver steatosis in ultrasound (USG) was graded according to Saverymuttu scale. The total intrahepatic lipid content was assessed by magnetic resonance proton spectroscopy (1HMRS). Twenty-four healthy children constituted the control group.

Results: NAFLD was confirmed in 34 children. The concentration of FGF-21 and SeP1 was significantly higher and SHBG significantly lower in children with NAFLD than in controls (p<0.000). Only FGF-21 level, among tested hepatokines, was significantly higher in children with NAFLD than in obese patients without NAFLD (p=0.046). NAFLD children demonstrate also significantly higher ALT, AST and GGT activities, insulin resistance (HOMA-IR), uric acid level, BMI, waist circumferences, degree of liver steatosis (USG) and total amount of lipids in 1HMRS. Moreover, hepatopathic obese children with advanced liver steatosis (grade=3) showed significantly higher values of FGF-21 compared to children with mild steatosis in USG (grade=1 or 2) (p=0.005). The significant FGF-21positive correlations with ALT (r=0.23), GGT (r=0.27), triglycerides (r=0.38), insulin resistance (HOMA-IR) (r=0.32), the degree of liver steatosis in USG (r=0.23) and total amount of lipids in 1HMRS (r=0.21) were found. Serum SeP1 levels were positively correlated with hsCRP (r=0.77) and SDS-BMI (r=0.24) and negatively with age (r=-0.24). We demonstrated also significant negative correlation between SHBG and age (r=-0.22) and HOMA-IR (r=-0.31).

Conclusion: Elevated FGF-21 levels and its significant correlation with hepatocyte injury, glucose and lipids metabolism and degree of liver steatosis suggest the role of this hepatokine in development and progression of NAFLD in children. Only FGF-21, among three tested hepatokines, seems to be a suitable non-invasive novel biomarker in predicting advanced liver steatosis and fatty liver in obese children.

Disclosure of interest: authors have no conflict of interest.
Evolution of incidence and characteristics of autoimmune liver diseases in children over 24 years in a French region

Delphine Hivert¹, Emmanuel Mas², Anne Breton¹, Jean-Pierre Olives¹, Karl Barange³, Janick Selves⁴, Pierre Broue⁵

¹Centre Hospitalier Universitaire Toulouse, Pédiatrie - 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
³Centre Hospitalier Universitaire Toulouse, Gastro-Entérologie Adulte, Toulouse, France
⁴Centre Hospitalier Universitaire Toulouse, Anatomopathologie, Toulouse, France
⁵Chu Toulouse, Pédiatrie - Gastro-Entérologie, Hépatologie, Nutrition et Diabétologie, Toulouse, France

Objectives and study: Autoimmune hepatitis (AIH) and autoimmune sclerosing cholangitis (AISC) are progressive inflammatory liver diseases of unknown etiology. Their epidemiology in children is still insufficiently known. This study evaluated the incidence of autoimmune liver diseases (AILD) in children in a French regional center over a period of 24 years and studied the pathological characteristics of these patients to improve their care.

Methods: We included 62 patients, observed between 1991 and 2014 (AIH-1, n = 27; overlap syndrome, n = 10; AIH-2, n = 5; AISC n = 16; AIH seronegative, n = 3; AIH with giant cell hepatitis with hemolytic anemia, n = 1) associated or not with inflammatory bowel disease (IBD). To assess incidence rates, we selected children under 15 years old at diagnosis who were domiciled in our administrative area (n = 51).

Results: We observed an average annual incidence of autoimmune liver diseases of 0.45 per 100,000 children (< 15 year old) over the 24-year period. This rate increased steadily over the period (1991-1996: 0.197/100,000; 1997-2002: 0.42/100,000; 2003-2008: 0.503/100,000; 2009-2014: 0.707/100,000). We found a significant increase in the incidence of AIH-1 (associated or not with AISC, n = 28), on average 7.6% per year (p = 0.028), but not with other type of AILD. The overall average follow-up was 7 years (range of 1 month to 19 years). 80% of AIH-2 were girls while the sex ratio was balanced for AIH-1 and AISC. 69% of AISC were associated with IBD. A viral triggering factor was suspected in 17% of cases of AIH. Cirrhosis was present at diagnosis in 24% of patients with AIH. After an initial induction therapy (corticosteroids and azathioprine, n = 35; cyclosporine, n = 7), treatment had to be increased for 50% of AIH-1 and 80% of AIH-2. After 5 years, treatment could be discontinued in 67% of children with AIH-1 (mean follow-up time of 4.8 years after end of treatment). The two children in the study who died had AIH-2 (after they underwent liver transplantation).

Conclusion: In our limited area, our study showed an increase by a factor of 3.6 of the incidence of AILD over the 24 years. The increase in incidence of all AILD types can be attributed to the increase in AIH-1; while AIH-2 and AISC remained constant over the period. Our results are in line with a recent study in Norway in adults and another one in Canada in children. A better understanding of the pathogenesis of this disease will help explain this increased incidence.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 559
Measurement of liver stiffness by Share Wave Elastography imaging technic in predicting oesophageal varices in portal hypertensive paediatric patients

Didem Gulcu¹, Mehmet Cingoz², Ibrahim Adaletli², Ahmet Bas², Hasret Ayyildiz Civan¹, Tufan Kutlu¹, Fugen Cullu Cokugras¹, Tulay Erkan¹

¹Istanbul University Cerrahpasa Medicine Faculty, Pediatric Gastroenterology Hepatology and Nutrition, Istanbul, Turkey
²Istanbul University, Cerrahpasa Medical Faculty, Radiology, Istanbul, Turkey

Objectives and study: To evaluate whether spleen stiffness and liver stiffness measured by Share wave velocity (SWV) imaging can identify patients who have oesophageal varices and the accuracy of liver SWV, spleen SWV and other noninvasive tests in predicting the presence and grade of oesophageal varices in portal hypertensive patients.

Methods: In a prospective study, we measured spleen stiffness and liver stiffness (left-right lob) in 43 patients with portal hypertension undergoing endoscopic screening for oesophageal varices and 63 healthy controls at Istanbul University, Cerrahpasa Medical Faculty in Istanbul, Turkey. Spleen diameter was measured by ultrasonography, spleen and liver stiffness was measured by SWV; endoscopy was used for detection of oesophageal varices. We assessed the ability of spleen diameter, portal venous flow, liver and spleen elastography, ALT/AST ratio and platelet count to identify patients with portal hypertension with oesophageal varices.

Results: Oesophageal varices were found in 25 of the 43 children (58%). Liver and spleen elastography measurements are high in portal hypertension group. Spleen enlargement was highly correlated with spleen elastography measurement. Mean spleen stiffness measurement is 62.98 kPa in portal hypertension patients with variceal bleeding, 33.20 kPa in patients without bleeding (Mann-Whitney U Test: p= 0.014). Mean liver stiffness measurement is 44.38 kPa in portal hypertensive patients in variceal bleeding, 22.84 kPa in patients without bleeding (Mann-Whitney U Test: p= 0.028). Platelet count is 100% sensitive, 71.1% specific in predicting variceal bleeding. In portal hypertensive patients with variceal bleeding, liver elastography measurements > 22.2 kPa is 100% sensitive and 65.8% specific (95% Confidence interval 0.656 to 0.910) and spleen elastography measurements > 36.8 kPa is 100% sensitive and 65.8% specific for predicting variceal bleeding (95% Confidence interval 0.699 to 0.935).

Conclusion: Measurement of spleen stiffness, liver stiffness can be used to identify portal hypertensive patients with varices. Spleen stiffness and liver stiffness measurements could be used as an initial noninvasive test screening for oesophageal varices in portal hypertensive patients.

Disclosure of interest: "None Declared".
A urinary metabolomic signature of pediatric obesity related liver disease

Jacopo Troisi¹, Luca Pierri¹, Annamaria Landolfi¹, Francesca Marciano¹, Antonella Bisogno¹, Federica Belmonte¹, Carmen Palladino¹, Salvatore Guercio Nuzio¹, Pietro Vajro¹

¹University of Salerno, Department of Medicine and Surgery, Pediatric Section, Baronissi, Italy

Objectives and study: Pediatric obesity-related NAFLD is an increasingly important condition with still incompletely understood pathogenesis, and poor efficacious treatment and monitoring options as well. Here we investigated its urinary metabolomic signature, which has hitherto been scarcely characterized.

Methods: Forty Italian children/adolescents (mean age 9.8 years) were enrolled in this pilot case-control study. Inclusion criteria were: age 5 to 16 years, normal weight (NW) [body mass index (BMI) < 85th percentile], overweight/obese (OW/OB) (BMI >85th and >95th percentile, respectively). The presence of medical conditions other than obesity ± ultrasonographic bright liver (=hepatic steatosis) were considered exclusion criteria. Weight, height, BMI, waist circumference, waist-to-height ratio, blood pressure, hepatosplenomegaly were recorded by trained staff members using calibrated instruments. Urinary metabolome was obtained by GCMS 2010 (Shimadzu, Kyoto). Sample extraction, purification and derivatization was made by MetaboPrep GC Kit (Theoreo, Italy) according to manufacturer. PLS Discriminant Analysis (PLS-DA) was performed to improve groups separation, by rotating PCA (Principal Components Analysis) components for achieving a maximum separation among classes, and understanding which variables carry class separating information.

Results: A well-defined differentiation of patients with and without steatosis and controls was obtained by using the model with 22.4% of the total variance explained in the first two latent components. Fifteen variables important in projection (VIPs) were identified by PLS-DA setting the VIP score=2 as a cut-off value. Two VIPs were not identified as known metabolites. The other 13 VIPs were:

A. xylitol, 4-phenyl acetic acid, oleic acid, threose and N-metyl nicotinate= higher mean concentrations in NW control group;
B. oxalic acid and cresyl sulphate= higher concentrations in OW/OB without steatosis group;
C. glucose, 1-methyl histidine, sebacic acid, 2-deoxy uridine, glucono-1,4-lactone and cysteine= higher mean concentration in OW/OB with steatosis group.

The Table illustrates the individual VIP metabolites fold change versus controls. The metabolite are ordered by decreasing VIP score.

<table>
<thead>
<tr>
<th>VIP</th>
<th>Metabolite</th>
<th>Pts without hepatic steatosis</th>
<th>Pts with hepatic steatosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose</td>
<td>1,22</td>
<td>2,46</td>
<td></td>
</tr>
<tr>
<td>Xylitol</td>
<td>0,71</td>
<td>0,46</td>
<td></td>
</tr>
<tr>
<td>Phenylacetic acid</td>
<td>0,06</td>
<td>0,25</td>
<td></td>
</tr>
<tr>
<td>Methyl histidine</td>
<td>2,11</td>
<td>16,33</td>
<td></td>
</tr>
<tr>
<td>Oleic acid</td>
<td>0,94</td>
<td>0,15</td>
<td></td>
</tr>
<tr>
<td>Sebacic acid</td>
<td>0,93</td>
<td>1,22</td>
<td></td>
</tr>
<tr>
<td>Deoxy uridine</td>
<td>1,02</td>
<td>3,44</td>
<td></td>
</tr>
<tr>
<td>Threose</td>
<td>0,74</td>
<td>0,59</td>
<td></td>
</tr>
<tr>
<td>Glucono-1,4-lactone</td>
<td>0,62</td>
<td>3,42</td>
<td></td>
</tr>
<tr>
<td>Oxalic acid</td>
<td>0,80</td>
<td>0,79</td>
<td></td>
</tr>
<tr>
<td>Cresyl sulphate</td>
<td>1,79</td>
<td>0,97</td>
<td></td>
</tr>
<tr>
<td>Unknown1</td>
<td>0,42</td>
<td>1,61</td>
<td></td>
</tr>
<tr>
<td>Cysteine</td>
<td>2,42</td>
<td>3,48</td>
<td></td>
</tr>
<tr>
<td>N-methyl</td>
<td>0,47</td>
<td>0,96</td>
<td></td>
</tr>
<tr>
<td>Unknown2</td>
<td>2,15</td>
<td>2,01</td>
<td></td>
</tr>
</tbody>
</table>
**Conclusion:** Pediatric obesity and its related liver disease appear having distinct metabolomic signatures. The difference emerges especially from metabolites involved in energy, peptide and organic acid metabolism, and in intestinal bacteria metabolism. This piece of information expands the current understanding of NAFLD pathogenesis, potentially translating into future better targeted treatment and monitoring strategies.

**Disclosure of interest:** None Declared.
Clinical practices among healthcare professionals concerning neonatal jaundice and pale stools

Helena Moreira Silva¹, Lia Azevedo Lijnzaat², Cláudia Melo³, Esmeralda Martins⁴, Ermelinda Santos Silva¹

¹Centro Hospitalar Do Porto, Paediatric Gastroenterology Service, Department of Child and Adolescent, Oporto, Portugal
²Instituto de Ciências Biomédicas Abel Salazar, Universidade Do Porto, Oporto, Portugal
³Centro Hospitalar Do Médio Ave, Paediatric Service, Porto, Portugal
⁴Centro Hospitalar Do Porto, Metabolic Diseases Unit, Paediatric Service, Department of Child and Adolescent., Oporto, Portugal

Objectives and study: Neonatal jaundice is a common clinical finding in the first two weeks after birth, occurring in 2% to 15% of newborns. However, prolonged and/or cholestatic jaundice is abnormal and should prompt early referral. Pale stools are a major indicator of cholestatic liver disease, mainly of biliary obstruction. In Taiwan, since 2004, an infant stool color card has been integrated into the child health booklet and used for universal screening of biliary atresia. Since then several authors have recognized the feasibility and cost-effectiveness of such screening method. Yet, to accomplish this purpose both healthcare professionals and parents must be prepared. The aims of our study were: 1) evaluate knowledge and clinical practice among healthcare professionals concerning jaundiced newborns, and 2) evaluate diagnostic accuracy in recognizing pale stools.

Methods: We included physicians (Family Physicians, General Pediatricians and Neonatologists) and nurses from primary care system and A- and B-level hospitals, from National Health Service, in the Northern region of Portugal. We applied a questionnaire including 8 or 10 questions (nurses and physicians, respectively) to evaluate knowledge and clinical practice, and a panel of eight stools photographs. Each stool should be classified as 'normal' or 'suspect'. Diagnostic accuracy in recognizing pale stools was evaluated using the number right answers.

Results: 266 participants completed the questionnaire [37.6% physicians (n=100) and 62.4% nurses (n=166)]. Regarding physicians’ answers we highlight that: 30.9% do not immediately request conjugated bilirubin (cBt) assay to jaundiced newborns with other possible signs and symptoms of cholestatic disease; in the breastfed-ones, 27.8% request cBt only if they are > 28 days old and 28.9% do not request cBt regardless of their age. Regarding nurses’ answers, 58% ask for medical observation depending on the jaundice intensity. The suspicious stool photographs were correctly identified by physicians and nurses, at all healthcare levels, with more than 90% of accuracy, except for a photograph with higher difficulty degree, correctly identified by 66% of professionals in primary care setting, 66.1% in B-level hospital and 89 % at A-level hospital (p<0.05).

Conclusion: A significant percentage of health professionals assumed clinical practices that preclude the timely recognition of cholestasis and pale stools. Training and continuous education programs regarding the importance of early recognition of cholestatic infants should be reinforced, mainly in the primary care setting. Further studies are needed to determine whether the use of a stool color card would be cost-effective in our country.

Disclosure of interest: None Declared.
HEPATOLOGY: General Hepatology

H-eP-027

Tissue copper concentrations are lower in children with non-alcoholic fatty liver disease, but only in those with more advanced disease

Harry Hubbard¹, Kishor Raja², Adrian Bomford³, Anil Dhawan¹, Emer Fitzpatrick¹

¹Paediatric Liver, GI and Nutrition Centre, King's College Hospital, London, United Kingdom
²Department of Clinical Biochemistry, King's College Hospital, London, United Kingdom
³Institute of Liver Studies, King's College Hospital, London, United Kingdom

Objectives and study: There has been recent observation of reduced liver copper and decreased ceruloplasmin levels in non alcoholic fatty liver disease (NAFLD) and much interest in the role of this abnormality in pathogenesis of the condition. The aim of this study was to compare liver copper concentration in children with NAFLD to normal controls and those with other chronic liver diseases.

Methods: Liver biopsies were obtained from children presenting to a paediatric liver centre as part of routine evaluation. The samples were dried, weighed, acid-digested, diluted and analysed for copper using Thermo XII Series Inductively Coupled Plasma Mass Spectrometry. Results were expressed per unit dry weight. NAFLD was further classified as simple steatosis (NAS score <3) borderline or true steatohepatitis (NASH) (≥3) and also scored for fibrosis. Eight normal controls (paediatric donor organs) were used for comparison.

Results: Median liver copper concentrations were: Wilson’s disease (n=56), 464µg/mg (IQR 272, 833), Autoimmune Liver Disease (n=29), 54µg/mg (33, 106) and NAFLD (n=55), 13µg/mg (8, 21), p<0.001. There was no significant difference in concentration between NAFLD and controls (median 13µg/mg (10, 16)). Tissue copper varied with degree of steatohepatitis and fibrosis (NAS score and Fibrosis score). Hepatic copper concentrations declined with increasing severity of NASH with copper concentrations in those with simple steatosis having a median leve of 18 microg/mg dry weight (IQR 17 – 18); those with NASH or borderline NASH, a median of 12 microg/mg (IQR 8 – 19). Copper concentrations also decreased with increasing severity of fibrosis; those who had a score <F2 had a median value of 15microg/mg (IQR 12-18) versus those scoring ≥F2 with a median value of 9 microg/mg (IQR 6 – 20). This variation was not reflected in serum levels of copper / caeruloplasmin nor in urinary copper measurements.

Conclusion: Though this study did not find that children with NAFLD had significantly lower liver copper measurements than normal controls, those with more severe NAFLD demonstrated lower tissue copper concentrations than those with mild disease.

Disclosure of interest: None declared
Autoimmune sclerosing cholangitis (AISC) in two cohorts in Europe and North America (NA): presentation of disease and follow-up

Jones Keaton¹, Laura Pirringer², Wallihan Daniel¹, Makeschin Marie Christine³, Mayr Doris³, Sibylle Koletzko⁴, Philip Bufler⁵, Alexander Miethke¹

¹Cincinnati Children’s Hospital Medical Center, Pediatric Hepatology, Cincinnati, United States
²University of Munich, Pediatric Gastroenterology and Hepatology, Munich, Germany
³University of Munich, Institute of Pathology, Munich, Germany
⁴Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
⁵Ludwig-Maximilians-Universität Munich, Pediatric Gastroenterology and Hepatology, Munich, Germany

Objectives and study: The prevalence of primary sclerosing cholangitis (PSC), which varies geographically, is highest in the northern hemisphere. We hypothesize that PSC overlap with Autoimmune Hepatitis (AISC) differs between geographically distinct cohorts.

Methods: Disease courses of 75 children with PSC or AISC referred to two tertiary centers in NA and in Europe between 2009 and 2013 were delineated by retrospective review of medical records, cholangiograms and liver biopsies.

Results: In the North American cohort of 56 subjects, 38 were diagnosed with PSC without overlap, of which 16 (39%) had Crohn’s disease (CD). In contrast, among the corresponding European cohort, only 2/14 (14%) had CD. AISC was primarily associated with UC in both cohorts. Consistent with the clinical diagnosis of AISC, the simplified AIH scores were significantly higher in these patients. ANA or SMA were positive for all patients who had undergone testing in Europe, including PSC subjects without overlap, whereas the prevalence of ANA and SMA was significantly lower among the subjects with PSC alone in NA. The grade of interface hepatitis on a 1 to 4+ scale was higher in European AISC subjects than in patients with PSC alone (mean score 3.0 vs 1.2, p=0.03) but the grade of periductal sclerosis was similar. Compared with PSC, European subjects with AISC presented at younger age and had lower serum total bilirubin and ALT levels, but not in NA. The Majoie score classifying the degree of large duct disease on images from MRCP or ERCP was significantly higher for intrahepatic abnormalities in the PSC cohort compared with the AISC group in NA, but not in Europe. At last follow up, bilirubin levels tended to be lower in the European AISC patients, but were significantly higher in the AISC compared with the PSC group in NA. Levels of gGT, alkaline phosphatase, ALT and AST were lower at last follow up in both PSC and AISC of NA and Europe. The majority of AISC patients were treated with corticosteroids and 6-mercaptopurine in both centers, but only 52% of PSC patients were treated with ursodeoxycholic acid in NA compared with 100% in Europe.
Conclusion: AISC is primarily associated with UC in both centers, whereas pediatric onset PSC without overlap was also associated with CD in NA. AISC appeared to be more active in regards to biochemistries whereas large duct disease was more advanced in the PSC subjects in NA. Current treatment strategies are associated with an improvement of biochemical markers in the majority of patients with PSC and AISC. Whether the differences in presentation and disease course are related to geographic variations or confounded by specific referral patterns to both institutions requires further investigation.

Disclosure of interest: None declared.
The role of plasma oxysterol measurement in the diagnosis of Niemann Pick C Disease in Children in Infantile Liver Disease

Marumbo Mtegha1, Teresa Hoi-Yee Wu2, Mick Henderson2, Patricia McClean1

1Leeds Teaching Hospitals NHS Trust, Department of Paediatric Hepatology, Leeds, United Kingdom
2Central Manchester University Hospitals NHS Foundation Trust, Manchester Centre for Genomic Medicine, Manchester, United Kingdom

Objectives and study: Niemann-Pick type C (NPC) is a progressive neurodegenerative disorder caused by defective lysosomal enzyme activity leading to multi-organ accumulation of cholesterol. It has autosomal recessive inheritance and is caused by mutations in NPC1 and NPC2 genes.

Children with liver disease with suspicion of NPC undergo extensive investigations including: white cell enzyme activity, bone marrow aspirate and liver biopsy. These are not specific or sensitive for NPC.

The diagnostic standard is filipin staining of cultured fibroblasts following skin biopsy and DNA analysis. Assay results are not available for up to 6 weeks due to technical requirements.

Cellular oxidative stress in NPC leads to formation of oxidised cholesterol products (oxysterols) identified as biomarkers specific to NPC. 3 biochemical species of oxysterols are known to be produced by non-enzymatic processes. These are 3β,5α,6β–cholestane-triol (3β,5α,6β–triol), 7β-hydroxycholesterol and 7-ketocholesterol.

We report our experience in the use of this new assay in the investigation of children presenting to our unit the in the past 20 months

Methods: Patients presenting to our centre who had 3β,5α,6β–triol levels measured were selected. Records were obtained to gain follow up status and document all investigations undertaken. 3β,5α,6β–trio levels were measured using the liquid chromatography-tandem mass spectrometry.

Results: 6 cases were identified (M:3). Median age at time of oxysterol measurement was 4.5 months (range 0.5-82 months). All patients presented with hepato-splenomegaly. 2/6 were not cholestatic. Of these, there were no significant differences in serum bilirubin & lipid profiles.

3β,5α,6β–trio levels were elevated in all patients. 2/6 had levels greater than 6X the normal range. These cases were confirmed as NPC on mutational analysis.

Table:

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (months)</th>
<th>Clinic</th>
<th>3β,5α,6β-triol ng/ml</th>
<th>WCE</th>
<th>Filipin Stainin</th>
<th>BMA</th>
<th>Liver Biops</th>
<th>Genetic s</th>
<th>Diagnosi s</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>F</td>
<td>2</td>
<td>HSM, CH</td>
<td>335.6</td>
<td>Raised</td>
<td>POS</td>
<td>POS</td>
<td>POS</td>
<td>POS NPC</td>
</tr>
<tr>
<td>B</td>
<td>F</td>
<td>7</td>
<td>HSM, TA</td>
<td>244.6</td>
<td>Raised</td>
<td>POS</td>
<td>*</td>
<td>*</td>
<td>POS NPC</td>
</tr>
<tr>
<td>C</td>
<td>M</td>
<td>82</td>
<td>HSM</td>
<td>41</td>
<td>NEG</td>
<td>*</td>
<td>*</td>
<td>NEG</td>
<td>Unknown</td>
</tr>
<tr>
<td>D</td>
<td>M</td>
<td>0.5</td>
<td>HSM, CH</td>
<td>72</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>Neonatal Sclerosin Cholangitis</td>
</tr>
<tr>
<td>E</td>
<td>F</td>
<td>7</td>
<td>HSM, CH</td>
<td>50.7</td>
<td>NEG</td>
<td>NEG</td>
<td>*</td>
<td>NEG</td>
<td>Unknown</td>
</tr>
<tr>
<td>F</td>
<td>M</td>
<td>1</td>
<td>HSM, CH</td>
<td>69.1</td>
<td>Raised</td>
<td>NEG</td>
<td>NEG</td>
<td>NEG</td>
<td>Unknown</td>
</tr>
</tbody>
</table>
HSM = hepato-splenomegaly, TA = transaminitis, CH = cholestasis
WCE = white cell enzyme activity (measuring chitotriosidase)
BMA = bone marrow aspirate, POS = positive result, NEG = negative result, NPC = Niemann Pick C disease
* = not performed
Reference range 3β,5α,6β-triol levels = 8.1-37.7ng/ml

**Conclusion:** 3β,5α,6β-triol levels may be mildly elevated in children with liver disease. Greatly elevated 3β,5α,6β-triol levels (6 times the upper limit of normal) correctly identified patients with NPC in our case series.

Larger cohorts will help in establishing specific references ranges in liver disease.

The assay represents a potential quick, non-invasive and specific method for correctly identifying patients with NPC that may lessen the need for invasive investigation.

**Disclosure of interest:**
“None Declared”
Study of Familial Tendency and PNPLA3 Polymorphism in Pediatric Non Alcoholic Fatty Liver Disease

Vikrant Sood¹, Seema Alam², Dinesh Rawat², Rajeev Khanna², Shvetank Sharma²

¹Institute of Liver and Biliary Sciences, Pediatric Hepatology, New Delhi, India
²Ilbs, Delhi, India

Objectives and study: Nonalcoholic fatty liver disease (NAFLD) is one of the most common liver disease worldwide both in adults as well as in children. There is a strong suggestion that familial/genetic factors are a major determinant of whether an individual will have NAFLD or not. No data on family clustering and PNPLA3 polymorphism in pediatric population is available from Indian subcontinent. We, therefore, aimed to establish correlation of pediatric NAFLD with predictive metabolic risk factors and PNPLA3 polymorphism in families.

Methods: As observational, prospective study was performed including overweight/obese children (aged 8-18 years) with or without NAFLD (ultrasonography based) and their parents. Detailed evaluation of subjects was done including metabolic screening, PNPLA3 I148M polymorphism and liver biopsy (as applicable).

Results: A total of 65 patients completed the study with fifty patients included in the NAFLD and 15 patients in the non NAFLD group. In the NAFLD group, in more than 3/4ths of the families, atleast one of the parents had shown evidence of fatty liver (82%) or low HDL (84%). Similarly there was high incidence (> 2/3rd) of IR, HTN and high TG in atleast one of the parents in NAFLD group. Metabolic syndrome was diagnosed in one-third (36 %) of the NAFLD cases versus 10 % in non NAFLD group. Homozygosity (GG status) and heterozygosity (CG status) for PNPLA3 polymorphism was seen in 34 % and 28 % of NAFLD patients respectively.

Higher HOMA 1 & 2 indices, higher systolic BP, higher weight, higher BMI, higher ALT, higher uric acid, higher cholesterol, lower HDL, higher insulin levels in the children as well as presence of IR in any one parent were risk factors significantly associated with NAFLD in overweight/obese children on univariate analysis. Presence of NAFLD in both parents, presence of acanthosis in the children and PNPLA3 homozygosity in the children were found as independent risk factors. Presence of fatty liver in both parents (11.47 fold higher risk), presence of acanthosis (10.25 fold higher risk) and homozygosity for PNPLA3 polymorphism in children may independently predict occurrence of NAFLD. Presence of NAFLD in both parents, presence of acanthosis nigricans and homozygosity for PNPLA3 polymorphism had high specificity (93.3 %, 86.7 %, 100 %) and positive predictive value (95.7 %, 93.1 %, 100 %) respectively.

Conclusion: Pediatric NAFLD is not an uncommon problem in Indian population with upto one-third showing evidence of frank metabolic syndrome. There is significant prevalence and family clustering of metabolic risk factors and PNPLA3 polymorphism in such children. Presence of NAFLD in both parents, presence of acanthosis in the children and PNPLA3 homozygosity in the children can predict occurrence of NAFLD in progeny. This data could guide us to prognosticate the families so as to allow better management and prevent future risk of various metabolic complications.

Disclosure of interest: None declared (for all authors)
Capturing t-cell receptors - a potential new modality for targeting hepatic tumours and post-transplantation lymphoproliferative disease (PTLD)

Nicola Ruth¹, David Millar², Sarah Penny³, Deirdre Kelly¹, Lora Steadman³, Nico Buettner³, Paloma Garcia⁵, Paisley Trantham⁴, Donald Hunt⁴, Khalid Sharif¹, Graham Anderson³, Mark Cobbold²

¹Birmingham Children's Hospital, Hepatology, Birmingham, United Kingdom
²Harvard Medical School, Boston, United States
³University of Birmingham, Immunology, Birmingham, United Kingdom
⁴University of Virginia, Chemistry, Virginia, United States

Objectives and study: Malignant cells express specific proteins on their cell surface. It is widely believed that it is these proteins that the immune system uses to recognise tumours and eventually eradicate them. When this process goes wrong, a tumour forms.

Aim: (1) To identify tumour specific MHC class I phosphopeptide antigens on lymphoblastoid cell lines LCL’s (an in vitro model for PTLD) as well as hepatic tumour tissues. (2) T-cells are immune cells which are notoriously difficult to maintain in long-term culture and as a result it is difficult to establish an ‘off the shelf’ T-cell product, however the aim of this project was to explore potential modalities for capturing the T-cell receptor (TCR), important in recognising tumour specific antigens and the resultant product could be used to establish a non patient-specific, but tumour specific product.

Methods: Paediatric and adult patients were identified with hepatic malignancy and consented as per current policy. Cells were isolated and tumour specific phosphopeptide antigens were identified. These provide the targets for T-cells, and more specifically TCR’s. Having identified these antigens, modalities have been explored for expanding these cells. Human Induced Pluripotent Stem Cell (hiPSc) technology was used to immortalise target T-cells of interest. Other modalities were subsequently used to transform these cells into stable T-cell products.

Results: A number of novel phosphopeptide antigens have been identified both in vitro as well as on patient tissues. This information has been used to identify potential T-cell targets and by formation of hiPSc we have established a method for expanding specific T-cell’s in vitro. Following on from this we have developed a technology for expanding these and transforming them into a target cell of interest with potential for future clinical application in paediatric tumours.

Conclusion: Identifying a modality for expanding cells with a specific TCR repertoire clearly allows us to target tumour specific phosphopeptide antigens and has the potential to be developed as an immunomodulatory therapy in patients with hepatic tumours or PTLD.

Disclosure of interest: “None Declared”. 
Objective and study: While the neurotoxic effects of increased ammonia have been extensively studied, the effects of ammonia on hepatocytes have been less characterized. Histopathological changes in the livers of patients with urea cycle defects, whom are often repeatedly exposed to high ammonia levels, may indicate that ammonia affect the liver as well. The purpose of this study was to investigate how ammonia affects hepatocytes considering metabolic activity, urea production and gene expression of some selected genes.

Methods: HepG2 (hepatocellular carcinoma) and H1 (human embryonic stem cell line differentiated to hepatocyte-like cells) cells were incubated with ammonium chloride or ammonium acetate. Metabolic activity was assessed with MTT assay, and production of urea was measured by an enzymatic method. Gene expression analysis was assessed with quantitative real-time PCR. Data are given as mean ± standard deviation.

Results: Incubation with 10 mmol/L ammonium chloride or ammonium acetate for 24 hours reduced metabolic activity in HepG2 cells measured as MTT cleavage to 75 ± 4%, n=3 and 75 ± 2%, n=4 of controls, respectively. Extending the incubation to 48 hours for ammonium acetate lowered the MTT cleavage further to 56 ± 2% of controls, p<0.01, n=3. A similar pattern was shown for ammonium chloride. Incubation with 10 mmol/L ammonium chloride for 48 hours significantly increased production of urea (p<0.01) in both HepG2 (4.3 ± 0.3 mmol/L, n=3) and H1 (17.8 ± 0.6 mmol/L, n=3) cells compared to controls, 1.7 ± 0.09 mmol/L (n=6) and 1.0 ± 0.04 mmol/L (n=3), respectively. Ammonium chloride (10 mmol/L) significantly increased mRNA level of aquaporin 8 (AQP8) after 24 hours (1.67 ± 0.04 change fold of controls, n=3) and 48 hours (4.22 ± 0.41 change fold of controls, n=4). Similar results were obtained with ammonium acetate. Ammonium chloride did not significantly change expression of multidrug resistance protein 4 (MRP4).

Conclusion: Ammonium dose-dependently reduced metabolic activity in HepG2 cells and increased formation of urea. Ammonium increased the expression of mRNA AQP8, but did not affect mRNA expression of MRP4.

Disclosure of interest: The authors have nothing to disclose.
Leukocyte MMP-2, TIMP-2 and IGF-1R expression are preferentially increased in children with NAFLD as compared to their healthy obese counterparts

Wojciech Janczyk, Joanna Trojanek, Piotr Socha, Aldona Wierzbicka, Lidia Gackowska, Izabela Kubiszewska, Mieczyslaw Szalecki, Jacek Michalkiewicz

1Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
2Children’s Memorial Health Institute, Clinical Microbiology and Immunology, Warsaw, Poland
3Children’s Memorial Health Institute, Biochemistry and Experimental Medicine, Warsaw, Poland
4Collegium Medicum Nicolaus Copernicus University, Immunology, Bydgoszcz, Poland
5Children’s Memorial Health Institute, Endocrinology, Warsaw, Poland

Objectives and study: Non-alcoholic fatty liver disease (NAFLD) and obesity are related to a low-grade systemic inflammation, vascular remodeling, visceral obesity, insulin resistance and dyslipidemia. Peripheral blood leukocytes may act as highly sensitive responders to many inflammatory stimuli that appear in the course of NAFLD and obesity. The aim of this study was to assess leukocyte gene expression profiles of mediators engaged in extracellular matrix degradation and inflammation in NAFLD compared to obese children.

Methods: The study included: 35 NAFLD children (diagnosed by combination of US and increased ALT) aged 14.2±2.6 years and 27 obese children aged 12.3±2.6yrs. Total leukocyte mRNA expression levels were analyzed by quantitative RT-PCR (real-time reverse transcriptase-polymerase chain reaction). Relative target gene expression level, compared to control group of healthy lean subjects was normalized by expression of the reference gene - G3DPH. The expression of MMPs (MMP-9, MMP-2, MMP-12, MMP-14), their inhibitors: TIMP-1, TIMP-2 as well as insulin like growth factor -1 receptor (IGF-1R), transforming growth factor beta (TGF-beta) and interleukin-6 (IL-6) were tested.

Results: We found that obese children had increased leukocyte MMP-9 (5.2±7.4), MMP-12 (2.2±2.5), TIMP-2 (1.5±1.4), IGF-1R (1.7±0.85) but low MMP-2 (0.62±0.84) expression levels as compared to the lean controls. The children with NAFLD had also elevated MMP-9 (5.6±8.2) and MMP-12 expression (3.3±5.2) but their MMP-2 expression levels (3.6±8.1) were higher than those in the obese ones (p<0.01). TIMP-2 (3.9±4.3) and IGF-1R (3.8±4.9) were slightly increased in NAFLD (p<0.05). Leukocyte MMP-2 expression levels in NAFLD were positively related to SDS-BMI (R=0.36) and selected parameters of liver function: ALT (R=0.4) and GGTP (R=0.5) as well as total cholesterol (R=0.37) and LDL-C (R=0.35).

Conclusion: NAFLD leukocytes differ from their non-NAFLD obese counterparts by relatively higher expression of MMP-2, TIMP-2 and IGF-R1. Increase in TIMP-2 (potential role in MMPs inhibition) and IGF-R1 (pro-fibrotic effects) may indicate pro-fibrotic potential of leukocytes infiltrating the liver. Increase of MMP-2 may reflect ongoing systemic inflammation.

Disclosure of interest: None Declared.

This project was supported by a grant number UMO-2011/01/B/NZ6/02661 from National Science Centre, Poland.
Further Evidence of Immune Mediation in Extrahepatic Biliary Atresia

Mohamed Shagranì¹, Martin Burdelski¹, Hussah Alhussini²

¹King Faisal Specialist Hospital & Research Center, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia
²King Faisal Specialist Hospital & Research Center, Department of Pathology, Riyadh, Saudi Arabia

Objectives and study: The etiology of Extrahepatic Biliary Atresia (EBA) is still unknown. It’s most likely that different etiologies are inducing this rapidly progressing cholestatic disease (1). Without liver transplantation the prognosis of these patients is poor (2). The experience of a recent ABO-Incompatible liver transplantation in a child with EBA who we suspected acute antibody-mediated (humoral) rejection confirmed by C4d immunofluorescence staining, but there was no signs of humoral antibody induced liver damage. This observation raised the hypothesis of immune mediation in Biliary Atresia so we did our retrospective study.

Methods: Twelve patients out of 196 patients were enrolled in our study (8 boys, 4 girls, and mean age at transplant, 14 months). They had received Living Donor Liver Transplantation (LDLT) 11 patients and one had cadaveric liver transplantation between November 2011 and December 2014. All was alive and/or followed-up for more than one yr and retrospectively investigated.

6 patients with EHB, 3 patients with Crigler Najar Syndrome and 3 patients with Progressive Familial Intrahepatic Cholestasis type 2 (PFIC2).

All explanted liver biopsies for all patients were tested for C4D Staining.

A rabbit polyclonal anti-human C4d antibody (BIOMEDIA, BL-RC4D, 1:50 dilution) was used to detect C4d. Sections were treated with protease (Ventana, 0.5 U/mL) at 37 °C for 20 minutes for antigen retrieval. C4d immunostaining using formalin-fixed, paraffin embedded tissue was available in our laboratory since August 2010, but it was applied only to selected cases and was not used routinely before this study. Staining was recorded as diffuse when linear C4d deposition around the portal tract vascular endothelium was seen in 50% or more of portal tracts. Staining of fewer than 50% of portal tracts was considered focal.

Results: All cases with EBA reported as positive for C4D based on our criteria of finding linear C4D deposition around the portal tract vascular endothelium both venin and artery but nothing was seen either around the hepatocytes or the sinusoidal space. The three cases with CNS and the rest with PFIC2 all reported as negative as no C4D deposition could be detected on liver biopsy.

Conclusion: Historically, EBA is an inflammatory cholangiopathy of still undetermined etiology. Correlations between histologic findings and clinical outcome in this disease have largely been based on evaluation of liver parenchyma. New data published recently(1) showed association between specific inflammatory cell subtypes within the fibrous plate and the length of transplant-free interval also supports the role of the immune system in the initial process of bile duct damage in biliary atresia. Our data support this hypothesis and add more evidence that EBA has a progressive immune-mediated injury of the biliary system.

Disclosure of interest: No conflict of interest, “None Declared”.
Serum resistin elevation occurs specifically in the NAFLD in children

Aldona Wierzbicka¹, Joanna Trojanek², Wojciech Jańczyk³, Lidia Gackowska⁴, Izabela Kubiszewska⁵, Mieczysław Szalecki⁶, Jacek Michalkiewicz⁷, Piotr Socha⁷

¹The Children's Memorial Health Institute, Department of Biochemistry, Radioimmunology and Experimental Medicine, Warsaw, Poland
²The Children's Memorial Health Institute, Department of Clinical Microbiology and Immunology, Warsaw, Poland
³The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology and Eating Disorders, Warsaw, Poland
⁴Collegium Medicum, Umk, Department of Immunology, Bydgoszcz, Poland
⁵Collegium Medicum Nicolaus Copernicus University, Department of Immunology, Bydgoszcz, Poland
⁶The Children’s Memorial Health Institute, Department of Endocrinology, Warsaw, Poland
⁷The Children's Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland

Objectives and study: Obesity is related to systemic chronic, sub-acute inflammatory responses and hormonal dysregulation of weight control which can lead to organ injury including cardiovascular and liver damage. Still, some specific features of immune disturbances seem to lead to liver steatosis and fibrosis which develop only in vulnerable obese subjects. We aimed to assess the serum levels of certain immune and hormonal regulators to find out if they differ in the groups of NAFLD and obese children.

Methods: The study included: 35 NAFLD children aged 13.44 ± 2.81 years, 26 obese children aged 14.57 ± 2.02 years, and 39 healthy lean controls aged 13.29 ± 3.81 years. Plasma levels of sCD14, IL-1beta, IL-6 as well as leptin and resistin concentrations were evaluated by ELISA test. We used Mann-Whitney U test for two groups comparisons and Spearman R test for testing associations.

Results: The NAFLD children as compared to their obese counterparts were characterized by highly elevated resistin elevation (6.30 ± 6.2 vs 3.85 ± 1.7 ng/mL, p=0.03) with no changes in the other parameters tested. Both the NAFLD and obese children as compared to the lean controls had increased concentrations of leptin (17.1 ± 14.5 vs 13.7 ± 6.5 vs 2.4 ± 1.7 ng/ml) and sCD14 (1317 ± 145 vs 1354 ± 198 vs 1047 ± 186 ng/ml). The following correlations were found in the NAFLD children: sCD14 vs WHR (R=0.391), IGF-1R vs TG (R=0.371), resistin vs ALT (R=0.509) and AST (R=0.486) and leptin vs waist circumference (R=0.429), and IL-6 vs TG (R=0.379).

Conclusion: Increase in resistin levels was specific for NAFLD possibly reflecting macrophages inflammatory status (both in the liver and adipose tissue). The levels of other serum mediators tested did not significantly differ between obese and NAFLD children. Only leptin and sCD14 levels were equally elevated in both in the NAFLD and obese children as compared to the lean control. Overall, the data obtained strongly suggest early contribution of resistin to liver steatosis in the course of NAFLD in children (insulin resistance induction).

Disclosure of interest: None Declared.

This project was supported by a grant number UMO-2011/01/B/NZ6/02661 from the National Science Centre, Poland.
Iron Overload In The Liver of Two Children: Nonalcoholic Steatohepatitis and Juvenile Hemochromatosis

Aysel Ünlüsoy Aksu1, Angela Caleffi2, Antonello Pietrangelo3, Sinan Sari1, Ödül Eğritaş Gürkan1, Zeliha Demirtaş1, Güldal Yılmaz4, Buket Dalgıç1

1Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
2University Hospital of Modena, Division of Internal Medicine 2 and Center for Hemochromatosis, Modena, Italy
3Azienda Ospedaliero-Universitaria Policlinico DI Modena, Internal Medicine, Modena, Italy
4Gazi University, Pathology, Ankara, Turkey

Objectives and study: Iron overload disorders are hereditary hemochomatosis (HH) and secondary etiologies other than HH. There are few reports about iron overload in childhood excluding hematological disorders. Here we present two children with juvenile hemochromatosis and NASH-related iron overload are the genetic and secondary causes, respectively.

Methods: Patient 1: A fifteen-year old boy was admitted to hospital with fatigue and an increase of transaminases levels, glucose, uric acid, transferrin saturation (TS), ferritin. He had central obesity, his body mass index was 306 kg/m². During follow-up, insulin resistance and high blood pressure were diagnosed; metformin and calcium channel blocker were initiated. Blood tryglyceride was 418 mg/dl. Abdominal ultrasound showed diffusely increased echogenicity of the liver, probably secondary to moderate steatosis. Abdominal magnetic resonance imaging (MRI) showed no evidence in favor of iron overload in any organ. Liver biopsy revealed severe steatosis (80%), minimal fibrotic activity, and mild accumulation of hemosiderin. The treatment with weekly phlebotomy for 8 weeks reduced TS to 19%, and the serum ferritin concentration decreased to 37 ng/ml; aminotransferases fell to normal, and phlebotomy was suspended. The patient was disagreed with the recommended diet and exercise. So the patient’s iron tests and aminotransferases are alternating. Phlebotomy is performed bimonthly or trimonthly.

Patient 2: This 15-year-old boy was referred to the pediatric gastroenterology department for elevated serum TS and ferritin concentrations and hair loss. He was on 25th percentile for weight and on 50th percentile for height. Abdominal MRI showed that T2-weighted signal intensity was lower in the liver parenchyma and pancreas versus the spleen and iron overload in the pancreas. Liver biopsy revealed mild periportal fibrotic activity and severe hepatocellular citoplasmic and periportal iron deposits. Mutation analysis showed hepcidin antimicrobial agent gene (HAMP) homozygous mutation and he was diagnosed with juvenile hemochromatosis. He was treated for 14 weeks with weekly phlebotomy. According to the iron tests, phlebotomy was required 3 times in 12 months.

Results: Both patients benefited from phlebotomy even if they had different etiologies.

Table: Laboratoty and clinical characteristics of two patients

<table>
<thead>
<tr>
<th></th>
<th>Patient 1</th>
<th>Patient 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin (g/dl)</td>
<td>15</td>
<td>14</td>
</tr>
<tr>
<td>TS (normal:16-45%)</td>
<td>87</td>
<td>91</td>
</tr>
<tr>
<td>Ferritin (normal:22–322 ng/mL)</td>
<td>735</td>
<td>495</td>
</tr>
<tr>
<td>AST (normal:5-40U/L)</td>
<td>98</td>
<td>22</td>
</tr>
<tr>
<td>ALT (normal:5-40U/L)</td>
<td>141</td>
<td>28</td>
</tr>
<tr>
<td>Uric asid (normal:202-416 micromol/L)</td>
<td>487,7</td>
<td>309,3</td>
</tr>
</tbody>
</table>
**Table:**

<table>
<thead>
<tr>
<th>Test</th>
<th>Value 1</th>
<th>Value 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulin (normal: 3-25 mU/L)</td>
<td>28.9</td>
<td>15</td>
</tr>
<tr>
<td>Hepatic iron concentration</td>
<td>16.5</td>
<td>120.7</td>
</tr>
<tr>
<td>(normal: 5-40 micromol/g)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hepatic iron index (normal &lt;2)</td>
<td>1.1</td>
<td>8.05</td>
</tr>
</tbody>
</table>

*ALT: Alanine amino transferase; AST: Aspartate amino transferase*

**Conclusion:** In childhood, the diagnosis of iron overload syndromes is crucial because they do not confront us with obvious symptoms and findings. Early initiation of a phlebotomy program before the onset of clinical manifestations can prevent mortality, especially in cases of juvenile hemochromatosis. In addition, NASH might lead to iron overload and iron overload might aggravate the clinical course of NASH. In patients with iron overload symptoms and/or findings, HH must be excluded, but other chronic liver diseases like NASH should be kept in mind.

**Disclosure of interest:** None Declared. Informed consent was obtained from both individuals included in the study.
Autoimmune Liver disease in Children with Sickle Cell Disease

Suttiruk Jitraruch¹, Emer Fitzpatrick¹, Maesha Deheragoda², Giorgina Mieli-Vergani³, Sue Height¹, Nedim Hadzic⁴, Marianne Samyn⁵

¹King's College Hospital, London, United Kingdom
²King's College Hospital, Institute of Liver Studies, London, United Kingdom
³King's College London School of Medicine at King's College Hospital, London, United Kingdom
⁴King's College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom
⁵King's College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom

Objectives and study: Sickle cell disease (SCD) is an autosomal recessive haemoglobinopathy resulting in intermittent haemolysis and microvascular occlusions. Hepatic involvement varies from asymptomatic gallstones to life-threatening acute liver failure (ALF) and cirrhosis. The aim of this study was to characterise the clinical features, natural history and outcome of autoimmune liver disease (AILD) in patients with SCD.

Methods: We performed a retrospective review of SCD patients with hepatic dysfunction referred to our centre from 1999-2015. The demographic, clinical, laboratory, histological and radiological features, management and outcome were studied. The diagnostic criteria included: positive serum autoantibodies, hypergammaglobulinemia, compatible histology and absence of viral/metabolic causes.

Results: Eighty-three SCD patients with hepatic dysfunction were identified. Six who presented with neonatal cholestasis were excluded. Of 77 patients, 13 (17%) were diagnosed with AILD and 2 had fulfilled criteria for systemic lupus erythematosus. The 13 patients with AILD (10 female) were diagnosed at a median age of 11 (range, 3.4-16) years. Eleven were homozygote for HBSS and 2 required regular transfusions. Family history for autoimmune disease was positive in 2. Two patients presented with ALF (INR 2.7 and 1.8). In two patients parvo B19 induced aplastic crisis preceded AILD diagnosis, 2 and 6 months, respectively. At presentation, anti-nuclear and anti-smooth muscle autoantibodies were in range 1/20-1/2560 and 1/10-1/320, respectively, median AST 294 (range, 67-814) U/L, IgG 33.5 (range, 13.7-43.7) g/L and INR 1.32 (range, 1.01-2.7). Ultrasonography showed enlarged lymph nodes at porta/superior to pancreas in 4, gall stones in 3, and splenomegaly in 5 patients. On MRCP five children had radiological features of cholangiopathy; 4 at presentation and 1 three years later. Liver biopsy was performed in 11 (6 via transjugular route) without complications; 9 showed interface hepatitis without cholangiopathy, one obtained after treatment and another one was inadequate. Treatment included ursodeoxycholic acid (12), prednisolone (12), azathioprine (8) and mycophenolate mofetil (1). After a median follow up of 3.8 (range, 0.2-14.3) years, 10 patients are alive with 2 lost to follow up. One patient died following intracranial haemorrhage. One patient required liver transplantation, 6.4 years after diagnosis due to recurrent biliary sepsis. Four patients were in full and five in partial remission. Four patients (2 males) were diagnosed with ulcerative colitis 2 before and 2 after AILD.

Conclusion: AILD is not uncommon in patients with SCD with a strong female preponderance. It responds well to standard treatment. Liver biopsy can be helpful to confirm the diagnosis. Ulcerative colitis was more common in the boys and should be excluded.

Disclosure of interest: “None Declared”.
HEPATOLOGY: General Hepatology

H-P-008

Kasai portoenterostomy in Biliary Atresia- single centre experience with adjuvant therapy

Sanjay Rajwal¹, Naved Alizai¹, Suzanne Davison¹, Patricia McClean²

¹Paediatric Liver Unit, Leeds General Infirmary, Leeds, United Kingdom
²Leeds Teaching Hospitals NHS Trust, Department of Paediatric Hepatology, Leeds, United Kingdom

Objectives and study: Biliary atresia (BA) is a cholangiopathy of unknown cause requiring timely referral for Kasai portoenterostomy (KP). Steroids are used following KP with a variable success rate. Objective of this study was, to determine the success of KP in a single centre cohort of children who received adjuvant therapy.

Methods: Retrospective analysis of database and case notes of all children with biliary atresia from Jun 1994 - Jul 2015. Children who received adjuvant therapy following KP were included in the study. Adjuvant therapy consisted of : oral dexamethasone 0.3mg/kg twice daily for 5 days, 0.2 mg/kg twice daily for 5 days, 0.1 mg/kg twice daily for 5 days, beginning on postoperative day 5 (along with ranitidine). In addition to steroids, oral ursodeoxycholic and phenobarbitone were given until 1yr of age. All children received intravenous antibiotics postoperatively for 5 days then prophylactic antibiotics for another 4 weeks.

Results: 179 children with BA were identified, of which 164 underwent KP. Fifteen did not undergo KP due to late presentation or cirrhosis (10), anatomical reasons (3), co-existing life limiting conditions (2). Nine children were excluded as they were participants in a trial which required them not to receive adjuvant therapy. 155 children were therefore studied, of which 22 (14%) had biliary atresia splenic malformation syndrome (BASM).

KP was performed at a median age of 49 d (10 - 144). Seventy two percent of children (112/155) cleared jaundice (serum bilirubin < 20 µmol/L). The median age of KP in those who cleared jaundice was 49 d (10 - 99) v not cleared jaundice 51d (11 - 144). After a median follow up of 6.1y (0.3- 21), 59% children (91/155) were alive with native liver and 55/155 needed liver transplant (4 died post transplant). Another nine children died either waiting for liver transplant (3) or associated illnesses( 6).

Conclusion: Using adjuvant therapy 72 % of children had a successful KP. This compares very favourably with clearance of jaundice rates in major paediatric hepatobiliary centres elsewhere in the world. Adjuvant therapy may have a role in contributing to these good outcomes.

Disclosure of interest: “None Declared”.
Long-term developmental outcome in extremely preterm infants with cholestasis

Jonas Teng1, Emelie Öberg2, Björn Fischler3, Antal Nemeth4, Kajsa Bohlin5

1 Södertälje Hospital and Karolinska Institutet, Dept. of Pediatrics and Dept. of Clinical Science, Intervention and Technology (Clintec), Stockholm, Sweden
2 Karolinska Univ Hospital and Karolinska Institutet, Dept. of Pediatrics and Dept. of Clinical Science, Intervention and Technology (Clintec), Stockholm, Sweden
3 Dept. of Pediatrics, Karolinska University Hospital, Clintec, Stockholm, Sweden
4 Karolinska University Hospital, Alb Childrens’ Hospital, Pediatric Gastroenterology, Hepatology & Nutrition, Stockholm, Sweden
5 Karolinska Institutet, Dept. of Pediatrics and Dept. of Clinical Science, Intervention and Technology (Clintec), Stockholm, Sweden

Objectives and study: Cholestasis is common among extremely preterm babies. The developmental outcome among cholestatic patients may theoretically be hampered by deficiencies in fat-soluble vitamins and essential fatty acids second. However, data on this topic are scarce. The objective of this study was to examine long-term motor, language and cognitive outcome at age 2.5 years among extremely preterm infants with cholestasis.

Methods: EXPRESS (Extremely Preterm Infants in Sweden Study) is a prospective national cohort study of infants born before 27 full weeks of gestation in 2004-2007. At 30 months of corrected age, development was assessed using Bayley scales of infant and toddler development, third edition (BSID-III). Live born infants within EXPRESS, born or treated in Stockholm County, were included and those who had neonatal cholestasis were identified retrospectively through medical chart reviews. Cholestasis was defined as conjugated s-bilirubin ≥30 µmol/L (approx. 1.8 mg/dL), with a ratio of conjugated to total serum bilirubin exceeding 20% on at least two occasions before discharge from the neonatal unit. Non-cholestatic infants formed the control group, and BSID-III composite scores were compared between groups.

Results: The incidence of neonatal cholestasis was 17.8% (31 out of 174 infants) in the Stockholm EXPRESS cohort. BSID-III assessment at 30 months of corrected age was performed in 81 infants, 16 cholestatic and 65 non-cholestatic. Of remaining 93 infants (15 cholestatic), 38 had died, 7 moved out of the County and 48 declined participation or were lost to follow-up. Significantly lower median motor composite score was seen among infants with neonatal cholestasis compared to non-cholestatic controls (Table). No significant differences were seen in cognitive or language composite scores. A multivariate stepwise forward linear regression analysis was performed to identify and correct for other factors correlated to BSID-III outcome. Cholestasis remained significantly correlated to lower motor composite score (p=0.007) when adjusted for the variables most strongly correlated to lower motor score, i.e. postnatal steroids given (p=0.028) and days on respiratory support (p=0.043).

Table:

Univariate analysis of BSID-III composite scores at 30 months corrected age

<table>
<thead>
<tr>
<th></th>
<th>Cholestasis n=16</th>
<th>Controls n=65</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BSID-III’ cognitive score</td>
<td>95 (85-120)</td>
<td>95 (65-130)</td>
<td>0.22</td>
</tr>
<tr>
<td>BSID-III’ language score</td>
<td>103 (53-115)</td>
<td>97 (56-135)</td>
<td>0.91</td>
</tr>
<tr>
<td>BSID-III’ motor score</td>
<td>97 (73-112)</td>
<td>107 (73-130)</td>
<td>0.04*</td>
</tr>
</tbody>
</table>

*Statistical significance, p <0.05. Data presented as median (range).
**Conclusion:** Neonatal cholestasis in extremely preterm infants is associated with impaired motor development at 2.5 years of age, but not with cognitive or language function. If there is a link to fat malabsorption and brain growth remains to be further elucidated.

**Disclosure of interest:** None declared.
Role of different cytokine polymorphisms in predicting the response to Pegylated interferon alfa-2a plus ribavirin in Egyptian children with chronic hepatitis C genotype 4

Sana Barakat1, Wessam El-Gendy2, Dalal El-Gezery2, Mona Abd El-Kader3, Amal Mansou2, Eman Shehata5, Shireen Hefny2

1University of Alexandria, Faculty of Medicine, Pediatrics, Alexandria, Egypt
2Faculty of Medicine, University of Alexandria, Clinical and Chemical Pathology, Alexandria, Egypt
3Faculty of Medicine, University of Alexandria, Pathology, Alexandria, Egypt
4Faculty of Medicine, University of Alexandria, Pediatrics, Alexandria, Egypt

Objectives and study: Information about treatment predictors, and even the response rates, in children with chronic hepatitis C (CHC), genotype 4 is limited. The aim of this study was to investigate the ability of different factors including the genotype polymorphism of a panel of cytokines, with a known role in the modulation of immune responses and subsequently the antiviral response, in predicting the response to Pegylated interferon (PEG-INF) and ribavirin(RBV) in a group of Egyptian children with CHC, genotype 4.

Methods: 57 children aged 5-17 years (48 males&8 females) with previously untreated CHC, Genotype 4 were analyzed for single nucleotide polymorphisms of interleukin(IL) IL-28B, IL-10, IL-6, interferon-gamma(IFN-γ), tumor necrosis factor-alpha (TNF-α), transforming growth factor-beta (TGF-β) by polymerase chain reaction using sequence-specific primers (PCR-SSP). They received a dose of PEG-INF alfa-2a equivalent to the dose licensed for adults based on calculated conversion to body surface area (BSA) [BSA/1.73x160ug /week] plus RBV (15 mg/kg/day) for 48 weeks. The primary end point was sustained virologic response (SVR). Pretreatment liver biopsy was done and evaluated using METAVIR fibrosis and activity scores.

Results: The Majority of studied children (82.5%) have low baseline viral load (<600,000 IU/ml). Concerning fibrosis, 30 (52.6%) children had no fibrosis(F0), 21(36.8%) had nonsignificant fibrosis (F1) and only 6(10.5%) had significant fibrosis (F2). The frequencies of different dimorphic polymorphisms were as follow: IL-28B- 12979860 C/T 82.5%, C/C 12.2%, T/T 5.3%; IL-10-1082 G/G 40%, A/A 37.5%, G/A 22.5%; IL-10-819 C/T 47.5%,C/C 45%, T/T 7.5%; IL-10-592 C/C 55%,C/A 37.5, A/A 7.5%; IL-6-174 G/G 67.5%, G/C 17.5%, C/C 15%; IFN γ +874 T/A 40%, T/T 35%, A/A 25%; TNF-α G/G 72.5 %,G/A 25%, A/A 2.5%; TGF-β codon10 T/T 40%, T/C 35%, C/C 25%. Overall, SVR was attained by 71.9% (41/57) of all children with higher response in older (>11y) than in younger children (<11) [86.4 vs. 62.8%. P=.05]. 77% of studied males attain SVR, versus 44% of females (p=.045), 87% of those with early virologic response (EVR) attained SVR (p=0.000).AFs were generally mild or moderate in severity, primarily flu-like symptoms. Dose was modified because of hematological AFs in 24% of children. All children continued Their treatment. SVR was not influenced by any of the studied cytokine polymorphism except for the polymorphism of IL-10-1082,where the G/A genotype which was significantly associated with bad response to treatment(p=0.016). Multi variants analysis showed that male sex, and achievement of EVR are independent predictors of SVR( Odd,s ratio and 95% CI were 0.98,0.36-0.98; 0.99,0.29-0.74 respectively). No effect of other factors like viral load, duration of infection, presence of auto antibodies, degree of fibrosis or high ALT levels was observed on SVR in this population infected with genotype 4.

Conclusion: Treatment of children with CHC with PED-IFN alfa-2a plus RBV is associated with favorable SVR rates and acceptable safety, which alleviates the long-term consequences of hepatitis C during adulthood when treatment is associated with additional negative prognostic factors. EVR, is a strong predictor of SVR in children as in adult. However, SVR in this population does not seem to be influenced by cytokine gene polymorphisms or other pretreatment predictors reported in adults.

Disclosure of interest: None Declared.
Hepatoblastoma in Explanted Livers of Patients with Biliary Atresia

Achiya Amir¹, Ajay Sharma², Ernest Cutz², Yaron Avitzur², Furqan Shaikh², Binita Kamath², Simon Ling², Anand Ghanekar², Vicky Ng²

¹The Tel-Aviv Sourasky Medical Center, The Pediatric Gi, Hepatology and Nutrition Unit, Tel-Aviv, Israel
²The Hospital for Sick Children, Toronto, Canada

Objectives and study: Surveillance of hepatic nodules for malignant transformation to hepatocellular carcinoma is important in the monitoring of patients with Biliary Atresia (BA). To-date, only two published case reports describe the finding of Hepatoblastoma (HB) in this setting. This study aimed to investigate this association of HB and BA, and to assess the utility of alpha-fetoprotein (aFP) as a marker in the diagnosis.

Methods: A retrospective study of all patients who underwent isolated liver transplantation (LTx) for the primary diagnosis of BA at a single center, between January 1999 and June 2014, was conducted. Patient demographics, pre-LTx aFP levels and histologic examination of native liver explants were reviewed.

Results: 102 (44% male, median age 11 months) patients underwent LTx for BA. Two (2%) explants examinations were confirmatory for a co-diagnosis of HB; both patients had abnormally elevated aFP. Overall, 56 (55%) patients had available pre-LTx aFP levels. In 24 (43%) patients aFP levels were always within normal range leading up to LTx surgery; 12 (21%) patients had initial elevated serum aFP levels that normalized prior to the LTx; and 20 (36%) patients proceeded to LTx surgery with abnormally elevated aFP levels. Recipients with persistently abnormal aFP levels were older at hepatopportoenterostomy (107d vs. 68d, P=0.02) and younger at LTx surgery (359d vs. 1713d, P<0.01), compared to patients with constantly normal levels.

Conclusion: In our cohort, HB was found to co-exist in approximately 2% of BA patients undergoing LTx, far exceeding the anticipated incidence of 1:10 billion for the concomitant diagnoses. Elevated serum aFP levels may be sensitive but not specific for HB in this context. Further research is required to identify specific mechanisms and risk factors.

Disclosure of interest:

Funding source: No external funding for this manuscript.

Financial disclosure: All authors have indicated they have no financial relationships relevant to this article to disclose.

Conflict of interest: All authors have indicated they have no potential conflicts of interest to disclose.
HEPATOLOGY: General Hepatology

H-P-013

Efficacy and security of TIPS in children

Etna Masip 1, Begoña Polo 1, Ester Donat 1, Maria Jesus Esteban 1, Juan Jose Vila 1, Carmen Ribes-Koninckx 1

1Hospital La Fe, Valencia, Spain

Objectives and study: The transjugular intrahepatic portosystemic shunt (TIPS) is a therapy well established in adults with portal hypertension, but it is not so frequent in children. There are only a few studies on TIPS published in pediatrics; we report three cases of children with severe portal hypertension where TIPS has been a good choice and has offered a short-term benefit and has become a therapeutic issue as a bridge to the liver transplantation.

Methods: three children with complications due to severe portal hypertension were elected to undergone TIPS placement in the last year (2015) in our center. We reviewed the clinical files and the indications and the efficacy of this therapy.

Results: three patients received TIPS in 2015. All of them had developed severe portal hypertension and were included in the waiting list for liver transplantation due to different diseases: biliary atresia, primary sclerosing cholangitis and cryptogenic liver cirrhosis. When the TIPS was placed the age of the patients was 26 months, 6.5 years and 15 years, and the median weight was 25 kg (range: 11.8 – 44.3 Kg). The indications for TIPS were: hepatic decompensation with progressively worsen hyperbilirubinemia, refractory ascites and bleeding from esophageal varices plus ascites. The TIPS was placed by the interventional radiologist accessing by the right internal jugular vein in 2 patients and by the left internal jugular vein in the other one. The youngest patient required 2 stents in the same procedure, and the other 2 patients required only 1 stent, but none of them developed any complication immediately after the procedure. The portosystemic gradient previous the TIPS was 14.3 mmHg (range 11-21mmHg), following the procedure the transhepatic gradient decreased to a mean of 4 mmHg (4-5 mmHg), which was statistically significant p<0.05. In the three cases the complications from the portal hypertension were resolved, none of them developed encephalopathy. No revision of the shunt was required in any case. Two of the cases have already received a liver transplantation (3 and 6 months after the procedure). The other patient is actually in transplant waiting list, but has not developed further episodes of bleeding and/or ascites.

Conclusion: In our series the TIPS has been a successful therapy for the portal hypertension and has acted as a bridge to the liver transplantation. 1. TIPS has shown a good efficacy in children with severe portal hypertension and refractory symptoms as gastrointestinal bleeding or ascites. 2. TIPS is a safe technique for children at any age and for the portal hypertension of different etiologies. 3. TIPS should be considered as a part of the therapy for children with portal hypertension at least in short-term or as a bridge to a liver transplantation.

Disclosure of interest: The authors do not declare any conflict of interest
Postvaccination immunity against hepatitis B virus in children

Barbara Santangelo¹, Giovanna Nardella¹, Sara Gorgoglione¹, Anna Pacilio¹, Agostino Petraccaro¹, Michele Conoscitore¹, Massimo Pettoello Mantovani¹, Angelo Campanozzi¹

¹University of Foggia, Pediatrics, Foggia, Italy

Objectives and study: A genetic predisposition was suggested to explain Hepatitis B Virus vaccine (HBVv) nonresponse. Several studies have found, in children with celiac disease (CD), an association between HBVv nonresponsiveness and "celiac HLA haplotypes". We aimed: 1) to assess the responsiveness to HBVv in a group of children; 2) to evaluate the possible link between inadequate response to HBVv and "celiac HLA haplotypes".

Methods: From November 2014 to March 2015, 158 children HBV vaccinated were recruited for measuring antiHBV antibodies (antiHBs): 25 (15.8%) with CD, 63 (39.9%) with obesity, 42 (26.6%) with poor growth and 28 (17.7%) with abdominal pain. We considered responsive antiHBs levels >25IU/ml. To estimate the role of HLA type in HBVv failure, in the subgroup with antiHBs levels <25IU/ml, HLA typing for CD was evaluated; in these patients antibodies against transglutaminase (tTGA) and endomysium (EMA) were evaluated as well.

Differences in frequencies between the groups were calculated by χ² test, considering significative values of p<0.05 (STATA MP12.1 Software).

Results: A total of 69 (43,7%) children were seronegative for antiHBs; a significantly high proportion of subjects in the celiac group (18/25 - 72%) failed to respond to HBVv (p=0.0019). There was not a statistically significant association between obesity and HBVv response (29/63 - 46%; p=0.6261). Among nonresponders, 40/69 subjects (44,4%) had celiac-genotypes, without any positivity for tTGA/EMA.

Conclusion: We suggest to investigate children for HBV immune status; nonresponders should be revaccinated to achieve the goal of universal protection. No clear association was observed between celiac-genotypes and HBVv responsiveness.

Disclosure of interest: “None Declared”.
Non-invasive assessment of liver fibrosis in children: correlations between transient elastography and biochemical markers

Tudor Lucian Pop¹, Ana Stefanescu¹, Alina Grama¹, Monica Platon², Anca Maniu², Horia Stefanescu²

¹University of Medicine and Pharmacy Iuliu Hatieganu, 2nd Pediatric Clinic, Cluj-Napoca, Romania
²University of Medicine and Pharmacy Iuliu Hatieganu, 3rd Internal Medicine Clinic, Cluj-Napoca, Romania

Objectives and study: The liver biopsy remains the gold standard for assessing liver fibrosis, but with many limitations (invasive method, sampling errors, and major risks). There is an increasing interest in the use of non-invasive methods for the assessment of liver fibrosis. The most used and validated methods in adults are the biochemical markers (FibroTest, Biopredictive) and transient elastography (FibroScan, Echosens), but with few studies in children. The aim of the study was to evaluate the correlation between these two methods in liver fibrosis evaluation in children.

Methods: We evaluated the liver fibrosis in 62 children and young adults (age between 6 months to 25 years, 35 males and 27 females) with liver diseases: chronic hepatitis B or C, Wilson disease, autoimmune hepatitis, glycogen storage disease, cirrhosis and other. We used non-invasive methods, both biochemical markers and transient elastography for 87 measurements. We analysed the relationship between the evaluations of fibrosis obtained by both methods. Due to different ways of grouping fibrosis stages using these methods, we have analysed the results using the following groups: no fibrosis (F0), moderate fibrosis (F1 and F2 by transient elastography and F0-F1, F1, F1-F2, F2 by biochemical markers), severe fibrosis (F3) and cirrhosis (F4).

Results: Biochemical markers scores were between 0.06-0.98 and transient elastography results were between 2.8 to 75 kPa. There was a very good relationship between the values obtained by the two methods (p=0.00002, r=0.4383). Also there is a good correlation when patients were grouped in different stages of fibrosis. No fibrosis was evaluated in 38 measurements using transient elastography and 24 using biochemical markers, moderate fibrosis in 46 measurements using transient elastography and 30 using biochemical markers, severe fibrosis in 7 measurements using transient elastography and 9 using biochemical markers (Pearson χ²=19.88, p=0.0186, Maximum Likelihood χ²=20.68, p=0.0141). In 12 measurements biochemical markers scored more than two stages of fibrosis compared with transient elastography. Inversely, in 8 measurements transient elastography scored more than two stages of fibrosis. Wilson disease (9 cases) and autoimmune hepatitis (four cases) respectively, were the most important causes in these different evaluations of fibrosis.

Conclusion: The results obtained using biochemical markers and transient elastography are consistent to each other. Those two methods can be used with good results for the assessment of liver fibrosis, if we respect the indications and limitations of each. Further studies are needed to assess the usefulness of these methods in children and to the validation in specific causes of liver diseases.

Disclosure of interest: Tudor L. Pop and Ana Ștefănescu funded by Partnership Grant PN-II-PT-PCCA-2011-3.2-0917.
HEPATOLOGY: General Hepatology

H-P-016

Hepatic lesions associated with McCune Albright Syndrome

Lauren Johansen¹, Wolfram Haller², Deirdre Kelly¹, Patrick McKiernan¹
¹Birmingham Children's Hospital, Paediatric Liver Unit, Birmingham, United Kingdom
²Birmingham Children's Hospital NHS Foundation Trust, Gastroenterology Department, Birmingham, United Kingdom

Objectives and study: McCune Albright Syndrome (MAS) has an estimated prevalence of 1 in 100,000 – 1 in 1000,000. It results from an early embryonic postzygotic somatic-activating mutation in the GNAS gene, encoding the cAMP pathway-associated G-protein, Gsa. Known hepatobiliary and pancreatic manifestations of MAS include neonatal cholestasis, hepatitis, hepatic adenoma, intraductal papillary mucinous neoplasm and pancreatitis. A number of studies have demonstrated a link between MAS and malignancy; however malignant hepatic lesions haven’t previously been reported.

We aim to describe the hepatic lesions associated with MAS following resolution of cholestasis.

Methods: Retrospective review of all cases of MAS presenting to a National Paediatric Liver Unit over a 20 year period (n=3).

Results: All infants had presented by 4 weeks with high GGT cholestasis, poor growth, hepatomegaly, raised liver transaminases and progressively acholic stool. Extensive diagnostic work-up was non-confirmatory. USS demonstrated gallbladder abnormalities in 2 of the infants and TIBIDA scans were non excretory. Liver biopsy showed neonatal hepatitis with associated microabscess formation in 2 cases, bile duct paucity in 2 cases, necrosis in 1 and severe cholestasis in 1. Of the 2 infants with bile duct paucity, 1 proceeded to ERCP, which showed a hypoplastic biliary tree, and the other underwent an intra-operative cholangiogram, which was normal. All infants were treated with ursodeoxycholic acid, fat-soluble vitamins and a MCT feed. In all cases cholestasis resolved by 1 year but transaminases remained raised.

MAS was diagnosed during infancy in 2 cases and in late childhood in one case. All children had café au lait skin patches and polyostotic fibrous dysplasia, 2 had renal tubular acidosis, 2 had precocious puberty and 1 developed thyrotoxicosis and prolactinoma.

1 child presented with abdominal mass and vomiting aged 5. Imaging showed a well-defined lobulated lesion involving multiple segments of the liver. AFP was raised and hepatoblastoma was confirmed on biopsy. He was treated with chemotherapy, right hepatectomy and cholecystectomy and is currently in remission.

The other 2 children developed hepatic lesions at ages 6 and 7. The lesions are progressive, increasing in both size and number, distorting the liver architecture and exerting a mass effect on the hepatic vasculature. On MRI, they show enhancement at the peripheries post contrast, followed by enhancement of the central scar on delayed imaging suggestive of atypical focal nodular hyperplasia (FNH). AFP levels are normal.

Discussion: FNH is a non-specific hyperplastic reaction to vascular abnormalities. Its cause is unknown but it may be instigated by inflammation within GNAS mutated hepatic tissue or by the associated endocrine abnormalities seen in MAS.

Hepatoblastoma is associated with Beckwith-Wiedemann syndrome and Familial Adenomatous Polyposis: both of which can have co-existent GNAS defects. GNAS defects are pro-inflammatory leading to fibrosis and STAT 3 activation in hepatic tissue.

Conclusion: Neonatal cholestasis in children with MAS resolves spontaneously. However, subsequent mass lesions seem common and appear to have a malignant potential. We theorize that the somatic activating GNAS mutation in MAS is involved in tumorigenesis within the liver and recommend that children with MAS and neonatal cholestasis undergo regular ultrasound and AFP monitoring.

Disclosure of interest: None Declared
Analysis of Hepatic Steatosis in Children (a single center experience)

Asuman Karhan1, Zuhal Akcoren2, Inci Nur Saltik Temizel1, Hulya Demir3, Hasan Ozen3, Aysel Yuce3

1Hacettepe University, Pediatric Gastroenterology, Ankara, Turkey
2Hacettepe University Faculty of Medicine, Pediatric Pathology, Ankara, Turkey
3Faculty of Medicine, Hacettepe University, Department of Pediatric Gastroenterology, Hepatology, and Nutrition, Ankara, Turkey

Objectives and study: We aim to identify the etiologies of steatosis in liver biopsies. The data was obtained retrospectively from 166 patients with hepatic steatosis diagnosed histologically.

Methods: The study included 166 patients, aged 4 months to 18 years, with hepatic steatosis diagnosed by liver biopsy between January 2005 and December 2015. Data was collected from patient files including: medical histories, baseline demographics, physical examination findings and anthropometric measurements (height, weight, body mass index Z scores based on WHO standards), biochemical findings, liver ultrasound findings and causes of hepatic steatosis. The type of steatosis (micro-/macrovesicular, or mixed), fibrosis and inflammation on biopsies were recorded. Statistical analysis was performed using the SPSS (version 18.0.0, IBM Corp). A p value of <0.05 was considered to be statistically significant. To compare the prevalence of variables among different diagnoses, chi-square or Fischer’s exact tests were used for categorical data. Student’s t test was used to compare means.

Results: Initially, 190 patients with steatosis were identified. Twenty-four (12.6%) of them were excluded due to missing information and the remaining 166 patients were included and reviewed in the analysis. Of 166 patients, 106 (64%) were male and 60 (34%) were female. The median age was 5.6 years (range, four months to 18 years). Metabolic diseases (45%), non-alcoholic fatty liver disease (NAFLD) (24%) and Wilson’s disease (11%) were the most common causes. The remaining 20% included cystic fibrosis, toxic hepatitis, mitochondrial diseases, and cholestatic hepatitis due to different causes. Macrovesicular steatosis was seen in 61% of the patients, mixed steatosis in 28%, and microvesicular steatosis in 11%. In those three major groups, macrovesicular fatty change was the most common type. Patients diagnosed as NAFLD were older with a mean age of 11±0.69 years while patients with metabolic diseases were younger with a mean age of 3±0.58 years. Fifty-eight patients had a BMI Z score of >+2, and 33 of these 58 (56.9%) patients had NAFLD. Hepatomegaly was noted in 113 (68%) of the 166 patients. Hepatosteatosis was detected by ultrasound in 55 patients (33%). Fibrosis was seen in 48% of the patients and more common in metabolic disease group, while necrosis was seen 8% of the patients and more common in the group diagnosed with Wilson’s disease. Triglyceride, total cholesterol, alanine transaminase and gamma-glutamyl transpeptidase levels were statistically different between disease groups (p<0.05).

Conclusion: The etiologies of hepatic steatosis in children are varied. The most common cause of hepatic steatosis in children is metabolic diseases, however NAFLD is another increasing cause of steatosis during childhood. Physical examinations, anthropometric measurements and laboratory tests may provide clues about the etiologies.

Disclosure of interest: We have no conflict of interest.
Studies on gut liver axis dysfunction in obese children with and without hepatic complications

Salvatore Guercio Nuzio¹, Luca Pierri¹, Martina Di Stasi¹, Marco Poeta¹, Grazia Massa¹, Jacopo Troisi¹, Massimo Boffardi¹, Pierpaolo Cavallo³, Luigi Cinquanta⁴, Doreen Ziegenhardt⁵, Claudia Mandato⁶, Ina Bergheim⁵, Pietro Vajro¹

¹Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi (Sa), Italy
²Clinical Pathology, Hospital S. Maria Dell’olmo, Cava De’ Tirreni, Italy
³University of Salerno, Department of Physics, Fisciano (Sa), Italy
⁴Laboratory Medicine, Aou of Salerno, Salerno, Italy
⁵Institute of Nutritional Sciences, University of Jena, Germany
⁶Aorn Santobono-Pausilipon, Pediatrics, Naples, Italy

Objectives and study: Gut-liver axis (GLA) dysfunction appears to play a role in obesity and obesity-related hepatic complications (HC). This study sought to concurrently explore several GLA components in a pediatric obese population with or without liver disease.

Methods: Thirty-two children (mean age 11.2 years) were enrolled: 9 normal weight (NW) controls and 23 obese (OB+) patients. Of the 23 OB(+) patients, 13 did not have steatosis (ST(-)), and 10 did have steatosis (ST+) [associated (n=7) or not (n=3) with hypertransaminasemia (HALT+)]. All subjects were characterized using auxologic, ultrasonographic, and standard laboratory parameters. Moreover, a glucose hydrogen breath test (H2BT) was performed to test for small intestinal bacterial overgrowth (SIBO), a urinary lactulose/mannitol ratio (LMR) was obtained to assess intestinal permeability (IP), and tests for transaminases, blood endogenous ethanol (ETH) endotoxin (ETX) and fecal calprotectin (FC) were also conducted.

Results: Eleven out of 23 OB(+) patients exhibited pathological LMR (p<0.05), with values paralleling the grade of liver involvement [NW < OB(+) < OB(+)ST(-)ALT(-) < OB(+)ST(+)/ALT(+) (p<0.05)]. LMR was significantly correlated with ETH (r=0.38 p=0.05) and ETX (r=0.48 p=0.015) levels. Elevated IP was a risk factor (OR > 1 p<0.002) for the development of US steatosis. SIBO was present only in obese patients and not in control patients. Fecal calprotectin levels were within normal limits in all subjects.

Table:

<p>| Urinary lactulose/mannitol (L/M) ratio, Endotoxemia, Ethanolemia and Fecal Calprotectin levels |
|-----------------------------------------------|----------------------------------------|---------------------------------|---------------------------------|---------------------------------|---------------------------------|</p>
<table>
<thead>
<tr>
<th></th>
<th>Group I</th>
<th>Group II</th>
<th>Group IIa</th>
<th>Group IIb</th>
<th>Group IIc</th>
</tr>
</thead>
<tbody>
<tr>
<td>NW</td>
<td>OB(+)</td>
<td>OB(+)ST(-)</td>
<td>OB(+)ST(+)/ALT(-)</td>
<td>OB(+)ST(+)/ALT(+)</td>
<td>OB(+)ST(+)/ALT(+)</td>
</tr>
<tr>
<td>n</td>
<td>9</td>
<td>23</td>
<td>12</td>
<td>3</td>
<td>8</td>
</tr>
<tr>
<td>LMR</td>
<td>0.017±0.005*</td>
<td>0.039±0.034</td>
<td>0.022±0.026*</td>
<td>0.055±0.015*</td>
<td>0.059±0.039*</td>
</tr>
<tr>
<td>Endotoxemia</td>
<td>0.049±0.012</td>
<td>0.054±0.030</td>
<td>0.049±0.012</td>
<td>0.038±0.019</td>
<td>0.068±0.044</td>
</tr>
<tr>
<td>Ethanolemia</td>
<td>0.016±0.070</td>
<td>0.020±0.012</td>
<td>0.018±0.005</td>
<td>0.016±0.007</td>
<td>0.025±0.018</td>
</tr>
<tr>
<td>Calprotectin</td>
<td>22.74±4.75</td>
<td>27.15±13.90</td>
<td>25.10±16.57</td>
<td>28.70±12.27</td>
<td>29.74±11.48</td>
</tr>
</tbody>
</table>

ANOVA with Bonferroni correction; ^ = p<0.05; T-test between Group I and Group II; * = p<0.05

Conclusion: IP, ETH, ETX, appear to be associated with GLA dysfunction in obesity and its HC. Pending further results to establish potential causative roles of these factors, the modulation of the GLA appears to represent a promising target for the prevention and treatment of these conditions.

Disclosure of interest: None Declared.
Viraemic Relapse After Apparent Spontaneous Clearance in a Child Vertically Infected by Hepatitis C Virus

Giuseppe Indolfi1, Giusi Mangone2, Elisa Bartolini1, Maria Moriondo2, Daniele Serranti3, Chiara Azzari3, Massimo Resti4

1Meyer Children's University Hospital of Florence, Paediatric and Liver Unit, Florence, Italy
2Immunology Lab, Meyer Children's University Hospital of Florence, Italy
3Department of Health Sciences, University of Florence, Florence, Italy
4Paediatric and Liver Unit, Meyer Children's University Hospital of Florence, Florence, Italy

Objectives and study: Spontaneous clearance of hepatitis C virus (HCV) is defined by the presence of anti-HCV antibodies and by the disappearance of HCV RNA from serum in at least two consecutive samples taken at least six months apart. So far, no study has been published on the durability of spontaneous clearance in children. The present study describe a 3-month-old child vertically infected by HCV. At 55 months of age the plasma viral load became undetectable. Accordingly, aminotransferases levels, that were raised initially, became normal while anti-HCV antibodies persisted in absence of HCV RNA. After six months of undetectable HCV RNA, in accordance with the guidelines currently available, spontaneous clearance of HCV was diagnosed. HCV RNA remained undetectable and aminotransferases normal through 33.9 months of follow up. At the age of 6 years and 8 months aminotransferases levels raised again and the plasma viral load rebounded. These results were confirmed with repeat testing and over the following 24 months. The child was otherwise healthy and no clinical sign or clue for an underlying immunodeficiency were identified. A complete diagnostic work up for raised aminotransferases was negative. Epidemiologic risk factors for reinfection such as intravenous drug use, exposure to unsafe therapeutic procedures, or to contaminated/unscreened blood were denied. Virologic testing was performed in order to demonstrate that viraemia reappearance was not due to de novo infection.

Methods: Cloning and sequencing of the HCV NS5B coding region was performed. After NS5B sequences were obtained, the degree of identity was tested among 2 child's strains amplified from 2 plasma samples collected before the putative clearance and 1 collected after viral rebound (GenBank KU286155-KU286157). Sequences from 2 previously described HCV genotype 2-infected patients with demonstrated intrahost evolution were included in the analysis for comparison of interpatient diversity (FJ024182-5 and FJ024187-90). Sequences were aligned using the MUSCLE program and the distance matrix under the Kimura two-parameter mode was calculated using the MEGA program. Phylogenetic trees were created by the Unweighted Paire Group Method. As a measure of the robustness of each node, we employed the bootstrap method (1,000 pseudo-replicas).

Results: De novo infection was excluded by sequencing of the NS5B gene that confirmed HCV genotype 2a infection with minor genetic variations suggestive of intrahost evolution of the strains collected before and after the putative clearance. During the period of virologic remission, HCV RNA was not detected in circulating P. The child is actually 8-year-old, persistently viraemic and with raised aminotransferases levels.

Conclusion: The present report provides evidence of HCV viral rebound in a child vertically infected by HCV and diagnosed with spontaneous clearance of the infection according to standard criteria. This report casts doubt on the complete eradication of the virus in presumed recovered children highlighting the need of exploring the burden of misdiagnosed cases and of revisiting the serologic and molecular criteria for HCV clearance. Further studies are needed to confirm and evaluate the burden of this phenomenon. Although many classes of potent drugs for HCV are available, the search for the HCV cure and eradication is not finished and should start with the correct identification of all the infected people.

Disclosure of interest: None Declared.
Improved adhesion and rolling of adult derived human liver stem cells (ADHLSC) cultured on thermosensitive polymer and attached with sialyl Lewis X.

Pierre-Edouard Dollet¹, Sharat Varma¹, Jérome Ambroise², Catherine Lombard¹, Etienne Sokal³

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, Pediatric Gastroenterology, Hepatology and Nutrition, Brussels, Belgium

Objectives and study: ADHLSC (adult-derived human liver stem/progenitor cells) infusions are undergoing clinical trials in treatment of inborn errors of metabolism. One objective is to increase the hepatic engraftment of the infused ADHLSC. Rolling and adhesion are essential steps for a successful engraftment. Alternative methods are considered to avoid trypsinization, known to damage integrins during culture passages, and subsequently adhesion. Selectin ligands are in addition insufficiently expressed, which may be compensated by attachment of sialyl Lewis X to the cells.

Methods: ADHLSC were cultured on thermosensitive polymer and harvested by non-enzymatic dissociation solution, and their adhesion properties was compared to that of control cells cultured on CellBind® (Corning®, Wiesbaden, Germany) and harvested by trypsinization. Adhesion was evaluated by shear stress test utilizing μ-Slide I Luer (ibidi GmbH, Martinsried, Germany) coated with vascular cell adhesion protein 1 (VCAM-1) or collagen type I. Secondly, the effect of the selectin ligand sialyl Lewis X attached to ADHLSC was compared to control cells for the rolling capacity, using the shear stress test with μ-Slide I Luer coated with E-selectin.

Results: ADHLSCs cultured on thermosensitive polymer and harvested by non-enzymatic dissociation solution showed a 38% higher adhesion to VCAM-1 coated μ-Slide I Luer (465 cells/field versus 338 cells/field in controls, 95% CI [92.2, 161.3] (p<0.01, n=4)). No significant change in adhesion potential was seen on collagen type I coated μ-Slide I Luer (573 cells/field versus 579 cells/field in controls).

Attachment of sialyl Lewis X to ADHLSC led to considerable increase of rolling to E-selectin coated μ-Slide I Luer (from 5 cells/field in controls to 289 cells/field (p<0.01, n=3).

Conclusion: We demonstrate that ADHLSC cultured on thermosensitive polymer, harvested by non-enzymatic dissociation solution and attachment of sialyl Lewis X significantly increase respectively their adhesion to VCAM-1 and rolling percentage to selectin as compared to cells cultured on CellBind and trypsinized.
HEPATOLOGY: General Hepatology

H-P-021

Development of an adherence self-help leaflet for the parents of children with liver disease.

Faith Matcham1, Anna Hames2, Marianne Samyn3

1King's College London, London, United Kingdom
2King's College Hospital, Institute of Liver Studies, London, United Kingdom
3King's College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom

Objectives and study: Medication non-adherence in liver disease is considered to be a crucial target for intervention, given its prevalence and implications for long-term health and survival. Medication adherence behaviour in adolescence and adulthood is likely to be modelled on adherence behaviour experienced as a child; targeting parental adherence prior to transition is a crucial, yet infrequently studied. The aim of this project is to develop a resource for the parents of children with liver disease, focusing on barriers to medication adherence.

Methods: Qualitative interviews with parents and clinicians, and literature reviews informed several of the key barriers for parental medication adherence. A self-help leaflet was developed using adherence techniques informed by health behaviour change literature. The leaflet was designed in a modular fashion, with a brief questionnaire identifying individual barriers to adherence at the start and then the appropriate module(s) provided to target the intervention accordingly.

Results: Five key areas relating to adherence were identified via qualitative interviews and literature reviews: understanding medications; remembering the right doses at the right time; children refusing or finding it difficult to take their medication; keeping track of complicated medication regimes; and adjusting to changes in routine. Behaviour change techniques drawing from models of health belief, visual reminders, implementation intentions and goal-setting have been utilised in brief, relevant and easy-to-use materials, with practical advice, frequently asked questions, and information about other resources available through the paediatric liver service. By the time of presentation this will have been piloted with parents, using “think aloud” methods to evaluate the usefulness and comprehensiveness of the pilot material, with preliminary results available.

Conclusion: Non-adherence is a crucial target for intervention amongst adolescents with chronic health problems, but is also prevalent amongst younger age groups. Targeted self-help literature can support parental adherence. This is also likely to improve adherence as the responsibility is handed over to young people.

Disclosure of interest: None declared
Predictive Factors of Positive Response to Interferon Treatment in Chronic B Active Hepatitis in Children

Oana Belei¹, Ioan Simedrea¹, Laura Olariu¹, Maria Pop², Georgiana Brad¹, Tamara Marcoci¹, Otilia Marginean¹

¹University of Medicine and Pharmacy Victor Babes, First Pediatric Clinic, Timisoara, Romania
²University of Medicine and Pharmacy Victor Babes, Third Pediatric Clinic, Timisoara, Romania

Objectives and study: The objective of this study was to assess the predictive factors of positive response to interferon (IFN) treatment in pediatric patients with chronic B virus active hepatitis (CBAH).

Methods: We performed a retrospective analyze of 2 lots of children with CBAH admitted between 2000-2015. The first lot consisted in 40 patients with positive response to IFN treatment and the second lot consisted in 42 patients non responders to IFN treatment. Both studied lots received the same treatment protocol: IFN α2B 3x3 MU/week, 6-12 months. The patients were assessed clinical, biological, virusological (HBs/HBeAg/Ab, DNA-HBV) and histological (Knodell score). A complete response was established when HBsAg/HBeAg became negative, aminotransferase level normalized, viremia became non-detectable and Knodell score decreased.

Results: The length of HBV infection was predictive for treatment response: in the first lot the length of infection was significantly shorter (29 +/- 7 months) compared to second lot (47.8 months), p<0.001. Presence of high aminotransferases level improved treatment response (180 +/- 18 // 194 +/- 26 UI/l) in responders against non-responders lot with lower aminotransferases level (56.7 +/- 5 // 73.1 +/- 12 UI/l), p<0.001. High DNA-HBV viremia level decreased the response to IFN treatment. HBeAg positivity was a predictive factor for treatment response (35.5% against 14.2%, p < 0.001). Higher necro-inflammatory activity predicted the response to treatment (7.6 +/- 1.7 against 4.8 +/- 1.2, p < 0.001).

Conclusion: This study identified the following positive prediction factors for IFN treatment in chronic B active hepatitis in children: recent infection, high aminotransferases serum level, low viremia levels, presence of HBe Ag and high necro-inflammatory activity.

Disclosure of interest: “None Declared”.
**Portal Vein Obstruction: The Challenge of Timely Diagnosis**

Dalia Belsha¹, Suzanne Davison², Stephen Hodges², Sanjay Rajwal², Patricia McClean³

¹Sheffield Children's Hospital NHS Foundation Trust, Sheffield, United Kingdom  
²Paediatric Liver Unit, Leeds General Infirmary, Leeds, United Kingdom  
³Leeds Teaching Hospitals NHS Trust, Department of Paediatric Hepatology, Leeds, United Kingdom

Objectives and study: Portal vein obstruction (PVO) due to portal vein thrombosis with portal cavernoma formation is a major cause of portal hypertension in children. Significant morbidity occurs due to oesophageal variceal bleeding. Early diagnosis permits appropriate counselling and provides an opportunity for prophylactic intervention. We aimed to evaluate the spectrum of clinical presentation of PVO, and identify opportunities for early diagnosis.

Methods: All children born after 1990 with a final diagnosis of PVO who were referred to a single centre between 2000 and 2015 were identified. A proforma was devised and data collected retrospectively from case notes including initial symptoms, signs and investigations, incidence of gastrointestinal (GI) bleeding and time to diagnosis.

Results: Fifty-six children with PVO were identified, one was later excluded due to insufficient data. Mean age at presentation was 3y 10m (range 1 m -13y 8 m), 26 were male. Risk factors were identified in 28/55 (51%) including umbilical vein instrumentation (12), congenital heart disease (10: 4 also had non-cardiac abnormalities) and other congenital anomalies (6: renal, anorectal, tracheo-oesophageal fistula and Goldenhar syndrome).

Four patterns of presentation were identified: (a) incidental finding of PVO on US (n=9); (b) neonatal with jaundice +/- ascites leading to US diagnosis of PVO (n=4); (c) upper GI bleed (n=22) and (d) “haematological presentation” with splenomegaly and/or symptoms/signs of hypersplenism (n=20)

Of 22 who presented with GI bleeding (mean age 3y 6m, range 6m-10y6m) 15 had diagnosis of PVO made during their initial admission. The remaining 7 were discharged without PVO being identified. All were subsequently readmitted after a median of 1m (range 7d - 18m) with further GI bleeding, after which the diagnosis was established. Three children with GI bleed at presentation were initially referred to haematology for investigation of thrombocytopenia, two undergoing bone marrow (BM) assessment.

Of 20 children (mean age 5y 2m, range (17m-13 y), without GI bleed who had a “haematological presentation”, 13 (65%) were referred to specialists in haematology (11) or immunology (2). BM assessment by trephine or aspiration was performed in 9/20 (45%) and was normal. Only 9/20 (45%) in this group had diagnosis of PVO established within 2 weeks of presentation. In the remaining 11 median interval to diagnosis was 10 m (range 2m - 6y). Of these, 10 had a significant upper GI bleed during the interval from presentation to diagnosis. In those who had evidence of splenomegaly on initial US, PVO was not initially identified.

Conclusion: PVO has a wide spectrum of clinical presentation. Associated risk factors are seen in 51% and may provide a clue to diagnosis. In this series diagnosis was delayed in 18/42 (43%), most frequently in those with a “haematological” presentation (55%) but also in those presenting with GI bleed (32%). Diagnosis by US can be technically challenging even when splenomegaly is detected. Carefully focussed imaging by US with Doppler studies and/or other radiological modalities should be undertaken in a child with history, symptoms or signs compatible with PVO.

Disclosure of interest: None Declared.
Stool colour cards allow specific identification of infant cholestasis: results of a prospective, experimental, monocentric, non-profit pilot study

Paola Gaio1, Enrico La Pergola2, Edoardo Rosellini1, Chiara Boscardin1, Piergiorgio Gamba2, Mara Cananzi3

1Dpt. of Woman and Child Health, University Hospital of Padua, Italy
2Unit of Pediatric Surgery, Dpt. of Woman and Child Health, University Hospital of Padua, Italy
3Unit of Pediatric Hepatology, Dpt. of Woman and Child Health, University Hospital of Padua, and Genius Group, Padua, Italy

Objectives and study: Infant cholestasis is an uncommon (1:2500 infants) but potentially serious condition that always indicates a hepatobiliary dysfunction. Early recognition of the underlying cause is essential to ensure rapid treatment and optimal prognosis. At present no neonatal screening is available and the detection of cholestasis, exclusively based on the identification of jaundice and acholic stools at paediatric visits, is often delayed. Recent Asian studies have demonstrated that stool colour cards allow prompt recognition of acholic stools by parents thus anticipating the age at diagnosis of biliary atresia, which worldwide represents the most frequent cause of infant cholestasis.

Aim of the study: to validate a screening method for infant cholestasis based on the evaluation of stool pigmentation employing a colour card.

Methods: An experimental, prospective, monocentric, uncontrolled, non-profit study was designed and approved by the Local Ethical Committee. A Stool Colour Card (SCC) was created employing pictures representative of cholic and acholic infant stools. After obtainment of informed consent, the SCC was provided to all parents of neonates born at the University of Padova at discharge from the hospital. Parents were required to inform investigators about stool colour at the end of the first, second and third month of life either by phone or employing a website/smartphone-app specifically designed for the study. In the occurrence of persistent acholic stools (>48 hours), parents were exhorted to immediately contact the investigators or to require a prompt paediatric evaluation; in case of medical confirmation of acholic stools, measurement of serum total/conjugated bilirubin was performed to prove the presence of cholestasis. To determine SCC specificity statistical power was calculated and resulted equal to 1200 subjects.

Results: 205 infants were enrolled (91% European; 4% Asian; 3.5% African; 1.5% Latin American); only 3 subjects were excluded because parents denied consent (98.5% adherence to the study). All enrolled subjects completed the study. 20.5% of the parents employed the website/smartphone-app to communicate stool colour records; remaining data were collected by phone. The SCC permitted the identification of a subject with acholic stool due to choledocal obstruction from biliary stones (true positive). No false negative or false positive cases were reported along the study period. The SCC showed a specificity of 100% (CI 98-100%).

Conclusion: these preliminary data support that SCCs are economic, easy to use, non-invasive tools for the identification of cholestasis during the first 3 months of life. Achievement of statistical power is needed to confirm SCC specificity. Larger studies will be needed to evaluate SCC sensitivity and capacity of diagnosing biliary atresia.

Disclosure of interest: None Declared
Clinical and immunological aspects of patients with chronic D hepatitis

Nicolae Bodrug¹, Doina Barba¹, Ecaterina Luca¹, Corina Cazan², Bogdan Neamtu²

¹University of Medicine and Pharmaceutics „Nicolae Testemitanu”, Chisinau, Moldova
²Pediatric Clinic Hospital, Ceforaten, Sibiu, Romania

Objectives and study: The viral hepatitis are widespread in the Republic of Moldova. In the pathogenesis of the hepatitis, a special role is played by the immunological mechanisms, responsible for the evolution and therapy responsiveness. The objectives of the study are: determination of the clinical and biochemical features of patients with the chronic viral D hepatitis (HDV); assessment of the cellular immunogram disorders (CD3⁺, CD4⁺, CD8⁺, CD16⁺, CD19⁺, CD4/CD8) of patients with the chronic HDV; identification of humoral immunological disorders (IgA, IgM, IgG, IgE) of patients with chronic HDV.

Methods: In the course of the study, 33 patients, with the average age of 11 ± 4.6 years, predominantly girls - 54%. Criteria of participation in the study: age < 18 years, presence of HDV total antibodies, anti-HDV IgM, positive HDV RNA. Exclusion criteria: age > 18 years, decompensated liver cirrhosis, hepatocellular cancer, acute Delta hepatitis, mixed infection HBV+HDV+HCV, HIV infection. All the patients underwent a clinical, a hematologic, a biochemical (ALT, AST, alkaline phosphatase, GGTP, total bilirubin, albumin, coagulation), and an immunologic (HBsAg, HbeAg, antiHBeAg, anti-HBcor, HDV total antibody and anti-HDV IgM ELISA) examination; quantitative determination of HBV DNA through PCR (detection limit 5 IU/ml) and HDV RNA (detection limit 500 IU/ml) and instrumental determination (ultrasound + Doppler portal system, upper digestive endoscopy, the degree of liver fibrosis through Fibroscan or Fibrotest - Fibromax (Biopredictive). The evolution prediction score was calculated - BEA (Baseline Event - anticipation score). The statistical method used - Epi Info.

Results: All the patients had positive HBsAg and anti-HDV antibodies, 76% - negative HBeAg, 83% - positive HDV RNA, 23% - positive HBV DNA. Biochemically, the cytolyis prevailed in the cases of the majority of patients (ALT 79.9 ± 11.3 IU/ml), just as cholestasis syndrome (total bilirubin 32.7 ± 4.3 mmol/l). Thrombocytopenia was revealed in the cases of 78% of patients with chronic HDV (83.3 ± 4.3×10⁹/l), leukopenia was revealed in 34% of the cases(2.4 ±0.23 ×10¹²/l). Hepato-splenomegaly was observed in the cases of most patients. In cases of patients with chronic HDV, the F2 and F3 degree of fibrosis prevailed (36% and 33%, accordingly). The evaluation of the BEA score has identified: 53% of patients with BEA-A, 35% - BEA-B and 12% - BEA- C. The analysis of the immunological indices in the cases of patients with chronic HDV revealed a clear increase of IgE (169.0 ± 48.9 IU/ml) in a half of patients and of IgG in 25 % cases of patients (25.8 ± 9.7 g/l), with the reduction of IgA in the cases of ¼ of patients (0.5 ± 0.05 g/l). The evaluation of the cellular immune parameters revealed an increase of the CD4⁺ (50.7 ± 3.8), CD8⁺ (32.67 ± 8.9) in the cases of half of the patients, CD3⁺ (81.1 ± 22.9) and CD16⁺ (29.9 ± 7.8) in the cases of 1/3 of the examined patients.

Conclusion: In such a way, some clinical and evolutionary features were distinguished in the cases of patients with chronic HDV, namely: 1. Chronic HDV remains a major public health problem in our country, creating a reservoir of HDV infection. 2. Awareness of chronic persistence mechanisms and evolutionary aggressiveness of chronic HDV, which is due to the defective involvement of the cellular and humoral immune system, certainly creates new immunopathogenetic directions in the prevention and treatment of the viral Delta hepatitis.

Disclosure of interest: None Declared
A Hidden Cause of Toxic Hepatitis: Herbal Anti-Colic Remedies

Asuman Karhan¹, Ayse Mete Yesil², Mustafa Senol Akin², Hulya Demir¹

1Hacettepe University, Pediatric Gastroenterology, Ankara, Turkey
2Hacettepe University, Faculty of Medicine, Pediatrics, Ankara, Turkey

Objectives and study: Herbal products have been used as medications since ancient times and are increasingly used by parents as a way to treat children. The use of these herbal products is growing due to the common misconception that they are natural, must therefore be harmless, and healthy alternatives to conventional medical treatment. The side effects of drugs are generally reported; however, toxin levels in herbal products are underestimated and not reported by doctors. We present three cases of herbal anti-colic drug associated toxic hepatitis and highlight the dangers of these herbal products.

A one-month-old girl was admitted to our hospital for the evaluation of high transaminase levels that were detected incidentally. The baby was being breastfed and there were no problems other than symptoms of colic since birth. The physical examination of the patient was normal but laboratory tests revealed high transaminase levels (ALT: 334 U/l, AST: 778 U/l) with a prolonged international normalised ratio (INR): 1.34. Infectious and metabolic tests were normal. With a detailed anamnesis, we learned that the parents were giving her fennel tea, a herbal product, including pimpinella anisum, oregano, fennel tea, fructus cumini and anethum graveolens to treat her colic symptoms. The patient’s transaminase and INR levels decrease to normal levels within four days of stopping the usage of the herbal products.

A formerly healthy four-month-old girl was brought to our emergency department for a possible nonfebrile seizure display with rolling eye movements and pallor. The physical examination was normal and there were no signs of infection or neurological disorder. The patient’s laboratory tests revealed high transaminase levels (ALT: 1828 U/l, AST: 1713 U/l) with a prolonged INR of 1.8. Her metabolic and infectious disease tests were normal. Cranial imaging and electroencephalography were also normal. A detailed anamnesis revealed that the patient received a herbal product that included fructus cumini, fennel tea, anethum graveolens, ginger, menthol and pimpinella anisum for symptoms of colic over one month. After the discontinuation of these herbal products, the patient’s liver enzymes returned to normal levels within one week and we did not observe any more seizures.

A formerly healthy four-month-old boy was admitted to our hospital because he was refusing to feed and was crying excessively. The patient’s physical examination was normal. Laboratory tests were normal, except for high transaminase levels (ALT: 317 U/l, AST: 415 U/l) with a prolonged INR of 1.3. Metabolic and infectious tests were normal. We discovered that patient’s family had given him herbal and non-herbal anti-colic drugs including fructus cumini, fennel tea and probiotics. The patient’s liver enzymes and INR levels normalised within few days of ending the use of these herbal and non-herbal drugs.

Conclusion: The toxic effects of these products are already known. However, toxic hepatitis due to anti-colic herbal drugs has not previously been reported. We have attempted to emphasise the importance of the detailed anamnesis regarding complementary and alternative medicine while investigating the patients.

Disclosure of interest: We have no conflict of interest.
A retrospective study of the outcomes for paediatric chronic hepatitis B infection post adefovir dipivoxil treatment

Adam Arshad1, Samantha Lissauer 2, Maxine Brown3, Deirdre Kelly 3

1University of Birmingham Medical School, MBChB Year 3, Birmingham, United Kingdom
2University of Birmingham, Centre for Human Virology, Birmingham, United Kingdom
3Birmingham Children's Hospital, The Liver Unit, Birmingham, United Kingdom

Objectives and study:

- To retrospectively evaluate Hepatitis B Virus (HBV) status in children who had received adefovir dipivoxil (ADV) as part of a trial within the past 11 years.
- To determine whether ADV treatment pre-conditions patients to spontaneous HBeAg seroconversion and ALT/HBV DNA reduction in later years with no additional further treatment.

Methods: 9 children with chronic HBV from a single centre that had received ADV as part of a 4 year, double blind multi centre trial in 2004-2005 were identified. Clinical data was collected (May-July 2015) from both paediatric and adult services from pre/post trial periods including:

- HBV serology and DNA
- Liver function tests
- Adverse events
- Other treatments received

Results: 6 of the 9 cohort children completed the original trial; with one undergoing HBeAg seroconversion within the study period and rest deemed 'failed responders'.

In subsequent years, the remaining 5 have all had HBeAg seroconversion at varying time points post-treatment (100 % vs 16.7% in the original trial). Mean duration post-treatment to seroconversion was 2112.8 days. No other treatments were given after the trial to confound results. No correlation can be found with time to seroconversion and age/ethnicity/sex/ original ADV treatment length/HBV genotype.

All 6 children had falling HBV DNA post ADV treatment (Figure 1). Baseline mean for all participants (at original study recruitment) was 3 x 10^8 copies/ml (with 2 outliers at higher levels), compared to end mean of 1.711 x 10^5 copies/ml. This was similar for ALT (baseline 39 – end 23 means). No adverse effects were noted in any of the cohort.

Conclusion: There is a high rate of spontaneous seroconversion post ADV treatment in children and adolescents. This suggests that treatment may provide hepatic pre-conditioning for long-term HBeAg seroconversion, above that expected without additional treatment. HBV DNA and ALT are further reduced. No safety issues are noted. Patients from other centres will be examined to study the wider implications of this study and whether this is a paediatric specific effect. Further biological and clinical studies are warranted to understand the potential for hepatic conditioning for spontaneous HBV seroconversion in children.

Disclosure of interest: No conflict of interest for any author.
Fig. 1

HBV DNA (mean copies/ml)

Years post follow up

Baseline

1×10^8
2×10^8
3×10^8
4×10^8
5×10^8
6×10^8
0
2
3
4
5
7
8
9
10
**An international survey regarding management of coagulopathy in children undergoing liver biopsy**

Maria Magnusson¹, Eugene Kua², Björn Fischler³, Winita Hardikar⁴, Paul Monagle⁵

¹Karolinska Institutet, Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Clintec, DIV. of Pediatrics, Mmk, Clinical Chemistry and Blood Coagulation Research, Stockholm, Sweden
²University of Melbourne, Murdoch Children’s Research Institute, Department of Paediatrics, Haematology Research, Melbourne, Australia
³Karolinska Institutet, Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Clintec, Division of Pediatrics, Stockholm, Sweden
⁴University of Melbourne, Royal Children’s Hospital, Department of Paediatrics, Department of Gastroenterology, Melbourne, Australia
⁵University of Melbourne, Murdoch Children’s Research Institute, Royal Children’s Hospital, Department of Paediatrics, Haematology Research, Melbourne, Australia

**Objectives and study:** Many children with liver disease need to undergo liver biopsy for diagnostic purposes or in the prognostic assessment of known liver disease. Bleeding complication rates of 1.5-2.8% has been reported in paediatric patients undergoing liver biopsy. A position paper regarding liver biopsy in children has recently been published from ESPGHAN Hepatology Committee *(Dezöfi A et al. JPGN 2015;60(3):408-20).* There are no evidence-based guidelines regarding management of coagulopathy specifically in children undergoing liver biopsy. Our objectives were to study how children with liver disease and coagulopathy are evaluated and if pro-haemostatic treatment is used prior to liver biopsy in centres for paediatric hepatology.

**Methods:** A survey regarding management of coagulopathy in children with liver disease in the setting of liver biopsy was sent to 18 centers for paediatric hepatology in Europe, North America and Australia in 2015.

**Results:** Data from 13 out of 18 centers in Europe (n=8), North America (3) and Australia (2) showed that all centers used at least INR and platelet count as preoperative tests, although cut-off levels for preoperative treatment or cancellation of biopsy differed between centers. Several liver biopsy methods were used, of which the most common were percutaneous ultrasound-guided (n=10), transjugular (9) and percutaneous ultrasound-assisted (8). Nine centers changed liver biopsy method in case of coagulopathy. Types of preoperative treatments are given in the figure. Vitamin K, fresh frozen plasma and platelet transfusion were used in most centers. Reported complications (2014) included bleeding (n=6), pneumothorax (1) and haemobilia (1).
**Conclusion:** Children undergoing liver biopsy are evaluated regarding haemostatic defects and the results are used for preoperative decision-making. Preoperative coagulation tests, liver biopsy methods and types of preoperative treatments differ between centers for paediatric hepatology.

Disclosure of interest: None Declared.
The impact of serum bile acid levels on the mRNA expression of pro-and anticoagulant proteins in liver tissue

Maria Magnusson¹, Cecilia Gälman², Björn Fischler³, Eva Beijer³, Henrik Arnell³, Antal Németh³, Gösta Eggertsen²

¹Karolinska Institutet, Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Clintec, DIV. of Pediatrics, Mmk, Clinical Chemistry and Blood Coagulation Research, Stockholm, Sweden
²Karolinska Institutet, Karolinska University Hospital, Labmed, Dept. of Laboratory Medicine, Stockholm, Sweden
³Karolinska Institutet, Astrid Lindgren Children’s Hospital, Karolinska University Hospital, Clintec, Division of Pediatrics, Stockholm, Sweden

Objectives and study: Coagulation factors are used as prognostic markers in liver disease, i.e. the levels are expected to decrease as the liver function deteriorates. However, in cholestatic liver disease, increased rather than decreased levels of coagulation factors have been demonstrated in patients with highly elevated levels of bile acids. The mechanism for this paradoxical finding is unclear and these effects are overlooked when coagulation factors are used as prognostic markers in patients with cholestatic liver disease. Our aim was to investigate if serum bile acid levels have an impact on the mRNA expression of pro-and anticoagulant proteins in hepatocytes.

Methods: Six patients (0.5-9.8 years) with progressive familial intrahepatic cholestasis (PFIC), who consecutively underwent the surgical procedure partial external biliary diversion (PEBD) to reduce high serum levels of bile acids, were enrolled in this cohort study at our tertiary referral center for pediatric hepatology. Informed consent was obtained and the study was approved by the ethics committee. INR, total fasting serum bile acids and liver biopsies were collected before and after the procedure. Eight age-matched non-cholestatic patients with α1 antitrypsin deficiency, undergoing liver biopsy, served as controls. mRNA specific for coagulation factor II (FII), FV, FVII, fibrinogen, protein C and Farnesoid X receptor (FXR) were extracted and analyzed for each liver biopsy.

Results: The mRNA levels of Factor V, Factor VII, the three fibrinogen chains and protein C were significantly higher compared to controls, prior to PEBD. A reduction in bile acids levels from median 298 µmol/L (range 83-687 µmol/L) to 4 µmol/L (range 2-145 µmol/L) after PEBD was seen. The mRNA levels after the procedure did not differ from controls, except for Factor V-mRNA which remained significantly higher than in the controls.

Conclusion: High levels of bile acids may stimulate the mRNA expression of both pro-and anticoagulant proteins.

Disclosure of interest: None Declared
Evolution of fulminant liver failure in mushroom poisoning in children

Alina Grama¹, Aurel Bizo², Dan Delean³, Cornel Aldea³, Ana Stefanescu², Tudor Lucian Pop²

¹University of Medicine and Pharmacy Carol Davila Bucuresti / University of Medicine and Pharmacy Iuliu Hatieganu, 2nd Pediatric Clinic, Cluj-Napoca, Romania
²University of Medicine and Pharmacy Iuliu Hatieganu, 2nd Pediatric Clinic, Cluj-Napoca, Romania
³Emergency Hospital for Children, Nephrology Clinic, Cluj-Napoca, Romania

Objectives and study: Mushroom poisoning occurs quite frequently in our country, especially in some rural area where the socioeconomic status is low. Fulminant liver failure is the cause of death in some of these patients with mushroom poisoning. The aim of our study was to analyse the prevalence and evolution of fulminant liver failure in mushroom poisoning in children during the last 15 years.

Methods: We have analysed retrospectively all patients with wild mushroom poisoning hospitalized between 2000 and 2015 in our hospital, the main Toxicology Centre in North-Western Romania. All clinical data and laboratory parameters from patients with mushroom poisoning with fulminant liver failure were analysed in order to evaluate the evolution, prognostic factors and utility of therapeutic measures in children.

Results: From 320 children with mushroom poisoning, 83 patients (25.93%, mean age 7.82 years, 45 males, 54.21%) presented fulminant liver failure. In our study 66.26% of the patients had delayed toxicity symptoms (over 12h). The most common first-noticed symptoms were gastrointestinal. The clinical features and biochemical parameters at admission were correlated with evolution. The encephalopathy presence (45/45 vs 17/38, p=0.0000), transaminases level (AST 4158 vs 1439 UI/dl, p=0.006, ALT 3420 vs 1524 UI/dl, p=0.009) and total bilirubin level (3.7 vs 1.5 mg/dl, p=0.0000), the severity of coagulopathy (INR 1.27 vs 6.85, p=0.0000), the presence of metabolic acidosis (41/45 vs 17/38, p=0.0001) were found to be significantly higher in patients who died compared to the survivors. Renal failure was associated in 14 patients (16.87%). 68 patients (81.93%) were treated by penicillin G. 63 patients (75.90%) were treated with hemoperfusion, plasmapheresis or hepatic dialysis. There was no case with possibilities for emergency liver transplantation. Even though the mortality rate of all mushroom poisoning cases was low (14.06%), in children who developed fulminant liver failure mortality was high (54.21%). The mortality varied in time (between 0% and 100% of cases from one year), but for the last years it was decreasing.

Conclusion: Fulminant liver failure in mushroom poisoning is associated with a high mortality in children, despite optimal medical therapy, including hemoperfusion, plasmapheresis and hepatic dialysis but without emergency liver transplantation. Improvement in health education and use of media during the last years has played an important preventive role in decreasing the frequency of mushroom poisoning and subsequently fulminant liver failure in children.

Genotype-phenotype correlation in Wilson’s disease with haemolytic anaemia and acute liver failure in children

Tudor Lucian Pop1, Ana Stefanescu1, Alina Grama1, Nicolae Miu1, Claudia Willheim-Polli2, Peter Ferenci2

1University of Medicine and Pharmacy Iuliu Hatieganu, 2nd Pediatric Clinic, Cluj-Napoca, Romania
2Medical University of Vienna, Department of Internal Medicine III, Vienna, Austria

Objectives and study: Wilson's disease is an autosomal recessive inherited disorder of copper metabolism, with phenotypic variation in children and adolescents: liver, neurological and rarely haemolytic anaemia with acute liver failure. There are more than 500 mutations of ATP7B gene responsible for this disease. There is an interest for correlations between genetic mutations (missense or nonsense / frame-shift) and clinical forms or evolution disease, with importance for the prognosis of the disease. The aim of our study was to analyse the most common genetic mutations in children with Wilson's disease with non-immune haemolytic anaemia and acute liver failure and to compare with the other forms of disease.

Methods: Data from 34 children with Wilson's disease were analysed in terms of clinical manifestations (acute or chronic liver disease, neurologic disease, acute liver failure with non-immune haemolytic anaemia), hepatic parameters, copper metabolism, and genetic mutations. The molecular analysis of ATP7B gene was performed using semi-nested polymerase chain reaction-based restriction fragment length polymorphism assay for H1069Q mutation detection and if negative or heterozygous then screening for mutations on exons 6 to 20 by denaturating high-performance liquid chromatography, followed by sequencing on a genetic analyser.

Results: Of the 34 children with Wilson’s disease, seven children presented with non-immune haemolytic anaemia and acute liver failure (20.59%; in four cases with severe fulminant hepatitis). The mean age at onset in patients with haemolytic anaemia was 14.7 years (10.5 to 17 years), compared to 12.3 years in the other patients. Wilson’s disease has been confirmed by the presence of gene mutations in all 34 cases, as homozygous or compound heterozygous status. The most common mutations in patients with non-immune haemolytic anaemia were W939C (42.86%) and K844K-fr (28.57%), while in other clinical forms H1069Q and G1341D (40.74%) were the most frequent. No patients with H1069Q mutation presented non-immune haemolytic anaemia.

Conclusion: It remains very difficult to make genotype-phenotype correlations in Wilson’s disease patients, due to the very small number of patients. In our patients, in those with non-immune haemolytic anaemia with acute liver failure the nonsense mutations non-H1069Q (as W939C mutation is) and frame-shift mutations (K844K-fr) are the most frequent, compared to other milder form of disease. As genetic diagnosis is usually time consuming and the results are late (except in the screening of the relative of an index patient), the importance for the prognosis of the disease at onset of the acute liver failure is questionable.

Disclosure of interest: Tudor L. Pop and Ana Stefanescu funded by Partnership Grant PN-II-PT-PCCA-2011-3.2-0917.
Prevalence of the ATP7B gene mutations among children with Wilson's disease from North-Western Romania

Tudor Lucian Pop¹, Ana Stefanescu¹, Alina Grama¹, Gabriel Domnariu¹, Claudia Willheim-Polli², Nicolae Miu¹, Alexandru Pirvan¹, Mariana Andreica¹, Simona Sorana Cainap¹, Bianca Simionescu¹, Rodica Elena Cornean¹, Daniela Elena Serban¹, Andreea Rachisan¹, Maria Pop³, Iulian Puiu Velea³, Ioan Simedrea³, Oana Belei³, Peter Ferenci²

¹University of Medicine and Pharmacy Iuliu Hatieganu, 2nd Pediatric Clinic, Cluj-Napoca, Romania
²Medical University of Vienna, Department of Internal Medicine III, Vienna, Austria
³University of Medicine and Pharmacy Victor Babes, Department of Paediatrics, Timisoara, Romania

Objectives and study: Wilson's disease is an autosomal recessive genetic disease of copper metabolism, involving mainly the liver in paediatric population. The ATP7B gene mutation analysis may confirm the diagnosis, especially in controversial cases. There is a great variability of the genotype in different geographic areas, with H1069Q mutation as the most frequent in Central and Eastern Europe. There is no report of ATP7B gene mutations in children from Romania. The aim of our study was to find the prevalence of different ATP7B gene mutations in the paediatric population from the North-Western Romania as a pre-requisite for developing of a DNA microarray chip for direct molecular diagnosis in Wilson's disease.

Methods: We have retrospectively analysed the data from the patients with Wilson’s disease diagnosed or followed-up in our unit. The diagnosis was done using the clinical features, copper metabolism tests and genetic testing, following the up-to-date Wilson’s disease guidelines. The molecular analysis of ATP7B gene was performed using semi-nested polymerase chain reaction-based restriction fragment length polymorphism assay for H1069Q mutation detection. In patients without this mutation or in those with heterozygous status, the screening for mutations on exons 3 to 21 was also done by denaturating high-performance liquid chromatography, then by direct sequencing. The Wilson’s disease patients without genetic analysis were not included in the cohort.

Results: Wilson’s disease was diagnosed including genetic analysis in 43 patients (22 males, 21 females), with mean age at diagnosis of 12.44+/−3.88 years (range from 5 to 18.16 years). The clinical manifestations at presentation were hepatic in 33 patients (76.74%, three of them with autoimmune features and one as acute hepatitis), haemolytic anaemia with acute liver failure in 7 patients (16.27%), neurologic in two patients (4.65%) and by screening as a relative of an index case in one patient (2.32%). Molecular analysis of ATP7B gene revealed the presence of a Wilson’s disease characteristic mutation in 39 patients in homozygous or compound heterozygous status. The most frequent mutations in our cohort were H1069Q, detected in 30.23% of the alleles, and G1341D, detected in 26.74% of the alleles. Also, W939C mutation (11.62%) and K844K fs mutation (5.81%) were frequently detected. Other mutations were rarely detected only in compound heterozygous status: W779X, V890M, R969Q, G1030S, A1135T, D1222N, IVS 6-2: A>G, IVS 4-1: G>A, IVS +1: g>A.

Conclusion: The majority of the children with Wilson’s disease in our population presented with hepatic manifestations. H1069Q was the most frequent mutation detected in children from North-Western Romania, similar to the other populations from Central and Eastern Europe. H1069Q, G1341D, W939C and K844K fs mutations represent almost 75% of the mutations detected in children with Wilson’s disease from our cohort. These results confirm the opportunity to develop a diagnostic microarray chip to detect Wilson’s disease mutations in most of our patients.

Disclosure of interest: None Declared.
**HEPATOLOGY: General Hepatology**

H-P-033

**APRI as a fibrosis marker in children with autoimmune hepatitis (AIH)**

**Karolina Piwczyńska**, Woynarowski Marek, Dądalski Maciej, Woźniak Małgorzata

1Children's Memorial Health Institute, Warsaw, Poland

**Objectives and study:** AIH has a progressive course thus it is important to find easy and reliable clinical test that could allow early detection of the disease progression. Liver biopsy is a standard for the assessment of staging of liver disease but the procedure is invasive, painful and there is risk of complication thus alternative methods of liver fibrosis assessment are under investigation. APRI - AspAT-to-Platelet Ratio Index is simple indirect fibrosis test and could be obtain during routine blood test. The aim of the study was to correlate the APRI with staging of liver disease assessed by liver biopsy in children with AIH.

**Methods:** Blood samples and standard liver biopsies were taken from 46 children (F-33, M-13) aged 5.5-18 (14.5±3.8) with AIH. Routine blood samples were collected from all patients and AspAT to Platelet Ratio was calculated. All children had routine liver biopsy. Liver biopsies were scored according to Batts and Ludwig classification and patients were classified according to staging into two groups. Patients with no or minimal fibrosis (staging 0-1) and patients with well visible fibrosis (staging 2-4). APRI between two groups was compared and receiver operating characteristics (ROC) analysis was used to calculate the power of the assay to detect advanced liver fibrosis (AccuROC, Canada).

**Results:** Mild liver fibrosis was present in 8 and advanced fibrosis was found in 38 patients. Children with advanced fibrosis had significantly higher APRI (1.59 vs 0.30, p<0.01)) than children with mild or no fibrosis. Significant ability to differentiate children with advanced fibrosis from those with mild or no fibrosis was found. Area under ROC curve was 0.736111 (AUC=0.7361) with sensitivity (95% CI) 0.58 (0.407565 to 0.744859) and specificity (95% CI) = 1 (0.630583 to 1 [97.5% one-sided CI])

**Conclusion:** APRI can differentiate children with advanced fibrosis from those with mild or no fibrosis. AspAT to Platelet Ratio Index can be useful to detect the progression of the fibrosis in AIH children.

**Disclosure of interest:** None Declared
Biliary atresia outcome in Greek children: a 14 year experience in a tertiary referral center

Aglaia Zellos¹, Lilia Lykopoulou², Daphne Margoni³, Maria Rogalidou⁴, George Chrousos⁵, Eleftheria Roma⁶, Nina Manolaki⁷, Maria Maragkoudaki⁸

¹Division of Gastroenterology, Hepatology & Nutrition, University of Athens School of Medicine, Agia Sofia Children's Hospital, Athens, Greece
²Agia Sofia Children's Hospital, First Department of Pediatrics, Athens, Greece
³University of Athens, Athens, Greece
⁴University of Ioannina School of Medicine, Department of Pediatrics, Ioannina, Greece
⁵University of Athens School of Medicine, First Department of Pediatrics, Aghia Sophia Children's Hospital, Athens, Greece
⁶University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
⁷Agia Sofia Children's Hospital, 2nd Department of Pediatrics, Athens, Greece
⁸Division of Gastroenterology, Hepatology & Nutrition, University of Athens, Agia Sofia Children's Hospital, Athens, Greece

Objectives and study: There is no previously reported data regarding time of referral for diagnosis and outcome in children with biliary atresia (BA) in Greece. This study aimed to describe the current outcome of a Greek national cohort of children with BA in the largest referral hospital in Athens.

Methods: All cases of BA diagnosed in our tertiary University Hospital “Aghia Sofia” between 2001 and 2015 were reviewed retrospectively. Data was extracted regarding presenting patient history, portoenterostomy timing and outcome and referral for liver transplantation (LT).

Results: A total of 53 children (17 males/36 females) initially referred for persistent cholestatic jaundice were diagnosed with BA between 2001-2015. The average period of follow-up was 7.7 ± 4.3 years (median 8 years). Median age of referral for evaluation of jaundice to the hospital was 52 days. Only 15% of patients were exclusively breastfed. Portonenterostomy was performed in 46/53 at 73±30 days (median age of 70 days). In 7 patients, the portoenterostomy was not performed due to technical difficulties and they subsequently underwent liver transplantation (LT). After portoenterostomy, 22/46 (47%) survived without LT during a mean follow-up of 8.1 ± 4.6 years (median 9 years). LT was performed in 29/53 (55%) with 93% survival during a mean follow-up of 7.4 ± 4.1 years. Two children died awaiting LT and 2 died after complications following LT. Patients with native liver survival had portoenterostomy at a median age of 63 days (range 27-83), while those who were eventually transplanted had portoenterostomy at a median age 71 days (range 40-135).

Conclusion: The majority of Greek patients with BA were referred late. Despite delayed referral, when portoenterostomy was successfully done even at a median age of 63 days, a significant number survived without LT during childhood years.

Disclosure of interest: Aglaia Zellos MD: None Declared; Lilia Lykopoulou MD: None Declared; Daphne Margoni MD: None Declared; Maria Rogalidou MD: None Declared; Maria Maragkoudaki MD: None Declared, George Chrousos MD: None Declared; Eleftheria Roma, MD: None Declared; Nina Manolaki MD: None Declared.
Autoimmune hepatitis in greek children: a 14 year experience in three tertiary referral centers

Aglia Zellos1, Lilia Lykopoulou2, Maria Maragkoudaki3, Daphne Margoni4, George Chouliaras3, Konstantina Dimakou5, Maria Rogalidou6, Maria Fotoulaki7, Alexandra Papadopoulou3, Eleftheria Roma8, Nina Manolaki9
1Division of Gastroenterology, Hepatology & Nutrition, University of Athens School of Medicine, Agia Sofia Children's Hospital, Athens, Greece
2Agia Sofia Children's Hospital, First Department of Pediatrics, Athens, Greece
3Division of Pediatric Gastroenterology, Hepatology & Nutrition, University of Athens, Agia Sofia Children's Hospital, Athens, Greece
4University of Athens, Greece
5University of Ioannina School of Medicine, Department of Pediatrics, Ioannina, Greece
6Aristotle University of Thessaloniki, 4th Department of Paediatrics, Papageorgiou Hospital, Thessaloniki, Greece
7University of Athens School of Medicine, First Department of Pediatrics, Athens, Greece
8Agia Sofia Children's Hospital, 2nd Department of Pediatrics, Athens, Greece

Objectives and study: Autoimmune hepatitis (AIH) is a progressive inflammatory disease of unknown etiology presenting alone or in association with other autoimmune diseases. There is no previous data regarding presentation of the disease in Greek children. The aim of the study was to describe the clinical and histological presentation and response to treatment in Greece.

Methods: A retrospective review of a cohort of patients < 18 years diagnosed with AIH between 2001-2015 in three tertiary pediatric centers in Greece. Data was extracted from medical records and patient history, laboratory data, radiology studies, liver histology and therapy were reviewed. All patients were diagnosed after positive serology and a percutaneous liver biopsy while the majority had magnetic resonance cholangiopancreatography (MRCP) within the first year after diagnosis.

Results: A total of 73 children with mean age 5.8 ± 3.3 (25 males/ 48 females) were diagnosed with AIH type 1 (n= 28), AIH type 2 (n= 21), or autoimmune sclerosing cholangitis (ASC) (n= 21). Most patients were referred for evaluation of persistently elevated transaminases and were asymptomatic upon initial evaluation. Four patients presented with jaundice. The age of diagnosis was similar in all 3 groups: median age was 6 years (range 0.8-13) for AIH type 1, 5 years (range 1.5-9) for AIH type 2 and 6 years (range 2.2-12) for ASC. On liver biopsy, fibrosis (mean fibrosis score: stage 2 by Ishak) was noted in 43/73 (59%) of cases at initial presentation. Associated autoimmune diseases were noted in 22/73 (30%), such as celiac disease (n= 1), inflammatory liver disease (n= 2), hypothyroidism (n=2), juvenile rheumatoid arthritis (n=3). Preexisting or concomitant liver disease was noted at presentation in 7 patients: choledochal cyst (n=1), recent acute EBV infection (n=3), recent acute HAV infection (n=1), a1 antitrypsin MZ phenotype (n=1), posterior lacerative injury (n=1). One patient had beta (β000) thalassemia. All children responded to treatment induction with prezonol +/- azathioprine in the first year. Duration of follow-up was 3.9 ± 2.8 years (range 0.5-14). About 97 % of children were treated long term with 1 medication and maintained biochemical and clinical remission. Five patients (7%) relapsed after discontinuation of therapy following clinical remission, while two have stopped therapy without relapse of their disease. None of the patients required liver transplantation during the study period.

Conclusion: Overall, children with AIH in Greece presented with mild clinical symptoms, although liver fibrosis was noted on liver biopsy in more than half upon initial diagnosis. All children responded well to initial and maintenance therapy and none progressed to liver failure during follow-up. However, in one third of patients, there was association with other autoimmune diseases that required concomitant treatment. Long-term follow-up is needed to evaluate for further disease progression.

Disclosure of interest: Aglia Zellos: None Declared; Lilia Lykopoulou: None Declared; Maria Maragkoudaki: None Declared; Dafne Margoni: None Declared; George Chouliaras: None Declared; Dina Dimakou: None Declared; Maria Rogalidou: None Declared; Maria Fotoulaki: None Declared; Ioanna Panayotou: None Declared; Alexandra Papadopoulou: None Declared; Eleftheria Roma: None Declared; Nina Manolaki: None Declared;
Evaluation Of Thyroid Hormones in Paediatric Acute Liver Failure Patients

Zeren Barış¹, Meltem Gülşan², Figen Özçay³

¹Baskent University Faculty of Medicine, Pediatric Gastroenterology and Hepatology, Ankara, Turkey
²Baskent University Faculty of Medicine, Pediatric Gastroenterology, Ankara, Turkey
³Başkent University Hospital, Paediatric Gastroenterology, Ankara, Turkey

Objectives and study: Serum TSH, free T4 and free T3 can be prognostic factors in ALF

Methods: We retrospectively collected clinical and laboratory data of 32 ALF cases with available thyroid function tests out of 91 ALF cases who applied to Baskent University Hospital between 2000-2015.

Results: There were a total of 32 patients, 14 of them were female. Patients' mean age was 64.17±52.39 months. ALF was idiopathic in 43.5% (n=14), due to hepatitis A in 25% (n=8), Wilson's disease in 6.3% (n=2), otoimmune hepatitis in 6.3% (n=2) and toxic causes in 6.3% (n=2). Thirteen patients (40.7%) had encephalopathy grade 1-2, 14 (43.8%) had encephalopathy grade 3-4, while 5 (15.6%) patients did not show any sign of encephalopathy. The mean value of INR was 4.98±3.36, total bilirubin was 19.93±10.9 mg/dl, albumin was 3.4±0.61 g/dl. The mean period from jaundice to encephalopathy was 25.19±17.98 days. The mean level of TSH was 0.81±1.14 µIU/ml (n: 0.7-6.4), fT4 was 1.5±1.29 ng/dl (n: 0.7-1.48) and fT3 was 1.60±0.71 pg/ml (n: 1.71-3.71). Free T4 levels were normal in 23 (71.9%) of the patients, while 19 (59.4%) patients had low TSH levels, and 16(50%) of the patients had low fT3 levels.

Hepatic failure resolved spontaneously in 11 (34.4%) of the patients, 10 (31.3%) patients underwent liver transplantation and 11 (34.4%) patients died. Patients were divided into two groups according to disease course: group 1 (n=11) included patients with spontaneous resolution and group 2 (n=21) included patients who either died or underwent liver transplantation. Age, mean period from jaundice to encephalopathy, INR and albumine levels did not show any significant difference between the two groups, while total bilirubin levels were significantly higher in group 2 (24.21±9.72 mg/dl) compared to total bilirubin levels of group 1 (11.76±8.21 mg/dl) (p=0.001).

Thyroid functions were evaluated between two groups. Serum TSH levels in group 1 (1.13±1.63 µIU/ml) were higher than the TSH levels in group 2 (0.63±0.78 µIU/ml) but this difference was not statistically significant. Free T3 and free T4 levels did not differ significantly between two groups.

Serum TSH levels were found to decrease with increasing levels of total and direct bilirubin levels, and these correlations were statistically significant (r=-0.41, p=0.021 and r=-0.39, p=0.024, respectively). Serum free T4 levels were found to decrease significantly with decreasing levels of serum albumin levels (correlation coefficient: 0.43, p=0.019). There wasn't any significant correlation between thyroid hormones and patients' age, grade of encephalopathy and serum levels of INR.

Conclusion: Although serum TSH and free T3 levels are suppressed in pediatric patients with ALF, patients with spontaneous survival seem to have higher TSH levels.

Disclosure of interest: None Declared.
Predictors of liver steatosis and fibrosis measured by Fibroscan in children with Wilson’s disease.

Wojciech Janczyk, Maciej Pronicki, Wieslawa Grajkowska, Diana Kaminska, Jakub Kmiotek, Magdalena Naorniakowska, Malgorzata Podlaska, Piotr Socha

1Children’s Memorial Health Institute, Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
2Children’s Memorial Health Institute, Pathology, Warsaw, Poland

Objectives and study: Wilson’s disease in childhood may present with mild or significant liver injury as indicated by liver biopsy and liver function tests. Zinc or D-penicillamine (D-pen) seem to stop progression of liver damage but zinc effectivity is often questioned. As liver biopsy is not usually repeated in the course of the disease only surrogate markers can be used for assessment of liver disease. Recently non-invasive transient elastography - Fibroscan® (Echosens, France) has been applied in many chronic liver diseases for assessment of fibrosis and steatosis. We aimed to evaluate progression of liver disease and response to treatment assessed by Fibroscan in relationship to the extent and type of liver damage before treatment as assessed by liver histology and liver function tests.

Methods: We retrospectively analyzed liver histology, liver copper content and biochemical markers of 34 children with Wilson’s disease aged 12.8±4.1 years at the time of diagnosis and compared them to liver stiffness (LSM) and steatosis (CAP) using Fibroscan® after mean period of 9.7yrs of treatment with zinc (n=21) or D-pen (n=13). In addition LSM and CAP results of pts with Wilson’s disease were compared to a control group of 20 healthy controls aged 11.8±5.3yrs. Liver histology was described semiquantitatively including micro- and macrovesicular steatosis (modified NAFLD scoring system by Kleiner et al.), portal and lobular inflammation and cholestasis. The associations were tested with Spearman R test and differences between groups were tested with Mann-Whitney U test.

Results: The selected cohort of patients with Wilson’s disease presented with variable fibrosis (grade 3-4 in 13 patients), lobular inflammation (grade 2-3 in 2 pts), portal inflammation (grade 2-3 in 3 pts), microvesicular (grade 2-3 in 3pts) and macrovesicular steatosis (grade 2-3 in 12pts) and without cholestasis. There were no differences in pre-treatment parametres between children treated with Zn and D-pen. Liver fibrosis (LSM) assessed by Fibroscan® was slightly but significantly higher in pts with Wilson’s disease than in healthy controls [5 (4.1-6.1) vs. 4.2 (3.8-4.5) kPa] and steatosis expressed by CAP was also increased [252 (218-292) vs. 182 (119-194) dB/m]; p<0.05. We found a significant relationship between liver steatosis assessed by Fibroscan® (CAP) and macrovesicular liver steatosis on liver biopsy (r=0.68) while LSM was not related to liver fibrosis. LSM significantly correlated with baseline total bilirubin levels (r=0.4) but not with other liver function tests, ceruloplasmin or liver copper content. We found no difference in Fibroscan results between groups treated with D-pen or zinc [LSM 5.4 (4.3-6.1) vs 4.5 (4.1-5.8) kPa; CAP 251 (208-266) vs. 256 (235-307) dB/m].

Conclusion: Liver steatosis in children with Wilson’s disease seems not to respond to treatment and the extent of steatosis in the course of the disease is closely related to pre-treatment values. Fibrosis at start of therapy is affected by treatment and may change significantly with time. D-pen and Zn therapy seem to be equally effective when tested with Fibroscan in children with mild liver injury.

Disclosure of interest: None Declared.
Portosystemic shunt surgery in children: Gazi university experience

Aydın Dalgıç1, Billur Demiroğulları2, Hakan Sozen3, Sinan Sarı4, Neslihan Ekgül Bozbulut4, Özül Eğritaş Gürkan4, Buket Dalgıç4

1Gazi University, Department of General Surgery, Ankara, Turkey
2Gazi University, Department of Pediatric Surgery, Ankara, Turkey
3Gazi University, Division of Transplantation, Ankara, Turkey
4Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey

Objectives and study: We evaluated the results and complications of portal hypertension patients who underwent portosystemic shunt surgery.

Methods: In this retrospective study, we reviewed patients with non-cirrhotic portal hypertension (PH), who underwent portosystemic shunt surgery at Gazi University Faculty of Medicine, Department of Pediatric Gastroenterology. Demographics, preoperative and postoperative anthropometric parameters (weight and height), hemoglobin, white blood cell, platelet counts, spleen size, degree of esophageal varices, variceal bleeding, potency of surgical shunt with Doppler ultrasound, complications after shunt surgery were obtained from hospital files and electronic medical records. We compared preoperative and postoperative records.

Results: Portosystemic shunt surgery was applied to 27 patients (19 boys, 8 girls) between 2006-2015. Their mean age was 9.64 ± 5.4. Shunt surgery indications were severe, rebleeding variceal bleeding, hypersplenism and portal biliopathy. Diagnosis of patients were prehepatic PH (portal vein thrombosis), presinusoidal PH (congenital hepatic fibrosis, hepatoporal sclerosis). Twelve (44.4%) patients underwent distal splenorenal shunting and 15 (55.6) underwent proximal splenorenal shunting. The mean postoperative follow-up time was 16.6 (range 1-49) months. Portocaval shunt occlusion occurred in 6 patients. Other complications were portal vein thrombosis (1), shunt thrombosis and thrombectomy (1), splenic embolization (1), chylous ascites and acalculous cholecystitis (1) and infection (1). One patient who had been followed with a patent proximal portosystemic shunt for three years, died after living donor liver transplantation performed for Budd-Chiari syndrome. Preoperative and postoperative weight for age, height for age Z scores, hemoglobin, white blood cell, platelet counts, spleen size, the degree of esophageal varices, frequency of variceal bleeding are shown at table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Pre-op (median, range)</th>
<th>Post-op (month 12) (median, range)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight, SDS</td>
<td>-1.35 (-3.89 - 1.96)</td>
<td>-0.54 (-2.74 - 1.63)</td>
<td>0.013</td>
</tr>
<tr>
<td>Height, SDS</td>
<td>-1.19 (-3.26 - 0.57)</td>
<td>-0.56 (-2.72 - 1.13)</td>
<td>0.046</td>
</tr>
<tr>
<td>*Hemoglobin, g/dl</td>
<td>9.8 (7.2 – 16.0)</td>
<td>11.6 (6.7 – 13.5)</td>
<td>0.26</td>
</tr>
<tr>
<td>*Leukocyte, /mm3</td>
<td>5105 (2200 – 22000)</td>
<td>4222 (2430 – 6870)</td>
<td>0.21</td>
</tr>
<tr>
<td>*Thrombocyte, /mm3</td>
<td>97300 (39800 – 2798000)</td>
<td>112000(65600 – 334000)</td>
<td>0.051</td>
</tr>
<tr>
<td>*Spleen size, cm</td>
<td>17 (13 – 20)</td>
<td>13.5 (12 – 17)</td>
<td>0.138</td>
</tr>
<tr>
<td>Esophageal varice grade</td>
<td>3 (0 – 4)</td>
<td>2 (0 – 3)</td>
<td>0.013</td>
</tr>
<tr>
<td>Frequency of variceal bleeding</td>
<td>1 (0 – 1)</td>
<td>0 (0 – 1)</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Table 1. Values are median (minimum-maximum). *Cases with splenectomy were excluded. SDS, standard deviation score.
**Conclusion**: Variceal bleeding due to PH is an important factor for morbidity and mortality. Portosytemic shunt surgery especially performed for non-cirrhotic PH patients, improved growth and development and decreased the degree of esophageal varices.

**Disclosure of interest**: None declared.
Use of the Paediatric End-stage Liver Disease Score for prediction of the evolution in fulminant liver failure caused by mushroom poisoning in children

Tudor Lucian Pop, Alina Grama, Ana Stefanescu, Dan Delean, Cornel Aidea, Aurel Bizo

1University of Medicine and Pharmacy Iuliu Hatieganu, 2nd Pediatric Clinic, Cluj-Napoca, Romania
2Emergency Hospital for Children, Nephrology Clinic, Cluj-Napoca, Romania

Objectives and study: Fulminant liver failure is a rare but fatal disease in children in the absence of the emergency liver transplantation. In our area mushroom poisoning is the most frequent cause of fulminant liver failure in children. Early evaluation of the prognosis and referral of the patient to a liver unit could be lifesaving. The Paediatric End-stage Liver Disease (PELD) Score was developed for children under 12 years of age to assess the severity of chronic liver disease and for prioritization of liver transplantation. The King’s College Criteria are used to predict the need of liver transplantation in acute liver failure. The aim of our study was to evaluate the usefulness of PELD Score as a prognostic factor in fulminant liver failure in children with mushroom poisoning.

Methods: We have retrospectively analysed the data of children with fulminant liver failure caused by mushroom poisoning during four consecutive years: clinical features, laboratory parameters and patient’s survival function to the PELD Score and the King’s College Criteria, calculated using data from the first day of hospitalization. We have included in the study only the children under 12 years of age. There was no patient with liver transplantation in our cohort.

Results: During 2008-2011, 69 children with mushroom poisoning were hospitalized, 28 of them with fulminant liver failure (40.57%). 22 children were under 12 years of age and their data were analysed (13 boys, 9 girls, mean age of 7.36+/−2.78 years). At admittance, 12 children (54.54%) presented severe encephalopathy. The evolution was fatal in 13 patients (59.09%). PELD score was significantly increased in non-survivors patients compared to survivors (19.41±20.49 vs -7.72±5.92, p=0.001). In deceased patients PELD Score was between -8.5 and 47 and in survivors was between -18 and -0.5. Based on our small cohort, the PELD Score over 10 can predict the mortality of the patient with a positive predictive value (PPV) 100%, negative predictive value (NPV) 69.23%, sensibility 69.23%, and specificity 100% (accuracy of 81.81%). The PELD Score over 3 can predict the mortality with PPV 100%, NPV 75%, sensibility 76.92%, and specificity 100% (accuracy of 86.36%) compared with King’s College Criteria that predict the indication of liver transplantation with PPV 100%, NPV 52.94%, sensibility 38.46%, and specificity 100% (accuracy of 63.63%).

Conclusion: Fulminant liver failure caused by mushroom poisoning had an increased mortality in our cohort, in absence of the emergency liver transplantation. The PELD Score at admittance can be used as a predictive factor for the evolution of the disease and for the need of the patient referral to a specialized liver unit, with emergency liver transplantation possibilities. In our small cohort, the PELD Score based on the admittance data was a better indicator of fatal evolution compared with the King’s College Criteria. Further studies are needed to permit a stronger conclusion.

Disclosure of interest: Tudor L. Pop and Ana Stefanescu funded by Partnership Grant PN-II-PT-PCCA-2011-3.2-0917.
Autoimmune hepatitis or Wilson’s disease or both? Analysis of challenging cases

Magdalena Naorniakowska¹, Małgorzata Woźniak¹, Maciej Pronicki², Diana Kamińska¹, Wojciech Jańczyk¹, Maciej Dądalski¹, Piotr Socha²

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology and Nutritional Disorders, Warsaw, Poland
²The Children’s Memorial Health Institute, Department of Pathology, Warsaw, Poland

Objectives and study: Comorbidity of autoimmune hepatitis (AIH) and Wilson’s disease (WD) can be considered, but has never been proven based on therapeutic response. There is a risk of misdiagnosis with standard diagnostic approach. We describe challenging patients where final diagnosis could not be established at primary diagnostic approach and we question coexistence of AIH and WD.

Methods: We identified 4 cases among 165 WD (diagnosis according to Ferenci score - FS) and 321 AIH patients, in whom primary diagnosis was changed or questioned.

Results: 3 patients were diagnosed because of elevated serum transaminases (TA) activity, and one due to acute hepatic failure.

Case 1: diagnosed with AIH based on liver histology (steatohepatitis and fibrosis), ANA 1:640, IgG: 2824.5mg/dl, without WD tests performed. Prednisone and azathioprine (AZT) was not effective and 1 year later diagnosis of WD was done based on results of ceruloplasmin, urine copper excretion, liver copper and molecular test. Penicillamine was introduced, steroids and AZT were withdrawn leading to normal liver tests.

Case 2: primarily did not fulfill criteria of WD: ceruloplasmin 16 mg/dl, normal urine copper excretion. Based on ANA 1:640 and ASMA 1:160, liver histology (severe inflammation and fibrosis) prednisolone was started. After 1 year the child developed psychiatric and neurological symptom, brain MRI revealed abnormalities. Based on ceruloplasmin concentration, neurological symptoms and molecular test (1 mutation) WD was diagnosed and zinc therapy was started. Meanwhile the patient was diagnosed with Crohn disease. Patient was treated with zinc, AZT and 5-ASA with good clinical and laboratory response.

Case 3: had normal serum ceruloplasmin and urine copper excretion. Based on histology (periportal inflammation), positive ANA 1:320 and ASMA 1:80, prednisolone was initiated. After 1 year TA were still elevated. At 2nd diagnostic approach WD was diagnosed based on ceruloplasmin 14mg/dl and molecular test (FS: 7 points). Penicillamine was initiated and steroids were withdrawn leading to normal liver function tests.

Case 4: diagnosed with WD based on ceruloplasmin 16mg/dl, urine copper excretion 4901ug/24h, K-F ring present and molecular test (2 mutations) (FS: 9 points). Penicillamine was started but 1 month later because of hipertransaminasemia and positive ANA (1:40), ASMA (1:40) steroids were added. After next 4 weeks trientine was started and penicillamine withdrawn due to neutropenia. Tapering of steroids led to TA elevation so steroids were continued. Liver biopsy performed after coagulation normalization showed steatohepatitis and fibrosis.

Conclusion: WD usually can be distinguished from AIH but in selected cases differential diagnosis is challenging. WD should be retested in patients with poor response to steroids. In a big cohort of WD and AIH patients only one seems to have comorbidity but even in this case AIH was not fully confirmed.

Disclosure of interest: None Declared.
Role of plasmapheresis in acute liver failure of autoimmune etiology

Banu Bal Çermik¹, Mustafa Ertugrul², Selim Gokce¹, Selcuk Uzunuer¹, Nurettin Onur Kutlu¹

¹Bezmialem Vakif University, Istanbul, Turkey
²Memorial Hospital, Istanbul, Turkey

Objectives and study: Autoimmune hepatitis (AIH) is characterized by increased levels of immunoglobulin G (IgG), the presence of autoantibodies and various degrees of lymphocyte predominant inflammation and fibrosis histologically. Immunosuppressive therapy induces remission in around 80% with the exception of fulminant presentation with encephalopathy. Several liver supporting methods including plasma exchange (PE) could make possible to bridge patients to transplantation or to spontaneous recovery in setting of liver failure. Herein, we report three AIH patients with fulminant presentation whose symptoms markedly improved with PE.

Methods Case 1: A previously healthy 6-year-old girl was admitted to hospital with nausea, vomiting and jaundice. Laboratory findings at presentation were AST 824 IU/L, ALT 721 IU/L, total bilirubin (TB) 7.62 mg/dl, direct bilirubin (DB) 5.98 mg/dl, INR 1.33. Viral serology for hepatitis A, B, C, E, Epstein-Barr virüs (EBV), and Cytomegalovirus (CMV) were all negative. Laboratory investigation revealed elevated IgG and positive antinuclear antibody. In due course of the disease, she rapidly progressed to grade 2-3 hepatic encephalopathy. Prednisolone together with PE has been started. After 3 daily sessions of PE treatment, patient was non-encephalopathic with decreased levels of transaminases, bilirubin and INR. At the end of one month, patient was well tolerating prednisolone and azathioprine with near normal transaminases and normal INR.

Case 2: 10-year-old boy with no history of previous illness presented with abdominal pain and jaundice. In laboratory, transaminases, LDH, GGT, TB, DB levels were elevated. INR was 1.96 that is unresponsive to vitamin K and fresh frozen plasma. Viral serology was negative for hepatitis A, B, C, EBV and CMV. Anti-smooth muscle antibody was positive together with increased titers of gammaglobulin. Liver biopsy was ignored due to coagulopathy and prednisolone was started. At the 4th day of prednisolone, patient developed grade 2 encephalopathy. After 3 PE sessions patient showed clinical and laboratory improvement. He was discharged on prednisolone treatment.

Case 3: A 2-year-old girl was referred to hospital with hepatic encephalopathy. INR value was 3.51. Viral, toxic and metabolic causes were excluded. She had positive antinuclear antibody together with increase gammaglobulin titers. Prednisolone and PE treatments were commenced on immediately. After 3 daily sessions of PE, she was non-encephalopathic and INR was 2.02. INR value was completely normalized at the end of first month of admission while she was on prednisolone and cyclosporine treatment.

Conclusion: In acute liver failure, spontaneous recovery rate ranges within 5-80%. Decompensation of liver function results in decreased biotransformation and excretion of toxic substances as well as synthetic properties. PE removes water soluble or albumin-bound toxic substances and replaces essential substances and temporarily supports liver functions until functional recovery or liver transplantation. In liver failure resulting from etiologies other than autoimmune and toxic causes, PE may not change eventual fate of the liver disease. In setting of AIH, however, it may have a special therapeutic role as an adjunct to immunosuppressive treatment by removing autoantibodies and cytokines, so therefore preventing further liver damage and decompensation, and allowing time for the recovery.
Portal hypertensive biliopathy as a cause of cholestasis in children with congenital hepatic fibrosis

Aydin Dalgıç¹, Sinan Sarı², Hakan Sozen³, Neslihan Gürcan Kaya², Buket Dalgıç²

¹Gazi University, Department of General Surgery, Ankara, Turkey
²Gazi University, Pediatric Gastroenterology, Hepatology and Nutrition, Ankara, Turkey
³Gazi University, Division of Transplantation, Ankara, Turkey

Objectives and study: Portal hypertensive biliopathy (PHB) is characterized with abnormalities of the intrahepatic and extrahepatic bile ducts and gallbladder in patients with portal hypertension. Extrahepatic portal vein obstruction is the most common cause of the PHB. Biliary changes were also described in the other causes of portal hypertension like cirrhosis and non-cirrhotic portal fibrosis. We report a child with PHB secondary to congenital hepatic fibrosis.

Methods: A 16-years-old female referred to our clinic for liver transplantation with diagnosis of congenital hepatic fibrosis. Four years ago, she suffered from upper esophageal variceal bleeding due to portal hypertension. She did not have any symptoms for four years and presented with bloody vomiting, icterus and severe pruritus for a month. On physical examination, she had icterus, hepatomegaly and splenomegaly. Laboratory tests revealed hemoglobin, 8.4 g/dL; leukocyte, 1900/mm³; platelet, 37000/mm³; AST, 44 U/L; ALT, 40 U/L; GGT, 20 U/L; ALP, 115 U/L; total bilirubin, 14.3 mg/dL; direct bilirubin, 8.1 mg/dL; albumin, 3.9 g/dL; prothrombin time, 10.3 sec. Upper gastrointestinal endoscopy showed esophageal and fundic varices. MRCP showed mild dilatation of the intrahepatic bile ducts. Liver biopsy was reported as congenital hepatic fibrosis and severe bilirubinostasis in the bile ductules and parenchyma. After other causes of cholestasis, including infections, autoimmune and metabolic liver diseases, Caroli disease, ductopenia and extrahepatic biliary system disorders were excluded on the basis of appropriate serologic, histopathologic and radiologic tests, she was diagnosed as PHB with clinical and radiologic findings.

Results: Proximal splenorenal shunt was performed. Within postoperative 20 days her clinical and laboratory findings was completely resolved. One year after the surgery there is no varices in upper gastrointestinal endoscopy.

Conclusion: Non-cirrhotic hepatic fibrosis is a rare cause of PHB. Management of PHB should be focused on the management of portal hypertension and relief of biliary obstruction. In symptomatic PHB, portal decompression surgery by proximal splenorenal shunt is one of the successful treatment option.

Disclosure of interest: “None Declared”
The Effect of Vitamin D Deficiency on Nonalcoholic Fatty Liver Disease Development in Obese Children

Makbule Eren1, Birgul Kirel2, Tuna Tekin3, Yalcin Kara3

1Eskisehir Osmangazi University, Pediatric Gastroenterology and Hepatology, Eskisehir, Turkey
2Osmangazi University, Eskisehir, Turkey
3Eskisehir Osmangazi University, Eskisehir, Turkey

Objectives and study: Non-alcoholic Fatty Liver Disease (NAFLD) is one of the major obesity-associated comorbid conditions. Factors influencing development of hepatosteatosis, initiating inflammation and progression to steatohepatitis are not elucidated yet. Decreased bioavailability of vitamin D in obese children is highly accepted. Our primary aim was to evaluate the effect of vitamin D deficiency on development of NAFLD in obese children. Our secondary aim was to clarify the effect of vitamin D status on certain well-known obesity related conditions.

Methods: 91 patients with obesity were enrolled in this study. Their data of demographic, anthropometric, laboratory and radiological findings were analysed retrospectively. Findings were evaluated according to their Vitamin D status. Patients were allocated into 2 groups as group 1 (vitamin D <20 ng/ml) and group 2 (vitamin D≥20 ng/ml). Hepatosteatosis was defined with ultrasonography. Liver enzyme elevations along with hepatosteatosis were referred as steatohepatitis.

Results: The median age of our study group was 13 (9-14). 53 (57.8%) of them were female. Vitamin D deficiency was observed in 74 (81.3%). Although 75.8% of patient with abdominal obesity, 77.3% with hepatosteatosis, 82.9% with insulin resistance, 76.5% with steatohepatitis, 83.3% with hypertension and 91.4% with hypertriglyceridemia had vitamin D deficiency, except the latter none of the other findings were significant (p=1.0, p=0.33, p=0.72, p=0.39, p=1.0, p=0.046). There wasn’t any difference between groups in terms of median levels of systolic-diastolic blood pressures (mmHg) [100 mmHg (90-120) vs. 100 mmHg (90-120) p=0.73; 60 mmHg(60-80) vs. 60 mmHg (57.5-70) respectively, p=0.31], ALT [21 U/l (14.7-35.2) vs. 18 U/l (12-36) p=0.51] and AST [22 U/L (18-30) vs. 23 U/l (15.5-28.0) p=0.91]. Neither mean levels of waist circumference (102.35±19.99 cm vs. 96.37±16.22 cm, p=0.28) nor HOMA-IR (4.34±2.75 vs. 4.03±2.28, p=0.66) was different between groups. Except calcium [9.8 mg/dl (9.7-10.0) vs. 9.7 mg/dl (9.4-9.8), p= 0.02] the other bone mineralization parameters was not significantly different among groups. Although higher triglyceride levels were observed in children with vitamin D deficiency (114 ± 44.39 mg/dl vs. 80.88 ±28.9 mg/dl, p= 0.004); there was no association with other lipid profile components.

There wasn’t any difference in terms of vitamin D levels between patient with or without insulin resistance [12. 0 ng/L(10.6-15.94) vs. 12.8 ng/L (8.9-18.2), p=0.78], hepatostetosis [11.6 ng/L(8.07-15) vs. 12.9 ng/L(10.9-17.77), p=0.22], steatohepatitis [12 ng/L (9.36-16.56) vs. 12.1ng/L (11.2-18.8, p=0.61) and hypertension [12.6 ng/L(11.07-18.35) vs. 12.1ng/L (9.26-16.64), p=0.6]. Median vitamin D levels at pubertal and prepubertal stage [11.75 ng/L(9.39-15.07) vs.15.0 ng/L(11.2-18.4, p=0.79 respectively] were not significantly different. We couldn’t demonstrate any correlation between vitamin D level and HOMO-IR (r=-0.087 p = 0.41), waist circumference (r= -0.11, p=0.21) and grade of steatosis r= 0.13, p=0.19

Conclusion: There is a high prevalence of vitamin D deficiency in obese children. Hypertriglyceridemia is more frequent in decreased vitamin D levels. However no association was found between vitamin D deficiency, hepatosteatosis, steatohepatitis and other obesity related conditions.

Disclosure of interest: None Declared
Antenatal and postnatal clinical spectrum of congenital portosystemic shunts: experience from a university hospital with high patient turnover

OBJECTIVES AND STUDY: Congenital portosystemic shunts (CPSS) are reported increasingly with different clinical associations in paediatrics. In this report we wanted to analyse the diagnosis and outcome of both foetuses and children with CPSS.

METHODS: We searched retrospectively for the foetuses and paediatric patients diagnosed and followed in our hospital with CPSS between 2008 and 2015. Databases of Obstetrics and Gynaecology and Paediatric Gastroenterology and Hepatology were used for this research.

RESULTS: Overall 8 cases of CPSS were diagnosed.

Antenatal diagnosed cases:
Four foetuses had been diagnosed as type I CPSS by foetal ultrasound in our perinatology clinic. All were the product of spontaneous conception in mothers aged between 24-33 years. Smallest foetus was 400 g at 22 weeks gestation at the time of diagnosis. All but one mother had at least one previous abort. One foetus diagnosed at 26 weeks gestation had to be terminated because of the associated severe cardiac anomalies. One other foetus diagnosed at 28 weeks of gestation displayed intrauterine growth retardation and oligohydramnios.

Postnatal diagnosed cases:
There were 4 children diagnosed with CPSS: 2 girls (age range 7-15). They were followed in our clinic at least for 2 years (range 2 years – 8 years). Demographics and specific data about children diagnosed postnatally with CPSS are summarized in the Table below.
<table>
<thead>
<tr>
<th>Case</th>
<th>Age at diagnosis (years) / Sex</th>
<th>Age and nature of first event</th>
<th>Physical Examination Findings</th>
<th>Laboratory Findings</th>
<th>Imaging Findings</th>
<th>Liver Biopsy</th>
<th>Treatment</th>
<th>Outcome</th>
<th>Follow-up time</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>7 / Female</td>
<td>Newborn hypoglycaemia</td>
<td>Premature adrenarche</td>
<td>Hypoglycaemia</td>
<td>Hamartomatous lesion in pancreas tail and focal nodular hyperplasia in the liver</td>
<td>PET-CT with octreotide: Normal CPSS</td>
<td>Diazoxide for hypoglycaemia</td>
<td>Conservative for liver and pancreatic masses</td>
<td>Uneventful</td>
</tr>
<tr>
<td>2</td>
<td>14 / Male</td>
<td>14 years Bloody vomiting</td>
<td>Mild mental retardation</td>
<td>Hyperammonemia</td>
<td>Multiple masses (6cm in diameter) 2004: Multiple masses (6cm in diameter) 2007: progression of lesions in size (8 cm) CPSS</td>
<td>2004: Fibrosis with regenerative nodules 2007: Adenoma or well differentiated hepatocellular carcinoma (HCC)</td>
<td>Living donor liver transplantation (LDLTx) due to suspicion of HCC</td>
<td>Improvement in mental retardation No HCC in explant Transferred to Adult Care</td>
<td>8 years</td>
</tr>
<tr>
<td>3</td>
<td>15 / Male</td>
<td>11 years Elevated LFTs of unknown origin</td>
<td>NR</td>
<td>Hyperammonemia</td>
<td>Multiple masses less than 4 cm in diameter in the liver CPSS</td>
<td>Loss of portal venules with mild fibrosis</td>
<td>L-ornithine L-aspartate</td>
<td>Uneventful Transferred to Adult Care</td>
<td>4 years</td>
</tr>
<tr>
<td>4</td>
<td>15 / Female</td>
<td>14 years Right upper quadrant pain</td>
<td>NR</td>
<td>Multiple masses in the liver (range 5-9 cm in diameter)</td>
<td>Regenerative nodules</td>
<td>LDLTx</td>
<td>Uneventful</td>
<td>3 years</td>
<td></td>
</tr>
</tbody>
</table>
Conclusion: CPSS can present in different ways with different outcomes. Number of children diagnosed with CPSS will probably increase due to technical improvements and increased availability of imaging modalities. More studies are needed to analyse the nature of masses seen in CPSS.

Disclosure of interest: None Declared
Novel Mutation of ABCB11 Heterozygote Associated with Transient Neonatal Intrahepatic Cholestasis

Jae Young Kim, Myung Seok Shin

1Chungnam National University Hospital, Pediatrics, Daejeon, Rep. of South Korea
2St. Mary's Hospital, Pediatrics, Daejeon, Rep. of South Korea

Objectives and study: Bile salt export pump (BSEP), encoded by ABCB11 (2q24-31), is key function of conjugated bile salts transport from the hepatocyte cytoplasm into biliary canaliculi. Numerous BSEP mutations have been defined in patients with progressive intrahepatic cholestasis type 2, benign recurrent intrahepatic cholestasis, intrahepatic cholestasis of pregnancy, drug induced cholestasis, and primary sclerosing cholangitis. In contrast, some novel mutations/variants of ABCB11 reported as attributing to the transient neonatal cholestasis (TNC). We experienced a case of novel heterozygous ABCB11 in a patient with TNC.

Case: A 45-days old male was hospitalized in our unit due to cholestasis. He was delivered cesarean section at 40 week gestation with a weight of 3500 g. Gestational and birth history were nonspecific. On physical examination, he had icteric sclera, bright copper color skin but yellowish stool color. He had no cardiac murmur, hepatomegaly, and splenomegaly. The initial hematologic findings showed hemoglobin 10.9 g/dL, white blood cell 14,080/uL, platelet 497,000/uL, and PT/PTT 10.8 (INR 1.04)/35.8 second. Liver function tests were as follows: AST/ALT 288/303 U/L, total bilirubin 5.44 mg/dL, direct bilirubin 4.86 mg/dL, GGT 55 U/L, ALP 411 U/L, albumin 3.7 g/dL and total cholesterol 152 mg/dL. Other tests showed α1-antitrypsin 144 mg/dL and normal thyroid function. TORCH tests, CMV PCR, EBV-PCR, and viral marker for hepatitis A, B and C were negative. Liver ultrasonography showed nonspecific. Blood and urine for amino acid and organic acid analysis were also nonspecific. Genetic analysis of 27 exon and exon-intron boundary for ABCA11 in chromosome 2q24 revealed novel heterozygote c.2053G>T (p.G685W) and 13 polymorphism in exon 16. Ursodeoxycholic acid was administrated and liver function tests on his age of 94 days showed AST/ALT 34/43 U/L, total and direct bilirubin 0.41/0.36 mg/dL, and GGT 26 U/L.

Conclusion: c.2053G>T (p.G685W) of ABCB11 might be associated with TNC.

Disclosure of interest: None Declared.
Lysosomal acid lipase activity deficiency in children with liver disease: What Else Could It Be?

Giusey Ranucci1, Giada Zollo1, Federica Leone1, Fabiola Di Dato1, Giovanna Puoti1, Lorenza Lepore1, Raffaele Iorio1

1University of Naples Federico II, Department of Translational Medical Science, Section of Pediatric, Liver Unit, Naples, Italy

Objectives and study: The deficit of lysosomal acid lipase (LAL-D or CESD) is a rare lysosomal storage disease. The total enzyme deficiency is associated with Wolman disease. In partial deficiency of LAL the onset of the disease is variable and the clinical features are less well defined. It is not known if other liver diseases can affect the activity of the LAL, resulting in an enzyme deficiency. Aims of our study were: to identify the prevalence of LAL deficiency in patients with liver disease of unknown origin; to evaluate the activity of LAL in patients with known liver disease such as Wilson’s disease (WD), biliary atresia (BA) and autoimmune hepatitis (AIH); to evaluate the existence of a relation between LAL activity and severity of liver disease (ALT level), dyslipidemia and other parameters of metabolic syndrome.

Methods: We evaluated 51 patients (36 males) with a median age of 13 years (2-33 years), followed at the Pediatric Hepatology Unit of University "Federico II" of Naples, belonging to two different groups: with a liver disease of unknown origin and with a liver disease secondary to a known cause. Recorded data of the patients included: anthropometric parameters; abdomen ultrasound evaluation; laboratory markers of liver disease including all markers of metabolic syndrome; acid lipase activity determination by blood spots according to the Hamilton's method; genetic analysis for patients with LAL activity deficiency.

Results: None of our patients resulted affected by LAL disease genetically determined. In 22% of subjects in the study a partial enzyme activity deficiency was found (reduction of LAL activity from 15% to 50% of the lower limit of the controls). Of these patients: 3 were in the first group; 8 were in the second group (6 patients with WD and 2 with BA). Steatosis was found in all patients with LAL activity deficiency. An inverse correlation between LAL activity and serum triglyceride levels (R = 0.08479) and age of the patients (R = 0.1192) was found. It was not found a significant correlation between LAL activity and BMI, ALT, glucose, cholesterol, insulin and HOMA index. Finally WD patients with LAL deficiency had both cholesterol and triglyceride levels higher if compared with not deficient patients; they also had a higher BMI.

Conclusion: Our study shows that liver disease may determine a secondary partial LAL deficiency and that in these patients the enzyme activity is inversely related to serum triglycerides, but it seems not to be related with the biochemical severity of liver disease. The direct correlation between LAL activity and age of patients could suggest that enzyme deficiency may facilitate over time liver disease progression, probably enhancing lipid deposition in the liver. The study for the first time demonstrate an high prevalence of LAL deficiency in patients with WD, related with an higher BMI and dyslipidemia. This finding may have a role in WD liver disease progression. Our results could be considered a good start point for the future development of prognostic biomarkers of liver disease (including LAL activity) and also for the development of new targeted therapies. These data should be confirmed on a larger series of children with liver disease.

Disclosure of interest: None to declare
Liver ciliopathies in children; a single centre 20-year experience

Natalia Nedelkopoulou, Ioannis Roilides, Anil Dhawan, Richard Thompson, Marianne Samyn, Tassos Grammatikopoulos

1 King's College Hospital, Paediatric Liver, GI and Nutrition Centre, London, United Kingdom
2 Aristotle University of Thessaloniki, 3d Pediatric Department, Thessaloniki, Greece
3 King's College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom
4 King's College Hospital, Paediatric Liver, GI & Nutrition Centre 2. Institute of Liver Studies, Division of Transplantation Immunology and Mucosal Biology, King's College London, London, United Kingdom
5 King's College Hospital, Paediatric Liver, Gastroenterology and Nutrition Centre, London, United Kingdom
6 King's College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom

Objectives and study: Ciliopathies are a heterogeneous group of multisystemic disorders with Caroli's disease (CD) and congenital hepatic fibrosis (CHF) being the most common liver manifestations reported in children. We present our experience in children with ciliopathies and liver involvement.

Methods: Demographic, clinical/ laboratory data of children with ciliopathies and liver involvement referred to our centre between 1995-2015 were reviewed.

Results: 58(33M) children were identified; 14 with autosomal recessive polycystic kidney disease (ARPKD), 2 with autosomal dominant polycystic kidney disease with autoimmune hepatitis and intestinal failure respectively, 15 with ARPKD and CHF, 16 with ARPKD and CD, 4 with Joubert syndrome, 1 with nephrocalcinosis and CD, 1 with nephronophthisis, 3 with CD, 1 with renal, liver, pancreatic cysts. Median age at referral was 5.5y [range, 1m-16y]. 47/58 were referred with established renal disease at median age 5.2y (1m – 15y) with bile duct dilatation (8), hypersplenism (4), GI bleed (2), hepatosplenomegaly (2), deranged liver function tests (LFTs) (3), family history of ARPKD with liver involvement (2), liver transplant (LT) assessment (1) for advanced liver disease and small bowel transplant assessment (1) for intestinal failure. All other patients were referred for liver review in the context of possible liver involvement in ARPKD. 2 were referred for abdominal distention/ pain. 7/47 with established renal/liver disease were referred from other paediatric centres. Isolated liver disease (CD) was identified in 3 patients (CD) with portal hypertension and abnormal LFTs (2) and 1 was diagnosed with a choledochal malformation. 1 patient was diagnosed with oro-digital syndrome type 4 with multiple liver cysts. Out of 4 patients with Joubert syndrome, 2 had abnormal LFTs and hypersplenism, 1 pruritus and 1 had biliary atresia and underwent LT. All patients underwent an abdominal uss (Table) and 26/58 underwent MRCP. Common findings on MRCP were intra/extrahepatic duct dilatation (15), cystic dilatation of bile ducts (12), liver cysts (4), hepatosplenomegaly (3) and cholangiopathy (3). Liver biopsy was performed in 10 patients to assess the degree of fibrosis as part of a transplant assessment (5) or to establish a diagnosis (5). Only 8 patients underwent genetic testing and mutations in TMEM and PKHD1 were identified in 2 and 2 children, respectively. Median follow up was 6.2 years [3m-20y]. In total, 18 children underwent transplantation; 10/18 isolated renal transplantation (RT), 5/18 combined liver-kidney (LRT) and 3/18 isolated LT. Two patients are currently listed for RT and another 2 for LRT.

Table:

<table>
<thead>
<tr>
<th>Liver uss</th>
<th>At presentation</th>
<th>Follow up</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heterogeneous liver parenchyma</td>
<td>23/58 (39%)</td>
<td>24/49* (48.9%)</td>
</tr>
<tr>
<td>Splenomegaly</td>
<td>25/58 (43%)</td>
<td>26/49 (53%)</td>
</tr>
<tr>
<td>Bile duct dilatation</td>
<td>26/58 (45%)</td>
<td>23/49 (47%)</td>
</tr>
<tr>
<td>Intrahepatic cysts</td>
<td>16/58 (28%)</td>
<td>13/49 (26.5%)</td>
</tr>
</tbody>
</table>

Table: Liver ultrasound scan (uss) findings at time of presentation and last review. *8 patients underwent LT, 1/58 no liver involvement identified.
Conclusion: Liver involvement is identified in a wide spectrum of ciliopathies. Early referral is recommended, as severity of liver disease can be variable at time of presentation, often resulting in portal hypertension (53%) and requiring transplantation (31%). In our cohort, diagnosis is based mainly on radiological findings with only a minority confirmed on genetic screening (14%).

Disclosure of interest: None
Subclinical neurological involvement does not develop if Wilson’s disease is treated early

Giusey Ranucci1, Raffaele Dubbioso2, Marcello Esposito2, Fabiola Di Dato1, Federica Leone1, Antonietta Topa2, Mario Quarantelli3, Margherita Matarazzo4, Lucio Santoro2, Fiore Manganelli2, Raffaele Iorio1

1University of Naples Federico II, Department of Translational Medical Science, Section of Pediatric, Liver Unit, Naples, Italy
2University of Naples Federico II, Department of Neurosciences, Reproductive and Odontostomatological Sciences, Naples, Italy
3University of Naples Federico II, Institute of Biostructure and Bioimaging, National Research Council (Cnr), Naples, Italy
4University of Naples Federico II, Department of Translational Medical Sciences, Section of Internal Medicine, Naples, Italy

Objectives and study: Wilson’s disease (WD) is a genetic disorder of copper metabolism in which metal deposits cause dysfunctions of various organs, mostly the liver and brain. If untreated, WD is fatal, but early treatment results in a good prognosis, although the long-term neurological outcome has not yet been clarified. To address this issue, we evaluated the neurological status of early-treated WD patients without overt nervous system impairment using neurophysiological, neuropsychological and neuroimaging procedures at least 10 years after treatment onset.

Methods: Thirty-eight WD patients (18 females and 20 males, aged 24.47 ± 7.50 years), who received an early diagnosis in presymptomatic or mild or moderate liver disease stages without neurological involvement and prompt treatment, were clinically evaluated with the Global Assessment Scale. Presentation was hepatic in 36 subjects (95%), while 2 patients (5%) were diagnosed in a presymptomatic stage. A neurophysiological study was performed to explore the central motor conduction time of the upper and lower limbs, and motor cortex excitability using single pulses and paired-pulse transcranial magnetic stimulation (TMS). Neuroimages were obtained with brain magnetic resonance scans. Cognitive abilities, and psychiatric and behavioral disturbances were evaluated with neuropsychological tests. TMS studies were also performed in a separate group of 15 WD patients with neurologic signs (8 males and seven females; mean age 28.2 ± 12.1 years, mean treatment duration 15.8 ±9.14 years). Fifteen age-, education-, and sex-matched healthy subjects, not affected by any neurological, psychiatric or other relevant clinical conditions (10 females and five males; mean age 26.7 ± 9.1 years; years of schooling 13.2 ± 2.4) served as the control group for clinical, neuropsychological, neuropsychological and neuropsychiatric evaluation.

Results: Patients were undergoing treatment with penicillamine (7 patients) or zinc salts (31 patients) with good adherence. They did not present any neurological signs at clinical evaluation or at specific scale of impairment, the mean Global Assessment Scale score was 0.3±0.7. Magnetic resonance imaging, transcranial magnetic stimulation studies and neuropsychological/neuropsychiatric assessment ruled out subclinical involvement.

Conclusion: Early diagnosis and treatment of WD can prevent the onset of neurologic damage, even at subclinical level.

Disclosure of interest: None Declared
The significance of portal hypertension in children with biliary atresia.

Maria Goliszek¹, Piotr Czubkowski¹, Natalia Oldak¹, Marek Woynarowski¹, Anna Chyżyńska¹, Joanna Pawłowska¹

¹The Children's Memorial Health Institute, Warsaw, Poland

Objectives and study: Portal hypertension (PH) is common consequence of progressive liver injury in children with biliary atresia (BA) affecting survival with native liver, quality of life and overall outcome. The aim of the study was to evaluate the significance of PH development in children with BA.

Methods: We retrospectively reviewed 390 children with BA who underwent Kasai hepatopportoenterostomy (HPE) between 1984 and 2014. Significant portal hypertension (SPH) was defined as gastrointestinal bleeding and/or varices of at least I grade and/or gastric varices. The statistical analyses were based on logistic regression and log-rank test for Kaplan Meier survival curves.

Results: The overall 5 and 10 year actuarial survival with native liver was 38% and 29% respectively. The main indicator of good prognosis was restoration of bile flow with decrease of total bilirubin below 2mg% within 6 months after HPE. SPH was observed in 171 (43%) patients and in 93 (24%) of them presented with variceal bleeding and mortality of 5% (n=20). An average age at the moment of bleeding was 2.3 years. Development of SPH was not significant for prognosis in the whole cohort, however in patients who survived initial 2 years after HPE without liver transplantation actuarial 10-year survival was 70% compared to 41% in patients who developed SPH (p<0.001). There was no correlation between SPH development and degree of liver fibrosis, anatomical pattern of BA, the presence of congenital anomalies or initial outcome of HPE. The only risk factor of SPH development was survival with native liver over 2 years (p<0.001).

Conclusion: The development of portal hypertension is a severe condition worsening prognosis in children with BA living over 2 years after Kasai operation without liver transplantation.

Disclosure of interest: None declared
Non Cirrhotic Portal Fibrosis in Pediatric Population- Breaking the Myths!!

Vikrant Sood1, Bikrant Bihari Lai2, Dinesh Rawat2, Rajeev Khanna2, Seema Alam2

1Institute of Liver and Biliary Sciences, Pediatric Hepatology, New Delhi, India
2Ilbs, Delhi, India

Objectives and study: Non-cirrhotic portal fibrosis (NCPF) has been classically described as a disease of young to middle age, with a mean age of onset in 3rd to 4th decade in different series. There is limited literature regarding its occurrence, onset or clinical presentation in children. We hereby present a series of 16 patients diagnosed and managed as NCPF in pediatric age group.

Methods: All patients presenting to the pediatric hepatology department (age < 18 years) were diagnosed as NCPF if they fulfilled 3 out of 4 following criteria (including liver biopsy), after excluding other etiologies:

1. Patent Portal Veins
2. Preserved Hepatic Functions
3. Moderate to Massive Splenomegaly with or without Hypersplenism
4. Liver Biopsy showing preserved lobular architecture with absence of cirrhosis

Results: A total of 16 patients were diagnosed as non-cirrhotic portal fibrosis (Male:Female 10:6) with a median age of 15 years (IQR 12 - 16). The median age of onset and diagnosis were 13 years (7.50 - 15.70) and 14.40 years (10.12 - 16.00) respectively. The clinical features included left upper quadrant mass in 14/16 (87.5 %), growth retardation in 13/16 (81.2 %), symptomatic hypersplenism in 7/16 (43.8 %), variceal bleed in 3/16 (18.8 %) and decompensation in 1 patient. Almost all patients had presence of varices (small or large) with Portal Hypertensive Gastropathy (mild or severe) on UGI endoscopy.

Following liver histopathological features were found suggestive of NCPF: Maintained lobular architecture (100 %), atretic portal tracts with fibrosis (100 %), partial or complete absence of portal vein profiles (75 %), abnormal approximation of portal-portal and portal-central vein (70 %), presence of aberrant portal channels at the periphery (30 %), sinusoidal congestion (30 %) and nodular regenerative hyperplasia (12 %).

Laboratory parameters showed hypersplenism with almost preserved liver synthetic functions in all patients. Median HVPG was 13.5 mm Hg which is higher than usually reported (Median 7 mm Hg). Median Fibroscan value was 10.95 K Pa suggesting mild to moderately high liver stiffness which is lower than cirrhotic range (>12-14 K Pa). Associated conditions included Hepatitis b infection and Gilbert’s syndrome in 2 each, severe symptomatic Hepatopulmonary syndrome in 1 and Hypothyroidism in 1 patient.

Conclusion: NCPF is not an uncommon entity in pediatric population with age of onset usually in the 2nd decade and younger than as depicted in majority of world literature. HVPG and Fibroscan values may overlap with those in cirrhotic patients and thus may not be diagnostic in isolation. Any patient presenting with evidence of portal hypertension (large spleen, evidence of varices with/out variceal bleed) with preserved hepatic functions, irrespective of the age, should be evaluated for possible NCPF etiology.

Disclosure of interest: “None Declared” (for all authors).
Revised scoring system for the diagnosis of Wilson disease in children

Palittiya Sintusek1, Anil Dhawan1

1King's College Hospital, Paediatric Liver, Gi & Nutrition Centre, London, United Kingdom

Objectives and study: Wilson disease (WD) is an inherited disorder of copper metabolism with diverse presentations. Although genetic mutations confirm the diagnosis but usually not available readily. Early diagnosis is sometimes warranted to start the treatment.

The aim of our study was to evaluate the diagnostic value of Modified scoring system in the wide spectrum of WD presentation in children compared to scoring system by the 8th International Conference on Wilson disease and Menkes disease in which we did not count the mark for positive genetic mutations.

Methods: We retrospectively studied the medical records of children with WD (n=52) as well as the mimic liver diseases; autoimmune hepatits (AIH) (n=63) and nonalcoholic fatty liver disease (NAFLD) (n=22) between 2005 and 2015 at King's college hospital. All WD children were initially diagnosed by King’s protocol and 43 patients were confirmed by genetic analysis later. The demographic data and parameters in the scoring system were collected. AIH and NAFLD patients with incomplete data were excluded from the study in order to reduce false negative and bias.

WD and non-WD (control group) patients with following parameters (in the table) will allocated score from 0-2. WD was diagnosed if the total score was more than 3.

Results: WD children were 11.61 (±3.93) years old while non-WD children (NAFLD and AIH) were 12.33 (±2.73) years old. In WD and non-WD group, 46% and 60% were female, respectively. According to scoring system by an international consensus in 2001 in which genetic analysis result was excluded; 12 patients had false negative and 11 patients had false positive. Using modified scoring system; only 2 patients had false negative and 1 patient had false positive. The sensitivity, specificity, positive predictive value and negative predictive value were 76.92%, 87.06%, 80.36%, 78.43 % and 86.05%, for conventional scoring system and 96.15%, 98.82%, 98.08%, 98.04% and 97.67% for modified scoring system, respectively.
### Table:

<table>
<thead>
<tr>
<th>Modified Scoring system</th>
<th>0</th>
<th>1-250</th>
<th>&gt; 250</th>
</tr>
</thead>
<tbody>
<tr>
<td>1) Liver copper, μg</td>
<td>&lt; 50</td>
<td>50-250</td>
<td>&gt; 250</td>
</tr>
<tr>
<td>2) Rhodanine or ocein stain</td>
<td>absent</td>
<td>present</td>
<td></td>
</tr>
<tr>
<td>3) Family history of WD</td>
<td>no</td>
<td>yes</td>
<td></td>
</tr>
<tr>
<td>4) Urinary copper, μmol/d</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>- basal 24 hour</td>
<td>&lt; 0.6</td>
<td>0.6-2</td>
<td>&gt; 2</td>
</tr>
<tr>
<td>- 24 hour after PCT</td>
<td>&lt; 5</td>
<td>5-25</td>
<td>&gt; 25</td>
</tr>
<tr>
<td>5) Serum ceruloplasmin, g/l</td>
<td>&gt; 0.2</td>
<td>0.1-0.2</td>
<td>&lt; 0.1</td>
</tr>
<tr>
<td>6) New parameters</td>
<td>normal</td>
<td>low ALP for age</td>
<td>triad*</td>
</tr>
<tr>
<td>(ALP, zinc and ultrasound finding)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>7) KF rings</td>
<td>absent</td>
<td></td>
<td>present</td>
</tr>
<tr>
<td>8) Neurological feature</td>
<td>absent</td>
<td>present</td>
<td></td>
</tr>
<tr>
<td>9) Coomb’s negative</td>
<td>absent</td>
<td>present</td>
<td></td>
</tr>
</tbody>
</table>

KF rings, Kayser-Fleischer rings; PCT, penicillamine challenge test, * triad: low ALP for age, serum zinc <11 μmol/L and finely heterogenous liver with splenomegaly on ultrasound finding

### Conclusion:
Modified scoring system increases the diagnostic values of WD diagnosis. Perspective validation is being undertaken.

### Disclosure of interest:
"None Declared"
Native liver survival in children with biliary atresia and ascites

Renata Rostirola Guedes¹, Carolina Mariano da Rocha¹, Fernando Schwengber¹, Carlos Oscar Kieling², Jorge Luiz dos Santos³, Sandra Maria Gonçalves Vieira³

¹Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil
²Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil
³Universidade Federal Do Rio Grande Do Sul / Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

Objectives and study: Biliary atresia is the leading cause of cirrhosis and liver transplantation in children. It is a rare disorder of infancy characterized by a destructive inflammatory and obliterative cholangiopathy which etiology has not yet been totally clarified. Ascites is the most prevalent complication of cirrhosis in all age groups and is associated with poor outcomes and decreased patient survival. The objective of this study is to evaluate one-year native liver survival in children with cirrhosis due to biliary atresia with and without ascites.

Methods: A hundred and six patients with cirrhosis due to biliary atresia (72 with ascites and 34 without ascites) from a Pediatric Gastroenterology and Hepatology Service in a tertiary hospital in the South of Brazil were included in a historic cohort between March 2000 and July 2014. Patients were included after the first ultrasound diagnosis of ascites and otherwise, the first ultrasound evidence of cirrhosis, in those who did not develop ascites. After enrollment, patients were classified into three groups: a) NA = no ascites; b) A1 = grade 1 ascites and c) A2-3 = grades 2-3 ascites, and followed by 12 months, death or liver transplantation.

Results: The incidence of ascites was 68%. The overall probability of 1-year native liver survival was 45.9%, while those observed in groups NA, A1 and A2-3 were respectively: 79.4%, 48.6% e 18.2% (p=0.000). In A2-3 group, among patients who lost their native livers, 18 (40.9%) underwent liver transplantation and 23 (52.3%) died in the waiting transplant list.

Conclusion: Ascites is a prevalent complication with an important impact on the native liver survival in children with cirrhosis due to biliary atresia. The one-year native liver survival in patients with moderate and severe ascites is extremely low.

Disclosure of interest: None Declared.
One-Year Native Liver Loss after Spontaneous Bacterial Peritonitis in Pediatric Patients compared to Adults

Fernando Schwengber¹, Carlos Kieling², Renato Borges Fagundes³, Carolina Mariano da Rocha¹, Mario Alvares-da-Silva⁴, Alexandre Araujo⁴, Sandra Vieira⁵

¹Universidade Federal Do Rio Grande Do Sul, Porto Alegre, Brazil
²Hospital de Clínicas de Porto Alegre, Unidade de Gastroenterologia Pediátrica, Porto Alegre, Brazil
³Universidade Federal de Santa Maria, Departamento de Clínica Médica, Santa Maria, Brazil
⁴Hospital de Clínicas de Porto Alegre, Serviço de Gastroenterologia, Porto Alegre, Brazil
⁵Hospital de Clínicas de Porto Alegre, Unidade de Gastroenterologia Pediátrica, Porto Alegre, Brazil

Objectives and study: Spontaneous bacterial peritonitis (SBP) is a frequent life threatening complication of cirrhosis, associated with liver decompensation, kidney injury, acute-on-chronic liver failure and death. Few studies address the prognosis after SBP in pediatric patients. Thus, this study aimed at evaluating the one-year native liver loss after the first episode of SBP in two different groups of cirrhotic patients: pediatric and adult.

Methods: This historical cohort study included patients with SBP followed by independent adult and pediatric liver transplantation units from a single tertiary hospital in southern Brazil. The diagnosis of cirrhosis was based either on clinical, biochemical, radiological or histological findings. The severity of the underlying liver disease was assessed according to the Child-Pugh classification, as well as PELD score or MELD score, for patients younger or older than 12 years of age, respectively. SBP was defined as an absolute neutrophil ascites count cell > 250 cells/µL, in the absence of an intra-abdominal source of infection. The primary outcome evaluated was one-year survival with the native liver, defined as patient survival without liver transplantation. This study has been submitted to and approved by the Institutional Review Board from the hospital in which it was conducted.

Results: Pediatric Cohort: 18 first episodes of SBP in pediatric patients with cirrhosis were reviewed. Biliary atresia was the most prevalent diagnosis (72.2%), and all patients were classified as Child-Pugh C. Positive ascites culture was observed in 50% of samples. The median hospital stay was 33 days. In-hospital mortality was of 38.9%. At the end of follow-up, seven patients were transplanted (38.9%) and eleven (61.1%) have died.

Adult Cohort: 42 first episodes of SBP in adult patients with cirrhosis and SBP were evaluated. Isolated hepatitis C virus infection was the most prevalent diagnosis (40.5%), and 35 (83.3%) patients were classified as Child-Pugh C. Positive ascites culture was observed in 13 (31.0%) samples. Median hospital stay was 10 days. In-hospital mortality of 26.2%. At the end of follow-up, seven patients were transplanted (16.7%) and 28 (66.7%) patients died.

Native Liver Survival: The cumulative probability of survival with native liver (no death nor liver transplantation) in children was 77.8% at 1 month, 27.8% at 3 months, 11.1% at 6 months. At 9 months of follow up no pediatric patients kept their native liver. For adult patients, the cumulative probability of native liver survival was 69.0% at 1 month, 54.8% at 3 months, 45.2% at 6 months. At 12 months of follow up, the survival of the native liver was 35.7%. One year survival was significantly higher in adults than in children (p=0.005). Mortality rate was similar between child C adults and children. The proportion of children who underwent transplantation in one year was of 39%, while in adults it was 14% (p=0.462).

Conclusion: SBP appears to be a late event both in adult and in pediatric patients, with high impact on native liver loss and on overall survival. Strategies should be more aggressively pursued for timely liver transplantation, particularly after the development of SBP.

Disclosure of interest: None Declared.
De novo autoimmune hepatitis in first high volume pediatric liver transplantation program in Saudi Arabia

Kishwer Kumar1, Mohamed Barr1, Talal Algoufi1, Dieter Clemens Broering2, Martin Burdelski1, Mohammad Ali Shagran1

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: The development of de novo autoimmune hepatitis (AIH) after liver transplantation (LT) has been described in both pediatric and adult populations. Unlike classic AIH, this condition does not have defined diagnostic criteria and is diagnosed mainly by the exclusion of other conditions. ANA and SMA, and less commonly anti-LKM1, have also been detected in de-novo autoimmune hepatitis developing after liver transplantation, a condition that may affect patients transplanted for non-autoimmune liver disease.

The histological findings are similar to those seen in AIH, and consist of a dense portal and interface mononuclear cell infiltrate rich in plasma cells as well as lobular lymphoplasmacytic hepatitis.

We examined the clinical presentation, pathologic features, association and treatment of De novo autoimmune hepatitis occurring after liver transplantation (LT) that is unrelated to disease recurrence.

Methods: Between January 2011 and December 2014, 156 pediatric liver transplants were performed at King Faisal Specialist Hospital and Research Centre, the first high volume pediatric liver transplant program in Saudi Arabia. Mostly from Living donors (n=145, 92.9%). Seven percent of transplants were performed from deceased donors (n=11, 7.1%).

The patient’s charts reviewed for possible causes or association, duration, and outcome. As per protocol we used to do autoimmune screen (ANA, ASMA, LKM and serum immunoglobulin twice per year for all patients). As observed by others Autoantibodies are frequently detected after liver transplantation (LT), but their role are unclear.

Results: Six cases were identified (3.8%). They were transplanted for Biliary Atresia (n=4), Urea cycle defect (n=1) and Sclerosing cholangitis (n=1), presented with the features of acute hepatitis in otherwise stable transplant recipients. All have positive autoimmune workup and positive histopathological findings without significant correlation of their serum immunoglobulin level which is usually the case in De Novo (AIH)

Four of them were associated with biliary stricture either at time of diagnosis or shortly after. All patients were successfully treated with steroids, Azathioprine and low dose of tacrolimus to keep level (2-4 ng/ml).

Conclusion: We are reporting that even with differ indications for liver transplantation (LT) and being purely living related donor (LRD) program still the incidence of de novo AIH is low and does not impact on long-term survival. Keeping in mind that Familial and metabolic cases are the major indications for liver transplantations in our Centre and the high percentage of De Novo (AIH) in biliary atresia cases (66.66%) strongly support that more studies need to look for the pathophysiology of biliary atresia as an autoimmune disease!

Disclosure of interest: "None Declared".
Liver transplantation from a donor with β-thalassemia intermedia is not contraindicated

Ersin Gumus\textsuperscript{1}, Osman Abbasoglu\textsuperscript{2}, Cahit Tanyel\textsuperscript{3}, Fatma Gumruk\textsuperscript{4}, Aysel Yuce\textsuperscript{1}, Hasan Ozen\textsuperscript{1}

\textsuperscript{1}Faculty of Medicine, Hacettepe University, Department of Pediatric Gastroenterology, Hepatology, and Nutrition, Ankara, Turkey
\textsuperscript{2}Faculty of Medicine, Hacettepe University, Department of General Surgery, Ankara, Turkey
\textsuperscript{3}Faculty of Medicine, Hacettepe University, Department of Pediatric Surgery, Ankara, Turkey
\textsuperscript{4}Faculty of Medicine, Hacettepe University, Department of Pediatric Hematology, Ankara, Turkey

Objectives and study: There is a growing gap between the number of available organ donors and the number of potential liver transplant recipients. The use of extended criteria (marginal) donors who might have been deemed unsuitable in earlier times is a strategy to fulfill this gap. To the best of our knowledge there hasn’t been any effort regarding the use of a hemosiderotic liver as a marginal donor. In the literature, there are a few case presentations reporting liver transplantation from a patient with hemochromatosis inadvertently. Iron overload seems to be the common serious problem following transplantation of iron loaded liver. We present a pediatric case of a successful liver transplantation from a marginal donor with β-thalassemia intermedia and discuss the unusual cause of iron overload in the transplant recipient.

Methods: This is a case report of an unusual and extraordinary pediatric liver transplantation experience.

Results: Extreme hyperferritinemia was detected in our patient shortly after liver transplantation from a thalassemic donor. Since high serum ferritin levels (18011 ng/ml, normal 10-300 ng/ml) were combined with increased transferrin saturation (95%, normal 20-50%) and moderately elevated plasma iron concentrations (289 µg/dl, normal 50-150 µg/dl), we presume that the most probable cause of hyperferritinemia in our patient was iron overload secondary to transplantation of hemosiderotic liver of a thalassemia intermedia patient. T2-­star magnetic resonance imaging (T2* MRI) of liver was consistent with hepatic iron overload (T2* 2.3 msn, 5.91 mg iron/g dry tissue). Hepatocellular injury and inflammation due to acute graft rejection, which was successfully treated with steroid and monoclonal anti-human CD3 antibody, probably contributed to elevated ferritin levels by causing release of stored iron from the hemosiderotic transplanted liver. Iron chelation and phlebotomy therapies were started simultaneously in the early postoperative period and follow up was done with monthly phlebotomies after discharge of patient. Patient's serum ferritin and transferrin saturation gradually decreased to 271 ng/ml and %10 respectively in six years after transplantation. The patient is now doing well with normal transplant functions, normal liver enzymes, normal liver T2* MRI results and slightly elevated ferritin levels (<300 ng/ml).

Conclusion: To the best of our knowledge this is the first report regarding a successful liver transplantation from a thalassemic deceased donor. Marginal donors are increasingly taken into consideration due to shortage of donor organs. Our case represents a good example of the use of marginal donors for liver transplantation. Tahalassemia intermedia patients can be candidates of marginal liver donors. After transplantation of a hemosiderotic liver inadvertently or purposely from a marginal donor, it is important to monitor the recipient after transplantation in terms of iron overload and related iron toxicity. Early attempts to lower iron burden including chelation therapy or phlebotomy should be considered to avoid organ toxicity and transplant failure.

Disclosure of interest: None Declared.
Outcomes of Patients Recommended for Transplant In a Cohort of Infants Born Less Than 30 Weeks Gestation with Intestinal Failure

David Mercer\(^1\), Brandi Gerhardt\(^2\), Brandy Hobson\(^3\), Ann Anderson Berry\(^4\)

\(^1\)University Of Nebraska Medical Center, Surgery, Omaha, United States
\(^2\)Nebraska Medicine, Surgery, Omaha, United States
\(^3\)Nebraska Medicine, Omaha, United States
\(^4\)University of Nebraska Medical Center, Pediatrics, Omaha, United States

**Objectives and study:** Our objective is to describe outcomes in a high risk patient population of infants born at less than 30 weeks gestation with referral to our center for intestinal failure. Intestinal failure (IF) requiring evaluation for intestinal transplantation and associated liver disease (IFALD) leading to liver transplantation for the pediatric population is relatively scarcely described in the literature. a case series of 93 infants and children described in 2010. (Cowles) Accordingly, very little is known about outcomes for infants born before 30 weeks estimated gestational age (EGA) requiring evaluation of and therapy for IF and IFALD. Many patients are candidates for intestinal rehabilitation programs (IRP) and do not require transplantation. Others are recommended for listing for transplantation but specific outcomes in this population are not well described.

**Methods:** We have assembled an IRB approved cohort of 98 infants born prior to 30 weeks EGA referred to our center for IF/IFALD who were evaluated for treatment. Using a retrospective medical records review we have examined the outcomes of infants referred for IF. This abstract will describe outcomes for patients in which transplant was recommended on initial evaluation.

**Results:** 98 infants were evaluated at our center, 2 were referred to palliative care, 89 were recommended for our intestinal rehabilitation program and 7 were recommended for transplant. All are living, 71.4% have received a transplant.

**Table:**

<table>
<thead>
<tr>
<th>Wait (days)</th>
<th>LTx alive/TF</th>
<th>LTx alive/TPN</th>
<th>LTx alive/IVF</th>
<th>LSBT alive/TF</th>
<th>LTx alive/TPN</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>112</td>
<td>LTx alive/TF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>113</td>
<td>LTx alive/TPN</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>100</td>
<td>LTx alive/IVF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>30</td>
<td>LSBT alive/TF</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>LTx alive/TPN</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Infants under 30 weeks EGA who are referred for IF and recommended for transplant have good outcomes with regards to mortality (0%). All listed patients have been successfully transplanted, 2/7 are total parenteral nutrition (TPN) dependent, 1/7 intravenous fluid (IVF) dependent, and 2/7 are tube feeding dependent. Infants born less than 30 weeks EGA with IF and IFALD who are recommended for transplant should be considered for treatment based on their disease state. Their gestational age does not appear to incur additional risk.

**Disclosure of interest:** None Declared.
Survival after liver transplantation in metabolic diseases and congenital liver diseases

Sirmen Kizilcan¹, Miray Karakoyun², Caner Turan³, Sema Aydogdu⁴

¹Ege University Medicine Faculty, Izmir, Turkey, Ege University Department of Pediatrics, Izmir, Turkey
²Ege University Medicine Faculty, Ege University Department of Pediatrics, Pediatric Gastroenterology, Hepatology and Nutrition, Izmir, Turkey
³Ege University Medicine Faculty, Ege University Department of Pediatrics, İzmir, Turkey
⁴Ege University Medicine Faculty, Ege University Department of Pediatrics, Pediatric Gastroenterology, Hepatology and Nutrition, Izmir, Turkey

Objectives and study: Liver transplantation (LT), has become a gold standart and only curative treatment for hepatic failure. Especially, children who have a bilier atresia(BA) , progressive fulminan intrahepatic cholestatis(PFIC), Wilson diseases( WD) and metabolic disease necessary LT in childhood. Last few decades, LT become an alternative treatment in metabolic diseases which develop the end stage liver failure. We compared prognosis of LT in metabolic diseases(MD) with other indications. Especially, we determined survival after transplantation or their liver in tyrosinemia, glycogen storage disease, hypercholesterolemia, citrulline with bilier atresia, Wilson disease, PFIC.

Methods: In our study, we included 189 children who have been liver transplantation in between 1997 and 2015 for hepatic failure caused by MD and chronic liver diseases in Ege University Medicine Faculty Pediatric Gastroenterology Department in Izmir. We examined the sex, age, transplantation age and type, donor type, rejection, complications, development and growth after transplantation.

Results: In our study, case gender varies as 54%(n=102) male. Total of 189, 23.8%(n=45) of cases were diagnosed as MD(14 progressive familial intrahepatic cholestasis, 7 Wilson disease, 3 alfa 1 deficiency, 2 glycogen storage disease type I, 1 glycogen storage disease type I, 1 glycogen storage disease type IV, 1 Aagenes syndrome, 13 tyrosinemia and 4 hyperlipidemia). We excluded 24.3%(n=46) children who were exitus after transplantations. Mean diagnose ages were 11.8(min 1-max 31) months in general groups and 18.7(min 12-max 24 ) months in MD group. In MD, their development and growth increased after the LT and in this groups, there were only 4 patient which recurrent after LT. Only three patients with hyperlipidemia and hypertrigliseridemi were transplanted. One of patients whom had PFIC re-diagnosed with same disease after the trasplantation. There were not any patologic sign deflected on other organs in group of the patients with tyrosinemia...In the group of patient with MD (n=45), 5 cases had shown the sign of the development of HCC. In general groups, 69.8%(n=132)patients have been transplanted from live donor. Also, we analyzed survival both of groups. PFIC is the most common disease in between MD which end up with LT, while the WD is the runner-up. Two over third of the patients with MD have been transplanted from live donor. In the group of patients with MD 15% rejection of the organ have been detected while in general group percentage for the rejection of the organ detected as 18%. In general group, survival rate for the first year after the transplantation were 82% and were dropped to 79% for the fifth year; while in group of patients diagnosed with MD, survival rate for the first year after transplantation were 80% and it dropped 77% at the fifth year. With these statistics not any significant differences between two groups were detected.

Conclusion: Liver transplantation has emerged from its position as a treatment of lastresort for inborn errors of metabolism to play a more robust role in a wider variety of diagnoses. LT, one of the curative treatment in hepatic failure, end stage of liver failure. Also, we remember that, LT is alternative and curative treatment in metabolic diseases.

Disclosure of interest: None Declared
Autoimmune BSEP disease after liver transplantation: effect of azathioprine

Nicolette Moes¹, Hubert van der Doef², Annechien Lambeck³, Klaas Nico Faber⁴, Annette Gouw⁵, Henkjan Verkade²

¹University Medical Center Groningen, Pghn, Groningen, Netherlands
²University Medical Center, Pghn, Groningen, Netherlands
³University Medical Center, Medical Immunology, Groningen, Netherlands
⁴University Medical Center, Research Institute for Gastro Intestinal Genetics and Immunology, Groningen, Netherlands
⁵University Medical Center, Pathology, Groningen, Netherlands

Objectives and study: After liver transplantation for Progressive Familial Intrahepatic Cholestasis type 2 (PFIC 2; BSEP deficiency), autoimmune BSEP disease may develop. The development of antibodies against BSEP transporter can cause immunological damage of the graft. Treatment options include increasing the level of immune suppression, plasmapheresis and B-lymphocyte depletion by rituximab. We herewith report the use of azathioprine, a B-lymphocyte and antibody blocking agent, as initial treatment for autoimmune BSEP disease.

Methods: A five year old boy developed cholestasis with jaundice and pruritus two years after liver transplantation for PFIC2. We diagnosed autoimmune BSEP disease by western blot analysis of serum samples and immunohistochemistry of liver biopsy. Tacrolimus and prednisolone levels were increased to trough levels between 10-12 ng/mL and 20 mg (1 mg/kg/ day), respectively. We additionally administered azathioprine (dosage 2.5 mg/kg/day). We measured BSEP antibody titers before and at monthly intervals after starting this treatment. After 1 month, the tacrolimus and after 6 month the prednisolone was lowered to initial dosages (trough levels of 6-7 ng/mL and prednisolone 2 mg every two days). We continued the azathioprine in order to assess the adequacy of maintenance therapy with azathioprine.

Results: Initial therapy with azathioprine and increased dosages of tacrolimus and prednisolone induced disappearance of pruritus and jaundice within 4 weeks, simultaneously with biochemical improvements of total/direct serum bilirubin from 241/215 µmol/L (13.9/12.4 mg/dL) to 17/15 µmol/L (0.98/ 0.78 mg/dL), serum bile salt from 140 µmol/L to 12 µmol/L and antibody titers from 1:6400 to 1:400. After 1 month tacrolimus could be weaned without recurrence of symptoms or biochemical deterioration. However, tapering of the prednisolone at 6 months was followed by recurrence of symptoms and by biochemical deterioration. Under the suspicion of prednisolone dependency, it was then decided to initiate rituximab.

Conclusion: Initial therapy for autoimmune BSEP disease with azathioprine, in combination to high dose of prednisolone and tacrolimus results in temporarily clinical and biochemical improvement. However, azathioprine alone seems insufficient for long term remission in autoimmune BSEP disease, if combined with regular dosages of post-transplant immunosuppression.

Disclosure of interest
"None Declared".

Vol. 62, Supplement 1, May 2016 635
Plasmapharesis, intravenous immunoglobulin and rituximab successfully treat recurrent progressive familial intrahepatic cholestasis type 2 (PFIC-2) after liver transplantation

Mohamed Shagrani¹, Faisal Aba Alkhail¹, Mohamed Alsebayel¹, Dieter Clemens Broering¹, Hussah Alhussini², Talal Algoufi¹, Hussein Elsiesy¹

¹King Faisal Specialist Hospital & Research Center, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia
²King Faisal Specialist Hospital & Research Center, Department of Pathology, Riyadh, Saudi Arabia

Objectives and study: In patients with PFIC-2, the Bile Salt Export Pump Protein (BSEP) is either absent or dysfunctional. Allo-immune mediated BSEP dysfunction may occur after liver transplantation in PFIC2 patients leading to a PFIC2 like phenotype. The IgG antibodies are reactive toward a canalicular epitope of BSEP, are of high affinity, and inhibited transport activity of BSEP, thus causing severe cholestasis. This phenomenon was first described in 2009 (1), since then, few cases of PFIC-2 recurrence were reported with mixed results(2). We report on two patients who developed recurrent normal GGT cholestasis mimicking primary BSEP disease, after liver transplantation.

Methods: A 14 years old boy and his 19 years old sister who had received cadaveric liver transplantation at the United States in 2011. In January 2014 the boy presented with severe itching, high bilirubin, high AST/ALT, high serum bile acid with persistently low GGT. Virology, Autoimmune screen, Abdominal CT Scan, ERCP and liver biopsy were negative. Immunosuppression were maximized with no improvement. A repeat biopsy of the 14 year-old boy on May 2014 showed recurrence of PFIC2, His Anti-BSEP came positive with a very high serum titer 1:1200, Treatment regimen for him started on June 2014, he received a course of 5 sessions of Plasmapharesis each session followed by IV immunoglobulin (IVIG), then received first dose of I.V. Rituximab 375/m². The second course of Plasmapharesis where modified by doing 5 sessions of Plasmapharesis every other day with an exchange volume of 1.5, followed by 3 days of IVIG to avoid washing out the IVIG by Plasmapharesis, followed by the second dose of IV Rituximab 375/m². His sister’s liver biopsy on July 2014 showed PFIC2 recurrence started treatment for recurrence September 2014, using the same modified protocol.

Results: Both patients showed excellent response to our regimen and currently they are symptoms free with normalization of their liver enzymes and total bilirubin

Conclusion: PFIC-2 recurrence after liver transplantation occur through an antibody mediated reaction against BSEP receptors on canalicular membrane and can successfully be treated with Plasmapharesis, IVIG and rituximab obviating the need for re-transplantation.

Disclosure of interest: “None Declared”.

1. De Novo Bile Salt Transporter Antibodies as a Possible Cause of Recurrent Graft Failure After Liver Transplantation, HEPATOLOGY, Vol. 50, No. 2, 2009
2. Rituximab as therapy for the recurrence of bile salt export pump deficiency after liver transplantation, Liver Transpl. 2013 Dec;19(12):1403-10
Adherence to treatment in adolescents after organ transplant and chronic disease and their psychological correlates.

Marta A. Biernacka¹, Anna Jakubowska-Winecka¹

¹Children Memorial Health Institute, Department of Health Psychology, Warsaw, Poland

Objectives and study: Mal-adaptive coping with chronic disease is associated with more adherence problems. In chronic disease it is essential to continue taking medication. Poor cooperation in the medical treatment leads to deterioration of well-being, complications of the disease, even danger or loss of life. Various resources are used to protect and facilitate adaptation to the illness but the most important is the family of a ill child, the relationship between parents and child, parents attitudes to the disease and treatment. The purpose of the study was to investigate whether parental attitude is related to patient adherence to medication regimens and the level of cooperation in kidney transplant patients, liver transplant, inflammatory bowel diseases and diabetes type I.

Methods: 136 children with different chronic disease: 66 boys aged 12 to 18 years (M=14.9; SD=1.81) and 70 girls aged 12 to 17 years (M = 14,2; SD=1.75) and 147 parents: 35 fathers and 112 mothers ages 32 o 59 years (M = 43,1; SD=5,73) participated in the study. To assess parental attitudes such as: Acceptance- Rejection, Demanding, Autonomy, Inconsequent Overprotective Parenting Attitude Scale (PAS) was used. The degree of patients adherence to medication regimen refers to whether patients take their medications was evaluated with the 8- item Morisky Medication Adherence Scale. To assess the degree of patients cooperation and the effects of treatment special questionnaire was prepared. It consisted of four aspects patients cooperation: Knowledge about the disease, Patient activity in the treatment process, Current treatment parameters and Doctor- patient cooperation satisfaction.

Results: In the statistical analysis the Pearson’s correlation coefficient was calculated. The critical level of significance was set at p < 0.05*, p<0.01**. The results are shown in the tables below.

Table: Tab.1. Correlation between the type of parental attitudes and MMAS-8 and four dimension of cooperation dependent on disease.

<table>
<thead>
<tr>
<th>Type of parental attitudes</th>
<th>Acceptance-Rejection</th>
<th>Demanding</th>
<th>Autonomy</th>
<th>Inconsequent</th>
<th>Over-protective</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MMAS-8</strong></td>
<td>- .404* D</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>.540** Ktx</td>
</tr>
<tr>
<td><strong>Knowledge</strong></td>
<td>n.s.</td>
<td>n.s.</td>
<td>.350* D</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Activity</strong></td>
<td>.398* D</td>
<td>- .435* Ktx</td>
<td>n.s.</td>
<td>.393* D</td>
<td>- .375*Ltx</td>
</tr>
<tr>
<td><strong>Treatment parameters</strong></td>
<td>.396* D</td>
<td>.336** Ktx</td>
<td>.371* Ltx</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
<tr>
<td><strong>Satisfaction with cooperation</strong></td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
</tr>
</tbody>
</table>
Ktx (patients after a kidney transplant), Ltx (patients after a liver transplant), IBD (patients with Inflammatory Bowel Diseases) and D (patients with diabetes type I)

Conclusion: 1. This study found that the relationship between the type of parental attitudes and regularity in taking medications was associated with the type of the disease. 2. Moreover the association between the type of parental attitudes and the various aspects of cooperation and the effects of treatment depended on the type of disease. 3. Parental attitude are important factors in the therapeutic contact with the patient. Acceptance and Autonomy attitudes seems to be beneficial and might positively influence patients medication adherence and improve their well-being, health and quality of life.

Disclosure of interest: Non declared
Sensorineural hearing loss in pediatric liver transplanted patients

Ayelet Mintz¹, Yael Mozer – Glassberg¹, Rachel Bergerin¹, Rivka Shapiro¹, Raanan Shamir¹, Joseph Attias²

¹Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel
²Schneider Children’s Medical Center of Israel, Institute of Audiology and Clinical Neurophysiology, Petah Tikva, Israel

Objectives and study: With increasing long-term survival of pediatric liver transplanted patients, systemic complications that do not necessarily involve the liver, have a significant impact on quality of life. Little is known about hearing impairment in children and adults after liver transplantation. Study aim was to evaluate the incidence and risk factors of hearing impairment among liver transplanted children.

Methods: we conducted a prospective study, with standard hearing and high frequency hearing tests administered to children who had undergone liver transplantation. The primary outcome measure was sensorineural hearing impairment over 20 decibels. Independent variables as demographic data as well as primary disease, pre and post-transplant treatments were evaluated. Especially looking at, average doses of aminoglycosides, loop diuretics, vancomycin and blood levels of tacrolimus at 1 week, 1 month, 6 months and 1 year post transplantation.

Results: Out of 78 followed, liver transplanted children, 45 (57.6%) fulfilled the inclusion criteria. Excluded, 22%, due to post transplant chemotherapy treatment, developmental delay, psychiatric illness and neurological deficit. Overall, 22/35 (62.8%) agreed to participate. After conducting hearing tests, another two were excluded due to technical difficulties. Finally, 5/20 (25%) had sensorineural hearing loss; (three had hearing impairment at the standard hearing frequency and all five at the high frequency range). The average dose of gentamycin was significantly higher in the hearing impairment group compared to the non-hearing impairment group (37.35 mg/kg versus 15.99 mg/kg respectively, p<0.04).

Conclusion: Despite the small sample size, it is reasonable to conclude that sensorineural hearing impairment is prevalent in pediatric patients following liver transplantation. We recommend that hearing tests should be performed as soon as possible after liver transplantation in order to achieve early detection and treatment of hearing impairment.

Disclosure of interest: None Declared.
Primary hyperoxaluria type 1 as an indication for liver-kidney transplantation—single center experience

Irena Jankowska1, Jacek Rubik2, Przemysław Sikora3, Dorota Wicher4, Małgorzata Markiewicz2, Joanna Cielecka-Kuszyk6, Joanna Pawłowska1, Marek Szymczak5, Mikołaj Teisseyre1, Ryszard Grenda2, Piotr Kaliciński5, Bodo Beck7

1The Children’s Memorial Health Institute, Gastroenterology, Hepatology, Nutritional Disturbances and Pediatrics, Warsaw, Poland
2The Children’s Memorial Health Institute, Nephrology, Kidney Transplantation and Arterial Hypertension, Warsaw, Poland
3Medical University, Paediatric Nephrology, Lublin, Poland
4The Children’s Memorial Health Institute, Department of Medical Genetics, Warsaw, Poland
5The Children’s Memorial Health Institute, Pediatric Surgery and Organ Transplantation, Warsaw, Poland
6The Children’s Memorial Health Institute, Pathology, Warsaw, Poland
7Institute of Human Genetics University of Cologne, Human Genetics, Cologne, Germany

Objectives and study: Primary hyperoxaluria type 1 (PH1) is a rare autosomal recessive disorder involving glyoxylate metabolism, caused by deficiency of liver-specific enzyme alanine: glyoxylate aminotransferase (AGT). The condition results in overproduction and excessive urinary excretion of oxalate. PH1 symptoms include early recurrent urolithiasis, nephrocalcinosis, progressive kidney injury and subsequent multiorgan involvement due to calcium oxalate (CaOx) deposition in different tissues. In many cases the diagnosis and specific treatment of PH1 is still delayed. Presently, the most recommended treatment option in PH1 patients with end-stage renal disease (ESRD) is combined liver-kidney transplantation (LKTx). The liver transplantation serves as a form of enzyme replacement therapy and usually prevents a recurrent CaOx deposition in renal graft and its failure.

Methods: Between 1990 and 2015 in The Children’s Memorial Health Institute in Warsaw in 6 children (3 boys and 3 girls aged 8-20 years) with PH1 LKTx was performed. In 4 of them PH1 diagnosis was made after failure of their primary renal transplant (KTx) due to recurrence of primary disease. All showed CaOx deposits in kidney grafts and in performed bone biopsies. Molecular analysis was possible only in 2 patients from this group and confirmed clinical diagnosis (mutations of AGXT gene). Only in 2 patients the molecular diagnosis of PH1 was made before ESRD (therefore primary LKTX was possible). In all presented cases organs for LKTX originated from deceased donors.

Results: In 5 patients the median follow-up time was 7 years (range 0.9-13 years) and currently all transplanted organs show satisfactory function. One patient developed renal graft failure after LKTX. He died with preserved liver function due to complications after third unsuccessful KTx at the age of 22 years.

Conclusion: Our results confirmed an effectiveness of LKTx in patients with PH1 and ESRD. However, only early diagnosis of PH1 allows appropriate choice of management and avoidance of unsuitable therapeutic decisions.

Disclosure of interest: “None Declared”.
Bone metabolism in children after liver transplantation

Dolóresz Szabó1, Nikolett Szabó1, Antal Dezsőfi1

1Semmelweis University, 1st Department of Pediatrics, Budapest, Hungary

Objectives and study: The favorable long term outcome after liver transplantation (LTx) gives opportunity to observe the late side effects of the immunosuppressive therapy. One of these effects is the changes of the bone metabolism.

Our aim was to assess bone metabolism after LTx in children with biliary atresia (BA). Bone mineral density (BMD), serum vitamin D, parathyroid hormone (PTH), osteocalcin (OC) and beta-crosslaps (BCL) levels were measured, and the changes were followed. Correlation of these parameters were also assessed.

Methods: In the first part of our study 21 patients with BA who underwent LTx were enrolled (16/21 girls, average age at the LTx: 8.5 month) and BMD was measured 4 and 6 years after LTx, prospectively. The second, cross-sectional analysis consisted of 44 patients (67 measurements, 28/44 girls, average elapsed time from LTx: 6.2 years), and BMD, vitamin D, PTH, OC and BCL serum levels were measured and correlation analysis was calculated between these parameters.

Results: The mean of lumbal z-score was -0.235 after 4 years LTx, and it did not change significantly two years later (z-score mean= -0.25; p=0.404). In contrast, whole body z-score decreased significantly 6 years after LTx, compared with the results of 4 years after LTx (z-score mean= -0.24 and -0.016, respectively; p=0.037), although children were supported with vitamin D. The cross-sectional analysis showed normal vitamin D and PTH level, the median was 32.5 ng/mL and 32.4 pg/mL, respectively. Markers of bone metabolism were also assessed, the median value of OC and BCL were 96.8 ng/mL and 1747.3 pg/mL, respectively. The second part of our study showed normal lumbal and whole body BMD (lumbal z-score mean= -0.004, whole body z-score mean=0.364). Based on the results of the correlation analysis mild negative correlation was observed between the level of vitamin D and PTH (r=-0.37), and between the level of vitamin D and BCL (r=-0.47). The relation between PTH and BCL showed positive correlation (r=0.685).

Conclusion: In our study we observed normal BMD 4 and 6 years after LTx. However, the decrease of the whole body BMD z-score emphasises the importance of the follow up. Markers of bone metabolism and serum vitamin D levels were in normal range on adequate vitamin D supplementation.

Disclosure of interest: None Declared.
HEPATOLOGY: Transplantation

H-P-065

The Incidence, Risk Factors And Clinical Course of De Novo Hepatitis B Infection in Paediatric Living Donor Liver Transplantation

Zeren Barış¹, Figen Özçay², Gökhan Moray³, Mehmet Haberal³

¹Baskent University Faculty of Medicine, Pediatric Gastroenterology and Hepatology, Ankara, Turkey
²Başkent University Hospital, Paediatric Gastroenterology, Ankara, Turkey
³Baskent University Faculty of Medicine, General Surgery, Ankara, Turkey

Objectives and study: We evaluated the incidence, risk factors and clinical course of liver transplanted paediatric patients with de novo hepatitis B infection and the clinical course of liver transplanted paediatric patients from anti HBc IgG positive donors.

Methods: We retrospectively collected the data of children who underwent liver transplantation between 2000-2015 in Baskent University Hospital and developed de novo hepatitis B infection or who had anti HBc IgG positive living donors. Patients who had a follow up period of minimum 18 months were enrolled.

Results: There were a total of 25 patients, 10 of whom had de novo hepatitis B infection. Patients were between 173,32±79.83 months old (min-max: 36-300 months). The mean follow up period of patients was 69,84±40,27 months (min-max: 18-144 months). The median time of diagnosis of patients with de novo hepatitis B was 28,67±25,61 months (min-max: 5-78 months) postoperatively.

Patients with and without de novo hepatitis B infection were compared. There wasn't any significant difference in age, gender, preoperative diagnosis, donor antiHBs and antiHBe titers, patient white blood cell, neutrophil and lymphocyte counts and time of steroid, tacrolimus or mycophenolate mofetil use between groups. The number of HBV immunizations (preoperative HBV vaccine doses) were significantly lower in patients with de novo hepatitis B infection (0,9±1,1 vaccine dose) when compared with the number of HBV immunizations in patients without de novo hepatitis B infection (2,67±0,86 vaccine dose), p=0,001. Preoperative anti HBs positivity were significantly lower in patients with de novo hepatitis B infection when compared with preoperative anti HBs positivity in patients without de novo hepatitis B infection, p=0,012). All of the patients in the group without de novo hepatitis B infection but one (14/15) had posttransplant lamivudin prophylaxis, while four patients in the group with de novo hepatitis B infection (4/9, 1 missing data) had lamivudin prophylaxis.

The clinical and laboratory features of patients with de novo hepatitis B infection were evaluated. The mean HBs Ag titers and mean HBV DNA titers of patients with de novo hepatitis B infection at the time of diagnosis were 954.55±1520.2 IU/ml and 581.68±1369.0 10^6 copy/ml respectively. Three patients with de novo hepatitis B infection had anti HBc IgG negative living donors. Immune suppressive (tacrolimus, sirolimus or cyclosporine) levels were normal in 5, high in 2 and unknown in 2 patients with de novo hepatitis B infection at the time of diagnosis.

Three (30%) of the patients with de novo hepatitis B infection had HBs Ag clearance at 10±7 months (min-max:3-17 months) and one patient had HBV DNA clearance and anti HBe positivity at 114 months. The mean HBs Ag titers and mean HBV DNA titers at the time of diagnosis of de novo hepatitis B infection did not differ significantly between patients with and without seroconversion. Two of the patients with de novo hepatitis B infection and without seroconversion had lamivudin and adefovir resistance during treatment course.

Conclusion: De novo hepatitis B infection is common in paediatric patients with anti HBc IgG positive living donor liver transplantation. The number of HBV immunizations and preoperative anti HBs positivity were important risk factors for development of de novo hepatitis B infection.

Disclosure of interest: None Declared
Donor specific antibodies (DSA) in children, five years after liver transplantation

Loreto Hierro1, Maria Jose Castro2, Esteban Frauca1, Gema Muñoz Bartolo1, Maria Dolores Lledin1, Angela de la Vega1, Carmen Camarena1, Manuel Lopez Santamaria3, Maria del Carmen Díaz1, Paloma Jara1

1H. La Paz, Pediatric Hepatology, Madrid, Spain
2H. 12 de Octubre, Immunology, Madrid, Spain
3H. La Paz, Pediatric Transplant Surgery, Madrid, Spain

Objectives and study: Antibodies anti-donor HLA may contribute to graft disease after solid organ transplantation. One study associated Donor specific antibodies (DSA) with centrilobular fibrosis in children with normal function after liver transplantation (Miyagawa-Ayashino A et al. Liver Transplant 2012). We aimed to determine DSA at a fixed point (5th year) after LT and to study correlations with clinical data.

Methods: PATIENTS: all 34 available patients from 2008-2009 cohorts. Median age at LT was 1.6 yrs. 53% had Biliary Atresia, 53% were male, 20% received a whole liver, 47% a Living donor. All were on low dose steroids, plus tacrolimus (85%) or cyclosporine (15%). Average tacrolimus level in the previous year was <3 ng/ml (16%), 4 ng/ml (45%) or 5 ng/ml (38%). 23% had developed food allergy. The graft in the previous year showed normal ALT (62%), transient dysfunction (26%), or chronic dysfunction (12%).

METHOD: a screening of antiHLA (Multiple Ag beads-Labscreen mix One Lambda) was done at 5th year posttransplant. Those with a positive result were further studied for DSA (single-antigen beads-LUMINEX). A second screening test was performed in all cases, averaging 10 months after the first determination. Clinical data at first determination and in the period between both tests were analyzed. There was no therapeutic intervention for DSA+ children.

Results:

1. First assessment: Screening showed antiHLA-I + (>15,000 SFI) in 3 (8.8%), anti-MICA in 1 (2.9%), and antiHLA-II + (>20,000 SFI) in 14 (41%). In 13 antiHLA-II patients: DSA were identified in 12: low (>500 MFI) DR in 1, intermediate (>2000 MFI) DQ in 2, strong (>4000 MFI) DQ in 9.
2. Follow-up determination: Screening technique averaging 9.8±3 months after the first determination showed: antiHLA-I in 2 (new cases), anti HLA-II in 7 (20.5%), all of whom previously positive. antiHLA-II became negative in half of the positive at first determination.
3. AntiHLA-II at first sample associated with living donor (p<0.01) and marginally to previous year tacrolimus <3ng/ml (p=0.11). No differences were observed in other clinical data including actual and previous year graft function.
4. AntiHLA-II at 2nd sample correlated with antiHLA-II + at first sample (p<0.01), male gender (p=0.05) and GGT value (normal in all+)(p=0.02). All “persisting antiHLA II” had normal graft function (ALT 23±8U/L, GGT 14±4 U/L) in the studied period.

Conclusion: No case of graft dysfunction was associated with DSA in this series. Positive DSA was frequent, usually against DQ as has been shown by others in adults and children. This study found at least half of positives, even with strong MFI, did not persist in follow up.

Disclosure of interest: "None Declared".

The study was supported by the Spanish Society of Liver Transplantation (SETH)’s grant “SETH-ASTELLAS 2014”
Does antiviral prophylaxis prevent cytomegalovirus associated complications in paediatric liver transplant recipients?

Palaniswamy Karthikeyan¹, Anil Dhawan², Anita Verma³

¹Kings College Hospital, Paediatric Gastroenterology Hepatology and Nutrition, London, United Kingdom
²King’s College Hospital, Paediatric Liver, GI & Nutrition Centre, London, United Kingdom
³Kings College Hospital, Institute of Liver Studies, London, United Kingdom

Objectives and study: CMV infection is more common in paediatric setting, as children are more CMV naïve than adults. Hence, the incidence and impact of CMV infection on the graft depends on Donor/Recipient (D/R) status at the time of transplant. Our aim was to analyze the CMV associated complications, graft survival, morbidity and outcome for paediatric liver transplant recipients (PLTR), who had CMV infection and those who received antiviral prophylaxis and pre-emptive antiviral therapy after liver transplantation.

Methods: We retrospectively analyzed data from 180 PLTR, who underwent transplant between 2008 and 2011. The follow-up period was 2 years from the date of transplant or until death. D+R- group with the highest risk for CMV infection received prophylactic intravenous ganciclovir treatment for 2 weeks after transplant, as per our protocol. The rest of the groups were on weekly CMV monitoring till discharge and received pre-emptive therapy only if they became symptomatic.

Results: Overall 88 patients (48.9%) developed CMV viraemia during the study period. PLTR who had CMV infection had significantly higher rate of graft rejection, hepatitis and hospital stay (table).

<table>
<thead>
<tr>
<th></th>
<th>CMV+ve (n=88)</th>
<th>CMV-ve (n=92)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rejection</td>
<td>42.1%</td>
<td>28.3%</td>
<td>0.05</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>28.4%</td>
<td>17.4%</td>
<td>0.07</td>
</tr>
<tr>
<td>Hospital Admission</td>
<td>48(7-270)</td>
<td>24.5(3-190)</td>
<td>-</td>
</tr>
</tbody>
</table>

Prophylaxis versus Pre-emptive groups

<table>
<thead>
<tr>
<th></th>
<th>Prophylaxis (n=54)</th>
<th>Pre-emptive (n=76)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rejection</td>
<td>29.6%</td>
<td>32.9%</td>
<td>0.69</td>
</tr>
<tr>
<td>Hepatitis</td>
<td>24.1%</td>
<td>28.9%</td>
<td>0.54</td>
</tr>
<tr>
<td>Re-transplantation</td>
<td>5.6%</td>
<td>6.5%</td>
<td>0.06</td>
</tr>
<tr>
<td>Length of hospital stay</td>
<td>27.5(10-190)</td>
<td>30.5(10-137)</td>
<td>-</td>
</tr>
</tbody>
</table>

The prophylaxis group (D+R-) had lower incidence of hepatitis and rejection compared with the pre-emptive group (patients from D-R+ & D+R+ group) However while comparing between two high risk groups (D+R prophylaxis group versus D-R+ preemptive group), the latter group had statistically significant highest incidence of hepatitis (35%) and longer hospital stay in the hospital after transplant. Re-transplantation was seen in 5.6% of patients who received prophylaxis as compared to 6.5% of patients in the pre-emptive group. The lowest incidence of hepatitis and re-transplantation were seen in the D-R- group.
**Conclusion:** CMV infection is associated with increased morbidity, graft rejection and hepatitis. Antiviral CMV prophylaxis against CMV infection reduces the incidence of graft hepatitis and rejection in comparison to other groups receiving pre-emptive therapy.

**Disclosure of interest:** None Declared.
Pulmonary function in children with cystic fibrosis (CF) after liver transplantation

Sebastian Więckowski¹, Piotr Czubkowski¹, Hanna Dmeńska², Mikolaj Teisseyre¹, Małgorzata Markiewicz-Kijewska³, Joanna Pawłowska¹

¹Children's Memorial Health Institute, Gastroenterology, Hepatology, Pediatric and Nutrition, Warsaw, Poland
²Children's Memorial Health Institute, Department of Lung Physiology, Warsaw, Poland
³Children's Memorial Health Institute, Pediatric Surgery and Organ Transplantation, Warsaw, Poland

Objectives and study: Pulmonary pathology remains the primary cause of morbidity and mortality in patients with cystic fibrosis (CF). Liver disease develops in approximately 25% of patients with CF, worsens lung disease and it is an independent risk factor for mortality. In patients with cirrhosis, liver transplantation (LTx) may exert beneficial effect on pulmonary function. Thus the aim of the study was to assess respiratory capacity in children with CF after LTx.

Methods: We performed the retrospective chart reviewed of 15 patients (5 girls, 10 boys) with CF who underwent LTx in our hospital from March 1990 to December 2015. We analyzed clinical data with special focus on lung function before and after LTx.

Results: LTX was performed at median age 13.3 years (7.25 – 18). All children presented with portal hypertension complicated with variceal bleeding in 8 patients. The median PELD and MELD before transplantation was 8 and 12 respectively. In almost all patients we observed positive influence on nutritional status and overall increase in quality of life. Seven patients before LTx did not have significant pulmonary dysfunction. Before LTx, median forced expiratory volume in one second (FEV1) was 84.6 (range 43 to 130.6), forced vital capacity (FVC) was 86 (range 55 to 116.2), the FEV1/FVC ratio ranging from 63.99 to 97.14 % (median 84.51). In the early post-transplant follow-up (from 6 to 12 month after LTx), FEV1 was 66 to 128.9 (median 87.1), FVC 79.35 to 113.3 (median 88), FEV1/FVC 69.78 to 91.16 (median 84.12). Two patients were deceased after LTx due to septic complications (2.5 and 16 months after LTx). Currently, median post-transplant follow-up of the remaining 13 patients is 3.3 years (range 0.9 to 10.5) and FEV1 is 45.67 to 122 (median 84), FVC 56 to 126 (median 102), FEV1/FVC 62.84 to 83.05 (median 72.91).

Conclusion: Liver transplantation for CF patients with advanced cirrhosis and mild to moderate pulmonary dysfunction offers encouraging results with possible beneficial effect on lung disease in long-term follow-up.

Disclosure of interest: None Declared
Bloodstream infections in children after living related liver transplantation. One center experience.

Mohamed Barr¹, Kishwer Kumar², Aly Akhtarul Hassan², Dalal Al Bogamí², Jessica Burkholder², Mohammad Ali Shagraní¹, Talal Algoufí², Laszlo Szonyí²

¹King Faisal Specialist Hospital and Research Centre, Pediatric Transplant Hepatology, Organ Transplant Centre, Riyadh, Saudi Arabia
²King Faisal Specialist Hospital and Research Centre, Organ Transplant Center, Pediatric Liver Transplant, Riyadh, Saudi Arabia

Objectives and study: Bloodstream infections remain as life-threatening complications and are associated with significant morbidity and mortality among solid organ transplant recipients. The widespread and local practice use of antibiotics could lead to a change in the pathogen pool which can modify the antimicrobial therapy. The goal of the study is to characterize the incidence and the main characteristics of the bloodstream infections in children who underwent living related liver transplantation. We studied 156 pediatric liver transplantations, of which 145 (92.9%) were performed from living donors and 11 (7.1%) were from deceased donors. Most of our transplanted children (n=129, 82.7%) were below 5 years of age (2 mo - 57 mo) with a mean of 18.6 mo ± 14.1 mo. They were 83 (53.2%) boys and 73 (46.8%) girls. Indications for transplantation were mainly biliary atresia (n=38, 24.4%) and progressive intrahepatic cholestasis (PFIC) type II (n=21, 13.5%). Other indications included Crigler Najjar syndrome type I, sclerosing cholangitis, urea-cycle defects, ductal plate malformations, PFIC type III, hepatoblastoma, primary hyperoxaluria type I, tyrosinemia type I, Wilson Disease, PFIC type I, and others.

Methods: Positive blood cultures from children post-living related-donor liver transplantation (LRDLT) operated between 2011 and 2014 were retrospectively studied. Cultures positive for skin contaminants including coagulase negative Staphylococci and Diphtheroids were excluded. Patients were then categorized according to the post-transplant duration before positive blood cultures and the number of episodes with positive blood cultures.

Results: Forty five children (28.8% of the study population) had positive blood cultures post LRDLT. Twenty seven children (60%) had Gram positive organisms, 13 children (28.8%) had Gram negative organisms, and 5 children (11.1%) had Candidemia. Cultures positive for coagulase negative Staphylococci (n=13) and for Diphtheroids (n=1) were excluded. Thirty six children (80%) had one positive blood culture, 6 children (13.3%) had two episodes, 3 children (6.67%) had three episodes, and 1 child (2.2%) had four episodes. Early post-transplant bacteremias were mainly detected within the first month (n=23, 51.1%) and after 2-6 months (n=10, 22.2%). Late post-transplant bacteremias were less detected after 6 months (n=12, 26.7%). The most common pathogens retrieved were E. coli (n=11, 24.4%) and Klebsiella (n=8, 17.8%).

Conclusion: Bloodstream infections are common after pediatric LRDLT. Early post-transplant bacteremias are mainly encountered during the first month. Escherichia coli and Klebsiella are the most common pathogens involved in early post-transplant bacteremias and should be considered in the treatment plan awaiting the culture and sensitivity results.

Disclosure of interest: None Declared.
Predictors of non-compliance to a gluten free diet in coeliac disease - a tertiary centre experience

Betina Lorentzen¹, Sara Mancell¹, Babu Vadamalayan¹

¹King's College Hospital, Paediatric Liver, Gi and Nutrition Centre, London, United Kingdom

Objectives and study: Complying with a gluten free diet is imperative to the health and well-being of patients with coeliac disease. Non-compliance to a gluten free diet increases the risk of developing complications. In our tertiary GI unit coeliac patients are seen at least yearly by the multi-disciplinary team including dietitian, psychologist, nurse specialist and gastroenterologist. Non-compliant patients are seen more often (at least 4 times a year) and between clinic visits a dietitian provides telephone support when needed. The aim of this study was to review patients who are not compliant with diet and to identify factors that may predict non-compliance at an earlier stage.

Methods: We retrospectively collected data on all children with histologically confirmed diagnosis prior to September 2015. 148 children were identified. Newly diagnosed coeliac patients (within the past year) as well as patients deficient in immunoglobulin A were excluded. 82 patients (50 females and 32 males) were included in the study. The following data were collected: age of diagnosis, gender, regular attendance (at least yearly since diagnosis), anti Tissue Transglutaminase (tTG) (<7 units/ml) from one year post diagnosis, age (at date of most recent tTG level) as well as zinc levels.

Results: Analysing tTG levels from 1 year post diagnosis enabled us to group our patients. Group 1, Compliers (49) had a tTG <7 at 1 year post diagnosis and maintained this while Group 2, Non-compliers (18) never had a tTG level <7. Group 3, Improvers (12) did not have a tTG level <7 at 1 year post diagnosis but had a normal tTG at the most recent time point. Group 4, Fluctuaters (3) had a tTG >7 at 1 year post diagnosis and had fluctuating tTG levels over time, ending up with 67% (n=2) having a tTG level <7 at their most recent reading. We found no differences in median age of diagnosis between Group 1 (5.4) and 2 (5.8). Group 3 and Group 4 were older at age of diagnosis (7.4) and (11.5). A similar distribution was found in age at most recent tTG. Group 1 had the best attendance (96%); no difference in attendance was found between Group 2 (83%) and Group 3 (83%). The poorest attendance was seen in Group 4 (67%). The percentage of patients with Zinc levels >11 (normal) were Group 1 (50), Group 2 (61), Group 3 (67), Group 4 (67).

Conclusion: Persistently high tTG levels at 1 year post diagnosis is an indicator of non-compliance in the long term. If tTG levels were not <7 units/ml at 1 year post diagnosis, there was a 60% chance of staying non-compliant and a 40% chance of improving, achieving a tTG <7 at a later date. Age at diagnosis and gender are not predictors of non-compliance to a gluten-free diet in coeliac disease. Future studies should compare Non-compliers with Improvers for any significant differences between the patient profiles of these 2 groups.

Disclosure of interest: None
Reducing the maternal dietary intake of indigestible and slowly absorbed short-chain carbohydrates is associated with improved infantile colic: a pilot study

Marina Iacovou¹, Elise Mulcahy¹, Helen Truby², Jacqueline Barrett¹, Peter Gibson¹, Jane Muir¹

¹Monash University, Department of Gastroenterology, Melbourne, Australia
²Monash University, Department of Nutrition and Dietetics, Melbourne, Australia

Objectives and study: To investigate if reducing the maternal dietary intake of indigestible and slowly absorbed short-chain carbohydrates, referred to as FODMAPs (Fermentable Oligo-, Di- and Mono-saccharides and Polyols) in breastfeeding mothers is associated with reduced symptoms of infantile colic. Additionally, to investigate if FODMAPs are detected in breast milk samples and whether such maternal dietary changes leads to changes in infant faecal pH. This was an open-label, single-blinded, intervention study.

Methods: Exclusively breastfeeding mothers and their colicky, typically-developing, healthy infants who met the Wessel Criteria for infantile colic were recruited from the community. After assessment of habitual maternal diet, mothers who were provided a low FODMAP 7-day diet. Using the validated Barr diary, the behavioural patterns of infants (crying, fussing, sleeping, feeding and awake and content durations) were captured for seven days at baseline and daily during the dietary intervention. Analysis was corrected for infant’s age. At baseline and at the end of the 7-day dietary intervention, breast milk was analysed for FODMAP content, using high performance liquid chromatography (HPLC) and infant faecal pH, using a protein electrode. The mothers were followed for 14 days.

Results: Eighteen breastfeeding mothers (aged 27-40 y) adhered to the diet that reduced FODMAP intake by about 75%. The infants were of gestational age 37-40.3 weeks and aged 2-17 weeks. At entry, crying durations were a mean [95%CI] of 142 [106-61] min and fell by 52 [178-120] min (p=0.005; ANCOVA). Combined crying-fussing durations fell by 71 [301-223] min (n=13; p=0.007), as did crying episodes (p=0.01) and fussing durations (p=0.011). Infant sleeping, feeding, or awake-and-content durations did not change. Infant fecal pH did not change. Breast milk lactose content was stable and other known FODMAPs were not detected. One unknown peak identified by HPLC had markedly reduced in 8 out of 10 breast milk samples. In the weeks following the intervention, 16 mothers continued on a low FODMAP diet.

Conclusion: Consuming a low FODMAP diet was associated with a reduction of infantile colic that was greater than the anticipated clinical significance of >25%, as deemed by previous colic studies. Since infantile colic does spontaneously improve with time, a controlled evaluation of the low FODMAP diet in mothers is needed and mechanisms by which such an effect might occur require investigation.

Disclosure of interest: First author, Marina Iacovou was in receipt of a scholarship (Australian Postgraduate Award) from Monash University. The Department of Gastroenterology receives funds from the sale of a digital application and booklets on the low FODMAP diet. 5th author, Professor Peter R Gibson has published a book on the low FODMAP diet. The other authors have no conflicts of interest relevant to disclose.
Effect of fermented milk with Lactobacillus paracasei CBA L74 on gastrointestinal and respiratory infections in children: multicenter randomized controlled trial

Giovanni Corsello\textsuperscript{1}, Rita Nocerino\textsuperscript{2}, Maurizio Carta\textsuperscript{3}, Roberto Mariniello\textsuperscript{4}, Marina Picca\textsuperscript{5}, Giulio De Marco\textsuperscript{6}, Maria Micillo\textsuperscript{7}, Dante Ferrara\textsuperscript{8}, Patrizia Vigneri\textsuperscript{7}, Gaetano Cecere\textsuperscript{2}, Pasqualina Ferri\textsuperscript{2}, Paola Roggero\textsuperscript{8}, Giorgio Bedogni\textsuperscript{10}, Fabio Mosca\textsuperscript{8}, Roberto Berni Canani\textsuperscript{11}

\textsuperscript{1}University of Palermo, Operative Unit of Pediatrics and Neonatal Intensive Therapy, Mother and Child Department, Palermo, Italy
\textsuperscript{2}University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
\textsuperscript{3}Federazione Italiana Medici Pediatri Lombardia, Milan, Italy
\textsuperscript{4}Pediatric Society of Primary Health Care (Sicup), Milan, Italy
\textsuperscript{5}University of Palermo, Department of Sciences for Health Promotion and Mother and Child Care, Palermo, Italy
\textsuperscript{6}Family Pediatrician, Palermo, Italy
\textsuperscript{7}University of Milan, Department of Clinical Science and Community Health, Neonatal Intensive Care Unit, Fondazione I.R.C.C.S. Ca’ Granda Ospedale Maggiore Policlinico, Milan, Italy
\textsuperscript{8}Clinical Epidemiology Unit, Liver Research Center, Basovizza-Trieste, Italy
\textsuperscript{9}University of Naples “Federico II”, Department of Translational Medical Science, European Laboratory for the Investigation of Food-Induced Diseases and Ceinge, Naples, Italy

Objectives and study: Recently it has been demonstrated that cow’s milk or rice fermented with Lactobacillus paracasei CBA L74 are able to prevent common infectious diseases (CIDs) in children aged 12-48 months attending daycare. In this study we aimed to confirm in a multicenter study the efficacy of cow’s milk fermented with Lactobacillus paracasei CBA L74 in reducing CIDs.

Methods: Multicentre, randomized, double-blind, placebo-controlled trial on healthy children (aged 12-48 months) consuming daily 7 gr of cow’s milk fermented with L. paracasei CBA L74 (group A), or placebo (group B) attending daycare during the 3-month study course. Over this period, acute gastroenteritis (AGE) and upper respiratory tract infections (URTI) were recorded by family pediatricians. At enrollment and after 3 months of treatment a stool sample was obtained from all study subjects to determine the effects on α- and β-defensins, cathelicidin (LL-37), and secretory IgA production by ELISA.

Results: 126 children (71 males, 56.3%) with a mean (SD) age of 32.8 (9.2) months completed the study: 66 in group A and 60 in group B. ITT analysis showed that during the study 105 out of the 146 (72%) children experienced at least one episode of CID. The proportion of children presenting at least one episode of CID was significantly lower in group A compared with group B (60% vs 83%, p<0.05). The absolute risk difference (ARD) for the occurrence of at least one CID was -23% (95% CI: -37% to -9%, p < 0.01, binomial regression) for group A vs. group B. This correspond to a number of children needed to treat of 4 (95%CI 3 to 11) for group A vs. group B. Per-protocol-analysis (PPA) showed that the proportion of children presenting at least one episode of AGE was significantly lower in group A vs. group B (18% vs 40%, p<0.05). The ARD for the occurrence of at least one episode of AGE was -22% (95% CI: -37% to -6%, p < 0.01) in group A compared to group B. Similar findings were obtained at PPA regarding the proportion of children presenting at least one episode of URTI, that was significantly lower in group A vs. group B (51% vs 74%, p<0.05). The ARD for the occurrence of at least one episode of URTI was -23% (95% CI: -40% to -7%, p < 0.01) in group A vs. group B. Net changes in log₁₀α-defensin (p<0.001), log₁₀β-defensin (p<0.001), log₁₀LL-37 (p<0.001) and log₁₀sIgA (p<0.001) were seen at 3 months vs. baseline for group A vs. group B.

Conclusion: Dietary supplementation with cow’s milk with Lactobacillus paracasei CBA L74 can be recommended as a valid strategy in preventing CIDs in children attending educational program.

Disclosure of interest: This work was supported in part by an unrestricted grant from KraftHeinz Italia SpA, Latina, Italy, an affiliate of Kraft Heinz Company Pittsburgh, PA, USA devoted to the centers.
Children with eating disorders secondarily to artificial nutrition in the neonatal period have specific food preferences and saliva composition

Martine Morzel1, Eric Neyraud1, Geraldine Lucchi2, Helene Brignot3, Patrick Ducoroy4, Aline Jeannin5, Caroline Truntzer6, Cecile Canlet7, Marie Tremblay-Franco8, Ç Hirtz9, Irene Loras-Duclaux9, Alain Lachaux7, Segolene Gaillard9, Sophie Nicklaus9, Gilles Feron1, Noël Peretti10

1 Inra, Umr1324 Centre des Sciences du Gout et de L'alimentation, Dijon, France
2 Université de Bourgogne, Clip-icmub, Dijon, France
3 Université de Bourgogne, Clipp-Icmub, Dijon, France
4 Inra, Umr 1331 Toxalim, Toulouse, France
5 Inserm, U1040, Hopital Saint Eloi, , Montpellier, France
6 Hcl, Chu Lyon, Hopital Femme Mere Enfant, Pediatric Hepatogastroenterology and Nutrition , Lyon, France
7 Hôpital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology; Reference Centre for Wilson Disease, Lyon, France
8 Inserm, Cim 1407, Hospices Civils de Lyon, Cnrs, Umr5558, Lyon, France
9 Inra, Cnrs, Umr1324 Umr6265 Centre des Sciences du Gout et de L'alimentation, Dijon, France
10 Hcl Inserm, Université Claude Bernard Lyon 1, Faculté de Médecine Lyon-Est, Inserm U1060, Carmen Laboratory, Lyon, France

Objectives and study: In the neonatal period, some severe digestive diseases require the cessation of oral feeding and the use of enteral or parenteral nutrition for prolonged periods. In some cases, this by-pass of the oral cavity during the early stages of feeding results in the development of so-called oral disorders (OD). Oral disorders may persist for years after healing of the causal disease, and are expressed for example by an exacerbated gag reflex, difficulties in chewing and swallowing and high food selectivity.

The aim of this study was to describe the consequences on oral physiology of oral by-pass and enteral nutrition in a population of children who suffered oral disorder (OD) compared to a healthy control population.

Methods: The two populations were followed over one year with three samplings and compared regarding 1) their food sensitivity consisting in measured feeding difficulties, food preferences and food habits with a questionnaire approach; and 2) their salivary composition. Proteome analyses were performed with different methods. First, proteins were separated by 2D electrophoresis. Spots of interest, i.e. differentially expressed between the two groups, were manually excised and after tryptic digestion, MALDI-TOF/TOF acquisitions led to identifications. SELDI-TOF MS profiling with ProteinChips arrays was also carried out. Peptidome profiling by label-free MALDI-TOF allowed to detect discriminant peptides, and identification of discriminant peaks was attempted by MALDI-TOF-TOF and nanoLC-ESI MS-MS. Metabolome analyses were performed by 1H NMR. Discriminant buckets were assigned to metabolites using reference databases.

Results: We included 21 children who suffered oral disorder (OD) and 23 age- and sex-matched healthy controls.

1) On feeding difficulty aspects, OD children were separated significantly on 6 dimensions reflecting eating difficulties (oral tactile sensitivity, appetite and interest for food, sensitivity to food texture, sensitivity to tastes, and sensitivity to temperature). Moreover, consumption frequency, number of consumed foods and liking were lower for the OD compared to the controls children for specific food groups.

2) On salivary composition, despite heterogeneity within the groups (age, pathology, medication, etc.), the 3 spectral methods (MALDI-TOF, SELDI-TOF, 1H NMR) allowed discriminating OD and controls, confirming that oral stimulation by food intake plays a role in shaping the composition of saliva. Saliva of OD patients exhibited a lower antioxidant status and lower levels of the salivary protease inhibitors.
cystatins. Other discriminant features (IgA1, dimethylamine) may relate to modified oral and/or intestinal microbial ecology. Finally, salivary profiles of OD patients were partly comparable to those of subjects with exacerbated gustatory sensitivities, in particular with reduced abundance of cystatin SN and higher abundance of zinc-alpha-glycoprotein.

**Conclusion:** Despite heterogeneity within the groups in terms of age/developmental stage and initial pathology in the patients group, feeding preferences such as salivary profiles specifically associated to oral disorders were identified. Whether this translates taste hypersensitivity and contributes to the eating difficulties deserves further attention.

**Disclosure of interest:** "None Declared". Grant ANR-10-ALIA-001-ORALISENS
Soluble mediators from Lactobacillus rhamnosus GG improve intestinal barrier function in a rat model of short bowel syndrome

Jiang Wu¹, Yan Zhong², Gabriele Gross³, Tim Lambers³, Ric van Tol³, Wei Cai⁴

¹Xin Hua Hospital, Department of Clinical Nutrition, Shanghai, China
²Mead Johnson Pediatric Nutrition Institute, Shanghai, China
³Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands
⁴Xin Hua Hospital, Shanghai, China

Objectives and study: Intestinal barrier integrity plays an essential role for gastrointestinal health and disease. The aim of this study was to explore potential effects of specific preparations of soluble mediators derived from Lactobacillus rhamnosus GG (LGG) on intestinal barrier function in a rat model of short bowel syndrome (SBS).

Methods: 6-week old male SD rats underwent either 75% small bowel resection or bowel transection (sham-operated control), followed by re-anastomosis. Animals were supplemented with 5*10⁸ CFU viable LGG, LGG soluble mediator preparation in an equivalent dose or PBS by intragastric gavage daily from day 2 throughout day 14 after small bowel resection. Body weight of the animals was measured regularly. On day 15, intestinal permeability (FD-40), serum levels of endotoxin and bacterial translocation to mesenteric lymph nodes, liver and spleen were assessed. SIgA, TNF-α and IL-6 levels in ileum content and serum were determined by ELISA. Intestinal adaptation was evaluated by assessing villus height and crypt depth. Expression of tight junction proteins including occludin, ZO-1 and claudin-1 and -4 in ileum was measured by western-blotting. Statistical analysis was performed using a one-way ANOVA or a non-parametric test.

Results: Compared with the sham operated group, bowel resection led to significantly lower body weight, increased villus height and crypt depth. Intestinal permeability, endotoxin levels as well as bacterial translocation in SBS group were increased whereas expression of slgA and occludin, ZO-1 and claudin-1 and -4 was decreased compared with sham group, demonstrating impaired intestinal barrier function in SBS model. This was accompanied by local and systemic inflammation as reflected by increased cytokine levels. Most parameters detrimentally affected in this SBS model were improved by the supplementation with either viable LGG or LGG soluble mediator preparation, including increased weight gain, reduced bacterial translocation, decreased levels of FD-40 and endotoxin as well as increased levels of slgA and tight junction protein expression at the end of the experiment. In addition, TNF-α and IL-6 levels in ileum and serum were reduced in the viable LGG and LGG soluble mediator preparation intervention groups.

Conclusion: Enteral supplementation of LGG or specific LGG soluble mediators improves intestinal permeability, reduces bacterial translocation, increases intestinal slgA level and lowers both local and systemic inflammation in a rat model of SBS. The LGG soluble mediator preparation not only mimics some of the biological effects of viable LGG, but even shows stronger effects on reducing inflammation and supporting intestinal barrier integrity and function, likely through up-regulation of specific tight junction protein expression.

Disclosure of interest: This study was supported in part by Mead Johnson Nutrition. Y. Zhong, G. Gross, T. Lambers and E. van Tol are employees of Mead Johnson Nutrition.
Maternal high dietary linoleic acid during gestation and lactation impairs rat offspring gut and metabolic homeostasis.

Charlene Alain¹, Justine Marchix², Sandrine David³, Frédérique Barloy-Hubler³, Céline Druart⁴, Nathalie Delzenne⁴, Philippe Legrand², Gaëlle Boudry¹

¹Inra Ur1341 Adnc, Saint-Gilles, France
²Usc Biochimie Nutrition Humaine, Rennes, France
³Ea1254, Rennes, France
⁴Metabolism and Nutrition Research Group, Louvain Drug Research Institute, Université Catholique de Louvain, Brussels, Belgium

Objectives and study: Linoleic acid (LA) consumption has increased over the last decades. This polyunsaturated fatty acid (PUFA) can be metabolized in various bioactive molecules that might impact gut barrier function, gut microbiota and lipid metabolism. Our objective was to assess if dietary LA excessive consumption during gestation and lactation affect offspring gut ecology and barrier function and lipid metabolism in a rat model.

Methods: Female Wistar rats were fed isocaloric and isolipidic diets (21% of energy from lipids) enriched in LA (LA, 12% of energy) or not (ctl, 2% of energy) during gestation and lactation. At weaning, male pups were fed either their dam diet or the other diet and were sacrificed at 3 or 6 months of age.

Results: At 3 months of age, offspring from LA dams displayed increased food intake (+9%, P=0.02), body weight gain (+13%, P=0.007) and visceral adiposity (+28%, P=0.04) compared to ctl pups. They also exhibited increased caecal epithelium permeability (flux of FD-4 in Ussing chambers +48%, P=0.05), tendency for increased colonic tnf-α mRNA levels (+27%, P=0.08) and decreased colonic intestinal alkaline phosphatase activity (-55%, P=0.02). Plasma IL-1β concentrations were greater (+25%, P=0.004) in LA pups than ctl ones. These maternal effects were not affected by the post-weaning diet. At 6 months of age, intestinal parameters of LA pups were restored to ctl levels. Yet, LA pups displayed enhanced fasted glycemia and insulinemia (+23%, P=0.04 and +36%, P=0.01, respectively) and liver steatosis compared to ctl pups. Again, this was independent of the post-weaning diet. Analyze of caecal microbiota by 16S sequencing and principal coordinate analysis revealed different microbiota signatures at 3 and 6 months. Within the 3-month old pups, the microbiota of LA pups clustered together irrespective of the post-weaning diet while those of ctl pups were separated due to the post-weaning diet. At 6 months of age, no clear clustering of the different microbiota was observed.

LA metabolic pathways were largely affected by the weaning diet, yet they were also affected by the maternal diet with different profiles at 3 and 6 months of age: plasma levels of anti-inflammatory PUFA metabolites were increased in 6 month-old LA pups compared to ctl ones (eicosanoids derived from n-3 PUFA, LTB5 +144%, P=0.0002 and 18-HEPE +55%, P=0.02 and epoxyeicosatrienoic acids 8,9-EET +93%, P=0.002 and 14,15-EET +58%, P=0.08). Those differences were not observed at 3 months of age. Concentrations of the conjugated linoleic acid t9,t11 (measured in the liver) were not different at 3 months of age but were decreased (-62%, P=0.004) in LA pups at 6 months of age.

Conclusion: Maternal high dietary LA intake has long-term consequences on offspring gut microbiota, gut function and lipid metabolism but with different patterns depending of the offspring age. While younger rats displayed altered gut homeostasis and greater visceral adiposity, older rats had restored gut homeostasis but glucose homeostasis defaults and liver steatosis. Whether the changes observed in intestinal microbiota composition and linoleic metabolic pathways between 3 and 6 months of age are involved in these different phenotypes needs to be explored.

Disclosure of interest: None declared
Probiotic supplementation in VLBW preterm infants improves feeding tolerance and reduces risk of gram negative sepsis

Deepa Hariharan¹, Lavanya Balasubramanian¹, Velmurugan Kannappan¹, Ganesh Veluswami¹
¹Sooriya Hospital, Neonatology, Chennai, India

Probiotic supplementation in preterm, VLBW infants: effect on feed tolerance, NEC and late-onset sepsis.

Objectives and study: Impaired gastrointestinal function and microbia predispose premature infants to sepsis and NEC, major causes of morbidity and deaths in this population. The aim of this study is to evaluate if probiotic supplementation reduces risk of feeding intolerance, NEC and late-onset sepsis in preterm VLBW infants in a busy referral NICU in India with >1000 high-risk admissions per year. Due to conflicting data on type of probiotic, a mixture of probiotics was used.

Methods: Infants with birth weight < 1250g, gestation <32 weeks admitted during the 16 month study period were randomly assigned to a protocol of enteral administration of mixture of probiotics: Lactobacillus acidophilus, Bifidobacterium bifidum, Saccharomyces boulardii 2.5 X 10⁹ UFC of each twice a day, from the 3rd day of life, for 6 week courses (STUDY GROUP), or only feeds with no probiotics (CONTROL GROUP). Standardized feeding protocol (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 or preterm formula were similar in the 2 groups. Surfactant, caffeine, ventilatory and inotrope use and PDA closure 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 or fungemia, time to reach full feeds, and death.

Results

<table>
<thead>
<tr>
<th></th>
<th>Study</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>93</td>
<td>103</td>
</tr>
<tr>
<td>Mean BW (g)</td>
<td>945</td>
<td>972</td>
</tr>
<tr>
<td>Mean GA (weeks)</td>
<td>28.7</td>
<td>29.3</td>
</tr>
<tr>
<td>Number of infants needing ventilator +/- inotrope support</td>
<td>34</td>
<td>38</td>
</tr>
<tr>
<td>Transient feed intolerance episodes</td>
<td>35</td>
<td>58*</td>
</tr>
<tr>
<td>Late-onset sepsis (gram negative rods/ fungus)</td>
<td>9</td>
<td>16*</td>
</tr>
<tr>
<td>Stage 2/3 NEC</td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td>Average time to full feeds (days)</td>
<td>23.6</td>
<td>32.4*</td>
</tr>
<tr>
<td>Death</td>
<td>4</td>
<td>5</td>
</tr>
</tbody>
</table>

* p<0.05
No episodes of probiotic sepsis

Conclusion: VLBW preterm infants receiving probiotics have lower incidence of feed intolerance and nosocomial sepsis and reach full feeds faster.

Disclosure of interest: None
Dairy lipids in infant formula: impact on the Omega-3 fatty acid content in membrane phospholipids of red blood cells in healthy term infants

Maria Lorella Gianni¹, Paola Roggero¹, Charlotte Baudry², Claudio Galli³, Pascale le Ruyet², Fabio Mosca¹

¹Neonatal Intensive Care Unit (Nicu), Department of Clinical Science and Community Health, Fondazione Ircs “ca’ Granda” Ospedale Maggiore Policlinico, University of Milan, Italy
²Lactalis R&d, Nutrition, Retiers, France
³University of Milan, Italy

Objectives and study: When breastfeeding is not possible, infants are fed formulas in which lipids are usually of plant origin. Blends of plant oils are used to provide the 2 essential fatty acids (FA): linoleic (LA) and α-linolenic acids (ALA). However, the use of dairy fat in combination with plant oils enables a lipid profile in formula closer to breast milk in terms of FA composition, triglyceride structure and cholesterol content. Moreover, experimental data in rats suggest that a mix of dairy fat and plant oils could stimulate the endogenous conversion of ALA to long chain polyunsaturated FA, resulting in higher brain levels of docosahexaenoic acid (DHA) than a blend of plant oils even supplemented with preformed DHA (Du et al., 2012). The main objective of this study was to determine the effect of an infant formula containing a mix of dairy fat and plant oils on Omega-3 FA (ω3 FA) content in membrane phospholipids (PL) of red blood cells (RBC).

Methods: This monocentric, double-blind, controlled, randomized trial was approved by the Ethical Committee of the Fondazione Irccs of Milan, Italy (Gianni et al., 2012; NCT01611649). After delivery, healthy term infants whose mothers decided not to breastfeed were randomly allocated to be fed with a formula containing either: a mix of dairy fat and plant oils (D; ALA 2.3% of total FA (TFA), LA/ALA=6), only plant oils (P; ALA 1.8% TFA, LA/ALA=10) or plant oils supplemented with AA (arachidonic) and DHA (PDHA; ALA 1.8% TFA, LA/ALA=10, DHA 0.2%, ARA/DHA=2). Breastfed infants were included in a reference group (BF). After 4 months, the sum of ω3 FA in membrane PL of RBC was evaluated by gas chromatography. The contents of the other FA in RBC at 4 months as well as FA profile in whole blood at enrollment and 4 months were measured as secondary outcomes. Differences between groups were assessed using an analysis of covariance with sex and gestational age as covariates.

Results: 70 formula-fed (FF) and 19 BF infants completed the protocol. At baseline, patients’ characteristics were similar between groups. Total ω3 FA and DHA levels in whole blood at baseline were similar in the 3 FF groups but DHA level was significantly higher in the BF group. A decrease in ω3 FA content in whole blood was observed between birth and 4 months, without any difference in groups D and PDHA but significantly higher in group P compared to BF. At 4 months, RBC total ω3 FA (in % of TFA) in infants fed formula D were significantly higher than in group P (8.6±1.2 vs. 5.7±0.8; P<0.001) and similar to those in group PDHA (8.8±1.1) and BF (9.7±1.8). RBC DHA levels in group D (4.1±0.8) were also higher than in group P (3.4±0.7; P=0.029) but lower than in group PDHA (6.8±1.0; P<0.001) and BF (7.0±1.4; P<0.001). However, levels of eicosapentaenoic (EPA) and docosapentaenoic acids (DPA) in group D were higher than in groups P, PDHA and BF.

Conclusion: A formula containing a mix of dairy lipids and plant oils increased the endogenous synthesis of ω3 long chain FA from precursor ALA, leading to higher total ω3 and DHA status in RBC than plant oil-based formula and to higher levels of ω3 intermediate FA, such as EPA and DPA, than a formula supplemented with DHA. Modifying lipid quality in infant formula by adding dairy lipids should be considered as an alternative method to improve ω3 FA status, especially concerning the three major long chain ω3 FA which play relevant and somewhat differential roles in newborn.

Disclosure of interest: This study was supported by Lactalis. C. Baudry and P. le Ruyet are employees of Lactalis.
Delayed vs early cord clamping in small for gestational age infants >35 weeks gestation: a randomized controlled trial

Abhisek Chopra¹, Neelam Kler¹, Anup Thakur¹, Pankaj Garg¹
¹Sir Ganga Ram Hospital, Neonatology, New Delhi, India

Objectives and study: To compare the effects of Delayed cord clamping (DCC) and Early cord clamping (ECC) on serum ferritin and hemoglobin at 3 months of age in small for gestational age infants born at ≥ 35 weeks

Methods:
Study design: Randomized controlled trial
Study population: All intramural infants of ≥35 weeks gestation with fetal growth restriction (weight less than 10th centile for age) based on Hadlock charts.

Intervention: Neonates with fetal growth restriction were eligible for enrollment. Neonates with gestational age < 35 weeks, Rh isoimmunisation, multiple gestation and congenital malformations were excluded. They were randomized to two groups, delayed cord clamping and early cord clamping. In DCC group, cord was clamped at 60 seconds while in ECC cord was clamped as soon as possible after birth.

Results: A total of 2514 women were screened. One hundred and forty two infants underwent randomization, 71 in each group. Total of 82 infants (38 in DCC and 44 in ECC) were analyzed at 3 months. There was no difference in baseline maternal and neonatal characteristics between the two groups. The mean (SD) gestation was 37.33 (1.57) weeks in DCC group and 37.54 (1.46) weeks in ECC group. The mean (SD) birth weight was 2157 (341) grams in DCC group and 2130 (382) grams in ECC group. The median (IQR) serum ferritin levels at 3 months were significantly higher in DCC group as compared to ECC group; 86(43.35-134.75) vs 50.5(29.5-83.5), p=0.01. The proportion of babies who had iron deficiency (ferritin <50 ng/ml) at 3 months was significantly less in DCC group (23.6% vs 47.7%). There was no difference in hemoglobin and hematocrit at 2 hrs. Mean (SD) hematocrit in DCC was 63.93 % (6.16) and 61.49 % (5.5) in ECC group. The proportion of infants who had polycythemia was significantly higher in DCC group; 48.7% vs 22.7 %, p=0.013. However there was no difference in the need of partial exchange transfusion and adverse clinical outcomes (hypoglycemia, respiratory distress and hyperbilirubinemia requiring phototherapy) in neonatal period.

Conclusion: Delayed cord clamping is a promising strategy to improve iron stores in SGA infant ≥ 35 weeks at 3 months of age, however it increases the risk of polycythemia without an increase in need for partial exchange transfusions.

Disclosure of interest: No conflict of interest to declare
A partly fermented infant formula containing scGOS/lcFOS supports adequate growth in healthy, term infants: the life study

Alfonso Rodriguez-Herrera1, Marieke Abrahamse-Berkeveld2, Martine Alles2, Hetty Boutrius2, Rocio P. Rubio3, Antonio Muñoz4, Massimo Agosti5, Gianluca Lista6, Luigi T. Corvaglia7, Juan L. P. Navero8

1Instituto Hispalense de Pediatría, Unidad de Gastroenterología Y Nutrición, Sevilla, Spain
2Nutricia Research, Utrecht, Netherlands
3Hospital Quiron, Barcelona, Spain
4Hospital Clínico Universitario San Cecilio, Granada, Spain
5Polo Universitario F. Del Ponte, Varese, Italy
6Ospedale Dei Bambini Vittore Buzzi, Milan, Italy
7Hospital S. Orsola Malpighi, Bologna, Italy
8Hospital Universitario Reina Sofia, Córdoba, Spain

Objectives and study: Nutrition in early life has a fundamental impact on the development of the gastrointestinal tract. Fermented formulae as well as a specific mixture of short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides (scGOS/lcFOS; 9:1) have a potential beneficial impact on gastrointestinal function and microbiota development in infants. The effect of a partly fermented infant formula (IF) containing scGOS/lcFOS on gastrointestinal tolerance as well as growth and safety during 3-4 months intervention was investigated (LIFE study, NTR3455). The focus of the current abstract is limited to growth and safety outcomes.

Methods: In a randomized, controlled, multi-center, double-blinded, prospective clinical trial, infants were enrolled before 28 days of age and assigned to receive one of two formulae until 17 weeks of age: 1) FIF+: an infant formula consisting of 30% fermented formula and containing 0.8g/100ml scGOS/lcFOS or 2) IF-: a non-fermented infant formula without scGOS/lcFOS. Apart from the presence of prebiotics and fermented formula, the composition of the formulas was similar (per 100ml: 66 kcal, 1.2 g protein and 3.4 g fat). As a reference, a group of infants was included being exclusively breastfed until 17 weeks of age. Growth was evaluated by equivalence analysis of weight gain per day during the intervention period using equivalence margins of ± 0.5 SD, between formula groups (per protocol) as well as compared to the breastfed reference group. In addition, other growth parameters as well as number and type of (serious) adverse events and formula intake was monitored monthly.

Results: A total of 300 infants were included, 200 in the formula groups and 100 in the breastfed reference group. Comparing both formula groups, equivalence was demonstrated for weight, length and head circumference gain (with margins of ± 0.5SD). Equivalence of weight gain per day was demonstrated when comparing the FIF+ group, but not the IF- group, to the breastfed reference group. The difference in means lay well within the pre-defined equivalence margins of ± 0.5SD (± 3.19 g/d) for the FIF+ group (1.26 g/d; 90%CI [-0.52; 3.02]), but not for the IF- group (2.43 g/d; 90%CI [0.76; 4.10]) with 0.5SD of 3.01 g/d) due to a significantly higher weight gain compared to the breastfed reference (P = 0.017). Equivalence in length gain compared to breastfed infants was demonstrated for both formula groups. Equivalence in head circumference gain was not demonstrated and higher in both formula groups compared to the breastfed reference group (P < 0.05), although head circumference values were not different between groups at any visit. Overall, the number of infants with at least one (serious) adverse events was not different between formula groups (n = 31 infants for both), nor the number of adverse events that were reported as related to the study products (n = 12 and n = 15 for the FIF+ and IF- group, respectively). No differences in severity of adverse events (mostly mild or moderate) or in use of concomitant medication were detected.

Conclusion: The current study suggests that a partly fermented infant formula containing scGOS/lcFOS is safe and supports an adequate growth until 17 weeks of age in healthy newborn infants.
Plasma metabolome in infants fed formula supplemented with milk fat globule membranes

Tove Grip¹, Olle Hernell¹, Bo Lonnerdal², Magnus Domellöf¹, Niklas Timby¹

¹Umeå University, Clinical Sciences/Pediatrics, Umeå, Sweden
²University of California, Nutrition, Davis, United States

Objectives and study: We previously showed that feeding term infants an experimental formula (EF) with reduced protein concentration, reduced energy density and supplemented with a bovine milk fat globule membrane (MFGM) concentrate had a positive effect on cognitive development and incidence of otitis media, compared to feeding a standard formula (SF). The aim of this study was to investigate effects of the intervention on the plasma metabolome in the same study population.

Methods: In a prospective, double-blinded, controlled trial, 160 exclusively formula-fed infants were randomized to EF or SF from <2 months to 6 months of age. A breast-fed reference (BFR) group consisted of 80 infants. Plasma samples were collected at 6 months of age. Metabolome analyses were done by liquid chromatography mass spectrometry (LC-MS) on 213 infants and gas chromatography mass spectrometry (GC-MS) on 192 infants. Both targeted and un-targeted data processing methods were used to identify metabolites and to analyse the metabolome. To examine differences of the general metabolome between the formula groups, orthogonal partial least squares discriminant analysis (OPLS-DA) was used. Multivariate analyses and model plots were performed in SIMCA (version SIMCA-P+ 13.0, Umetrics, Umeå, Sweden). Differences in concentrations of specific metabolites were analysed with two-sided t-test (SPSS statistics 22) and reported as unadjusted p-values.

Results: No separation was observed at 6 months of age between the EF and SF groups in the OPLS-DA in LC-MS or GC-MS. However, plasma concentrations of several specific metabolites of interest differed between the two formula groups. The EF group had a higher relative concentration of myo-inositol compared to the SF group (p = 0.02) and more similar to the BFR group. Other metabolites where the EF and SF groups differed in relative concentrations include 2-aminobutyric acid (p=0.001), fumaric acid (p= 0.008) and myristic acid (p=0.01).

Conclusion: The intervention led to effects on several plasma metabolites at the age of 6 months. The relative concentration of myo-inositol was higher in the EF compared to the SF group. Myo-inositol is necessary for optimal function of the nervous system, and brain concentration of myo-inositol has previously been shown to be positively associated with cognitive function in infants. Further, we found differences between the EF and SF groups in plasma concentrations of other metabolites involved in lipid and amino acid metabolism. We have previously reported differences in fat intake and plasma amino acids between the groups that may explain some of these differences. The effect of the EF on plasma metabolites may reflect any mechanisms explaining the positive effect of MFGM-supplemented formula on cognitive and immunological development.

Disclosure of interest: Olle Hernell and Bo Lönnerdal are members of Hero scientific advisory board. Semper/Hero has financed part of the study.
Evaluation of Hepcidin as iron status indicator at 4 months of age

Staffan Berglund¹, Ola Andersson², Lena Hellström-Westas², Magnus Domellöf¹

¹Umeå University, Department of Clinical Sciences, Pediatrics, Umeå, Sweden
²Uppsala University, Department of Women's and Children's Health, Uppsala, Sweden

Objectives and study: Infants are at risk of iron deficiency (ID) from 4-6 months of age and the risk can be reduced using delayed cord clamping. However, infants experience large physiological changes in iron status and sensitive indicators of ID are lacking. The iron regulatory hormone hepcidin is closely associated with iron status and may be a useful indicator of iron stores in infants.

Methods: Full-term infants (n = 382) were randomized to delayed (≥180 sec) or early cord clamping (≤10 sec) and iron status including ferritin, transferrin saturation [TS], mean cell volume [MCV], and transferrin receptor concentration [TfR] was assessed at 4 months. In the 8 cases who developed ID at 4 months (defined as 2 out of 4 variables in the lower range) and 98 randomly selected controls, we analyzed hepcidin using an immunochemical assay and explored its correlation to clamping intervention, iron status, and to ID.

Results: The delayed cord clamping group had significantly higher hepcidin at 4 months with median (10th; 90th percentile) 39 (14.4; 76.6) vs. 20 (5.37; 86.1) ng/ml (p<0.001). Log₁₀Hepcidin at 4 months correlated positively to ferritin (r=0.766, p<0.001), TS (r=0.368, p<0.001), and MCV (r=0.420, p<0.001), and negatively to TfR (r= -0.457, p<0.001). Cases with ID had significantly lower hepcidin levels 5.5 (3.0; N/A) vs. 34.5 (10.7; 72.2) ng/ml (p=0.012). All cases of ID at 4 months had hepcidin level below 16 ng/ml and all but one (87.5%) had a level below the 10th percentile for those with delayed cord clamping (14.4 ng/mL).

Conclusion: Delayed cord clamping improved iron status also when evaluated by hepcidin levels. Hepcidin is a relevant indicator of iron status at 4 months of age and may be useful in clinical practice to detect cases of ID.

Disclosure of interest: None Declared.
A randomised trial to test the effectiveness of maternal relaxation therapy during breastfeeding: effects on infant behaviour

Nurul Husna M Shukri, Jonathan Wells, Firdaus Mukhtar, Mary Fewtrell

1Ucl Institute of Child Health, Childhood Nutrition Research Centre, London, United Kingdom
2University Putra Malaysia, Department Of Psychiatry, Faculty of Medicine & Health Sciences, Serdang, Malaysia

Objectives and study: Lactation involves complex physiological and psychological signalling between mother and infant and is energetically costly. Postpartum distress may affect the energy allocated to breastfeeding (BF) and breast milk since it increases energy expenditure. If the mother is more relaxed, she may be able to allocate more energy to BF. We found that mothers randomised to use a relaxation tape during BF had a significant reduction in stress scores and their infants showed greater gains in weight and BMI. Thus, we would like to test the hypothesis that the BF relaxation intervention has favourable effects on infant behaviour.

Methods: Women were recruited at antenatal clinics in Malaysia (March-December 2014). After birth, exclusive BF mothers were randomised to control (n=31) or intervention groups (n=33). Intervention group mothers were asked to listen to a relaxation audiotape on a daily basis for at least 2 weeks during BF at post HV1-HV3, and encouraged to listen daily in between visits, or as often as they found it useful. Mothers were not informed about randomisation as this might influence their behaviour. Home visits (HV) were performed when the baby was 2-3 (HV1, pre-treatment), 6-8 (HV2) and 12-14 (HV3) weeks old to assess infant growth (weight, length) and maternal stress and anxiety using Perceived Stress Scale and Beck Anxiety Inventory respectively. Infant behaviour, categorised as mean time sleeping, awake and happy, feeding and distress (fussing, crying and colic), was recorded within 1-2 weeks post HV1 and HV2 using a validated 3-day diary. The duration and change (Δ) in duration of each behaviour from HV1-HV2 was compared between groups and correlations with frequency of use of the tape, maternal stress score and infant growth were examined.

Results: There were no significant differences between groups in socio-demographic factors, maternal stress score, infant weight or duration of sleeping, feeding, distress and awake at HV1. The intervention group infants had significantly longer sleep duration at HV2 (856±98 v 774±94 mins p=0.017). There was no significant difference in duration of behaviours from HV1-HV2 between groups. BMI at HV2 was positively associated with Δsleep time (r=0.49, p=0.003) and negatively associated with Δawake time (r=-0.39, p=0.025). Δawake time was also negatively correlated with weight gain from HV1 to HV3 (r=-0.41, p=0.019), and weight and BMI at HV3 (r=-0.47, p=0.06; r=-0.53, p=0.02 respectively). Higher maternal anxiety score at HV1 was positively associated with Δawake time (r=0.39, p=0.02) in infant. The frequency of use of the relaxation tape was positively associated with Δsleep time (r=0.43, p=0.008) and duration of sleeping at HV2 (r=0.35, p=0.035), and also with infant weight (r=0.45, p<0.01) and BMI (r=0.53, p<0.01) at HV3. All infants grew normally according to the WHO growth standards during the study.

Conclusion: Infants whose mothers were randomised to use relaxation therapy had higher sleeping duration at HV2 with a ‘dose-response’ effect. This altered behaviour pattern may have resulted in additional energy being available for growth, consistent with observed effects of the intervention on weight and BMI. Mothers who were less stressed may have favourably altered breast milk composition by either changing the calorie/hormonal levels that might affect infant growth and behaviour. This will be investigated in further analyses of breast milk composition.

Disclosure of interest: None Declared
A micronutrient-fortified young child formula improves the iron and vitamin D status of healthy young European children: a randomised double-blind controlled trial

Marijolijn Akkermans1, Simone Eussen2, Judith van der Horst-Graat3, Ruurd van Elburg2, Hans van Goudoever4, Frank Brus1

1Juliana Children’s Hospital/Haga Teaching Hospital, Paediatrics, The Hague, Netherlands
2Danone Nutricia Research, Utrecht, Netherlands
3Food & Biobased Research (Wageningen Ur), Wageningen, Netherlands
4VU University Medical Centre, Paediatrics, Amsterdam, Netherlands

Objectives and study: Iron deficiency (ID) and vitamin D deficiency (VDD) are common among young European children because of low dietary intakes. Studies to evaluate the effect of milk fortification on iron and vitamin D status of young European children are scarce. We therefore investigated the effect of a micronutrient-fortified young child formula (YCF) on the iron and vitamin D status of healthy 12-36 months old children living in Western-Europe.

Methods: This randomised, double-blind controlled trial was performed in Germany, the Netherlands, and the United Kingdom in 2012-2014. A total of 318 children received either YCF (1.2mg/100ml iron; 1.7µg/100ml vitamin D) or non-fortified cow’s milk (CM) (0.02mg/100ml iron; no vitamin D) for 20 weeks. Blood samples were taken before and after the intervention. ID was defined as serum ferritin (SF) <12µg/l in the absence of infection (defined as high-sensitivity C-reactive protein <10mg/l). VDD was defined as 25-hydroxyvitamin D (25(OH)D) <50nmol/l.

Results: Intention-to-treat analysis revealed that YCF preserved iron status (mean estimated SF change ± SE: 1.7µg/l ± 2.4) and improved vitamin D status (25(OH)D change ± SE: 17.4nmol/l ± 2.8). The ID prevalence decreased slightly in the YCF group (14.3% to 13.9%) and increased in the CM group (11.9% to 29.6%) (p=0.036). The VDD prevalence decreased in the YCF group (25.3% to 13.5%) and increased in the CM group (21.9% to 33.3%) (p<0.001).

Conclusion: Compared to cow’s milk, young child formula use for 20 weeks preserves iron status and improves vitamin D status in healthy young children in Western-Europe.

Disclosure of interest: This study was funded by Danone Nutricia Research. The statistical analyses and the interpretation of the data were performed independently from Danone Nutricia Research. Akkermans, Brus and Van Goudoever work in non-profit hospitals in the Netherlands. Van Goudoever is also member of the National Breastfeeding council, the ESPGHAN council, the National Health council, the neonatal nutrition section of the Dutch Paediatric Association and he is the director of the (Dutch) National Donor Human Milk Bank. He received honoraria for presentations and consultations from Danone, Nutricia, Mead Johnson Nutrition, Nestle, Nutrition Institute, Hipp, Prolacta and Nutrinia. Eussen and Van Elburg are employees and Van der Horst-Graat is a former employee of Danone Nutricia Research.
Optimising nutrition to improve growth and reduce neurodisabilities in neonates at risk of neurological impairment

Morag Andrew¹, Jeremy Ross Parr², Christine Montague-Johnson¹, Bonny Baker¹, Jane Holmes³, Karen Laler¹, Janette Atkinson⁴, Oliver John Braddick⁵, Peter Bernard Sullivan¹

¹University of Oxford, Department of Paediatrics, Oxford, United Kingdom
²Newcastle University, Institute of Neuroscience, Newcastle Upon Tyne, United Kingdom
³University of Oxford, Centre for Statistics in Medicine, Oxford, United Kingdom
⁴University College London, Faculty of Brain Sciences, London, United Kingdom
⁵University of Oxford, Department of Experimental Psychology, Oxford, United Kingdom

Objectives and study: Docosahexaenoic acid (DHA), choline and uridine-5-monophosphate (UMP) are important brain nutrients which form phosphatidylcholine, the most abundant membrane phospholipid in the brain and retina. Brain accrual of DHA is most rapid during the first 2 years of life, mirroring the period of maximal brain growth and connectivity. Western diets are lacking in DHA. Certain groups of infants are at particular risk of DHA insufficiency. For example, infants born preterm do not receive the normal third trimester transplacental transfer of DHA. DHA, choline and UMP supplementation increases rodent brain phospholipids, synaptic components, functional brain connectivity and cognitive performance. Clinical trials of infant DHA supplementation alone have shown inconclusive effects on cognition and visual performance. This novel pilot study is the first to supplement infants at risk of neurological impairment (ARNI) with a nutrient combination containing these neurotrophic compounds. The objective of the study was to investigate if intake of this specific nutrient combination improves neurodevelopmental outcome in infants ARNI.

Methods: Recruitment to this double blind randomised control trial (RCT) was from three UK neonatal units. Eligibility: ≤31 weeks, weight <9th percentile; <31 weeks with ≥ Grade II intraventricular haemorrhage (IVH) or preterm white matter injury (PWMI); 31-40 weeks with ≥ Grade II IVH or PWMI, ≥ Sarnat Grade II hypoxic ischaemic encephalopathy or defined brain MRI abnormalities. Stratification was by gender, gestation and brain injury severity. Randomised infants received daily neurotrophic supplementation or placebo, for 2 years. Primary outcome was Bayley Scales of Infant Development III (BSID III) composite cognitive score (CCS) after 2 years. Secondary outcomes included BSID III composite language score (CLS) and BSID III composite motor score (CMS). Ethical approval was granted by Oxfordshire Research Ethics Committee. Trial data was analysed using intention to treat and per protocol analyses.

Results: 62 neonates were recruited. Using an intention to treat analysis mean CCS at 2 years was 87.7 (SD 20.4) in the intervention group and 81.6 (SD 18.5) in the placebo group (χ²(1)=2.28, p=0.13; -0.2, 18.2). Mean CLS in the intervention group was 91.5 (SD 20.1) and 83.2 (SD 19.6) in the placebo group (χ²(1)=2.74, p=0.1; -2.4, 18.3). CMS was similar in both groups. Per protocol, mean CCS in the intervention group was 88.0 (SD 20.1) and 80.8 (SD 18.7) in the placebo group (χ²(1)=3.16, p=0.08).

Conclusion: The difference in CCS and CLS between intervention and placebo groups represents a clinically significant effect size. When analysed per protocol, the difference in mean CCS score between intervention and placebo groups approached statistical significance (p=0.08). Use of neurotrophic micronutrient supplementation in infants ARNI warrants exploration in a large multicentre RCT.

Disclosure of interest: The dietary intervention product was produced by Nutricia, Netherlands. Nutricia had no part in the design of the study or in data analysis. Professor Peter Sullivan is a member of the Nutricia Scientific Advisory Board.
**NUTRITION: Clinical nutrition**

N-O-016

**6th annual Paediatric Nutrition Week: e-Pinut 2015**

Arnaud De Luca¹, Marion Dumont², Michel Fischbach³, Dominique Guimber⁴, Noel Peretti⁵, Hugues Piloquet⁶, Regis Hankard⁷

¹Inserm U1069, Tours, France  
²Chu, Tours, France  
³Chu, Strasbourg, France  
⁴Chu, Lille, France  
⁵Hcl Inserm, Université Claude Bernard Lyon 1, Faculté de Médecine Lyon-Est, Inserm U1060, Carmen Laboratory, Lyon, France  
⁶Chu, Nantes, France  
⁷Inserm U1069, University of Tours, Tours, France

**Objectives and study:** The tracking of protein-energy malnutrition (PEM) is still an issue in Paediatrics. Infants below one year, having rapid growth, are particularly affected. We conduct annual surveys with systematic nutritional assessment in hospitalised children. The aims of this 6th edition were to assess the characteristics of PEM in infants and to appreciate the evolution of PEM.

**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. 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. Hospitalisation diagnoses (reason of hospitalisation and chronic disease if any) and nutritional support were recorded. Data were recorded using e-Pinut web-based tool (www.epinut.fr). Results are expressed as mean ± SD and infants below 1-year old were compared to older population using Khi² test.

**Results:** Eight countries were involved, including 72 centres (138 wards). Among the 2324 collected observations, 2215 were analysed (54% boys, mean age: 4.8±5.1 years). A weight-for-height z-score <−2SD (compatible with PEM) was present in 11% of cases: Gabon (G) 23%, Ivory Coast (IC) 19%, Colombia (C) 17%, Belgium (B) 15%, France (F) 10%, Democratic Republic of the Congo (DRC) 7%, Algeria (A) 6%, and Tunisia (T) 0%. Height-for-age z-score <−2SD was found in 14% of the whole population: IC 38%, DRC 29%, G 14%, A 14%, F 13%, C 11%, B 10%, and T 5%. In the whole population, 2071 diagnoses were recorded. PEM was more frequent in cardiosurgical (30%), cardiological (16%) and gastroenterological (14%) diseases. In infants below 1-year old (654 patients, 30%), the top 3 was nephrological (20%), all-surgical (16%), and cardiological (15%) diseases. PEM frequency was not different before or after 1-year old (11.9% vs. 9.9%, P=0.16). Enteral or parenteral nutritional supports were more frequent in infants (13.7% vs. 8.8%, P<0.001) but not nutritional care (28.2% vs. 24.8%, NS). Only 50% of malnourished children had a nutritional care.

**Conclusion:** PEM remains frequent in Paediatrics and is insufficiently treated. Infants below 1-year old had a nutritional status similar to older children but require more enteral or parenteral nutritional supports. This suggests that infants could be more severely malnourished, but associated with more invasive care. Diseases leading to PEM are quite different in this population than in older children. Small samples apart from France and imbalance between countries prevent from reliable comparisons. Since 6 years, the number of participating centres and countries is still important, showing a lasting mobilisation around awareness in nutritional assessment in hospitals.

**Disclosure of interest:** A. de Luca: Research support from Nutricia, Advanced Medical Nutrition-France.
Impact of pasteurization of human milk on its gastric digestion: an in vivo study in the preterm infant

Samira De Oliveira¹, Claire Bourlieu², Olivia Ménard¹, Yann Le Gouar¹, Amandine Bellanger³, Emelyne Dirson⁴, Florence Rousseau¹, Célia Moustiés¹, Candice Perrier¹, Patrick. Pladys⁴, Didier Dupont¹, Amélie Deglaire¹

¹Inra - Agrocampus Ouest, Umr1253 Science et Technologie du Lait et de L’œuf, Rennes, France
²Umr Stlo 1253 Inra-Agrocampus Ouest, Bioactivity and Nutrition, Rennes, France
³Chu Rennes, Service de Pédiatrie, Rennes, France
⁴Chu Rennes, Lactarium, Unité Nutrition et Diététique Infantile, Rennes, France

Objectives and study: Human milk is the ideal food for neonatal nutrition and optimal growth. When the mother’s own milk is unavailable or limited, pasteurized human milk from milk banks is preferentially administered instead of infant formula, especially for preterm hospitalized neonates. Holder pasteurization (62.5 °C, 30 min) is applied for sanitary reasons but alters human milk components such as enzymes and immunoglobulins. In vitro studies have also shown that pasteurization of human milk impacts its hydrolysis and disintegration in term newborns (De Oliveira et al., 2016). Our study aimed at investigating the impact of pasteurization of human milk on its gastric digestion in preterm infants.

Methods: In vivo study was conducted at Rennes Hospital on preterm infants (n=12) fed by a feeding nasogastric tube each three hours (NCT02112331). Over a six-day sequence, gastric aspirates were collected twice a day, before and after administration of raw or pasteurized human milk. Samples were collected at 35, 60 or 90 min after meal ingestion. Gastric volume and pH were measured. Structural changes of the digesta were evaluated by confocal microscopy and laser light scattering. In digesta, residual intact proteins left were followed by gel electrophoresis (SDS-PAGE) submitted to densitometry, and lipolysis degree was evaluated by gas and thin layer chromatography fitted to flame ionization detector.

Results: On average (±SD), infants were 27.5 ± 12.3 days old at the first day of the study. Birth weight was 1.4 ± 0.3 kg and gestational age 29.6 ± 1.0 weeks. Digestive kinetics presented high inter and intra-individual variabilities. Regarding proteins, results showed a rapid disappearance of intact caseins and lactoferrin, but a resistance of alpha-lactalbumin. The contribution of meal gastric emptying or hydrolysis in protein disappearance depended on the protein. Some pre-lipolysis was determined in milk before digestion and it was in overall significantly lower in pasteurized than in raw milk, likely due to the heat-denaturation of endogenous lipases. During gastric digestion the kinetics of lipolysis were not affected by pasteurization (p > 0.05). The lipolysis degree ranged from 6 to 20% at 90 min. This relatively limited extent of gastric lipolysis was observed for both raw and pasteurized human milk, and was illustrated by the microscopic observations: some native milk fat globule structure (hydrophobic core enveloped by an amphiphilic membrane) persisted through the gastric digestion for both raw and pasteurized human milk. Regarding the structure, pasteurization led to heat-induced protein aggregates in the soluble phase and at the interface of the human milk fat globule membrane, and also impacted the protein aggregation and emulsion disintegration during gastric digestion.

Conclusion: This study represents a unique and important dataset on the behavior of pasteurized versus raw human milk. The gastric digestion is a key step which can further modulate nutrient absorption and infant nutrition. Digestive hydrolysis may also impact on gut microbiota, a major contributor to the development of the intestinal and systemic immune systems in the neonatal period. Physiologic and metabolic consequences remain to be investigated.

Disclosure of interest: None declared.
NUTRITION: Nutrition and health outcomes

N-O-018

Human milk short chain fatty acid composition is associated with infancy adiposity outcomes

Philippa Prentice¹, Jacques Vervoort², Kelly Dingess³, Kasper A. Hettinga⁴, Marieke H. Schoemaker³, Tim T. Lambers³, Eric A.F. Van Tol³, Carlo A. Acerini¹, Ken K. Ong⁵, David B. Dunger¹

¹University of Cambridge, Department of Paediatrics, Cambridge, United Kingdom
²Wageningen University, Laboratory of Biochemistry, Wageningen, Netherlands
³Mead Johnson Pediatric Nutrition Institute, Global Discovery, Nijmegen, Netherlands
⁴Wageningen University, Dairy Science and Technology, Wageningen, Netherlands
⁵University of Cambridge, Mrc Epidemiology Unit, Cambridge, United Kingdom

Objectives and study: Presumed benefits of human breast milk (HM) in avoiding rapid infancy weight gain and later obesity could relate to its nutrient composition. However data on breast milk composition and its relationship with growth are sparse. We investigated whether short chain fatty acids (SCFA), known to be present in HM and linked to energy metabolism, are associated with infancy anthropometrics.

Methods: In a prospective birth cohort, 641 HM hindmilk samples, collected 4-8 weeks postnatally, were analyzed. Repeated infant anthropometry at 3, 12 and 24 months, using weight, length and skinfold thickness z-scores, was collected. HM SCFA measured by 1H-nuclear magnetic resonance spectroscopy (NMR) and Gas chromatography (GC-MS) were related to infant anthropometry data. Data were evaluated using multivariate analysis and Spearman correlations.

Results: NMR peaks for HM butyrate, acetate, formic acid, but not propionate, could be detected. SCFA levels were unrelated to infant sex, maternal BMI, mode of delivery, gestational age and birth weight. However, butyrate peaks were higher in HM from exclusively breast-feeding mothers than mixed-feeding mothers (p=0.003).

HM butyrate was inversely related to 12-month skinfolds (rₛ=-1.0,p=0.02), 12-month BMI (rₛ=-0.09,p=0.04), 3-12 month skinfolds gain (rₛ=-0.1,p=0.002) and 3-12 month weight gain (rₛ=-1.1, 1,p=0.01). No relationships were found with 3-month or 24-month anthropometry, or height gains. Additional GC-MS analysis further confirmed butyrate associations.

HM acetate and formic acid showed less pronounced associations with adiposity. HM formic acid was inversely related to 3-month BMI (rₛ=-0.1, p=0.008) and HM acetate with 3-month skinfolds (rₛ=-0.1, p=0.002). Acetate and formic acid were unrelated to 12-month adiposity or height outcomes.

Conclusion: Human milk SCFA, specifically butyrate, may play a beneficial role in infancy weight gain and adiposity. Further knowledge of human milk and exploration of HM SCFA origin may be critical to future strategies to support healthy growth and may reduce the risk for developing overweight and obesity.

Effect of early protein supply on body fat deposition during infancy and childhood: a randomized trial

Martina Weber\textsuperscript{1}, Veronica Luque\textsuperscript{2}, Joaquin Escribano\textsuperscript{2}, Ricardo Closa\textsuperscript{2}, Elvira Verduci\textsuperscript{3}, Alice ReDionigi\textsuperscript{4}, Joana Hoyos\textsuperscript{5}, Jean-Paul Langhendries\textsuperscript{6}, Dariusz Gruszfeld\textsuperscript{7}, Piotr Socha\textsuperscript{8}, Berthold Koletzko\textsuperscript{9}, Veit Grote\textsuperscript{10}

\textsuperscript{1}LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
\textsuperscript{2}Universitat Rovira I Virgili, Iispv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
\textsuperscript{3}San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
\textsuperscript{4}San Paolo Hospital, University of Milan, Milan, Italy
\textsuperscript{5}University Children's Hospital Queen Fabiola, Ulb, Brussels, Belgium
\textsuperscript{6}Service de Néonatologie, Département Pédiatrique, Liege- Rocourt, Belgium
\textsuperscript{7}Children’s Memorial Health Institute, Warsaw, Poland
\textsuperscript{8}The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Feeding Disorders and Pediatrics, Warsaw, Poland
\textsuperscript{9}Dr. von Hauner Children’s Hospital, University of Munich Medical Center, DIV. Metabolic and Nutritional Medicine, Munich, Germany
\textsuperscript{10}Von Haunersches Kinderspital, University of Munich Medical Centre, Munich, Germany

Objectives and study: Obesity rates in children and adults are rising worldwide. Opportunities for early prevention as well as methods to identify children at risk are of interest. As a key driver of metabolic programming infant nutrition plays a crucial role in early tissue deposition and might induce long lasting effects on body composition.

The Childhood Obesity Project (CHOP) is a multicentre double-blind randomized clinical trial with an intervention during the first year of life and a reference group of breastfed infants. We examined the impact of different infant feedings on body composition from three months to six years of age. Additionally we assessed overweight and obesity based on cut offs for BMI and fat mass index (FMI; fat mass (kg)/ height\textsuperscript{2} (m\textsuperscript{2})) since the commonly used BMI cut-offs were criticized to underestimate the real overweight /obesity prevalence in children.

Methods: Healthy formula fed (N=1090) and predominantly breastfed (N=588) infants were enrolled up to the age of two months (mean age 2 weeks). Formula fed infants were randomized to isoenergetic formulae with higher (HP) or lower protein (LP) provided for the first year of life. We evaluated body composition from measures taken at the ages of one year (n=1063), two (921) and six years (650). Body composition was calculated with the Slaughter’s equation\textsuperscript{1} based on skinfold thickness. We defined overweight and obesity at six years by the IOTF BMI cut offs\textsuperscript{2} and classified children as “over fat” and “obese fat” when FMI was above the 90.8th and 97.7th gender specific percentile at six years, respectively.

Results: Percentage body fat was not different in HP and LP at one year but higher in HP by 0.5 percentage points at two and at six years (95% confidence interval 0.1-0.8, P=0.008; 0.1-1.0, P<0.001). Fat Mass Index (FMI) at 6 years was 0.17 kg/m\textsuperscript{2} higher in HP than LP (0.06-0.27, P=0.002). Percentile based classification of over fat/ obese fat children was not comparable to the commonly used IOTF BMI cut-offs. Prevalence of overweight / obesity and over fat / obese fat at 6 years (Table) was highest in HP and similar in LP to previously breastfed (BF) children.
Table:

<table>
<thead>
<tr>
<th>Feeding group</th>
<th>Overweight</th>
<th>Over fat</th>
<th>Obese</th>
<th>Obese fat</th>
</tr>
</thead>
<tbody>
<tr>
<td>LP (N=221)</td>
<td>31 (14%)</td>
<td>5 (2%)</td>
<td>10 (5%)</td>
<td>3 (1%)</td>
</tr>
<tr>
<td>HP (N=218)</td>
<td>41 (18%)</td>
<td>14 (6%)</td>
<td>21 (10%)</td>
<td>6 (3%)</td>
</tr>
<tr>
<td>BF (N=208)</td>
<td>31 (15%)</td>
<td>6 (3%)</td>
<td>6 (3%)</td>
<td>2 (1%)</td>
</tr>
</tbody>
</table>

Conclusion: Higher formula protein intake in infancy induces increased body fat deposition up to school age. The active promotion of breastfeeding and improved formula composition are effective strategies to reduce later obesity risk.

Disclosure of interest: None Declared. Financially supported in part by the European Commission.

References


Aberrant adipose tissue partitioning with abdominal obesity, defined by MRI, is a hallmark of paediatric Crohn’s Disease

Dhamyanthi Thangarajah1, Karyn E. Chapell1, Sundhiya Mandalia1, Gary Frost2, John M.E Fell3

1Imperial College, Section of Academic Neonatal Medicine, London, United Kingdom
2Imperial College, Nutrition and Dietetic Research Group, Faculty of Medicine, London, United Kingdom
3Chelsea and Westminster Hospital NHS Foundation Trust, Department of Paediatric Gastroenterology, London, United Kingdom

Objectives and study: Paediatric Crohn’s disease (CD) is associated with alterations in body composition; deficits in fat free mass are well described [1], adipose tissue measures are less well defined. Visceral adipose tissue (VAT) is the adipose compartment most strongly associated with chronic inflammation and furthermore intestinal adipose tissue expansion described as ‘creeping fat’ is well recognised from surgical specimens as a hallmark of CD. The aim of this study was to measure body composition in paediatric CD, specifically to quantify VAT using magnetic resonance imaging (MRI).

Methods: Children (7-18 years) with CD and healthy children to act as controls, were recruited. Volumes (expressed in litres) of the following abdominal compartments; VAT, subcutaneous adipose tissue (SCA) and muscle were quantified from MRI at two time points, 10 weeks apart for all subjects. Intrahepatocellular lipid (IHCL), expressed as CH2 water, was determined using Magnetic Resonance Spectrometry. Analysis: Univariate and linear regression analysis was used to identify factors associated with the dependent variable (compartment volume). All variables found to be significantly associated with the dependent variable (p<0.2) were used to derive a multivariable linear regression model (significance p<0.05).

Results: 33 children were recruited (25 CD (16 males), and 8 controls (5 males)), mean age 14.0±2.3 years and 13.4±2.5years; median BMI z-scores -0.74 [-1.65 to 0.03] and 0.11 [-0.65 to 0.41] respectively, (non-significant differences). No participant with CD was receiving concurrent systemic steroids, or had a history of steroid dependent disease. For all compartment volumes, no significant differences were observed in any of the participants between the volumes at 10 weeks and at baseline. CD was significantly associated with more VAT and SCA when compared to healthy children; after adjusting for sex, weight-z score, height-z score, and pubertal status. CD had 0.39 l [0.16 to 0.63] more VAT than controls, (p<0.001) and had 1.82 l [1.36 to 2.45] more SCA than controls (p<0.001). Abdominal muscle volumes were lower in CD when compared with controls, but not statistically significant. There was no significant difference in IHCL between CD and controls.

Conclusion: For the first time in Paediatric CD we show an association with abdominal adipose tissue obesity (VAT and SCA) and a trend toward muscle deficit in the context of normal hepatic lipid and BMI measures. The drivers of this obesity phenotype in children with CD is unknown and may be the result of systemic chronic inflammation. VAT expansion could be driven by local intestinal inflammation, the more pronounced SCA expansion that we have identified implies mechanisms involving systemic mediators.


Disclosure of interest: J.M.E Fell conflict with: served as consultant to Jansen. No other conflict of interests declared.
Placental MFSD2a transporter is related to decreased DHA in cord blood of women with gestational diabetes

María Teresa Prieto-Sánchez¹, María Ruiz-Palacios², Jose Eliseo Blanco-Carnero¹, Ana Pagan², Christian Hellmuth³, Olaf Uhl³, Wolfgang Peissner³, Antonio Ruiz-Alcaraz⁴, Hans Demmelmaier³, Juan Jose Parrilla¹, Berthold Koletzko³, Elvira Larque²

¹University of Murcia, Obstetrics and Gynecology Service, Virgen de la Arrixaca Clinical Hospital, Murcia, Spain  
²University of Murcia, Department of Physiology, Murcia, Spain  
³Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany  
⁴University of Murcia, Department of Biochemistry, Molecular Biology B and Immunology, Murcia, Spain

Objectives and study: Maternal-fetal transfer of docosahexaenoic acid (DHA) is impaired by gestational diabetes mellitus (GDM), but the underlying mechanisms are still unknown. MFSD2a was recently recognized as a lyso-phospholipid (lyso-PL) transporter that facilitates DHA accretion in brain. The role of this transporter in placenta is uncertain. We evaluated effects of GDM and its treatment (diet or insulin) on phospholipid species, fatty acid profile in women, cord blood and placental fatty acid carriers.

Methods: Prospective observational study of pregnant women recruited in the third trimester (25 controls, 23 GDM-diet, 20 GDM-insulin). Fetal ultrasound was performed at gestational week 38. At delivery, maternal and neonatal anthropometry was performed, and fatty acids in total lipids and phospholipid species were analyzed in placenta, maternal and venous cord blood. Western-blot analyses were performed for placental fatty acid carriers.

Results: Fetal abdominal circumference z-score at 38 weeks tended to higher values in GDM (P=0.071), pointing toward higher fetal fat accretion in these babies. DHA percentages were reduced in cord serum total lipids (P=0.029) and lyso-PL (P=0.169) in GDM. Placental MFSD2a was reduced in both GDM groups and was positively correlated to DHA values in cord serum total lipids (r= 0.388, P= 0.003). Among established placental lipid carriers, only FATP4 was correlated to DHA concentration in placental lyso-PL. In all compartments, DHA percentage was inversely correlated to fetal abdominal circumference.

Conclusion: In offspring of women with GDM, higher fetal fat accretion and lower placental MFSD2a contribute to reduce DHA availability. Lyso-PL appear to contribute to materno-fetal DHA transport.

Disclosure of interest: There are no conflicts of interest, financial or otherwise, declared by any of the authors. Financially supported in part by Hero S.L. and the European Commission.
Effect of prebiotic inulin-type fructans on health parameters and intestinal microbiota composition in children aged 3 to 6 years: a randomized, double-blind, placebo-controlled explorative study

Szimonetta Lohner¹, Nóra Szili¹, Viktória Jakobik¹, Dorottya Soltész¹, Sara Soldi², Sotirios Vasileiadis², Stephan Theis³, Carolin Sieland³, Günther Boehm⁴, Tamás Decsi¹

¹University of Pécs, Department of Paediatrics, Pécs, Hungary
²Advanced Analytical Technologies Srl, Fiorenzuola D’arda, Italy
³Beneo-Institute, Obrigheim, Germany
⁴Nutritional Science Consulting, Leipzig, Germany

Objectives and study: We aimed to explore whether prophylactic dietary supplementation with prebiotic inulin-type fructans was able to stabilize intestinal microbiota and influence the frequency of infectious disease episodes during a winter period in kindergarten children and whether regular consumption of prebiotics was able to stabilize faecal flora during antibiotic administration.

Methods: Children aged 3 to 6 years were randomly allocated to consume either inulin-type fructans (Orafti®) or maltodextrin in a dose of 6.0 g/day for 24 weeks.

Infectious disease episodes and duration, prescribed antibiotics or other medications were recorded by physicians and parents. Absence from kindergarten was recorded via diaries by the parents.

Faecal samples were collected for bacteriological (quantitative PCR and next generation sequencing) analyses at the beginning (SD1) and the end (SD5) of the study; and on the 1st, 7th and 14th day of each antibiotic treatment. Stool consistency was evaluated on a Bristol Stool Chart. Dietary habits of participating children were assessed by 3-days food intake protocols.

Results: From the 270 children randomized, 110 children in the prebiotic and 109 in the control group finalized the study.

Bifidobacteria counts were significantly higher in children receiving the prebiotic than in controls at SD5 and during antibiotic treatment. Lactobacilli counts decreased from SD1 to SD5 within the placebo group, but remained stable in the prebiotic group. Parents reported significantly softer stools within the normal range in the prebiotic group already after 12 weeks of supplementation.

The number of febrile episodes requiring physician’s consultation (number of infections/child/24 weeks: 0.65 (1.09) vs. 0.90 (1.11); mean (SD)) and that of sinusitis (0.01 (0.1) vs. 0.06 (0.25)) were significantly lower in the prebiotic as compared to the placebo group. There was no significant difference between the prebiotic and the placebo groups in the number of infectious episodes reported by the parents, in the total number of infection days, febrile days, or total days of antibiotic treatment, absence from day-care and the days spent in hospital due to an infectious disease.

Conclusion: Prebiotic supplementation significantly modified the composition of the intestinal flora and resulted in softer stool consistency in children aged 3 to 6 years. The significant reduction in febrile episodes requiring physician’s consultation supports the concept of further studies with prebiotic supplementation in young children.

Disclosure of interest: S. Theis and C. Sieland are employees of the Suedzucker/ BENE Group. S. Lohner, N. Szili, V. Jakobik, D. Soltész, S. Soldi, S. Vasileiadis, G. Boehm and T. Decsi declare: The study was financially supported by the BENE Group, Germany.
Infant feeding is associated with growth trajectory patterns in childhood and body composition in adulthood

Wendy Oddy¹, Peter Rzehak², Luisa Mearin³, Merete Eggesbo⁴, Veit Grote⁵, Trevor Mori⁶, Martina Weber⁷, Lawrence J. Beilin⁸, Rae-Chi Huang⁹, Berthold Koletzko⁹, Hania Szajewska¹⁰, Raanan Shamir¹¹, Sibylle Koletzko¹²

¹Menzies Institute for Medical Research, University of Tasmania, Hobart, Australia
²DIV. Metabolic and Nutritional Medicine Dr. von Hauner Children’s Hospital, University of Munich Medical Centre, Munich, Germany
³Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
⁴Norwegian Institute of Public Health, Department of Genes and Environment, Oslo, Norway
⁵Von Haunersches Kinderspital, University of Munich Medical Centre, Munich, Germany
⁶The University of Western Australia, School of Medicine and Pharmacology, Perth, Australia
⁷LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
⁸The University of Western Australia, Telethon Kids Institute, Perth, Australia
⁹Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
¹⁰University of Warsaw, Pediatrics, Warsaw, Poland
¹¹Schneider 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
¹²Ludwig Maximilian’s University Munich Medical Center, Dr. von Hauner Children’s Hospital, Munich, Germany

Objectives and study: Evidence demonstrates that early infant feeding is associated with programming of growth in childhood and into adult life. However, effects on growth pattern and later body composition are still not fully investigated. Our objectives were to 1) identify growth patterns in children and 2) investigate early nutritional programming effects on these patterns up to six years and body composition at 20 years.

Methods: The West Australian Pregnancy Cohort (RAINE) Study and three European cohort studies (CHildhood Obesity Prevention Trial, HUMIS (Norwegian Human Milk Study), Prevent CD (Coeliac Disease) that collaborate in the European Union funded Early Nutrition project with data on infant feeding (predominant or full breastfeeding), anthropometry and body composition were harmonized and pooled. Latent growth mixture modelling was applied to identify growth patterns among the 6708 individual BMI-SDS trajectories. Combined with logistic regression, the impact of breastfeeding for <3 months compared to ≥ 3 months on growth patterns was assessed. Differences in body composition at six and 20 years among the growth patterns were tested by ANOVA.

Results: Identified growth patterns comprising BMI-trajectories were: Class 1 5%; Persistent, accelerating rapid growth Class 2 40%; Early, non-persistent rapid growth and Class 3 55%; Normative growth. A shorter duration of breastfeeding for <3 months, compared to ≥ 3 months was significantly associated with being in growth classes 1 and 2 (OR=2.75 and 1.97) following adjustment for maternal and infant factors. These adverse growth patterns continued to show differences in body composition between the growth pattern classes at both six and 20 years of age.

Conclusion: A shorter duration of breastfeeding of <3 months compared to ≥ 3 months, increases the risk of childhood obesity and has long-lasting effects on body composition into adulthood. Growth patterns in childhood may be the mediating link between infant feeding type and long-term obesity risk.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 673
The effect of different protein concentration in infant formula on growth, body composition, and later risk of obesity: a systematic review

Bernadeta Patro-Golab1, Bartłomiej Zalewski1, Stefanie MP Kouwenhoven2, Jacek Karaś1, Berthold Koletzko3, Johannes Bernard van Goudoever4, Hania Szajewska1

1Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
2VU University Medical Center Amsterdam, Department of Pediatrics, Amsterdam, Netherlands
3Ludwig-Maximilians-Universität, Dr. von Hauner Children’s Hospital, University of Munich Medical Centre, Division of Metabolic and Nutritional Medicine, Munich, Germany
4VU University Medical Center Amsterdam, Emma Children’s Hospital, Amsterdam Medical Center, Department of Paediatrics, Amsterdam, Netherlands

Objectives and study: Infant feeding, especially protein intake, may potentially influence important health outcomes in later life. We aimed to investigate current evidence on the effects of infant formula and follow-on formula with different protein concentrations on infants’ and children’s growth, body composition, and later risk of overweight, obesity, and metabolic syndrome.

Methods: In this systematic review, we searched several electronic databases (including MEDLINE, EMBASE, the Cochrane Library) and additional sources of data up until November 2014 for randomized controlled trials (RCTs).

Results: Twelve trials that recruited healthy term infants met our inclusion criteria. The vast majority of the identified studies evaluated only short-term outcomes related to growth of infants. During the first year of life, different protein concentration of infant formulas does not seem to affect linear growth significantly, apart from a transient effect in the first months of life. Lower mean weight (and weight z-scores) obtained in the infants fed a lower-protein formula were observed only from 6 to 12 months of age. Data from one, large RCT showed that lower-protein concentration of formula in infants may reduce body mass index (BMI) (from 12 months of age) and the risk of obesity in children at school age (6 years). No conclusions with regard to the effects of lower-protein formula intake on body composition can be formulated.

Conclusion: The evidence is insufficient to firmly assess the effects of reducing the protein concentration in infant formula on long-term outcomes, but this appears as promising intervention for reducing the risk of overweight and obesity in children. In view of the limited available evidence more studies replicating effects on long-term health outcomes are needed.

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].

Disclosure of interest: JB van Goudoever holds patents with regard to a specific blend of essential amino acids in order to develop a new infant formula. Dr JB van Goudoever is sponsor of a study designed to look at the effects of a low-protein formula on weight gain and body composition, which is funded by the EU. B Koletzko is a member of the National Breastfeeding Committee and tends to be biased towards breastfeeding. The Ludwig-Maximilians-University of Munich, Germany and it's employee BK have received support for scientific and educational activities by companies that market products for infants and children, including Abbott, Baxter, B. Braun, Dairy Goat Cooperative, Danone, Fresenius Kabi, Fonterra, Hipp, Mead Johnson, Nestlé, and Yakult, predominantly as part of publically funded research projects with support of the European Commission or German governmental research support. The study formula for the CHOP study was produced by Bledina, Steenvorde, France as part of a contract with the European Commission. H Szajewska has participated as a clinical investigator, and/or advisory board member, and/or speaker for Arla, Biogaia, Biocodex, Danone, Dicofarm, Hipp, Nestle, Nestle Nutrition Institute, Nutricia, Mead Johnson, Merck, Sequoia, and Yakult. B Patro-Golab and BM Zalewski have participated in a conference sponsored by Nestle. SM Kouwenhoven is PhD student of a study designed to look at the effects of a low-protein formula on weight gain and body composition. J Karaś, none declared.
NUTRITION: Nutrition and health outcomes

N-O-025

Longitudinal fat mass and visceral fat during the first 6 months after birth in healthy infants: support for a critical window for adiposity in early life

Laura Breij¹, Gerthe F. Kerkhof¹, Emanuella De Lucia Rolfe², Ken K. Ong², Marieke Abrahamse-Berkeveld³, Dennis Acton⁴, Anita C.S. Hokken-Koelega¹

¹Erasmus University Medical Center / Sophia Children’s Hospital, Pediatric Endocrinology, Rotterdam, Netherlands
²University of Cambridge, Mrc Epidemiology Unit, Cambridge, United Kingdom
³Nutricia Research, Utrecht, Netherlands
⁴Nutricia Research, Early Life Nutrition, Utrecht, Netherlands

Objectives and study: Body composition in early life influences the development of obesity during childhood and beyond. It is, therefore, important to adequately determine longitudinal body composition during the first months of life.

Methods: In 203 healthy term infants, we investigated longitudinal body composition, including fat mass percentage (FM%) and fat-free mass (FFM), by air-displacement plethysmography, at 1, 3 and 6 months of age, and abdominal visceral fat and abdominal subcutaneous fat, by ultrasound, at 3 and 6 months.

Results: We found a significant increase in FM% between 1 and 3 months, but not between 3 and 6 months (p<0.001, p=0.098, resp.). Girls had higher FM% than boys at 1 and 6 months (p=0.05, p<0.001 resp.) and less FFM than boys at 1, 3 and 6 months (p=0.02, p=0.02, p<0.001 resp.). There was a large variation in FM% at all ages, even between infants with similar weight SDS. Visceral fat and abdominal subcutaneous fat did not change between 3 and 6 months. FM% was highly correlated with abdominal subcutaneous fat, but not with visceral fat.

Conclusion: Changes in FM% occur mainly in the first 3 months of life, and FM%, visceral and abdominal subcutaneous fat do not change between 3 and 6 months, supporting the concept of a critical window for adiposity development in the first three months of life. In addition, our study provides longitudinal reference data of FM%, FFM, visceral fat and abdominal subcutaneous fat during the first 6 months of life.

Disclosure of interest: “AHK received an independent research grant from Nutricia Research”. 
NUTRITION: Nutrition and health outcomes

N-O-026

Serum lipid profile in infants fed formula supplemented with a bovine milk fat globule membrane fraction

Tove Grip1, Thomas F Dyrlund2, Linda Ahonen2, Magnus Domellöf3, Olle Hernell4, Tuulia Hyotylainen4, Mikael Knip5, Bo Lonnerdal6, Matej Oresic2, Niklas Timby1

1Umeå University, Clinical Sciences/Pediatrics, Umeå, Sweden
2Steno Diabetes Center A/S, Gentofte, Denmark
3Umeå University, Department of Clinical Sciences, Pediatrics, Umeå, Sweden
4Steno Diabetes Center, Gentofte, Denmark
5University of Helsinki, Helsinki, Finland
6University of California, Nutrition, Davis, United States

Objectives and study: We recently showed that term infants fed an experimental formula (EF) with reduced protein concentration and energy density, and supplemented with a bovine milk fat globule membrane (MFGM) concentrate performed better on cognitive testing at 12 months of age and had lower incidence of otitis media until 6 months of age compared to infants fed standard formula (SF). We hypothesized that the explanation would be that bioactive components, e.g. one or several of the lipid constituents of MFGM, also necessary for normal brain development, are present at lower concentration in SF than EF. The aim of the present study was therefore to evaluate the effects of the EF on the serum lipid profile.

Methods: In a prospective, double-blinded, controlled trial, 160 exclusively formula-fed infants were randomized to be fed EF or SF from <2 months to 6 months of age. 80 breastfed infants were recruited as a reference (BFR) group. Serum samples were collected at 4 and 12 months of age. Lipidomic analyses were performed on serum samples from a subgroup of 90 infants, 30 from each group (EF, SF and BFR). An ultra-high-performance liquid chromatography - mass spectrometry (UHPLC-MS)-based platform was applied to analyze molecular lipids. Total lipid extracts were obtained using a modified Folch extraction technique and the extracts were analyzed by UHPLC-MS in positive (ESI+) ion mode. MS data processing was performed using MZmine 2.17 software. Global lipid profile differences were analysed using orthogonal partial least squares discriminate analysis (OPLS-DA). Multivariate analyses and model plots were done using SIMCA (SIMCA-P+ 13.0, Umetrics, Umeå, Sweden). Differences in concentrations of specific metabolites were analysed using 2-sided t-test (SPSS statistics 22) and reported as unadjusted p-values.

Results: At 4 months of age, we observed a separation in the global serum lipid profile in the OPLS-DA between the EF and SF groups. Further, there were differences in several specific lipids of interest. For example, serum concentrations of sphingomyelin 39:1 (p <0.001), sphingomyelin 38:1 (p <0.001) and phosphatidylcholine 36:2 (p <0.001) were higher in the EF than the SF group. Sphingomyelin 42:2 (p <0.001) was lower in EF compared to SF. At 12 months of age, there was no difference in the serum lipid profile between the EF and SF groups.

Conclusion: MFGM supplementation had marked effects on the serum lipidomic profile during the intervention. The differences in serum lipids had disappeared 6 months after the intervention. Sphingomyelin and choline are important constituents of the nervous system and exogenous administration have been associated with enhanced brain function. The differences in lipidomic profile between the EF and SF group may contribute to the mechanisms underlying the improved cognitive development in infants fed MFGM-supplemented formula.

Disclosure of interest: Olle Hernell and Bo Lönnerdal are members of Hero scientific advisory board. Semper/Hero has financed part of the study.
The ability of body mass index and serum leptin to predict body composition in 8 year old Spanish children

Veronica Luque1, Joaquin Escribano1, Natalia Ferre1, Michelle Venables2, Priya Singh2, Les Bluck2, Dariusz Gruszfeld3, Piotr Socha4, Veit Grote5, Berthold Koletzko6, Ricardo Closa1

1Universitat Rovira I Virgili, ISPV, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
2Human Nutrition Research Centre, Cambridge, United Kingdom
3The Children’s Memorial Health Institute, Department of Neonatology and Neonatal Intensive Care, Warsaw, Poland
4Children’s Memorial Health Institute, Warsaw, Poland
5Von Haunersches Kinderspital, University of Munich Medical Centre, Munich, Germany
6Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany

Objectives and study: Body mass index (BMI) is a fast, non-invasive, and low cost method to diagnose obesity. However, it does not differentiate between fat mass (FM) and lean body mass (LBM). The purpose of the present study was to assess the prediction ability of BMI and leptin for FM determined by deuterium dilution.

Methods: A cross-sectional observation study was performed in a sub-sample of the European Childhood Obesity Project (EU CHOP). Sixty 8 year old children (25 boys) had weight, height and serum leptin levels measured and body composition assessed with deuterium dilution. To quantify the ability of BMI and leptin to predict fat mass in children, linear regression analysis was performed. The project was designed in agreement with the Declaration of Helsinki and was accepted by local ethical committees. Parents received written information and signed informed consent to participate in the study.

Results: Full data is reported for 59 children (25 boys). Description of main outcome measures is shown in Table 1.

FM was highly correlated with BMI (r=0.844, p<0.001) and leptin (r=0.801, p<0.001). BMI explained 64.4% of FM (B=1.248 (1.037, 1.458), p<0.001) while leptin explained 69.7% of FM variation (B=0.863 (0.705, 1.020), p<0.001). A multivariate linear regression model including BMI and leptin, adding gender for effects adjustment, explained 91.0% of the FM variation.

By using the already mentioned multivariate linear regression model, the derived equation to predict FM was FM [kg] = -11.939 + (0.940 * BMI [Kg/m2]) + (0.266 * Leptin [ng/ml]) + (2.118 * gender), were gender is 1= male, 2 = female.

The analyses of the residuals of the predicted model showed a normal distribution with a mean=0. The predictive equation was internally validated with 200 bootstrap resamples and the resulting simulated model showed that coefficients were still highly significant (p=0.005) and the analysis of the residuals was similar to the predicted model (normal distribution with a mean= 0).
Table:

<table>
<thead>
<tr>
<th></th>
<th>All</th>
<th>Boys</th>
<th>Girls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>n=59</td>
<td>n=25</td>
<td>n=34</td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>Mean (SD)</td>
<td>p-value</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>27.929 (4.517)</td>
<td>27.573 (3.859)</td>
<td>28.190 (4.985)</td>
<td>0.608</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>128.0 (4.5)</td>
<td>127.6 (4.1)</td>
<td>128.3 (4.8)</td>
<td>0.524</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>16.98 (2.15)</td>
<td>16.93 (2.15)</td>
<td>17.02 (2.18)</td>
<td>0.879</td>
</tr>
<tr>
<td>BMI (z score)</td>
<td>0.55 (1.04)</td>
<td>0.55 (1.16)</td>
<td>0.55 (0.97)</td>
<td>0.980</td>
</tr>
<tr>
<td>Fat Mass (kg)</td>
<td>8.364 (3.181)</td>
<td>6.898 (2.741)</td>
<td>9.442 (3.082)</td>
<td>0.002</td>
</tr>
<tr>
<td>Fat Mass index (kg/m²)</td>
<td>5.064 (1.775)</td>
<td>4.23 (1.63)</td>
<td>5.68 (1.64)</td>
<td>0.001</td>
</tr>
<tr>
<td>Leptin (ng/ml)</td>
<td>2.37 (1.67, 4.28)</td>
<td>1.88 (1.47, 2.40)</td>
<td>2.98 (2.12, 5.95)</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

P-value for Student’s T-test or Mann Whitney U-test between genders; BMI: body mass index; IQR: percentiles 25th and 75th.

**Conclusion:** Fat-mass specific parameters such as serum leptin used in conjunction with BMI could be used to predict FM in children. The present study generated a valid predictive equation to assess fat mass in 8 year old children. Further studies are needed to determine age and population specific equations to predict FM.

**Disclosure of interest:** Authors disclose no conflicts of interest.
**NUTRITION: Neonatal and infant nutrition**

N-O-028

**Safe discharge of preterm infants at <34 weeks PCA, weight less than 1.8kg by aggressive paladai feeding in Indian NICU**

Deepa Hariharan¹, Lavanya Balasubramanian¹, Velmurugan Kannapan¹, Ganesh Veluswami¹
¹Sooriya Hospital, Neonatology, Chennai, India

**Objectives and study:** Early discharge of premature infants from the NICU is common in India, due to low incidence of insurance coverage for neonates. Paladai, a beaked Indian cup, that allows infants to take enteral feeds as early as 30 weeks gestation is used in many Indian NICUs. Infants can be trained to take paladai feeds by mouth even if they have brief in-coordinated bursts of suck and swallow. This study looks at factors influencing time to achieve oral feeds by paladai in infants less than 32 weeks gestation by implementing an early discharge protocol with aggressive nutritional planning.

**Methods:** From February to September 2015, an early discharge program was implemented for 34 infants with birth weight less than 1500g, gestation less than 32 weeks, and following factors analyzed. Care-giver related factors studied included time spent by mother in NICU and seniority of nurses giving care. Neonatal factors studied included gestation, duration of ventilation or CPAP and need for >2 anticonvulsants. Duration of kangaroo mother care and oral stimulation exercises were studied. Infants with bacteremia, intracranial bleeds and NEC were excluded. The time to achieve full paladai feeds - speed of 10ml/minute, with no distress or cyanosis - after initiation of oral feeds was documented. The duration to discharge after full enteral feeds and incidence of exclusive direct breastfeeds were studied. 34 matched historical controls were used.

**Results:** Mean gestation in study group was 29.3 weeks, and mean BW 1095g. Mean time to start paladai feeds was 14 days, and to achieve full paladai feeds was 19.6 days in the early discharge group, (18 days and 27.3 days in the historical controls) [p<0.02]. Discharge after reaching full feeds happened 4.5 days earlier in the early discharge group (p<0.05). Exclusive breastfeeding was higher in the early discharge group (31/34) compared to controls (24/34). Multivariate analysis showed that caregiver related factors were more important in achieving paladai feeds earlier: mothers spending more than 8 hours per day at bedside (OR 4.1, 95%CI 1.6-13.4, p=0.012), and nurses with >4 years experience feeding babies (OR 4.4, 95%CI 1.9-12.50, p=0.003) resulted in earlier time to paladai feeds. Neonatal factors did not affect time to full paladai feeds. Duration of kangaroo mother care, but not oral stimulation exercises positively influenced time to full paladai feeds. Average weight at discharge in study group was 1.26 kg (1.1 – 1.63kg), and average corrected gestation at discharge was 31.6 weeks (31.1 – 33.3 weeks). 32 infants of the study group were followed up at 3 months of age, and had weight above 10th percentile.

**Conclusion:** Stable preterm infants can be fed orally by paladai, as early as 30 weeks PCA. Early discharge, before 34 weeks PCA or weight of 1.8kg is feasible and safe. Caregiver related factors play a major role in infants acquiring feeding skills.

**Disclosure of interest:** none
Growth during early infancy and anthropometry at 4 years of age: follow-up of the BeMIM study

Manja Fleddermann¹, Hans Demmelmaier¹, Veit Grote¹, Branca Trisic², Tatjana Nikolic³, Berthold Koletzko¹

¹Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
²Hipp Study Center, Belgrade, Serbia
³Institute for Gynecology and Obstetrics, Clinical Centre of Belgrade, Belgrade, Serbia

Objectives and study: Nutrition and growth during early infancy influence the risk to develop obesity in later life. We tested whether the protein intake of different formulae or breastmilk during early infancy have an impact on anthropometry at 4 years of age.

Methods: The BeMIM (Belgrade Munich Infant Milk) study was conducted as a double-blind, randomized clinical trial that enrolled healthy term infants. Formula-fed infants (n=213) were randomly assigned to receive a standard formula (CF, 1.5g protein/100mL) or a formula with a lower protein content (IF, 1.3g protein/100mL) and a higher content of alpha-lactalbumin enriched whey until the age of 120 days. Breastfed infants (BF, n=185) were enrolled as a reference group. Anthropometry (weight, height, body fat content measured via sum of skinfolds (Slaughter equation) and bioelectrical impedance analysis) was assessed at 4 years of age.

Results: Concentration of IGF-I (number of infants in IF: 81, CF: 79, BF: 87) at 120 days were significantly higher in IF than in CF infants 58.5 (15.0) vs. 53.7 (9.95) ng/mL, Median (IQR), p=0.02. BF infants showed a lower IGF-I level of 41.6 (10.7) ng/mL.

A follow-up of anthropometry in 187 children (IF: 65, CF: 59, BF: 63), corresponding to about 72% of children who completed the intervention study at 120 days of age, was achieved. There were no differences in weight, height, body mass index or body fat content between the formula groups at 4 years and anthropometry was similar in formula- and breastfed infants. About 9.2, 3.4 and 11.1 percent of the children showed an age-adjusted BMI≥25 in the IF, CF, BF group, respectively (no significant differences). A higher BMI was significantly related with a higher body fat content (group independent Spearman rank correlation, R=0.62 for body fat measured via skinfolds and R=0.36 via bioelectrical impedance analysis). BMI at 4 months, IGF-I levels at 4 months and BMI of the father might have been predictors or contributing factors of the BMI at 4 years. A significantly higher gain in weight-for-age and length-for-age z-score from 1 to 4 months in the IF (0.50±0.62 and 0.36±0.73) compared to the CF (0.23±0.76 and 0.07±0.81) infants (Follow-up children only, Students t-test, p=0.03 for weight and p=0.04 for length) was followed by a significantly lower gain in these z-scores from 4 months to 4 years in the IF (0.3±0.84 and 0.40±0.92) compared to the CF group (CF:0.72±0.66 and 0.72±0.85, p=0.01 and p=0.05). The respective changes in BF infants were 0.05±0.69 and -0.15±0.76 from 1 to 4 months and 0.63±0.80 and 0.37±0.85 from 4 months to 4 years.

Conclusion: Although the infant formula with slightly lower protein content and higher content of alpha-lactalbumin enriched whey induced significant higher IGF-I levels at 120 days of age, it has no significant impact on anthropometry at 4 years of age or obesity risk.

Disclosure of interest: This study was financially funded in part by HiPP GmbH and Co Vertrieb KG, Pfaffenhofen, Germany.
A Synbiotic Mixture of scGOS/lcFOS and Bifidobacterium breve M-16V is Able to Restore the Delayed Colonization of Bifidobacterium Observed in C-section Delivered Infants

Chua Mei Chien¹, Goh Eng Neo Anne¹, Chiang Wen Chin¹, Rajeshwar Rao¹, Chew Charmaine², Christophe Lay², Ben Amor Kaouther³, Knol Jan³, Chaithongwongwatthana Surasith ⁴, Khemapech Nipon ⁴, Chongrisawat Voranus ⁴

¹Kk Women and Children Hospital, Singapore, Singapore
²Danone Nutricia Research, Singapore, Singapore
³Danone Nutricia Research, Utrecht, Netherlands
⁴King Chulalongkorn Memorial Hospital, Bangkok, Thailand

Objectives and study: Infants born by C-section miss the exposure to the maternal vaginal microbiota and this absence of microbial inoculation has been associated with a delayed colonization of commensal bacterial members such as Bifidobacterium. This compromised microbial inoculation may impact the health of the newborn and epidemiological data from cohort studies indicate associations between C-section and immune and metabolic disorders such as asthma and obesity. The objective of this study was to determine the effect of a specific mixture of short-chain galactooligosaccharides and long-chain fructooligosaccharides (scGOS/lcFOS, ratio 9:1) and the probiotic strain Bifidobacterium breve M-16V in restoring the delayed colonization of Bifidobacterium observed in term C-section delivered infants.

Methods: In a multi-country, double-blind, randomised controlled study, 153 infants born by elective C-section were randomised to receive (1) an infant formula supplemented with scGOS/lcFOS (0.8g/100ml) and B. breve M-16V (7.5x10⁸ CFU/100ml), or (2) a formula supplemented with scGOS/lcFOS (0.8g/100ml), or (3) a control formula from birth until age 4 months. As a reference group, 30 vaginally born, breast fed infants were studied in parallel. Stool samples were collected at day 3 and/or day 5, week 2, week 4, week 8, week 12, week 16, and week 22 (6 weeks post-intervention). The total Bifidobacterium gene count, several Bifidobacterium species and B. breve were determined with molecular tools, pH and SCFA were also measured in the stool samples.

Results: 129 randomized infants were included in the modified ITT data analysis with 45, 39 and 45 infants in the synbiotic, prebiotic and control group, respectively. All the study groups including the reference group were mixed-fed. The data confirmed the delayed colonization of Bifidobacterium in C-section delivered infants. The synbiotic supplementation resulted in a significant higher estimated mean of total bifidobacteria gene count from the first days of life (p<0.0001) and this bifidogenic effect remained significant until week 12 (p=0.032) compared to the control group. In the prebiotic group, the estimated mean of total Bifidobacterium gene count was comparable to the control group. In the synbiotic group, B. breve M-16V was still detected in 38.7% of the infants at week 22 indicating a persistence of the probiotic strain. A significant lower estimated mean faecal pH was observed in the synbiotic group from the first days of life (p<0.0001) and this remained significant until 1 month of age (p=0.001) compared to the control group. A significant higher estimated mean amount of acetate was observed in the synbiotic group at day 3/5 (p<0.0001) compared to the control group. A lower number of subjects with adverse events of eczema/atopic dermatitis was reported in the synbiotic group (n=3) compared to the control (n=10), and prebiotic group (n=9), after correction for family allergy history (p<0.05).

Conclusion: An infant formula supplemented with scGOS/lcFOS and B. breve M-16V is able to restore the delayed colonization of Bifidobacterium in C-section delivered infants from the first days of life. This phenomenon is associated with the creation of a favourable gut ecosystem milieu. These biological effects may have potential long term health benefit in C-section born infants.

Disclosure of interest:
“None Declared”. 

Vol. 62, Supplement 1, May 2016 681
NUTRITION: Nutrition and health outcomes

N-O-031

Maternal CD does not influence human milk macronutrients, lipids and hormones

Maria Grunewald1, Luisa Mearin2, Renata Auricchio3, Gemma Castillejo4, Isabel Polanco5, Carmen Ribes Koninckx6, Ilma Korponay-Szabo7, Sabine Vriezinga8, Katharina Werkstetter9, Berthold Koletzko9

1Dr. von Hauner Children’s Hospital, Ludwig-Maximilians-University, Munich, Germany
2Leiden University Medical Center, Dept. of Pediatrics, Leiden, Netherlands
3University “Federico II”, Dept. of Medical Translational Sciences and European Laboratory for the Investigation of Food-Induced Diseases, Naples, Italy
4Hospital Universitari Sant Joan de Reus, Urv, lipv, Dept. of Pediatric Gastroenterology Unit, Reus, Spain
5La Paz University Hospital, Dept. of Pediatric Gastroenterology and Nutrition, Madrid, Spain
6La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain
7Heim Pál Children’s Hospital, Celiac Disease Center, Budapest, Hungary
8Leiden University Medical Center, Pediatrics, Leiden, Netherlands
9Dr. von Hauner Children's Hospital, LMU Munich, Divison of Metabolic and Nutritional Medicine, Munich, Germany

Objectives and study: Human milk (HM) provides important nutrients for healthy growth and development of the newborn infant. Maternal nutrition and disease status are known factors which influence HM composition. We investigated within the PreventCD study if maternal celiac disease (CD) and adherence to gluten-free diet (GFD) affect concentrations of selected milk components.

Methods: We analyzed HM samples from mothers who were participants in the PreventCD study from 5 European countries. Concentrations were determined for HM macronutrients (protein, carbohydrates and fat), the peptide hormones insulin, adiponectin and IGF-II, fatty acids, carnitines, phosphatidylcholines and sphingomyelins from HM samples collected 0 – 3 months (early sampling) and 4 – 5 months (late sampling) postpartum. A multivariate regression model for the analyte concentrations and maternal CD was applied adjusted for day of milk sampling and study center. P-values were corrected with Bonferroni for the 128 measured milk components.

Results: HM samples were available from 378 mothers of whom 187 (49.5 %) were diagnosed with CD, of which 180 were adhering to a GFD. No significant differences between HM from mothers with or without CD in the concentrations of macronutrients, hormones, polar lipids, carnitines, and the majority of fatty acids were found, neither in early nor late samples. The only exception was palmitic acid (C16.0) which was significantly lower in HM from CD mothers from early sampling (22.37 weight% vs. 22.00 weight%, p = 0.001). This effect was also shown for women with or without GFD in the early samples (22.26 weight % vs. 22.05 weight%, p = 0.007), but in the later samples palmitic acid did not differ between both groups.

Conclusion: Human milk macronutrients, hormones and lipids are similar in mothers with and without CD and adhering to a GFD does not affect them, with exception of lower palmitic acid during the first three months of lactation. Carbohydrate intake stimulates the synthesis of palmitic acid. As gluten is a content of grain based foods, it seems possible that reduced palmitic synthesis and hence lower levels in milk occur through the different dietary patterns between a normal and a GFD. The difference in the concentration is low, as palmitic acid is ubiquitous and is also supplied by other food sources. Mothers who have CD and adhere to a GFD should be encouraged to breastfeeding their children as their milk presents no relevant differences in growth-related nutrients in comparison to the milk of mothers on a normal diet.

Disclosure of interest: The authors declare no conflicts of interest.
Associating nutritional risk with clinical outcomes in pediatric patients: an appraisal of different tools

Nara Elizabeth Lara Pompa¹, Jane Williams¹, Sarah Macdonald², Katherine Fawbert³, Kathy Kennedy¹, Jane Valente³, Vanessa Shaw³, Jonathan Wells¹, Susan Hill⁴, Mary Fewtrell¹

¹UCL Institute of Child Health, Childhood Nutrition Research Centre, London, United Kingdom
²Great Ormond Street Hospital for Children, NHS Foundation Trust, London, United Kingdom
³Great Ormond Street Hospital for Children, London, United Kingdom
⁴Great Ormond Street Hospital for Children, Paediatric Gastroenterology, London, United Kingdom

Objectives and study: The high prevalence of malnutrition in hospitalized children has lead to a widespread interest for routine screening on admission. However, malnutrition screening tools (MSTs) with validation studies in children are still scarce, particularly regarding their association to relevant clinical outcomes. The study aimed to determine the associations between 3 MSTs and clinical outcomes (length of stay-LOS; complications: infection, delayed wound healing, transfer to another hospital or unplanned use artificial nutrition; nutrition status on discharge-NS) in children admitted to a tertiary referral hospital, in comparison to baseline weight and body composition (BC) scores.

Methods: 152 children (mean age 10.7yr; 50% male; 51.3% surgical) admitted under any specialty with an expected stay >3d were enrolled in the study. 3 MSTs (Paediatric Yorkhill Malnutrition Score-PYMS; Screening Tool for the Assessment of Malnutrition in Paediatrics-STAMP; Screening Tool for Risk of Impaired Nutritional Status and Growth-STRONG) were implemented on admission. Weight (WT), height and BC measurements (lean (LM) and fat mass (FM) using dual Energy X-ray Absorptiometry) were obtained within 48 hours of admission and SD scores (SDS) calculated using UK BC reference data (Wells et al., 2012). Discharge WT, LOS and complications during stay were also recorded.

Results: Most patients were classified as moderate risk (MR) by STAMP and STRONG, and low risk (LR) by PYMS. As expected, a decreased appetite significantly increased the risk of being classified high risk (HR) by all MSTs (risk ratio (RR)=1.9, 1.7, 2.2 PYMS, STAMP and STRONG respectively), while dietary restrictions and artificial nutrition support were also predictors of HR using STRONG (RR=3.5, 2.7). Patients with mobility issues also had an increased risk using STAMP (RR=1.8). All MSTs showed a significant association with LOS, with a high proportion of HR patients staying longer than predicted and having an increased risk compared to MR and LR patients. Although HR patients had a tendency for higher complication rates, this was not significantly different for any of the MSTs. A decreased weight during hospitalization as marker for worsening NS was found in 43% of HR patients by PYMS, but was not significant for the other tools. In comparison, low WT or BC scores (<-2 SDS) on admission indicated a significantly increased risk for longer than predicted stays and, particularly in the case of low LM, increased complications and worsening NS.
Table:

<table>
<thead>
<tr>
<th></th>
<th>RR&lt;sup&gt;a&lt;/sup&gt;</th>
<th>RR&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Increased LOS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PYMS</td>
<td>2.5*</td>
<td>2.9*</td>
</tr>
<tr>
<td>STAMP</td>
<td>1.7*</td>
<td>2.5*</td>
</tr>
<tr>
<td>STRONG</td>
<td>2.3*</td>
<td>2.9*</td>
</tr>
<tr>
<td><strong>Complications</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PYMS</td>
<td>1.6</td>
<td>0.9</td>
</tr>
<tr>
<td>STAMP</td>
<td>1.4</td>
<td>1.7*</td>
</tr>
<tr>
<td>STRONG</td>
<td>1.1</td>
<td>1.9*</td>
</tr>
<tr>
<td><strong>Decreased weight during stay</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PYMS</td>
<td>2.0*</td>
<td>1.5</td>
</tr>
<tr>
<td>STAMP</td>
<td>1.1</td>
<td>1.6*</td>
</tr>
<tr>
<td>STRONG</td>
<td>1.1</td>
<td>1.4</td>
</tr>
</tbody>
</table>

<sup>a</sup> Risk ratio of HR patients compared to MR and LR.<br><sup>b</sup> Risk ratio of patients with <-2SDS compared to normal scores; * significant with p<.05

**Conclusion:** Children had a high risk of malnutrition on admission, with proportions varying according to the MST used. All MSTs had significant associations with LOS and, in the case of PYMS, for worsening NS during hospitalization. Baseline BC, particularly low LM, was better able to predict complications and worsening NS in addition to increased LOS. The different MSTs seem to show strengths and limitations, as compared to BC/WT measurements, that suggest further validation in different settings with specific clinical outcomes might be necessary.

**Disclosure of interest:** None Declared

Wells JC et al. AJCN. 2012, 96:1316-26
Despite lower serum 25-hydroxy vitamin D concentrations, bone density was higher in dark than fair skinned children

Pia Karlsland-Akeson¹, Kristina Åkesson², Torbjörn Lind³, Sven-Arne Silfverdal³, Olle Hernell³, Inger Öhlund³

¹Department of Pediatrics, Lund University, Malmö/Lund, Sweden
²Department of Orthopedics, Lund University, Malmö/Lund, Sweden
³Department of Pediatrics, Umeå University, Umeå, Sweden

Objectives and study To evaluate the impact on vitamin D status and bone density in early winter of a 3-month vitamin D intervention in Swedish children based on skin color.

Methods: In this prospective, double-blinded, randomized, food-based intervention study in southern (55°N) Sweden, 5-7-year old, fair and dark skinned children received daily vitamin D supplement; 25µg, 10µg or placebo (2µg) during 3 winter months. Bone mineral density (BMD) and bone mineral content (BMC) were measured at baseline and at one month after end of intervention. Vitamin D (S-25(OH) D), PTH and ALP were analyzed at baseline and after 3 months.

Results: Sixty-six children with fair and 57 with dark skin were included. At baseline S-25(OH) D was lower (41.6 vs. 59.4 nmol/L; p<0.001), P-PTH higher (p=0.014) and BMD higher (total body (TB) (p=0.031), total body less head (TBLH) (p=0.005), femoral neck (FN) (p=0.007)) in dark than fair skinned children. After intervention, S-25(OH) D increased to above 50 nmol/L in almost all fair-skinned and in at least 88% of dark-skinned children. The 25µg dose was associated with higher TB-BMD and BMC (p=0.033 and p=0.038) and FN-BMC (p=0.47) compared to placebo in dark-skinned children and a greater increase in spine BMD (L1-L4) and BMC (p=0.034 and p=0.03) in dark compared to fair-skinned children. This was associated with decreasing PTH.

Conclusion: Despite lower S-25(OH) D concentrations, bone density was higher in dark than fair-skinned children in early winter. Bone density appeared more sensitive to vitamin-D intervention in dark than in fair skinned children.

Disclosure of interest: None
Protein intakes and their nutritional sources during the first two years of life in 5 European countries

Louiza Damianidi¹, Dariusz Gruszfeld ², Elvira Verduci³, Fiammetta Vecchi⁴, Annick Xhonneux⁵, Jean-Paul Langhendries⁵, Veronica Luque⁶, Melissa Ann Theurich⁷, Marta Zaragoza-Jordana⁶, Berthold Koletzko⁷, Veit Grote⁸

¹Dr. von Hauner Children’s Hospital, University of Munich Medical Center, Munich, Germany, DIV. Metabolic and Nutritional Medicine, Munich, Germany
²The Children’s Memorial Health Institute, Department of Neonatology and Neonatal Intensive Care, Warsaw, Poland
³San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
⁴San Paolo Hospital, University of Milano, Department of Pediatrics, Milan, Italy
⁵Service de Néonatologie, Département Pédiatrique, Liege- Rocourt, Belgium
⁶Universitat Rovira I Virgili, Ispv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
⁷Dr. von Hauner Children’s Hospital, University of Munich Medical Center, DIV. Metabolic and Nutritional Medicine, Munich, Germany
⁸Von Haunersches Kinderspital, University of Munich Medical Centre, Munich, Germany

Objectives and study: High protein intake in infancy affects future obesity risk and other health outcomes. We aim to describe total protein intake and its sources in a birth cohort in five European countries (Germany, Belgium, Italy, Poland, and Spain) over the first two years of life.

Methods: 746 formula-fed infants were included. Three-day weighed dietary records at 6, 7, 8, 9, 12, 18 and 24 months of age were used. Kruskal Wallis and Anova tests were used to assess differences in nutritional intake among countries.

Results: Dairy products were the main component of the infants’ diets and were gradually substituted by meat products. Unmodified cows’ milk was rarely introduced before 12 months of age, while infant formula was the main contributor of protein intake in infancy. Food choices and protein intake differed among countries (p< 0.001). Median energy intake increased from 686 (interquartile range: 614, 790) to 1097 (938, 1 263) kcal/day from 6 to 24 months of age. Median protein intake ranged from 19 (15, 25) to 44 (36, 54) g/day, providing 11 to 16% of energy intake and often exceeding recommended intakes from 9 months onwards, partly due to the substitution of dairy protein (mainly from infant formula) by meat protein. Two nutritional patterns could be discerned between countries: higher energy, fat, protein and animal protein intake was observed in Italy, Spain and Poland, while intakes were lower in Belgium and Germany.

Conclusion: During weaning, substitution of dairy products with meat and other protein sources resulted in high protein intakes in formula-fed infants that markedly exceed recommended intakes. Differences in the contribution of specific protein sources from complementary foods exist among European countries. There are major opportunities for improving early nutrition but cultural and geographical differences should be considered.

Disclosure of Interest: “None Declared”. Financially supported in part by the European Commission.
Micronutrient intake and prevalence of adequacy in European children, from birth to 8 years.

Marta Zaragoza-Jordana¹, Veronica Luque¹, Joaquin Escribano¹, Mariona Gispert-Llauradó¹, Veit Grote², Berthold Koletzko³, Ingrid Pawellek⁴, Elvira Verduci⁴, Alice ReDionigi⁴, Anna Stolarczyk⁵, Jerzy Socha⁵, Jean-Paul Langhendries⁶, Annick Xhonneux⁶, Ricardo Closa¹

¹Universitat Rovira i Virgili, Iispv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
²Von Haunersches Kinderspital, University of Munich Medical Centre, Munich, Germany
³Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
⁴San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
⁵Clinic of Paediatrics, Children’s Memorial Health Institute, Warsaw, Poland
⁶Service de Pédiatrie, Département Pédiatrique, Liege- Rocourt, Belgium

Objectives and study: Dietary intake evaluation aims at assessing whether intakes meet nutrient intake recommendations. In Europe, suboptimal intakes have been reported for several nutrients including calcium, iron, zinc, vitamin B₁ (thiamine), vitamin B₂ (riboflavin), vitamin B₆ (niacin), folate (vitamin B₉) and vitamin D. So far, no studies estimated nutrient intake data from healthy children across different European countries using the same methodology. Our aim was to describe nutrient intakes and the prevalence of inadequate intakes during the eight first years of life in children from 5 European countries.

Methods: Data from the prospective Childhood Obesity Project (EU CHOP) study were analysed. Breast and formula fed infants were enrolled within the first two months after birth, at a mean age of 2 weeks, and followed regularly until the age of 8 years. Dietary intake was collected with 3-day weighed/estimated food records at 3, 6, 12, 24, 36, 48, 60, 72 and 96 months of life and was converted into nutrients using food composition tables from all participating countries. Nutrient intake adequacy was estimated following the American Institute of Medicine (IOM) guidelines for population groups and individual assessment, based on Estimated Average Requirements of nutrients of FAO/WHO/UNU, or the IOM if FAO/WHO/UNU data were not available. The project was designed in agreement with the Declaration of Helsinki and was accepted by local ethical committees. Parents received written information and signed informed consent to participate in the study.

Results: 1679 infants were recruited after birth. Intake data was available for a decreasing number of children over time, from 904 children at 3 months to 396 at 8 years. Sodium, potassium, calcium, phosphorus, iron, zinc, magnesium, iodine, vitamin B₁₂, folate, vitamin A and vitamin D intakes at 3, 6, 12, 24, 36, 48, 60, 72 and 96 months were described (data not shown). Prevalence of adequacy to recommendations at group level was assessed for calcium, phosphorus, iron, zinc, magnesium, iodine, vitamin B₁₂, folate, vitamin A and vitamin D. Probability of adequate intake (PA) was calculated for calcium, phosphorus, iron, zinc (except at 12 months), magnesium, iodine (except at 2 and 4 years), vitamin B₁₂ (except at 1, 3 and 6 years) and folate. Figure 1 summarises adequacy results. Concerns arose for zinc, calcium, iron, iodine, folate and vitamin D which showed group adequacy levels below 80% at several timepoints; iodine and folate prevalence of PA>75% at individual level were under 20% at almost all timepoints.
**Conclusion:** The mean intakes of phosphorus, magnesium, vitamin B$_{12}$ and vitamin A among European children are adequate, whereas a high proportion of children did not achieve adequate intakes of zinc, calcium, iron, folate, iodine and vitamin D from infancy to 8 years.

**Disclosure of interest:** Authors disclose no conflicts of interest. Financially supported in part by the European Commission.
Duration of breastfeeding is an independent contributor to BMI z-score decrease after 12 months of lifestyle intervention in overweight and obese children

Elke Dorenbos¹, Jesse Rijks¹, Anita Vreugdenhil¹
¹Maastricht University Medical Centre, Paediatrics, Maastricht, Netherlands

Objectives and study: Absence of breastfeeding has been suggested to lead to epigenetic changes and metabolic alterations, thereby increasing the risk of becoming obese in childhood. It is likely that these metabolic alterations also have an adverse effect on therapy outcomes once a child has become overweight or obese. In this study the influence of breastfeeding on the outcomes of a lifestyle intervention in overweight and obese children was assessed.

Methods: Children were recruited from the Centre for Overweight Adolescent and Children’s Healthcare (COACH, Maastricht University Medical Centre), which offers a multidisciplinary, personalized lifestyle intervention for overweight and obese children and their families. During an initial assessment of physical health and social and mental well-being, anthropometric characteristics, blood pressure, polysomnography, food intake behavior, and physical activity were assessed. Furthermore, a fasting blood analysis was performed to assess total cholesterol, high-density lipoprotein (HDL) cholesterol, low-density lipoprotein (LDL) cholesterol, free fatty acids, triglycerides, glucose, insulin, homeostatic model assessment of insulin resistance (HOMA-IR), HbA1c, C-reactive protein, alanine transaminase, and aspartate transaminase concentrations. After 12 months of lifestyle intervention, all measurements were repeated. Breastfeeding and duration of breastfeeding was estimated during medical history taking, and children were classified as having received “any breastfeeding” (exclusive or partial breastfeeding) or “no breastfeeding”. Associations were tested using regression analyses.

Results: 149 children (67m/82f, age 11.9±3.2y; BMI z-score 3.5±0.7) were included in this study, of which 49 children (34.5%) had received breastfeeding. At baseline, children that were breastfed showed higher HDL-cholesterol concentrations than children that were not breastfed (1.28±0.04 vs. 1.17±0.83 mmol/L, p=0.020). After 12 months of lifestyle intervention, a significant reduction in BMI z-score (-0.2±0.5 SD, p=0.002), triglycerides (-0.2±0.5 mmol/L, p=0.003), and HbA1c (0.2±0.3%, p=0.000) was observed in children that were breastfed. Children that were not breastfed also decreased BMI z-scores (-0.12±0.42, p=0.006), as well as diastolic blood pressure z-score (-0.6±1.2, p=0.014), total cholesterol concentration (-0.3±0.6 mmol/L, p=0.000), and LDL cholesterol concentration (-0.3±0.6 mmol/L, p=0.000). In addition, an increase in fasting glucose concentrations (+0.2±0.6 mg/dl, p=0.010) was observed. Mean health parameter changes after one year of lifestyle intervention were not different between children that were breastfed and those that were not breastfed. After correcting for age, gender, and socio-economic status, breastfeeding duration was positively associated with a decrease in BMI z-score after one year of lifestyle intervention, explaining 18.2% of the variance in BMI z-score (B=-0.014, R²=0.182, p=0.021).

Conclusion: Overweight and obese children that were breastfed show higher HDL-cholesterol concentrations at baseline compared to children that were not breastfed. Longer duration of breastfeeding was positively associated with BMI z-score decrease after one year of lifestyle intervention.

Disclosure of interest: None Declared.
Circulating salicylic acid and metabolic profile in obese children: a case-control study

Elvira Verduci¹, Carlotta Lassandro¹, Giovanni Radaelli¹, Benedetta Mariani¹, Marta Brambilla¹, Alberto Battezzati², Giuseppe Banderali¹

¹San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
²International Center for the Assessment of Nutritional Status, University of Milan, Department of Food, Environmental and Nutritional Sciences, Milan, Italy

Objectives and study: Treatment with salicylates seems to reduce blood glucose and glycated haemoglobin levels in adults. Salicylic acid (SA) is normally present in blood even in people not taking salicylates drugs. The aim of this study was to evaluate the association between circulating salicylic acid and metabolic variables in obese children, compared to normal-weight children (control group).

Methods: Thirty-four obese children (18 girls and 16 boys) aged 6-14 years and 34 normal-weight children, sex and age-matched, were recruited for the study. Exclusion criteria comprised chronic or acute therapies with anti-inflammatory drugs. Children were defined as obese or normal weight according to the International Obesity Task Force. BMI z-scores were calculated. Anthropometric measurements and blood pressure of children were taken. Fasting blood samples were analyzed for lipids, insulin and glucose. The homeostatic model assessment of insulin resistance (HOMA-IR) was calculated and insulin resistance was defined as HOMA-IR >3.16, according to the cut-off for the paediatric population. The triglyceride glucose index (TyG-Index), an emergent useful indicator reflecting mainly muscle insulin resistance, was calculated. The quantitative insulin sensitivity check (QUICK) index was calculated to detect insulin sensitivity. Pancreatic β-cell function was evaluated by HOMA-β%. SA serum concentration (salicylaemia) was measured using a sensitive stable isotope dilution and gas chromatography-mass spectrometry (GC-MS) method. Comparison between obese and normal-weight children was performed for continues variables by the Mann–Whitney test. The associations were assessed by Spearman’s correlation coefficient. Statistical significance for all tests was set at a $p$-value of 0.05.

Results: Compared to control group, obese children showed higher BMI z-score (3.17 [0.83] vs 0.14 [0.89], $p < 0.0001$), higher insulin (16.90 [6.70] vs 7.69 [4.48] μU/mL; $p < 0.0001$), HOMA-IR (3.64 [1.56] vs 1.62 [1.00]; $p < 0.0001$), TyG (3.61 [0.15] vs 3.40 [0.15]; $p < 0.0001$) and HOMA-β indices (274.96 [145.53] vs 136.79 [77.23]; $p < 0.0001$) and lower QUICK index (0.32 [0.02] vs 0.37 [0.04]; $p < 0.0001$). No difference was observed for circulating salicylic acid (0.08 [0.04] vs 0.11 [0.05] μmol/L; $p = 0.081$). Twenty obese children (58.8%) showed insulin resistance. In obese children a positive association between salicylaemia and QUICK index ($p = 0.023$) and negative associations between salicylaemia and HOMA-IR ($p = 0.023$) and HOMA-β ($p = 0.012$) were shown. A negative association was observed with systolic blood pressure ($p = 0.014$). No association was observed between salicylaemia and lipids. In the control group, no association was found between salicylaemia and lipids and glucose-metabolism variables.

Conclusion: In obese children salicylaemia was associated positively with insulin sensitivity and negatively with insulin resistance. Given the increasing prevalence of insulin resistance among obese children, these results could be of interest. However, further larger studies are needed to verify the association between salicylaemia and metabolic pattern in obese children.

Disclosure of interest: None Declared.
Nutrition in preschool children and later risk of obesity: a systematic review and meta analysis

Julie Lanigan¹, Amanda Adegboye², Kate Northstone³, Catherine Salisbury¹, Atul Singhal¹

¹University College London, Institute of Child Health, London, United Kingdom
²University of Westminster, Department of Life Sciences, London, United Kingdom
³University of Bristol, School of Social and Community Medicine, Bristol, United Kingdom

Objectives and study: Nutrition in infants and preschool children has been suggested to influence the risk of later obesity. However, the evidence for this association is conflicting and few studies have investigated this prospectively or considered the role of energy and specific macronutrients. Here we report a systematic review and meta-analysis of studies that tested the hypothesis that nutrition in the preschool period, between the ages of 6 months and 3 years, is associated with later obesity risk.

Methods: MEDLINE, EMBASE and CENTRAL databases were searched from January 1988 to June 2015 for studies reporting nutritional intake in infants and preschool children aged 6-36 months and later measures of obesity. Bibliographies of included studies were hand searched and authors and other experts consulted to identify omissions. We included all studies that investigated dietary energy and/or macronutrient intake during 6-36 months in relation to later measures of obesity. Methodological quality was assessed using the Downs and Black checklist designed specifically to appraise both randomised and non-randomised studies¹. The checklist was adapted to include aspects of particular relevance to studies investigating nutritional exposures. Two reviewers independently scored studies against the 28 item checklist which included questions on study reporting, external validity, internal validity (bias and confounding), and statistical power. A statistician independently scored questions relating to statistical methods and their decision was final. Data from studies amenable to meta-analysis were analysed using STATA (StataCrop 12, Texas). For continuous outcomes, results were expressed as standardised mean difference (SMD) between the high and low protein intake groups. For dichotomous outcomes, results for each study were expressed as relative risk (RR). Both dichotomous and continuous outcomes were presented with 95% confidence intervals (CI). Between-study heterogeneity was assessed by the Q and I² statistics.

Results: 24 eligible articles (comprising 16 primary studies) were included in a narrative synthesis, and 13 studies in a random-effects meta-analysis. A higher protein intake was associated with later risk of obesity in 15 studies. In 13 studies included in the meta-analysis protein in the preschool period was associated with higher BMI z-score later in childhood (pooled effect size: 0.28 z-scores, 95% CI 0.20 to 0.35)(Figure 1). There was no significant heterogeneity between studies (F 0.0%, p = 0.932).

Associations of energy, fat and carbohydrate were inconclusive.

Figure 1: Protein intake and BMI z-score – pooled effect estimate
Conclusion: Our findings suggest that nutrition and particularly high protein intake in infants and preschool children is important for risk of later obesity. Although further experimental data are required to establish causality, these findings suggest that optimising the protein intake of these children could be important for their long term health.

Disclosure of interest: The authors declare no conflicts of interest.

Reference List


Protein intake and source during complementary feeding and growth up to 6 years of age, secondary data evaluation from the European Childhood Obesity Project.

Louiza Damianidi1, Dariusz Gruszfeld2, Elvira Verduci3, Fiammetta Vecchi4, Annick Xhonneux5, Jean-Paul Langhendries5, Veronica Luque6, Melissa Ann Theurich7, Marta Zaragoza-Jordana6, Berthold Koletzko7, Veit Grote8

1Dr. von Hauner Children’s Hospital, University of Munich Medical Center, Munich, Germany, DIV. Metabolic and Nutritional Medicine, Munich, Germany
2The Children’s Memorial Health Institute, Department of Neonatology and Neonatal Intensive Care, Warsaw, Poland
3San Paolo Hospital, University of Milan, Department of Pediatrics, Department of Health Science, Milan, Italy
4San Paolo Hospital, University of Milano, Department of Pediatrics, Milan, Italy
5Service de Néonatologie, Département Pédiatrique, Liege- Rocourt, Belgium
6Universitat Rovira i Virgili, Iispv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
7Dr. von Hauner Children’s Hospital, University of Munich Medical Center, DIV. Metabolic and Nutritional Medicine, Munich, Germany
8Von Haunersches Kinderspital, University of Munich Medical Centre, München, Germany

Objectives and study: Protein sources during early infancy may be associated to later growth. Thus, we aimed to investigate the possible impact of protein intake and different protein sources at 6 and 12 months on z-BMI at 1, 2 and 6 years of age using data from the CHOP (Childhood Obesity Project) study, a randomized intervention trial conducted in 5 European countries (Germany, Belgium, Italy, Poland, Spain).

Methods: 670 infants were included in the analysis. Three day weighed dietary records at 6 and 12 months and weight, height and BMI measurements at 1, 2 and 6 years were used. Simple and multiple regression analyses models (both crude and adjusted for: gender, mother’s BMI before pregnancy, z-BMI at baseline, study country, total energy intake) were chosen to identify possible associations between protein intake (% of energy) and z-BMI outcomes.

Results: Total protein intake in early life was positively related to later z-BMI (6 months intake to 1 year: β=0.04, P-value=0.001, 2 years: β=0.03, P-value=0.001, 6 years: β=0.04, P-value=0.049, 12 months intake to 2 years: β=0.05, P-value=0.001). Positive relations for animal protein intake to later z-BMI were recognized (Table). Dairy protein intake was related to z-BMI at 1, 2 and 6 years of age (6 months intake to 1 year: β=0.04, P-value=0.002, 2 years: β=0.03, P-value=0.019, 6 years: β=0.03, P-value=0.043, 12 months intake to 2 years: β=0.07, P-value=0.000). While also meat protein at 12 months was correlated to BMI at 2 years (β=0.04, P-value=0.013). No statistically significant relations were found for non-animal protein intake.
Table:

Effect of protein intake (% of energy) from different food groups at 6 and 12 months on z-BMI at 1, 2 and 6 years.

<table>
<thead>
<tr>
<th>z-BMI</th>
<th>1 year outcomes</th>
<th>2 years outcomes</th>
<th>6 years outcomes</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n/670 β P</td>
<td>n/670 β P</td>
<td>n/670 β P</td>
</tr>
<tr>
<td><strong>Animal</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6mo intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>666 0.03 0.020</td>
<td>552 0.02 0.086</td>
<td>402 0.03 0.095</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>642 0.04 0.002</td>
<td>532 0.03 0.019</td>
<td>391 0.04 0.039</td>
</tr>
<tr>
<td>12mo intake</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crude</td>
<td>- -</td>
<td>535 0.06 &lt;.0001</td>
<td>367 0.05 0.007</td>
</tr>
<tr>
<td>Adjusted*</td>
<td>- -</td>
<td>516 0.05 &lt;.0001</td>
<td>356 0.04 0.088</td>
</tr>
</tbody>
</table>

* Adjusted: adjusted for gender, mother’s BMI before pregnancy, z-BMI at baseline, study country, total energy intake

**Conclusion:** Protein intake in early life was related to z-BMI. Additionally animal- protein intake 6 and 12 months may affect BMI until 6 years of age; the effect of dairy protein on later BMI seemed to be stronger than that of meat. The intake of protein intake during complementary feeding should be kept within recommended limits.

**Disclosure of interest:** “None Declared”. Financially supported in part by the European Commission.

Maurizio Mennini¹, Federica Ferrari², Lucia Morcaldi², Luigi Principessa³, Laura Stronati⁴, Salvatore Cucchiara¹

¹Sapienza University of Rome, Pediatrics and Childhood Neuropsychiatry, Rome, Italy
²Sapienza University of Rome, Rome, Italy
³Sant’Andrea Hospital, Sapienza University of Rome, Rome, Italy
⁴Sapienza University of Rome, Cellular Biotechnology and Hematology, Rome, Italy

Objectives and study: Childhood obesity is considered a major worldwide problem, especially for the association with metabolic syndrome (MS). Many studies suggest a possible interplay in Body Mass Index (BMI) increase, visceral obesity and chronic low-grade inflammation with production of cytokines and acute-phase markers. Non alcoholic fatty liver disease (NAFLD) is considered as the hepatic manifestation of the MS, and its prevalence is 34.2% in obese children. It has been demonstrated that severity of liver steatosis correlates with an increased intestinal permeability (IP). The aim of the study was to assess the presence of systemic inflammation in overweight/obese children and the possible relationship between NAFLD, IP and fecal inflammatory markers.

Methods: We enrolled every pediatric patient without any known pathological condition showing BMI greater than 85th percentile according to CDC. Demographic and clinical features were recorded: age, sex, hip and waist circumference (WC). Laboratory evaluation included: aspartate aminotransferase (AST), alanine aminotransferase (ALT), fasting glucose, insulin, total, LDL and HDL cholesterol, triglycerides, ESR, CRP. Insulin resistance was determined by the HOMA index. MS was diagnosed using criteria modified from those of adults. All patients performed abdominal ultrasound to detect presence of mild, moderate or severe liver steatosis. All other causes of liver disease were excluded. We also determined serum TNF-α, IL-1, IL-6 and fecal calprotectin. Moreover, in order to evaluate IP, lactulose and mannitol test were performed.

Results: We enrolled 29 patients (23 Males; mean age 12.3±3.71 years): 5 (17.2%) and 24 (82.7%) were overweight and obese, respectively. Among 29 patients, 20 (68.9%) showed a WC greater than 95th centile; 8 (27.5%) and 10 (34.4%) had elevated value of insulin and HOMA Index, respectively. Five (17.2%), 6 (20.6%) and 2 (6.8%) patients had elevated triglycerides, Total and LDL Cholesterol respectively. MS was diagnosed in 2 patients. Ten (34.48%) children showed ALT higher than 40 UI/L. At ultrasound evaluation, the steatosis was mild in 12 patients (41.3%), moderate in 10 (34.4%), severe in 3 (10.3%), Only 4 (13.7%) children presented a normal liver. In all patients ESR and CRP were normal; in 2 of 12 patients fecal calprotectin was increased. Serum TNF-α, IL-1 and IL-6 were performed in 13 patients. TNF-α was increased in all children, IL-1 in 5 (17.2%) and IL-6 in 4 (13.7%). HOMA Index was significantly correlated to TNF-α (p<0.01) and IL-6 (p<0.01). Two out of 17 patients reported an altered IP: mean IP was higher in children with moderate/severe steatosis compared than those with mild or without steatosis (0.029 vs 0.018), but the difference was not significant. IP was found to correlate with TNF-α (p<0.01).

Conclusion: In our population, most of children were obese with a prevalence of MS lower than that commonly described. NAFLD was present in 34.48% of obese patients. TNF-α and IL-6 level seem to be related to insulin resistance. Assuming that these cytokines are secreted by adipose tissue, our results suggest a link between visceral obesity and systemic inflammation. We did not find a significant alteration neither of IP nor of fecal inflammatory markers. Our study is a first step toward understanding the close connections between obesity, MS and inflammation, while studies including larger populations with prolonged follow up are running.

Disclosure of interest: None Declared.
The impact of taurolidine-citrate locks implementation in a large pediatric cohort on home parenteral nutrition

Cecile Lambe¹, Catherine Poisson¹, Cecile Talbotec¹, Olivier Goulet¹

¹Hôpital Necker-Enfants Malades, Pediatric Gastroenterology, Hepatology and Nutrition, Paris, France

Objectives and study: Catheter-related bloodstream infections (CRBSIs) remain a major issue in patients on home parenteral nutrition. Several studies in patients with long-term central venous catheter (dialysis, oncology, parenteral nutrition catheters) have reported that the use of taurolidine or taurolidine-citrate locks decreases the incidence of CRBSIs. Taurolidine is an antimicrobial agent and prevents biofilm formation while citrate prevents clot formation. The aim of this prospective interventional study was to assess the impact of taurolidine-citrate locks on the CRBSI rate in the particular group of children with intestinal failure (IF) receiving long-term home parenteral nutrition (HPN).

Methods: One hundred and ninety three children with intestinal failure who received consecutively HPN in our Center from 2008 to 2014 were included prospectively. The rate of catheter infection was monitored every calendar year. Taurolidine-citrate locks were initiated from October 2011 in children with recurring CRBSI (2 CRBSI episodes in less than 12 months). Taurolidine-citrate solution was infused after each PN infusion into the catheter lumen and left in place until the next infusion (10 to 60 hours). CRBSI rate was compared before and after lock therapy initiation in these patients (Wilcoxon paired test) and over time in the whole cohort. The Kaplan Meier cumulative rates of patients free from CRBSI in patients with taurolidine-citrate locks and in controls were compared using log rank test.

Results: Taurolidine-citrate locks were used in 40 patients since October 2011. No adverse events were reported. In these 40 selected patients, only 5 CRBSI episodes occurred on treatment. The CRBSI rate per 1000 catheter days decreased from 4.16 (29547 days) before treatment to 0.25 (19688 days) on treatment (p<0.0001). In the whole cohort median annual CRBSI rate per 1000 catheter days decreased significantly from 2.20 (range 1.66-2.55) in 2008-2011 to 1.11 (range 1.08-1.55) in 2012-2014 (p<0.0001). The cumulative rate of patients free from CRBSI at 18 months was 92% in the 40 patients that received the taurolidine-citrate locks vs. 61% in the 86 patients who did not receive locks (p = 0.011).

Conclusion: Taurolidine-citrate catheter locks implementation dramatically decreased the incidence of CRBSIs in a large pediatric cohort of patients on long-term home parenteral nutrition. Its use should be widened to protect these fragile patients from further complications.

Disclosure of interest: None Declared.
NUTRITION: Clinical nutrition

N-eP-001

Nutritional status in neurologically impaired children and its relation with bone mineralization

Francesca Penagini¹, Stefano Mora², Stefania Bova³, Stefania Del Sesto¹, Domenica Brunetti¹, Dario Dilillo¹, Gian Vincenzo Zuccotti¹

¹ “V. Buzzi” Children’s Hospital, University of Milan, Department of Paediatrics, Milan, Italy
² San Raffaele Scientific Institute, Pediatric Bone Densitometry Unit, Milan, Italy
³ Ospedale Dei Bambini V. Buzzi, Neurology Unit, Milan, Italy

Objectives and study: Malnutrition and low bone mineral density (BMD) are common in neurologically impaired (NI) children, in particular in children with cerebral palsy (CP). The two conditions are related, as it is known that poor nutritional status can negatively impact on bone mineralization. The aim of our study was to assess nutritional status, bone health and the relation between the two conditions in our population of NI children.

Methods: A total of 26 NI subjects (mean age 9.9 ± 3.7 years, M:F ratio 11:15, all Caucasian except for one Hispanic), were enrolled between November 2014 and March 2015. Diagnoses were: cerebral palsy (CP) 42.3% (n=11), epilepsy of various etiology associated with mild or no motor impairment (epilepsy without CP) 57.7% (n=15). Patients receiving vitamin D supplementation were excluded. All subjects underwent: 1) Nutritional assessment including feeding history, anthropometric evaluation of weight, height, body mass index (BMI) and triceps skinfold thickness (TST); 2) Biochemical analyses for bone metabolism and serum markers of bone turnover including parathormone (PTH), 25-hydroxy-vitamin D (25OHvitD), bone alkaline phosphatase (BAP) and carboxy-terminal collagen (CTX); 3) BMD measurement at lumbar spine (L1-L4) with Dual Energy X-ray Absorptiometry (DEXA).

Results: Feeding difficulties were encountered in 42.3% of total patients, in 90.9% of children with CP. Nutrient intakes were compared to recommended dietary intakes for Italian population (LARN 2014), insufficient intake of energy, protein and calcium were found in 26.9%, 3.8%, 69.2% of total patients. A poor nutritional status (BMI< 10°c.le and/or TST< 10°c.le) was found in 38.5% of total patients, in 72.7% of children with CP. Vitamin D insufficiency (25OHvitD < 20 ng/dl) was found in 65.4% of total subjects, in 81.8% of children with CP. Values of CTX and BAP were significantly higher in epileptic children without CP compared to children with CP (p=0.0396 and 0.048 respectively). Results of nutritional status and bone metabolism are shown in table 1. A poor bone mineralization (BMD z-score < 2) was found in the lumbar spine of 38% of the total and in 73% of children with CP. Correlation analyses found positive correlation between BMD z-score and the anthropometric parameters BMI z-score and TST (r=0.8205; p< 0.0001 and r=0.7374; p< 0.0001 respectively). Negative correlation was also found between BMD z-score and severity of motor impairment measured by Gross Motor Function Classification Scale- GMFCS (r = -0.7216  p< 0.05).

Table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>CP (n=11)</th>
<th>Epilepsy without CP (n=15)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight SDS</td>
<td>-3.76 ± 2.04</td>
<td>-0.3 ± 1.1</td>
<td>0.0002a</td>
</tr>
<tr>
<td>Height SDS</td>
<td>-2.36 ± 1.23</td>
<td>-0.4 ± 1.08</td>
<td>0.0004a</td>
</tr>
<tr>
<td>BMI SDS</td>
<td>-3.22 ± 2.28</td>
<td>-0.1 ± 1.26</td>
<td>0.001a</td>
</tr>
<tr>
<td>TST (mm)</td>
<td>5.80 ± 2.00</td>
<td>8.86 ± 2.95</td>
<td>0.0045a</td>
</tr>
<tr>
<td>25OHvitD (ng/ml)</td>
<td>13.14 ± 2.6</td>
<td>18.38 ± 3.18</td>
<td>0.12</td>
</tr>
<tr>
<td>PTH (pg/ml)</td>
<td>61.98 ± 5.37</td>
<td>56.83 ± 5.29</td>
<td>0.89</td>
</tr>
<tr>
<td>BAP (UI/L)</td>
<td>99.6 ± 14.81</td>
<td>136.47 ± 16.74</td>
<td>0.048a</td>
</tr>
<tr>
<td>CTX (ng/l)</td>
<td>1210, 91 ± 118.4</td>
<td>1624 ± 209.15</td>
<td>0.0396a</td>
</tr>
</tbody>
</table>

Table 1: Anthropometric parameters and bone metabolism of our population.

a = statistically significant values
**Conclusion:** Our data confirm a high prevalence of malnutrition, vitamin D insufficiency and poor bone mineralization in NI children, particularly in those with CP. We also confirm that nutritional status and motor impairment are factors that negatively impact on bone mineralization.

**Disclosure of interest:** None declared.
Neurocognitive functions in infants with malnutrition; and its association with micronutrients, LC-PUFA and brain metabolites

Murat Cakir1, Sukran SENYUVA2, Sibel KUL3, Ulas Emre AKBULUT1, Ali Cansu4

1Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Gastroenterology Hepatology and Nutrition, Trabzon, Turkey
2Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatrics, Trabzon, Turkey
3Karadeniz Technical University, Faculty of Medicine, Dept. of Radiology, Trabzon, Turkey
4Karadeniz Technical University, Faculty of Medicine, Dept. of Pediatric Neurology, Trabzon, Turkey

Objectives and study: Neurocognitive impairment (NI) is common in malnourished infants. However, role of serum micronutrients and LC-PUFA levels for NI and relationship between the NI and brain metabolites are lacking. Therefore, we aimed to analyze the correlation between the neurocognitive function (NF) and (i) serum micronutrients and LC-PUFA levels and (ii) brain metabolites in malnourished infants.

Methods: The study included the 24 infants (group 1, 10.8 ± 7.6 months, 62.5% female) with malnutrition and 21 healthy infants (group 2, 12.7 ± 9.7 months, 66.7% female) without any chronic disease and malnutrition. NF of the infants were assessed by using Ankara Developmental Screening Inventory (ADSI). Peripheral blood was collected in all infants for micronutrients [calcium (Ca), iron (Fe), magnesium (Mg), vitamin B12, zinc (Zn), folic acid and vitamin A] and LC-PUFA [arachidonic acid (AA) and docosahexaenoic acid (DHA)] analysis. MRS was performed using multivoxel MRS (1.5 Tesla, Siemens Magnetom®), and measured the metabolites of N-acetyl aspartate (NAA), choline (Cho), and creatine (Cr) in the basal ganglia, thalami, white matter.

Results: 10 of 24 of infants had severe (group 1a) and others had mild/moderate (group 1b) malnutrition according to WHO guidelines. All parameters of ADSI [communication-cognitive, fine motor, gross motor, social skills-self care and total (T-points)] were lower in malnourished infants than the healthy infants (p<0.05 for all). In micronutrients; only Ca and Mg levels were significantly lower in malnourished infants (p<0.05). No significant difference was found in LC-PUFA levels between the malnourished and healthy infants, but AA levels were significantly low in group 1a than 1b (14.07 ± 2.26 vs. 15.74 ± 1.23%, p<0.05). NAA/Cho in the white matter were significantly low in group 1a than 1b (1.40 ± 0.32 vs. 1.71 ± 0.36), other parameters did not exhibit any significant difference. Correlation analysis revealed that T points in the ADSI were only positively correlated with serum Ca levels and white matter NAA/Cho ratio (r=0.381, p<0.05 and r=0.298, p<0.05, respectively) (Figure 1a, 1b).

Conclusion: NFs are impaired in infants with malnutrition, and serum Ca level is the main indicator of NI. NI effects the white matter NAA/Cho ratio. No association was found between NF and LC-PUFA levels. Effects of Ca supplementation in malnourished infants on NF and brain metabolites are needed to be studied prospectively.

Disclosure of interest: None Declared.
Eating behaviour and macronutrient intake before and during growth hormone treatment in short children born small for gestational age

Koen Huysentruyt¹, Muriel Thomas², François Inge³, Martine Cools⁴, france Annick⁵, Parent Anne-Simone⁶, Beauloye Véronique⁷, De Schepper Jean⁸

¹Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (Vub), Pediatrics, Brussels, Belgium
²Bespeed, Brussels, Belgium
³Uz Leuven, Belgium
⁴Department of Pediatrics, Division of Pediatric and Adolescent Endocrinology and Diabetology University Hospital Gent, Gent, Belgium
⁵University of Antwerp, Antwerp, Belgium
⁶Université de Liège, Liège, Belgium
⁷University Hospital Uclouvain, Louvain, Belgium
⁸Department of Paediatric Endocrinology, Uz Brussels, Belgium

Objectives and study: Although a reduced food intake is often reported by the parents in short children born small for gestational age (SSGA), few data exits in the literature. Therefore, we investigated the eating behaviour and macronutrient intake in SSGA children before and during growth hormone (GH) treatment.

Methods: 40 short (current height < -2.5 SD and height velocity < 1.0 SD during the last 6-18 months) SGA children, aged between 3-8 years, were randomized into a group with (TR; n=20) and without (NTR; n=20) GH treatment. Eating behaviour was assessed using the Children's Eating Behaviour Inventory (CEBI), food intake via a standardized 3-day food diary before randomization (t₀) and one (t₁) and two (t₂) years after randomization. CEBI scores were also assessed in a non-clinical control population. Mean energy and macronutrient intake was calculated from the nutritional diaries (n=35) using the Nubei® dietary software and compared with the Belgian recommended dietary intake (RDI).

Results: At start mean (SD) age was 5.3 (1.5) years, height for age Z-score -3.3 (0.8), mean (SD) weight for age Z-score -3.8 (1.4), and BMI Z-score -1.9 (1.3), with no significant difference between TR and NTR group. Mean (SD) caloric intake at t₀ was 1669 (325) kcal/day and 1300 (288) kcal/day in boys and girls <6 years respectively (RDI: 1134-1363 and 1040-1243 respectively), and 1423 (171) kcal/day and 1481 (347) kcal/day in boys and girls ≥6 years respectively (RDI: 1458-1842 and 1339-1702 respectively). Overall, 11 (31.4%) children had a caloric intake below the RDI when expressed as kcal/day, but only two (5.7%) when expressed as kcal/kg/day. Baseline protein-intake was excessive in all children (median (range) 3.9 (2.4-7.1) g/kg/day; RDI 0.85-0.92). Mean (SD) fat-intake at t₀ was 39.2 (6.0)% of total energy intake (RDI 30-35% of total energy intake), with 27 (79.4%) having a fat-intake > RDI. Compared to t₀, mean caloric intake rose significantly (p=0.04 and <0.01 respectively) in the NTR group at t₁ (mean difference 17.2 kcal/kg, 95% CI 1.1-33.3) and t₂ (mean difference 31.5 kcal/kg, 95% CI 16.1-46.9); in the TR group a significant (p<0.01) difference was noted at t₁ (mean difference 25.7 kcal/kg, 95% CI 9.5-41.8), but not at t₂ (mean difference 8.8 kcal/kg, 95% CI -1.75-19.3; p=0.09). TR and NTR group did not differ in caloric intake at any time point (p-values between 0.08-0.26). The number of children with a caloric intake below the RDI on follow-up was similar in both groups (p-values between 0.66 and 1.0). The baseline mean CEBI-score was significantly (p<0.01) higher than in the non-clinical control population (95.5±9.5 vs 86.7±11.5 respectively), whereas the mean perceived problem score was significantly lower than the mean of a non-clinical population (5.2±4.6 vs 13.26±13.26, p<0.01). At t₁ and t₂ mean perceived problem score was significantly (p<0.01) lower than at t₀ in the NTR group, while this difference was not noted in the TR group.

Conclusion: Mean caloric intake was low in older SSGA children compared to the RDI, but not when expressed in function of their body weight. Fat and especially protein intake were too high. GH treatment does not influence caloric intake in these children. Higher CEBI scores were noted than in a non-clinical population, but with a lower perceived problem score.

Disclosure of interest: None Declared.
Results of the ESPGHAN Nutrition Training Survey

Jörg Jahnel1, Ilse Broekaert2, Marta Tavares3, Nicolette Moes4, Hubert van der Doel5, Christos Tzivinikos6

1Medical University Graz, Austria  
2University of Cologne, Pediatrics, Cologne, Germany  
3University Hospital Porto, Portugal  
4University Medical Center Groningen, Pghn, Groningen, Netherlands  
5University Medical Center Groningen, Groningen Transplant Center, Dept. Pediatrics, Netherlands  
6Alder Hey Children's Hospital, Paediatric Gastoenterolpogy, Liverpool, United Kingdom

Objectives and study: Nutrition training is an essential part of fellowship in paediatric gastroenterology, hepatology, and nutrition (PGHN) as specified in the nutrition syllabus offered by ESPGHAN. We sought to evaluate nutrition training among fellows and professionals specialising in paediatric gastroenterology (GI).

Methods: Between 2/2014 and 5/2015, an ESPGHAN-wide call by email attracted participation by 56 PGHN fellows from 26 countries. We contacted trainee members of ESPGHAN and fellows who attended ESPGHAN activities like summer schools, in sum approximately 250 persons. An electronic survey comprised 17 questions regarding general information, year of graduation from medical school, paediatric GI training programs offered by the local hospital and/or national PGHAN organisation, time schedule of the local/national PGHAN education, composition of the local multidisciplinary nutrition team, current training opportunities in their local centres and countries, and nutrition topics covered during training.

Results: Among 56 fellows in the field of PGHN, 36% had already completed their training, whereas 54% were still in training. 39 fellows (71%) were participating in a local GI training program. 33 fellows (59%) were enrolled in a national PGHN fellowship program leading to subspecialty certification. The training of 24 fellows (43%) was entirely devoted to paediatric GI. Another 25 (45%) spent between >50-99% in this field. A multidisciplinary nutrition team was available to 59% of fellows (without exception, those enrolled in an official PGHN programme). These teams included dietitians (88%), fellows (84%), consultants (81%), specialist parenteral nutrition nurses (44%), psychologists (46%), and pharmacists (44%). 16 fellows (33%) used the recently published ESPGHAN syllabus for nutrition and 29 (60%) had attended a nutrition course (ESPGHAN-directed or other). Few used e-learning nutrition modules (16%) but many were willing to use e-learning modules in the future (70%); many asked for future ESPGHAN nutrition summer schools (84%) and some requested long-distance learning nutrition programs (51%). Most frequently covered during training were the topics of diagnosis and investigation of a patient with failure to thrive (63%), cystic fibrosis (43%), indications and contraindications for commencing enteral feeds (43%), benefits and risks of enteral and parenteral nutrition (43%), infant feeding (37%), and coeliac disease (34%).

Conclusion: This survey shows that nutrition training in Europe is variable and that the ESPGHAN nutrition syllabus is not yet implemented Europe-wide. ESPGHAN should motivate all individual trainers to apply the ESPGHAN nutrition syllabus. Future e-learning modules and summer schools may provide concomitant training.

Disclosure of interest: None Declared.
Does exclusive enteral nutrition affect the clinical course in paediatric Crohn's disease patients?

Elena Scarpato1, Caterina Strisciuglio2, Massimo Martinelli1, Clelia Tortora1, Sabrina Cenni1, Maria Rosaria Serra1, Annamaria Staiano1, Erasmo Miele1

1Federico II University, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
2Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy

Objectives and study: Crohn's disease (CD) is a chronic inflammatory condition that affects the gastrointestinal tract, characterized by a continuous relapsing and remitting course. The pathogenesis is complex and involves genetic and environmental factors. Diet is believed to be a major contributory factor to the onset or course of CD. The aim of this study was to evaluate the clinical effects of exclusive enteral nutrition (EEN) vs corticosteroids (CCS), in a cohort of paediatric patients diagnosed with CD.

Methods: A retrospective chart review of patients diagnosed with CD between January 2003 and December 2013, has been conducted. Demographical and clinical characteristics, laboratory parameters, and paediatric Crohn's disease activity index (PCDAI) were evaluated at diagnosis, and at 8 weeks, 6 months, 1 year and 2 years follow-up. Subjects were divided in 2 groups at CD diagnosis: Group 1, receiving EEN for 8 weeks followed by a gradual introduction of foods during the subsequent 4 weeks, and Group 2, treated with or al CCS with tapering off by week 11.

Results: We evaluated 33 patients in the EEN group (males 20; mean age at diagnosis 10.4±3.5 years) and 11 patients in the CCS group (males 6; mean age at diagnosis 11.7±4.6 years). At the baseline, there were no significant differences in clinical characteristics, localization, and disease's behavior between the two groups, with the exception of CRP values (Group 1, mean 19.4±30.2 mg/L vs Group 2, 9.7±11.7 mg/L; p=0.06). After 8 weeks from diagnosis, 27/33 (82%) patients from Group 1 and 9/11 (82%) from Group 2 were in remission (p=1). Four out of 33 (12%) from the EEN group and 2/11 (18%) from the CCS group needed to start immunomodulators after 8 weeks (p=0.6). Moreover, we detected a significant improvement in mean CRP values in the EEN group compared to the CCS group (mean 0.69±0.98 mg/L and 1.94±1.81 mg/L, respectively; p=0.006). At 1 and 2 years of follow up, BMI z-scores between the 2 groups were not significantly different (p=0.29 and p=0.57, at 1 and 2 years, respectively). Considering disease activity, PCDAI mean scores were significantly lower in EEN group vs CCS group after 1 year (T3) and 2 years (T4) of follow-up (mean PCDAI at T3: 5.7±3.8 in the EEN group and 12.7±13 in the CCS group, p=0.04; mean PCDAI at T4: 4.2±5.6 in the EEN group and 15.2±11.7 in the CCS group, p<0.001). After 2 years from diagnosis, 8/11 (73%) patients from the CCS group had at least one relapse, while in the EEN group the number of patients that experienced at least one relapse was only 16/33 (48.5%; p=0.147). In addition, 6/11 (54.5%) patients in CCS group needed to start immunomodulators, whilst in the EEN group a therapy with azathioprine or methotrexate has been started in 10/33 patients (30%; p=0.169). At the end of the follow-up period, 2/33 (6%) subjects in the EEN group and 2/11 (18%) children in the CCS group needed to start a therapy with infliximab (p=0.256).

Conclusion: This study confirms that EEN has the same effectiveness of CCS therapy in the induction of clinical remission, but with a significant better short and long-term outcome on inflammatory parameters and disease activity. In addition, EEN seems to be more effective in maintaining remission, and in reducing the need of immunomodulators and infliximab.

Is obesity due to precocious antibiotic therapy an iceberg phenomenon?

Luminita Dobrota¹, Mihai Leonida Neamtu²

¹Pediatric Clinic Hospital, Ceforaten, Sibiu, Romania
²Lucian Blaga University, Pediatric Clinic Hospital, Ceforaten, Sibiu, Romania

Objectives and study: Recent studies have shown that the broad-spectrum antibiotic therapy initiated within the first 2 years of life is linked with early onset obesity (younger than 5 years old). The process is due to gut microbiota alteration during its incomplete maturation (maturation appreciated around the age of 4). The interest of the study is amplified by “escalade” antibiotic therapy, as well by the increasing velocity of the obesity incidence in Romania. The objective is to evaluate the impact of precocious antibiotic therapy on small children weight (preschoolers).

Methods: The study group included subjects 3-7 years old, hospitalized between 01.01.2015-30.11.2015, for current conditions, known with proper lifestyle and diet, and complete medication history. Have been excluded those with family history of obesity, personal history of chronic medication (anabolics), chronic diseases (genetics, endocrine, neurologic ones, inclusively) which impact on weight control. Were studied the following parameters: weight and height on admission, the age at which the first broad-spectrum antibiotic were initiated, number of past antibiotic cures and the age at which antibiotics were administered, gut microbiota data (if any), metabolomics data – cholesterol, triglyceride (if any). BMI was calculated using 2000 CDC Growth Charts and was interpreted as overweight at or above the 85th percentile and below the 95th percentile for children of the same age and gender, and as obesity at or above the 95th percentile for children of the same age and gender.

Results: 546 subjects were observed. 108 (19.8 %) were obese (obese group) and 438 (80.2 %) had normal weight (control group). In obese group: 48 subjects were obese at 3 years old, 30 at 5 years old and 30 at 7 years old; 54 were females and 54 males; 6 (5.5 %) subjects never received antibiotics and 102 (94.5 %) received antibiotics in various cures: 18 subjects in the first years of life, 54 in the first 2 years and 30 in the first 3 or more years of life; 36 (35.2 %) subjects received a single cure of antibiotics and 66 (64.8 %) between 2-18 cures. The study groups were homogeneous in terms of gender (p 0.19).

In our study, “per se” antibiotic therapy does not seem to influence the weight until de age of 7 (p 0.17). More specifically and also contradictory, antibiotic therapy initiated in the first 2 years of life had a significant influence about weight around the age of 5 (p 0.04) and 7 (p 0.05), but no significance around the age of 3 (p 0.26). Unaccountable, antibiotic therapy initiated in the first year of life appears to greatly influence the weight only at age of 7 (p 0.000**).

“Per se” antibiotic multiple cures does not seem to influence the weight (p 0.15), but if these are initiated in the first year of life the influence becomes extremely significant (p 0.000**).

No data about gut microbiota composition and any other metabolomics, at all.

Conclusion: Precocious and multiplied cures of broad-spectrum antibiotics seem to have repercussions also on child weight, among other. The earlier antibiotic administration achieved, the obesity may persist more longer in time. The earlier and repeatedly antibiotic administration also achieved, the influence on child weight becomes extremely significant. The lack of biological data in our study (gut microbiota and metabolomics) proves that the link between precocious antibiotherapy and obesity is not well accounted.

Disclosure of interest: None Declared.
Growth assessment of preterm infants using detailed anthropometry

James Ashton¹, Mark Johnson², Jenny Pond², Philippa Crowley², Borislav Dimitrov³, Freya Pearson ², R Mark Beattie¹

¹Southampton Children's Hospital, Paediatric Gastroenterology, Southampton, United Kingdom
²University Hospital Southampton, Neonatal Medicine, Southampton, United Kingdom
³University of Southampton, Medical Statistics, Southampton, United Kingdom

Objectives and study: Preterm infants display slower ex-utero growth and altered body composition (lower fat-free mass, higher percentage body fat) compared to term counterparts; rendering them at risk of morbidity and mortality. Weight is known to fluctuate and does not represent accrual of lean mass or reflect changes in body composition. In older children mid-upper arm circumference (MUAC) is a validated measure of nutritional status (lean mass). This study aimed to investigate the utility of determination of growth using MUAC and mid-thigh circumference (MTC) in infants born below 30 weeks gestation.

Methods: Infants were recruited within 1 week of admission to the neonatal unit in Southampton. MUAC and MTC were measured in these infants at recruitment and at weekly intervals until discharge; each measurement was performed in triplicate on individual blank tapes to avoid bias (a mean value was calculated). All limbs were measured each week by the same 3 people. In addition weekly measurements of weight, length and head circumference were collected. Data were analysed by corrected gestational age; infants were added into the analysis at the week they were born and remained in the analysis (e.g. 23 week infants added 23 weeks CGA and included in 24 weeks CGA data when 1 week old etc.) and by unadjusted age (week of life). Statistical analysis was by SPSS v22.

Results: 46 infants have been recruited. Median duration of measurement was 7.5 weeks (1-19 weeks). Median gestational age at birth was 26 weeks (23-29 weeks).

Analysis of unadjusted data by curve estimation displayed a mean increase of 3.94mm/week for left MUAC (p=<0.0001), 3.92mm/week for right MUAC (p=<0.0001), 6.1mm/week for left MTC (p=<0.0001) and 6.3mm/week for right MTC (p=<0.0001). A significant change was also seen in MUAC and MTC when measured at weekly intervals using CGA data.

Unadjusted data were used to calculate coefficients of determination (R²) using a growth regression model for individual measures; left MUAC 0.992, right MUAC 0.989, left MTC 0.989 and right MTC 0.995. All 4 measures fitted a growth model as closely as weight (0.995), length (0.985) and head circumference (0.989).

There was high concordance between left and right MUAC/MTC; comparing unadjusted age data; mean left MUAC and right MUAC generated a correlation coefficient of 0.999 (Pearson) (p=<0.0001); left MTC and right MTC generated a correlation coefficient of 0.998 (Pearson) (p=<0.0001).

Correlation of mean weight and length with additional anthropometric measures demonstrated significant concordance for all measures. See table 1.
Table:

**Table 1** - Correlation of mean weight, length and head circumference with mean MUAC/MTC (unadjusted age) (Pearson Correlation)

<table>
<thead>
<tr>
<th>All significant at p=&lt;0.0001</th>
<th>Weight</th>
<th>Length</th>
<th>Head Circumference</th>
<th>Left MUAC</th>
<th>Right MUAC</th>
<th>Left MTC</th>
<th>Right MTC</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight</td>
<td>1</td>
<td>0.975</td>
<td>0.991</td>
<td>0.992</td>
<td>0.990</td>
<td>0.994</td>
<td>0.994</td>
</tr>
<tr>
<td>Length</td>
<td>0.975</td>
<td>1</td>
<td>0.989</td>
<td>0.987</td>
<td>0.982</td>
<td>0.987</td>
<td>0.988</td>
</tr>
<tr>
<td>Head Circumference</td>
<td>0.991</td>
<td>0.989</td>
<td>1</td>
<td>0.995</td>
<td>0.992</td>
<td>0.997</td>
<td>0.997</td>
</tr>
</tbody>
</table>

**Conclusion:** These data demonstrate the potential utility of MUAC and MTC as a measurement of growth in preterm infants and were accurately reproducible over time. These preliminary data show statistically significant correlation between currently used anthropometric measures and MUAC/MTC. Further study of more infants, combined with nutrient intake data, is vital to confirming MUAC/MTC as a useful and minimally invasive measure of growth and body composition in preterm infants.

**Disclosure of interest:**
None declared
A nutritional supplement beverage with and without probiotics during the third trimester of pregnancy and lactation show benefit on infant growth up to 12 months of age in the Philippines

Jojo Mantaring¹, Jalil Benyacoub², Raul Destura¹, Sophie Pecquet³, Karine Vidal², Sheri Volger ⁴, Valerie Guinto¹

¹Philippines General Hospital, Manila City, Philippines
²Nestle Research Center, Lausanne, Switzerland
³Nestlé Nutrition, R&d, Vevey, Switzerland
⁴Nestlé Nutrition, R&d, King of Prussia, United States

Objectives and study: Optimal nutrition during pregnancy and lactation plays a critical role in promoting positive maternal outcomes and appropriate infant growth and development. The timing and composition of maternal supplementation during critical periods of fetal and infant development may have an impact on short- and long-term growth parameters. The present study explored the effects of a maternal nutritional supplement beverage formulated with and without a probiotic mixture of Lactobacillus rhamnosus (CGMCC 1.3724) and Bifidobacterium lactis (CNCC I-3446) consumed during pregnancy and lactation on maternal health and fetal and infant growth.

Methods: Healthy women at the beginning of the third trimester of pregnancy who were willing to exclusively breastfeed for at least the first 2 months postpartum were recruited and enrolled in this randomized study conducted at the Community Hospital of Muntinlupa City, Philippines. A total of 233 women were randomized to the following groups: a daily nutritional supplement (S) 2 x 200 ml serving per day (140 kcal, 8 g protein, 21 g carbohydrate, 3.5 g fat including DHA) (n=78); the exact same supplement with probiotics (7x10⁸ cfu of B. lactis and 7x10⁸ cfu of L. rhamnosus per serving) (S pro) 2 x 200 ml serving per day (n=78); or no supplement (no-S), i.e., no additional kcal (n=77) during the third trimester of pregnancy and the first 8 weeks of lactation. Maternal health and morbidity was assessed monthly and at delivery; fetal in-utero development was measured with ultrasound between 24-28 weeks gestation and APGAR scores at birth; infant growth was measured at delivery, 2 weeks, and 1, 2, 3, 4 and 12 months.

Results: A total of 208 mothers and infants (male=109; female=99) were included in the analysis. Mean maternal weight gain in the third trimester and body mass index (BMI) at delivery were similar among groups. Infants were born at approximately 39 weeks gestation with no statistically significant differences between the S pro and S groups in mean birthweight, APGAR scores, anthropometrics, fetal biparietal diameter or abdominal circumference. Overall, there were no statistically significant differences between the S pro and S groups for infant growth parameters in the first year of life. Mean weight-for-age z-scores for all groups were below the WHO median value. However, at age 12 months, the combined S pro and S groups gained more weight (8.61 vs 8.97 kg, p=0.001) and height (73.4 vs. 74.2 cm, p=0.031) compared to the no-S group and had higher a weight-for-age z-score (-0.88 vs. -0.62, p=0.045). Maternal and infant morbidity were similar among groups.

Conclusion: Fetal growth and short-term infant growth parameters appeared similar between groups, regardless of supplementation. However, providing a nutritional supplement beverage during the last trimester of pregnancy and through the first 2 months of exclusive breastfeeding showed beneficial effects on infant growth at 12 months. Supplements were well tolerated. In addition, despite providing additional calories, supplementation did not result in excess maternal weight gain.

Disclosure of interest: This study was sponsored by Nestlé Nutrition. JB, SP, KV and SV are employees of Nestec SA.
Bone status in preterm infants: influences of maternal factors and nutritional regimens

Paola Gaio¹, Margherita Fantinato¹, Marco Daverio¹, Daniel Nardo¹, Valentina Favero¹, Marta Meneghelli¹, Francesca De Terlizzi², Giovanna Verlato¹

¹Dpt. of Woman and Child Health, University Hospital of Padua, Italy
²Igea. Laboratory of Clinical Biophysics, Carpi, Italy

Objectives and study: The goal of nutrition in preterm infants is to achieve the rate of growth of a normal fetus of the same gestational age (GA). Growth and bone mineralization occur mostly in the 3rd trimester. During pregnancy maternal nutrition and life style (sun exposure) could also influence fetal bone growth. Moreover extremely preterm infants are exposed to several postnatal risk factors such as prolonged parenteral nutrition (PN), long period of immobilization, fluid restriction and administration of steroids and diuretics. For these reasons preterms are at high risk of metabolic bone disease (MBD), with microarchitectural deterioration (osteopenia) and demineralisation (osteomalacia) of bone. A useful tool to analyze bone status is quantitative ultrasound (QUS). Our aim was to evaluate possible influences of maternal diet and an early aggressive PN on bone health in preterms and to search for useful markers of bone status.

Methods: We enrolled preterms weighing < 1250 g and in PN within 48 h of life, hospitalized in our NICU from May 2009 to January 2014. From May 2009 to December 2010 infants received later amino acids (AA) and lower energy intakes (group L: AA started on day 1-2 at 1.5-2 g/kg, advanced from 0.5-1 g/kg to 3.5-4 g/kg per day on day 4; maximum Non-Proteic Energy (NPE) 70 kcal/kg per day); from January 2011, as a result of a changing in our unit protocol, infants received earlier AA and higher energy intakes (group H: AA started on day 1 at 1.5-2 g/kg, advanced from 1 g/kg to 4 g/kg per day on day 4; NPE > 80 kcal/kg per day). We monitored patients from birth to 36 weeks (wk) of GA, through anthropometric, clinical and biochemical parameters. To assess bone status we performed QUS at birth, at day 21 and at 36 wk of GA and we tested the second metacarpus bone transmission time and metacarpus speed of sound (mc-BTT, mc-SOS). Independently, in the more recently enrolled patients (65) maternal nutritional intakes were evaluated by a specific food frequency questionnaire, data were elaborated with a dedicated software.

Results: We enrolled 244 patients (93 vs 151: group L and H). Evaluating bone status, we observed significantly higher value of mc-BTT at day 21 and 36 wk of GA in group H. Positive correlations were found between mc-BTT at day 21 and nutritional intakes (total protein intake in the 1st and 2nd wk of life, total energy intake in the 1st wk and in the 1st month of life, intravenous NPE in the 1st and 2nd wk of life). Searching for markers of bone status, we found that mc-BTT at day 21 was worse in patients with serum phosphate (P) on day 21 < 1.4 mmol/l, with urine calcium/creatinine ratio on day 21 ≥ 2 mol/mol and with mean total energy intake in the 1st wk of life <70 kcal/kg per day. Maternal vitamin D intake was lower than recommended, and positively correlated with basal ultrasound parameters (mc-SOS, r: 0.35, p=0.005).

Conclusion: An aggressive nutritional regimen improves bone status in preterm infants. Preterm newborns with energy intake in the 1st week of life < 70 kcal/kg/per day and P level < 1.4 mmol/l at day 21 have a worse bone status assessed by QUS at day 21 and at 36 weeks of GA. These indexes of growth and bone status positively correlated with QUS parameters until discharge, suggesting that improving growth early in life could influence later bone development. Maternal intakes could influence bone status of newborn: optimizing vitamin D levels during pregnancy should be recommended to improve bone health, particularly in high risk pregnancies.

Disclosure of interest: None Declared.
Extremely preterm infants experience hyperglycemia beyond the first days of life

Itay Zamir¹, Andreas Tornevi², Thomas Abrahamsson³, Fredrik Ahlsson⁴, Boubou Hallberg⁵, Ingrid Pupp⁶, Elisabeth Stoltz Sjöström, RD⁷, Magnus Domellöf¹

¹Pediatrics Unit, Department of Clinical Sciences, Umeå University, Umeå, Sweden
²Department of Public Health and Clinical Medicine, Division of Occupational and Environmental Medicine, Umeå University, Umeå, Sweden
³Division of Pediatrics, Department of Clinical and Experimental Medicine, Linköping University, Linköping, Sweden
⁴Department of Women’s and Children’s Health, Uppsala University, Uppsala, Sweden
⁵Department of Neonatology, Karolinska Institute, Stockholm, Sweden
⁶Department of Pediatrics, Institute of Clinical Sciences, Lund University, Lund, Sweden
⁷Department of Food and Nutrition, Umeå University, Umeå, Sweden

Objectives and study: Neonatal hyperglycemia is common among extremely preterm infants, but the research so far has focused mostly on its occurrence during the first week of life even though disturbances in glucose concentrations may be more long-lasting. Furthermore, there is no consensus regarding what constitutes normal values of glucose concentrations and there are no evidence-based guidelines for treatment of hyperglycemia in this population. This study aims to describe the occurrence of hyperglycemia in extremely preterm infants during the first month of life and evaluate how it is affected by enteral and parenteral nutrition.

Methods: Data from a population-based cohort of all infants born in Sweden at <27 weeks gestational age during a 3-year period 2004-2007 (the EXPRESS cohort) was used. Daily first, highest and lowest glucose measurements as well as nutritional intake data were retrospectively obtained from hospital records. We excluded infants who had major congenital malformations or chromosomal abnormalities, did not survive the first month of life, had more than 2 days without glucose measurements during the first week of life or more than 3 days without glucose measurements during either one of weeks 2 through 4.

Results: Mean (SD) gestational age and birth weight among included infants (n=194), were 24.8 (1.1) weeks and 702 (163) g, respectively. The prevalence of hyperglycemia (at least one blood glucose value > 10 mmol/L) on day 9 of life was 33% and decreased to 18% by day 28. Total and enteral carbohydrate intake significantly correlated with the highest daily plasma glucose (r=+0.17 and +0.11; p<0.001) but parenteral carbohydrate intake did not. However, a correlation with parenteral carbohydrate intake was observed when considering only days with parenteral fluid intake ≥75% (r=+0.11; p<0.001). Both gestational age and current weight at the day of glucose measurement correlated significantly with the highest daily plasma glucose (r=-0.30 for each; p<0.001).

Conclusion: Extremely preterm infants experience hyperglycemia well beyond the first week of life. High glucose infusion rates only partially account for the variance in glucose concentrations and only during the early period when most of the nutrition is given parenterally.

Disclosure of interest: None Declared.
Sialyllactose and galacto-oligosaccharides differentially modulate microbiota composition, intestinal epithelium gene expression, and dendritic cell development

Laurien Ulfman1, O. Perdijk2, P. van Baarlen3, M.H.C. Schoterman4, A. Nauta4, S. Brugman2, F. Schuren5, R.J. van Neerven6

1Frieslandcampina, Wageningen, Netherlands
2Wageningen University, Cell Biology and Immunology, Wageningen, Netherlands
3Wageningen University, Host Microbiome Interactomics, Wageningen, Netherlands
4Frieslandcampina, Amersfoort, Netherlands
5Tno, Zeist, Netherlands
6Wageningen University and Frieslandcampina, Cell Biology and Immunology, Wageningen and Amersfoort, Netherlands

Objectives and study: Human breast milk is unique for its wide variety and quantity of oligosaccharides. These human milk oligosaccharides (HMOs) can be divided into two different types: acidic oligosaccharides, and neutral oligosaccharides. The aim of the present study was to characterize the effects of two oligosaccharides, the acidic HMO sialyllactose (SL) and neutral galactooligosaccharides (GOS) on microbiota composition, intestinal epithelium gene expression, and dendritic cell development.

Methods: Pooled and pre-fermermented fecal samples from adults and infants were used as inoculum in batch culture vessels to study the effect of GOS or SL on microbiota composition on group level by QPCR, and short chain fatty acid (SCFA) production by HPLC. In addition IL-Chip analysis was performed to study the effects at species level. Further, the effects of SL and GOS on gene expression in Caco-2 intestinal epithelial cells was studied using Affymetrix microarrays. The effect of SL and GOS on dendritic cells was studied by differentiating human monocytes isolated from buffy coats with IL-4 and GM-CSF.

Results: GOS mainly promoted the growth and survival of Bifidobacteria, whilst SL primarily promoted the outgrowth of Bacteroides, and the levels of Bifidobacteria. These effects were most prominent in the batch cultures inoculated with adult fecal matter. SL and GOS induced different profiles of SCFA and lactate, with SL inducing higher propionate levels and GOS higher lactate levels. At species level SL but not GOS was shown to induce the growth of the anti-inflammatory bacteria Bacteroides fragilis, and Faecalibacterium prausnitzii in adult cultures, and Bacteroides fragilis and Bacteroides thetaiotaomicron in infant fecal cultures.

In human Caco-2 intestinal epithelial cells exposure to GOS induced pathways involved in regulation of cell cycle, intracellular signalling related to this, and related to cell proliferation and migration, as well as several aspects of metabolism. In this model no notable immune response-related pathways were modulated by GOS. In contrast, SL modulated pathways involved in cell cycle regulation, intracellular signalling, cell-cell contact and immunity. These data suggest that SL promotes intracellular signalling pathways that activate immune response and cell and tissue development and contributes to epithelial barrier strengthening.

On dendritic cells SL – but not GOS – was shown to induce a more tolerogenic phenotype of dendritic cells. The dendritic cells generated in the presence of SL produced lower levels of TNF-α and IL-12 compared to control DC and GOS-matured DC, but similar levels of IL-10. They also retained a more immature phenotype as evidence by lower expression levels of CD86 and increased expression of PD-L1 and CD80.

Conclusion: Overall this study shows that SL and GOS differentially influence microbiota composition, gene expression profiles in intestinal epithelial cells, and effects on DC maturation. These data support the notion that individual oligosaccharides may promote gastrointestinal immune homeostasis through different mechanisms.
Disclosure of interest:

The study was financed in part by FrieslandCampina. LU, MHCS, and RJJvN are employees of FrieslandCampina. OP and SB are financed by STW Open Technology Program (NWO).
Detection of bovine proteins in human milk and amniotic fluid using proteomics

Qi Bang Zhang, Judy Cundiff, Elizabeth McConnell, Carol Berseth, Sarah Maria, Robert McMahon, Shay Phillips, Christina Valentine, Beena Kamath-Rayne, Ardythe Morrow

1Mead Johnson Nutrition, Pediatric Nutrition Institute, Evansville, United States
2Mead Johnson Nutrition, Medical Affairs, Evansville, United States
3Cincinnati Children’s Hospital, Perinatal Institute, Cincinnati, United States

Objectives and study: Human milk (HM) and human amniotic fluid (HAF) have previously been thought to be “bovine–free”. However, mass-spectrometry (MS)-based proteomics have uncovered cow milk proteins (CMP) in human milk. It has been speculated that the presence of CMP may drive either tolerance or cow milk protein intolerance in early childhood. Further understanding of bovine proteins in both HM and HAF through proteomics may offer insights into the occurrence of allergies or development of tolerance in breastfed infants. Using MS-based proteomics, this study explores a possible mechanism of exposure of fetuses and infants to bovine proteins in human milk whey (HMW) and HAF through the mother-fetus/infant dyad.

Methods: This prospective analysis included preterm HM from 1 - 3 wks of lactation (n = 6) and HAF from 34 - 37 wks of gestation (n = 6), both collected by Cincinnati Children’s Hospital. Proteins were extracted and tryptically digested, followed by MS analysis and search against Uniprot database under human and bovine taxonomy. Peptides with association to both human and bovine organisms were excluded from comparison. An exponentially modified protein abundance index (emPAI) estimated relative intensities of proteins.

Results: A total of 36,882 human-specific and 3,044 bovine-specific peptides were characterized in HAF and assigned to 1,739 human and 267 bovine proteins, respectively. Analogously, 33,937 human-specific and 3,673 bovine-specific peptides were identified in HMW and assigned to 1,705 human and 330 bovine proteins, respectively. In this study, 124 bovine proteins including B-lactoglobulin were present in both HAF and HMW whereas alpha-s1-casein was specifically found in HAF and lactotransferrin only in HMW. Relative abundances of these three bovine proteins are at least four orders of magnitude lower than the most abundant human proteins in HAF and HM.

Conclusion: Using proteomic technology, bovine proteins beyond B-lactoglobulin and caseins were identified in human milk whey and/or human amniotic fluid. Future work is needed to validate the presence and composition of non-human proteins in HM/HAF through proteomic and complementary approaches and to examine correlation of these proteins with clinical outcomes such as cow milk protein intolerance.

Protective effects of Milk Fat Globule Membrane and L. fermentum CECT 5716 on gut functions and on T cells response in a newborn rat model

Tiphaine Vanhaecke1, Pierre-Antoine Grohard1, Philippe Aubert1, Julie Jaulin1, Julien Chevalier1, Tony Durand1, Hélène Boudin1, Philippe Naveilhan1, Amandine Ligneul2, Pascale le Ruyet2, Michel Neunlist3

1School of Medicine, University of Nantes, Inserm Umr 913, Nantes, France
2Lactalis R&d, Nutrition, Retiers, France
3University Hospital of Nantes, Inserm U913, Nantes, France

Objectives and study: Impaired intestinal functions together with an abnormal immune response is incriminated in the pathophysiology of gut disorders affecting infants and children, including the development of food allergies and colitis, associated with behavioral comorbidity. Recent studies highlighted the crucial role of intestinal microbiota, probiotics and MFGM lipids in promoting postnatal maturation and strengthening of the intestinal epithelial barrier (IEB). Therefore we characterized, in a rat pup model, the impact of oral administration of Lactobacillus fermentum CECT 5716 (LF) and Milk Fat Globule Membrane (MFGM) on gut functions, anxiety-related behavior and on spleen T cells cytokine production.

Methods: Healthy newborn rats received by gavage once a day, from postnatal day (PND) 7 to 24, a mixture of LF + MFGM (109 CFU and 150 mg/100g body weight/day, respectively), an isocaloric lipid solution or water (controls). Gut motility (total transit time (TTT)) and paracellular permeability were assessed in vivo at PND20. Anxiety-related behavior was studied at PND21 using the Elevated Plus Maze test. At the end of the supplementation period (PND24), representative Th1 and Th2 cytokines (IFNγ and IL-4, respectively) were assayed in the supernatant of CD3/CD28 activated spleen T cells. Morpho-anatomical data were collected (animal size and weight ; intestinal segments length). LF+MFGM effects on intestinal permeability were also characterized in response to maternal separation (MS) stress at PND10.

Results: Daily administration of LF+MFGM did not alter the morpho-anatomical parameters nor the anxiety-related behavior and associated plasmatic corticosterone levels compared to control group. In basal condition, LF+MFGM administration for 15 days induced a 41% decrease in paracellular permeability in vivo (n=18, p<0.01) together with a 12% decrease in TTT (n=18, p<0.0001) compared to controls. In addition, LF+MFGM administration for 17 days increased IFNγ/IL-4 ratios after anti-CD3/CD28 stimulation of isolated splenic cells (6<n<8, p<0.01). Furthermore, a 4 days administration of LF+MFGM prevented MS-induced increase in paracellular permeability in controls (+69%, n=6, p<0.001 ; +44%, n=6, p>0.05, respectively).

Conclusion: These results show the ability of Lactobacillus fermentum CECT 5716 and Milk Fat Globule Membrane combination, daily and orally administered, to strengthen the IEB not only in basal conditions but also in response to stress, in a rat model. Additionally, the administration of LF+MFGM could promote the maturation of the gut motility function. Furthermore, the co-administration of LF+MFGM shifted Th1/Th2 cytokine balance towards a Th1 response in isolated splenocytes. The use of these dietary compounds might therefore provide a new approach in the prevention and/or treatment of functional intestinal abnormalities and food allergies.

Disclosure of interest: The authors whose names are listed immediately below report a conflict with Lactalis : T. Vanhaecke, A. Ligneul, P. Le Ruyet.
High amino acid and energy intake influence the levels of zinc in the preterm neonate

Gianluca Terrin¹, Maria Di Chiara¹, Andrea Pietravalle¹, Sara Monaco¹, Francesca Cautilli¹, Etta D’Aquino¹, Mario De Curtis¹

¹“Sapienza” University of Rome, Department of Pediatrics, Rome, Italy

Objectives and study: Zinc is a key element for protein synthesis and growth in fetus and preterm newborn. Recent guidelines for preterm nutrition recommend an earlier and higher intake of amino acids (AA) and energy to avoid postnatal catabolism and approximate normal fetal growth. Adequate AA and energy supply, inducing anabolic state and promoting protein synthesis, may increase consumption of zinc in the preterm newborn. We performed a prospective observational study to assess the effect of nutrients intake on zinc levels and to investigate the relation between zinc and postnatal growth in preterm neonates.

Methods: We enrolled neonates with GA of 24-36 weeks consecutively observed in our Unit during a period of six months. We excluded subjects with major pre- and post-natal complications of preterm birth. Serum levels of zinc were measured at 0-24 h (T0), 7 (T1) and 28 (T2) days of life by atomic absorption spectroscopy. Data regarding demographic and clinical characteristics and nutritional intake were collected during the entire hospitalization period.

Results: We enrolled 54 neonates (birth weight 1786 g; gestational age 31 weeks; males 25.5 %). We observed a zinc deficiency in 50% and 87% of neonates, at T1 and T2, respectively. In subjects with zinc deficiency at T2, we observed an increased energy (103 vs 65 Kcal/Kg/day) and protein (3.4 vs 2.2 g/Kg/day) intake compared with neonates with normal serum value of zinc at the same time point. A significant correlation between energy (r=0.451, p=0.031) and protein (r=0.455, p=0.034) intake and serum zinc levels was also demonstrated at T2. In subjects with zinc deficiency, we observed a higher mean daily body weight increase in comparison with subjects with normal levels of zinc at T1.

Conclusion: Occurrence of zinc deficiency in preterm neonates was very high. Zinc status of preterm neonates was influenced by early protein and energy intake. Additional zinc supplementation could be considered when a high nutritional intake was provided to a premature baby.

Disclosure of interest: No conflict of interest.
Systematic review: early infant feeding practices and the risk of wheat allergy

Ania Chmielewska¹, Małgorzata Pieścik-Lech¹, Raanan Shamir², Hania Szażewska¹

¹Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
²Tel-Aviv University, Sackler Faculty of Medicine, Tel-Aviv, Israel

Objectives and study: In 2008, the European Society for Paediatric Gastroenterology, Hepatology and Nutrition recommended that complementary feeding should not be introduced before 17 weeks and not later than 26 weeks. For gluten, this was suggested specifically as potentially reducing risk of coeliac disease (CD), as well as type 1 diabetes and wheat allergy (WA). The recommendation was based on observational data. Recently, large interventional studies have shown that time of gluten introduction had no effect on the risk of developing CD during early childhood. Whether early feeding has an effect on WA risk needs further evaluation.

The objective was to systematically review the association of early infant feeding practices [breastfeeding (BF), timing of gluten/wheat introduction] and WA or elevated wheat-specific IgE concentration (wheat sensitization, WS).

Methods: The protocol for this systematic review was registered with PROSPERO (CRD42015023574). Up to June 2015, the Cochrane Library, MEDLINE, EMBASE, CINAHL, LILACS, Maternity and Infant Care, MEDLINE and Science Citation Index were search for studies of any design. The primary outcome measure was WA or presence of wheat-specific IgE.

Results: From 4491 publications yielded by search strategy, six studies (7550 participants) were included: one randomized controlled trial (RCT) and 5 observational studies. The majority (4 out of 6) were conference proceedings with only abstracts available. An attempt to obtain results from the authors was made. Breastfeeding: longer BF duration was associated with WA. BF compared to formula feeding did not affect rates of WS at age 15; exclusive BF for 6 months compared to 4 months reduced rates of WS at 1 year, but not at 5 years. BF at the time of gluten introduction did not have an effect on WS. Gluten introduction: risk for WS was higher when gluten was introduced > 7 months compared to earlier introduction. Timing of introduction of solids in general had no effect on rates of WS.

Conclusion: Prolonged breastfeeding might be associated with increased risk of WA. The risk of WS was not affected by breastfeeding at the time of gluten introduction. Delayed gluten introduction might increase risk for WS.

Disclosure of interest: None declared.
Synaptic maturation in newborn piglets is dependent on immunoglobulins

Kateryna Goncharova, Björn Weström, Liudmyla Lozinska, Nadiia Mosiichuk, Olena Prykhodko, Ester Arevalo Sureda, Jaroslaw Wolinski, Anna Socha-Banasiak, Stefan Pierzynowski

1Lund University, Biology, Lund, Sweden
2Vasyl Stefanyk Prycarpathian National University, Dept Biochemistry and Biotechnology, Ivano-Frankivsk, Ukraine
3Kiapn Polish Academy of Sciences, Dept Endocrinology, Jablonna, Poland
4Polish Mother’s Memorial Hospital Research Institute, Dept Gastroenterology, Allergology and Pediatrics, Lodz, Poland

Objectives and study: Piglets are born somewhat immunocompromised, without maternal passive immunity. The transfer of colostrum-derived immunoglobulins (Ig), across the gut mucosa into the blood circulation, occurs exclusively after birth. It has been shown that Ig which are absorbed can be transported into the cerebrospinal fluid (CSF), crossing the blood-brain barrier in a time-dependent manner (Harada et al., 2010). We have previously demonstrated that colostral Ig can affect neuronal migration and microgliogenesis (Pierzynowski et al., 2014) in neonatal pigs. The purpose of the present study was to investigate the effect of Ig intake on synaptic growth and maturation in the brain of neonatal pigs.

Methods: Newborn, un-suckled piglets were divided into 4 groups fed respective diets in amount 15 ml/kg b wt each 3 hours during first 12 hours: the 1st group was fed a lactose-based elemental diet (LED, n=3) via a stomach tube, the 2nd group was fed LED together with an intravenous umbilical infusion of purified swine serum Ig (IGV, n=3), the 3rd group was fed LED enriched with swine serum Ig (IGS, n=3), while the 4th group was fed with swine colostrum (Col, n=3). After 12 hours all piglets independently of group were further fed with LED up to 48 h and then sacrificed and the brain was dissected. Un-suckled newborn piglets (NB, n=3) and sow-reared piglets 48 h old (group S, n=3) were used as controls. The effects of the various diets on synaptic growth and maturation was monitored by analysis of synaptic proteins, identified by specific antibodies, and analyzed with a confocal microscope. Synaptophysin (major synaptic vesicle protein p38) was used as the main marker for synapse density, while synaptopodin, a protein associated with postsynaptic densities and dendritic spines, was used for estimation of synaptic maturation/function.

Results: Low levels of Ig were found in the CSF of piglets from groups IGV, Col and S, but not in the LED, IGS and NB groups. The total number of synapses increased by 50% after 48 h of feeding in groups IGV, Col, S, LED and IGS, compared to that of the NB group. With regards to synaptic maturation, the amount of synaptophysin-positive regions was significantly increased in piglets from groups IGV, Col and S, but not in the LED and IGS groups, as compared to the NB group. Moreover, the ratio between synaptophysin and synaptophysin-positive regions in groups IGV, Col and S, was close to 1,0 while in piglets from groups LED, IGS and NB it was around 0,5.

Conclusion: Newborn piglets totally devoid of maternal Ig provide an ideal model to study the impact of Ig on neonatal brain development. The piglets deprived of Ig revealed a reduction in postnatal synaptic maturation while the i.v infusion of Ig or absorption of colostrum Ig was found to stimulate synapse development. This may be of importance for brain development in preterm human neonates that are born with low immunoglobulin levels transferred in utero as compared to full term neonates.

Disclosure of interest: None Declared.
Lactobacillus rhamnosus GG derived soluble mediators modulate adaptive immunity in vitro

Irene S. Ludwig¹, Sarmauli Manurung², Eric A.F. Van Tol², Ruurd van der Zee¹, Tim T. Lambers², Femke Broere¹, Willem van Eden¹

¹Utrecht University, Department of Infectious Diseases and Immunology, Utrecht, Netherlands
²Mead Johnson Pediatric Nutrition Institute, Global Discovery, Nijmegen, Netherlands

Objectives and study: Probiotics and probiotic related nutritional interventions have been described to have beneficial effects on immune homeostasis and gut health. In previous studies, specific preparations of Lactobacillus rhamnosus GG (LGG) soluble mediators have been demonstrated to exert beneficial effects in preclinical models of allergic sensitization, bacterial infection, and intestinal barrier function. In the context of allergic diseases, differentiation of dendritic cells (DC) and their interactions with T cells are crucial for driving tolerogenic responses. In the current project we set out to evaluate whether these LGG soluble mediators can modulate DC differentiation and have an impact on prompting protective or tolerogenic T cell responses.

Methods: Monocytes were isolated from PBMC of healthy blood donors and cultured in the presence of GM-CSF, IL-4 and specific LGG soluble mediator preparations during 6 days to induce DC differentiation. Subsequently, these DCs were matured in the presence of TNF-alpha for 1 day, and analyzed for their phenotype and ability to induce autologous T cell activation and differentiation to model recall antigens (HA and TT). After 7 days of co-culture, T cells were analyzed for activation and differentiation by flow cytometry of intracellular cytokines (IFN-γ, IL-2), activation markers (CD25) and Foxp3 expression.

Results: LGG soluble mediators did not alter dendritic cell numbers or maturation status of DCs. However, these DCs did show improved capacity to induce a T cell response as shown by increased IL-2 and IFN-gamma producing T cell populations upon stimulation with recall antigens. These enhanced recall responses coincided with enhanced Foxp3 expression that was not observed when T cells were cultured in the presence of control treated DCs. In contrast, the number of activated T cells (determined by CD25 expression) was only slightly increased. Unconditioned bacterial culture medium subjected to the same processing steps as the LGG soluble mediator preparations did not affect any of the readouts.

Conclusion: This study reveals that LGG soluble mediators can influence adaptive immune responses as shown by the modulation of dendritic cell functionality. These mechanisms might contribute to the beneficial effects observed in preclinical models in vivo. Altogether, LGG derived soluble mediators may provide an alternative to live probiotics in case live bacteria may not be used because of health conditions.

Antibody-independent detection of bovine β-lactoglobulin derived peptides in human milk

Rita Nocerino¹, Gianluca Picariello², Pasquale Ferranti², Lorella Paparo¹, Annalisa Passariello¹, David C Dallas³, Randall C Robinson³, Daniela Barile³, Roberto Berni Canani⁴, Rosita Aitoro¹

¹University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
²Institute of Food Sciences, National Research Council (Cnr), Avellino, Italy
³University of California, Dpt. of Food Science and Technology, Davis, United States
⁴University of Naples “Federico II”, Department of Translational Medical Science, European Laboratory for the Investigation of Food Induced Diseases (Elfid) and Ceinge, Naples, Italy

Objectives and study: Data on the presence of mother’s diet-derived food allergens in breast milk are conflicting. In particular, the occurrence of cow’ milk proteins (CMP)-derived peptides is controversial, mainly due to the possible pitfalls of the immunochemical detection methods (antibody cross-reactivity between bovine and human milk proteins). Due to extensive gastro-intestinal processing of dietary proteins, the likelihood that CMP-derived peptides will occur in human milk is higher than for intact proteins. However, no attempt to detect peptides deriving from the mother’s diet in breast milk has been reported so far. The aim of the study was to evaluate the presence of CMP-derived immunogenic peptides in breast milk.

Methods: Using antibody independent techniques such as High Resolution Tandem Mass Spectrometry (HR-MS/MS) in double-blind assays we determined peptides from CMP in samples of mature breast milk collected from healthy lactating women (aged 21-42 years).

Results: 12 samples of mature breast milk were collected: 6 mothers on strict CMP-free diet (control) and 6 mothers on regular diet containing at least a cup of cow’s milk daily. We identified seven peptide fragments of minor CMP and two β-lactoglobulin (β-Lg)-derived peptides in breast milk from mothers (2 out 6 samples) who received a cup of bovine milk daily. The β-Lg fragments, namely β-Lg f(42-57) and β-Lg f(42-54), belong to an epitopic region of the protein and were not detected in milk from women on a strict milk/dairy-free diet (6 samples). Competitive ELISA and Western blot analyses failed to detect processed or intact β-Lg.

Conclusion: Human breast milk can contain immunologically active peptides deriving from the gastrointestinal processing of CMP. This finding also provides an indirect proof that immunological active peptides can be adsorbed and distributed at a systemic level. HR-MS/MS is required for a reliable identification of the peptides. In addition to the possible role in the sensitization of CMP allergic children, “processed” food allergens could be involved in “teaching” the newborn’s immune system, at its early developmental stages, to tolerate foreign antigens.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 717
N-eP-019

Dysbalanced polynsaturated fatty acids metabolism in cow milk allergy: new clues for pathogenesis understanding and dietary treatment in food allergy

Lorella Paparo, Rita Nocerino, Rosita Aitoro, Mario Capasso, Carlo Agostoni, Viviana Granata, Cinzia Pezzella, Antonio Amoruso, Roberto Berni Canani

1University of Naples "Federico II", Translational Medical Science, Naples, Italy
2University of Naples "Federico II", Ceinge Advanced Biotechnologies, Naples, Italy
3University of Milan, Clinical and Community Science, Milan, Italy
4University of Naples "Federico II", Translational Medical Science-Elfid-Ceinge Advanced Biotechnologies, Naples, Italy

Objectives and study. Preliminary evidences reported association between food allergy and dysbalanced polynsaturated fatty acids metabolism. We assessed the influence of crucial enzymatic activities in PUFAs metabolism, delta-5 (FADS1) and delta-6 (FADS2) desaturase, gene polymorphisms on n-6 and n-3 serum levels in children with IgE-mediated cow milk allergy (CMA).

Methods. A venous blood sample was collected from 100 children with sure diagnosis of CMA (64 male, all Caucasian, all no farm-living, median age 6.2, range 1-7 yrs) to determine plasma fatty acid profile by gas chromatography-mass spectrometry. Two variants of the FADS1-FADS2 gene cluster (rs174545 and rs498793, respectively) were tested by genotyping with TaqMan assay, performed on DNA extracted from peripheral blood mononuclear cells. 711 healthy subjects with similar demographic characteristics and no at risk for allergy were evaluated as controls.

Results. Children with IgE-mediated CMA showed significantly lower levels of linoleic acid (LA), eicopentaenoic acid (EPA), docoahexaenoic acid (DHA) and higher levels of arachidonic acid (ARA) compared to healthy controls. The frequency of heterozygotes for the rs174545 (FADS1 SNP) in children with CMA was 59.5%, compared to 42.2% in healthy controls (p<0.05). The heterozygous for the rs498793 (FADS2 SNP) showed a frequency of 68.8% compared with 8.72% in the control group (p<0.05). By an association analysis we observed that the heterozygous for the rs174545 showed lower levels of DHA (p=0.003) and the heterozygous for the rs498793 had a higher levels of ARA (p<0.05).

Conclusion. An increased rate in SNPs of FADS1 and FADS2 gene region has been observed in CMA children. This lead to a different conversion of n-3 and n-6 PUFAs catalysed by the delta5 and delta6 desaturase, respectively. These finding open the way to a better understanding of food allergy pathogenesis and dietary treatment.

Disclosure of interest: None declared
Growth of Infants Born to Obese Women: PREOBE Project

Liliana Ladino¹, Luz Garcia-Valdés ², Maria-Teresa Segura², Estefania Parejo-Laudicina², Maria-Teresa Miranda³, Cristina Campoy⁴

¹Institute of Research in Nutrition, Genetics and Metabolism ingm, El Bosque University, Bogota, Colombia
²Excellence Centre for Paediatric Research Euristikos, University of Granada, Granada, Spain
³Department of Biostatistics, Faculty of Medicine, University of Granada, Spain
⁴Department of Paediatrics, Faculty of Medicine, University of Granada, Spain

Objectives and study: We aimed to analyse the growth of infants born to obese women during the first 24 months of age based on infant feeding type in the first months of life.

Methods: The study was performed on 175 mother-child pairs participating in the PREOBE study (www.proyectopreobe.com, www.ClinicalTrials.gov NCT01634464). The study group was evaluated at infant ages of 3, 6, 12, 18 and 24 months of the infants as following World Health Organization growth standards. Infant feeding type at 3 months of age was classified into 3 groups: exclusive breastfeeding, infant formula feeding and mixed feeding. Anova-test with Bonferroni post-hoc correction was applied with SPSS software version 21.

Results: At 6 months of age the breastfed infants born to obese women showed lower z-scores for weight-for-length (-1.38+/-.79) and Body-Mass-Index (BMI) (-1.49+/-.78) than breastfed infants born to normal women (-0.04+/-.78 and -0.14+/-.78 respectively), both comparisons with p=0.01. Similarly, the z-score for middle-upper-arm-circumference in breastfed infants born to obese women was lower (-0.85+/-.74) than breastfed infants born to normal women (0.62+/-.82) p=0.00. Finally, infants born to obese women fed with infant formula showed a similar z-score for BMI (-0.59+/-.74) to breastfed infants born to normal women (-0.14+/-.78) p>0.05. These differences did not remain to 24 months of age.

Conclusion: Infants born to obese women fed with infant formula and breastfed infants born to normal women, show a similar BMI at 6 months of age, although this difference is short lived. Future studies are needed to investigate the growth of infants born to obese based on infant feeding type received.

Disclosure of interest: Only Ladino L has a conflict having received a research fellowship from Nestlé Nutrition Institute. * This study has been supported by the Andalusian Government. Economy, Science and Innovation Ministry (PREOBE Excellence Project Ref. P06-CTS-02341).
Attitudes and practices of coaches concerning rapid weight loss in competitive judo and taekwondo athletes

Ben-El Berkovich¹, Aliza Stark¹, Alon Eliakim², Dan Nemet², Tali Sinai¹

¹The Hebrew University of Jerusalem, School of Nutritional Sciences, Rehovot, Israel
²Meir Medical Center, Child Health and Sports Center, Kfar-Saba, Israel

Objectives and study: Many adolescents participate in weight category sports. Fasting, skipping meals and dehydration are common methods of rapid weight loss (RWL) used prior to competition. This study examines coaches’ attitudes and practices concerning RWL among Israeli judo and taekwondo athletes.

Methods: A convenience sample of coaches and instructors (n=68) completed structured questionnaires.

Results: Participants were on average ~34 years old, 85% male, 59% authorized coaches with 71% reporting 20+ years in the field and 68% having 10+ years of teaching experience. The majority (90%) reported that they usually guided their athletes through the weight loss process. Interventions for weight loss began at 12.7±1.9 years and average reduction of 1.5±0.7 kg. Although the majority of the participants recommended that their athletes lose weight gradually (92%), in practice, methods used included dehydration and/or increased physical activity (80.3%), sweat suits (50.8%), restricted fluid intake (39.3%), training in heated rooms (27%) and sauna (26.2%). Some coaches (28%) indicated recommending (at least once) weight loss by spitting (27.8%) or using laxatives, diuretics, diet pills or vomiting (21.3%).

Conclusion: Coaches and instructors often encourage athletes to cut weight before competition. The methods recommended are potentially harmful with significant health risks including compromised nutritional status, diminished physical performance and impaired growth and development. This is of particular concern in young athletes. Enhancing knowledge and awareness for coaches, athletes and parents regarding potential dangers is critical for reducing the magnitude and misuse of RWL methods.

Disclosure of interest: None Declared
Visual evoked potentials in offspring born to mothers with overweight, obesity and gestational diabetes

Francisco J Torres-Espinola¹, Staffan Berglund², Miguel Pérez-García³, Andrés Catena³, Cristina Campoy¹

¹University of Granada, Centre of Excellence for Paediatric Research Euristikos, Granada, Spain
²Umeå University, Department of Clinical Sciences, Pediatrics, Umeå, Sweden
³University of Granada, Mind, Brain and Behaviour International Research Centre (Cimcyc), Granada, Spain

Objectives and study: Obesity, overweight, and gestational diabetes (GD) during pregnancy may negatively affect neurodevelopment in the offspring. However, the mechanisms are unclear and objective measures of neurodevelopment in infancy are scarce. We hypothesized that these maternal metabolic pathologies negatively affect the cortical visual evoked potentials (cVEPs), a proxy for neuronal maturity.

Methods: We included 331 pregnant women stratified into four groups; normal weight (controls), overweight, obesity, and GD. In a subsample of the offspring, we assessed the P100 wave from cVEPs at 3 months (n=157) and at 18 months (n=136). At 18 months, we also evaluated the Bayley III Scales of neurodevelopment and its correlation to cVEP.

Results: At 3 and 18 months of age, offspring born to overweight and obese mothers did not differ in cVEPs compared to controls. However, infants born to GD mothers showed at 18 months, longer latencies when measured at 1 degree, 15 min, and 30 min of arc respectively. The correlations at 30 min of arc remained significant after confounder adjustment (121.0 vs. 112.6 ms, p=0.007). In the overall cohort a wave latency at 3 months above the 75th percentile correlated significantly to a lower cognitive scores at 18 months and an amplitude at 18 months above the 50th percentile correlated significantly to higher cognitive scores.

Conclusion: Infants born to mothers with GD have prolonged latencies of visual evoked potentials, suggesting non-optimal neurophysiologic development. The finding is further relevant considering that the latencies and amplitudes of cVEPs are correlated to cognitive development.

Disclosure of interest: None Declared.
**NUTRITION: Nutrition and health outcomes**

N-eP-023

**Antidiarrhoeal activity of milk derived compounds with enkephalinase inhibitory activity in a castor oil-induced diarrhoea in rats.**

Alba Garcia Just\(^1\), Blanca Grases Pintó\(^1\), Marc Andreu Garcia Cruz\(^2\), Joaquin Puigjaner Riba\(^3\), Maria Rodriguez-Palmero\(^3\), Montserrat Rivero Urgell\(^2\), Margarida Castell\(^1\), Francisco José Pérez Cano\(^1\), Angels Franch\(^1\)

\(^1\)University of Barcelona, Department of Physiology, Faculty of Pharmacy, Barcelona, Spain
\(^2\)Laboratorios Ordesa, Barcelona, Spain
\(^3\)Laboratorios Ordesa, Research Department, Sant Boi de Llobregat, Barcelona, Spain

**Objectives and study:** Acute diarrhoea is one of the most common causes of morbidity and mortality in children worldwide. Research in this field has focused on finding enkephalinase inhibitors in order to reduce the loss of water and electrolytes. We have developed a skimmed bovine milk hydrolysate (H1) with enkephalinase inhibitory activity and we have also identified a bioactive peptide (P1) responsible for part of its activity. The aim of this study was to establish the effect of both milk derived compounds on acute diarrhoea and intestinal transit in rat models.

**Methods:** The study of the antidiarrhoeal activity involved Wistar rats distributed in 5 groups which were diarrhoea-induced by oral administration of 1.5 mL of castor oil. A group did not receive any treatment, being the reference diarrhoea group (RD), two others received the dietary intervention with the milk derived compounds H1 (8.5 g/kg) and P1 (0.8 g/kg) 1 h prior to diarrhoea induction. A positive control group using the drug racecadotril and a negative control group receiving a non-hydrolysed skimmed bovine milk were also used. The diarrhoea process was monitored through the evaluation of the faecal outputs obtained every 60 min during the first 8 h post-induction (PI). The presence of diarrhoea and its severity was quantified by the faecal specimen in basis of its colour, consistency and volume. In a second study, the influence of H1 and P1 on intestinal transit was assessed in healthy rats. The animals received the above dietary interventions, but in this case using loperamide as a positive control, 30 min prior the oral administration of the charcoal suspension. After 20 min, intestinal transit was measured.

**Results:** The administration of castor oil to the RD group led to a fast diarrhoea apparition (2-3 h PI) and high incidence (90% at 4 h PI) that remained until the end of the study. The severity of the process was the highest when compared to the rest of the groups. The pretreatment with both H1 and P1 delayed the beginning of the diarrhoeic process up to about 7 h and 9 h PI, respectively (p<0.01 vs. RD). H1 also reduced the diarrhoea incidence during the 2-5 h PI as well as the severity during the first 8 h PI (p<0.05 vs RD). P1 completely inhibited the development of diarrhoea during the first 4 h PI (0% of incidence) and diminished the diarrhoea incidence during the 5-7 h PI (50%; p<0.05 vs. RD). P1 was also able to markedly reduce the diarrhoea severity, especially during the first 8 h PI (p<0.01 vs. RD). The protective effects of H1 and P1 were comparable with those found after racecadotril administration. In contrast, the non-hydrolysed milk powder did not have any effect on diarrhoea prevention. Regarding the second study, none of the milk compounds studied modified intestinal transit, in contrast to loperamide which caused inhibition (37%) of this variable.

**Conclusion:** These preclinical data demonstrate that these bioactive milk derived compounds, hydrolysate H1 and peptide P1, show strong antidiarrhoeal activity without affecting intestinal transit. Therefore, they can be suggested as potential agents in this very common disorder in the infant population.

**Disclosure of interest:** Garcia-Just A: None Declared, Grases-Pintó B: None Declared, Garcia-Cruz MA Conflict with: Laboratorios Ordesa, Puigjaner J Conflict with: Laboratorios Ordesa, Rodriguez-Palmero M Conflict with: Laboratorios Ordesa, Rivero M Conflict with: Laboratorios Ordesa, Castell M: None Declared, Pérez-Cano FJ: None Declared, Franch A: None Declared
Nutrition and health outcomes

Rice protein hydrolysate and probiotic bifidobacterium breve combined with omega-3 fatty acids prevent weight gain and associated metabolic changes in a porcine model of prepuberal obesity

José C Serrano¹, Anna Cassañé¹, Maria Font-Fornols², Joaquin Puigjaner Riba³, Jose Antonio Moreno³, María Rodríguez-Palmero³, Jesús Jiménez³, Raquel Quintanilla², Lluís Arola⁴, Manuel Portero-Otin⁵, Joan Tibau⁶

¹Nutren-Nutrigenomics, Irblleida, Lleida, Spain
²Irta, Monells, Girona, Spain
³Laboratorios Ordesa, Research Department, Sant Boi de Llobregat, Barcelona, Spain
⁴Ctns, Centre Tecnològic de Nutrició i Salut, Reus, Spain
⁵Institut de Recerca Biomèdica de Lleida, Medicina Experimental, Lleida, Spain
⁶Irta, Animal Breeding, Monells, Girona, Spain

Objectives and study: Obesity during the transition to puberty is linked to increased cardiometabolic risk in adulthood. In a previous study in rodents fed western diet, we showed that a combination of rice protein hydrolysate and a probiotic (Bifidobacterium breve) decreased weight gain in comparison with the control group, whereas individual ingredients did not (unpublished data). Taking profit from the physiological similarities of human and porcine metabolisms, in the present work we studied the metabolic effect of a western-type diet supplemented with these bioactive ingredients compared to a standard diet in a porcine model of prepuberal obesity.

Methods: We fed 42 female littermates from 12 litters of a high intramuscular fat Duroc line ad libitum with 4 different diets from 60 to 130 days of age (equivalent to humans at 8-12 years old) at IRTA Pig Experimental Station. Diets used were a Standard diet (SD1): 2480 Kcal/kg and 5% of fat; Western diet (WD2): 3680 Kcal/kg and 12% fat; Western diet (WD3) with 50% of protein as rice protein hydrolysate and supplemented with the probiotic B. breve (5x10¹⁰ ufc/day); Western diet (WD4) with the same composition as WD3 and containing 2% omega-3 fatty acids. Daily consumption and weekly weight were individually measured. Image analysis and blood biomarkers of fat tissue deposition were evaluated by computerized tomography and biochemistry respectively.

Results: Weight gain in WD2 fed animals was higher compared with SD1 fed group (p<0.01). Interestingly, despite similar calorie intake, weight gain was significantly attenuated in WD3 and WD4 (p<0.007 ANOVA, adjusted for false discovery rate (FDR)=0.01). Though calorie intake was higher in all western diet groups (p=5.73 E-7, FDR 4.01 E-6), rate of growth (weight gain adjusted for caloric intake) was significantly minor in the WD3 and WD4 groups (p=1.15 E-7, FDR 1.21 E-6). WD2 intake led to an increase of LDL cholesterol and it was significantly decreased in the WD4 group (p=0.01, FDR p=0.03). WD4 also diminished plasma triacylglycerol levels in comparison with WD2 (p<0.05). Interestingly, multivariate analyses showed that rate of growth was the variable with highest projection importance (VIP score 2.5) in partial-least discriminant analyses (65% accuracy with 3 components) followed by amount of subcutaneous fat, HDL cholesterol and glucose (VIP scores 1.8, 1.6 and 1.5, respectively). Considering all the individuals LDL cholesterol correlated significantly with pelvic renal fat amount, representing a visceral fat depot (Spearman correlation coefficient: 0.37, p<0.013), as well as with total fat amount (coefficient 0.37, p<0.016), plasma triacylglycerol concentration (coefficient 0.36, p<0.017) but not with subcutaneous fat amount (p=0.09). This is in line with data in humans, showing that metabolic consequences of fat partly depend on the anatomical location.

Conclusion: Porcine models, even those selected for fat accumulation, show hypercholesterolemia and other metabolic disarrangements after intake of a high-calorie, high-fat diet. The use of a diet containing rice protein hydrolysate, the probiotic B. breve and omega-3 fatty acids prevented excessive weight gain and dyslipidemic alterations associated with obesity in this model.

Disclosure of interest: Joaquin Puigjaner, José A. Moreno, María Rodríguez-Palmero and Jesús Jiménez are employees of the company Laboratorios Ordesa. This study was funded by Laboratorios Ordesa and CDTI.
**NUTRITION: Nutrition and health outcomes**

N-eP-025

**Nutritional and antibiotic intervention during lactation attenuates development of offspring measured by novel developmental score for mice, the “mouse-D-score”**.

Joline Attema¹, Christa De Ruiter¹, Nanda Keijzer¹, Marry Barrett-Bergshoeff¹, Stef van Buuren², Wim van Hartingsveld³, Robert Kleemann¹, Peter Wielinga¹

¹Tno, Metabolic Health Research, Leiden, Netherlands
²Tno, Child Health, Leiden, Netherlands
³Tno, Healthy Living, Zeist, Netherlands

**Objectives and study:** Worldwide, awareness is growing that the first 1,000 days spanning a woman’s pregnancy until her child’s 2nd birthday is a crucial period for the health programming of the child for the rest of his/her life. Hallmarks of early-life development can be monitored using the “D-score”, a composite measure of multiple developmental items (S van Buuren, Stat Methods Med Res. 2014). To study the effects of nutritional interventions during this critical period, translational preclinical models are needed. Here we present the “mouse-D-score” to monitor mice during the first three weeks of their life, and study the effects of (nutritional) interventions during pregnancy and lactation on the offspring.

**Methods:** In a first study we developed the mouse-D-score algorithm. In a second study, the effects of interventions during lactation were analysed using the mouse-D-score. In the first experiment, ten litters of heterozygously bred ApoE*3Leiden (E3L) mice, containing two male E3L, two female E3L, two male WT and two female WT, were studied for their development using thirteen items of development; negative geotaxis, cliff aversion, rooting, pina unfolding, lower incisor eruption, hair growth, surface righting, forelimb grasp, open field, air righting, auditory startle, ear twitching and eye opening. These scores together were combined into a “mouse-D-score”. In the second experiment, fifteen litters of six homozygously bred LDLr/-.Leiden mice (three female and three male) were used and randomized in three groups. The mothers of the first groups received regular chow, the mothers in the second groups received an antibiotic treatment via drinking water between day 3 and 8, and the mothers of the third group received chow supplemented with butyrate.

**Results:** In the first study, we observed that the development of male mice was significantly faster than in female mice. In particular, the items negative geotaxis, cliff aversion, rooting, surface righting and forelimb grasp were passed earlier by males than by females. The development of WT was faster than the development of E3L mice, in particular forelimb grasp and air righting. Both antibiotic treatment and nutritional intervention by butyrate resulted in transiently decreased development rate compared to chow control. This was observed in multiple items of the mouse-D-score.

**Conclusion:** The mouse-D-score is a composite score of multiple developmental items during the first three weeks of life in mice. Using this score in different mouse lines we have shown that female mice show a different development rate than male mice, that genotype influences development rate and that this development can be modified by nutritional interventions on the mothers. This model may be used to study the effects of novel nutritional interventions on early life development.

**Disclosure of interest:** None Declared.
Effectiveness of a primary prevention program of overweight in 0-3 year old children, the BBOFT+ study; a cluster randomized trial.

Vlasblom Eline¹, Monique L’Hoir¹, van Grieken Amy², Raat Hein², Boere-Boonekamp Magda³

¹TNO, Child Health, Leiden, Netherlands
²Erasmus MC, Public Health, Rotterdam, Netherlands
³Twente University, Health Technology and Service Research, Enschede, Netherlands

Objectives and study: Prevention of overweight and obesity during early childhood is more promising than prevention during childhood or adolescence. BBOFT+ is an early prevention Youth Healthcare (YHC) program that aims to promote breastfeeding, physical activity, daily breakfast, sufficient sleep, and to decrease sugar sweetened beverage intake and screen (TV and computer) time by increasing parenting skills. The aim of this study was to evaluate the effectiveness of BBOFT+ compared to Care as Usual (CAU).

Methods: We conducted a cluster randomized controlled trial. Parents of newborn infants were invited to participate. Measurements were assessed after birth (2-4 weeks T0), 6 months (T1), 13 months (T2) and 36 months (T3). Parents received advice on healthy behaviors and parenting during all regular youth healthcare visits. Primary outcomes were BMI standard deviation scores, breastfeeding, daily breakfast, daily outdoor activity, sleep duration, sugar sweetened beverages and screen time. Secondary outcomes were parenting styles and practices.

Results: In total 901 children were included in the BBOFT+ group and 1094 in the CAU group. No significant differences were found on BMI standard deviation scores and daily breakfast (yes/no) between the two groups at any assessment moment. At 36 months, overweight/obesity percentages were < 5% in both groups. In the BBOFT+ compared to the CAU group, after correction for confounders, the children at 6 months: drank sugared drinks less often (OR 0.78 (CI 0.62-0.97), went outside less often (OR 0.79 (CI 0.63-0.98), at 13 months: had received breastfeeding more often 6 months or longer (β 1.324 (CI 1.04-1.69), at 36 months: used less often TV/pc (≥1 hour per day (vs. <1 hour) on weekdays and in the weekend (OR 0.65 (CI 0.53-0.87) and OR 0.68 (CI 0.53 - 0.87), went outside daily more often (OR 1.44 (CI 1.098 - 1.91) and parents more often had a controlling parenting style (β 0.07 (CI 0.01 - 0.12).

Conclusion: A primary prevention program that focuses on enhancing parenting skills related to healthy behaviors of children 0-3 years old had some advantages (less screen time, physically more active and a more controlling parenting style) over CAU, but not on BMI standard deviation scores. The YHC in the Netherlands is of high quality and at 36 months in both groups overweight/obesity percentages < 5%.

Disclosure of interest: “None Declared”.
Extensively hydrolyzed casein formula containing L. rhamnosus GG prevents the occurrence of other allergic manifestations in children with cow’s milk allergy: 3-year randomized controlled trial

Roberto Berni Canani 1, Giorgio Bedogni 2, Margherita Di Costanzo 3, Antonio Amoroso 3, Carmen Di Scala 3, Linda Cosenza 3, Viviana Granata 3, Rita Nocerino 3

1 University of Naples “Federico II”, Department of Translational Medical Science, European Laboratory for the Investigation of Food-Induced Diseases and Ceinge, Naples, Italy
2 Clinical Epidemiology Unit, Liver Research Center, Basovizza-Trieste, Italy
3 University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy

Objectives and study: Children with cow’s milk allergy (CMA) have an increased risk to develop other allergic manifestations. We performed a randomized controlled trial (RCT) to test whether the early administration of an extensively hydrolyzed casein formula containing L. rhamnosus GG (LGG) can reduce the 3-year incidence of other allergic manifestations in CMA children.

Methods: A parallel-arm RCT was performed in children aged 1 to 12 months with IgE-mediated CMA. Patients were allocated to one of two groups of dietary interventions: EHCF (Nutramigen®, Mead Johnson, Evansville, USA) and EHCF+LGG (Nutramigen LGG®, Mead Johnson, Evansville, USA). All subjects were evaluated during a 36 months follow-up. Other allergic manifestations (atopic eczema, allergic urticaria, asthma and oculorhinitis) were diagnosed by experienced team unaware on group assignment according to standard criteria. Tolerance acquisition was evaluated every 12 months by the result of oral challenge.

Results: 220 subjects (147 male, 67%) with a mean (SD) age of 5.7 (3) months were randomized, 110 to EHCF and 110 to EHCF+LGG. Binomial regression using intention-to-treat analysis revealed that the absolute risk difference (ARD) for the occurrence of at least one allergic manifestation over 36 months was -0.22 (95%CI: -0.35% to -9%, p<0.001) for EHCF+LGG vs. EHCF. The ARD for the occurrence of atopic eczema was -0.13 (95%CI: -0.25% to -1%, p<0.05), -0.14 (95%CI: -0.25% to -2%, p<0.001) for allergic urticaria, -0.11 (95%CI: -0.22% to 0%, p>0.05) for asthma, and -0.17 (95%CI: -0.29% to -6%, p<0.01) for oculorhinitis in EHCF+LGG vs. EHCF group. Binomial regression for repeated measures using per-protocol-analysis with Bonferroni’s correction for 3 comparisons (contrasts) revealed that the ARD for the acquisition of cow’s milk tolerance was 0.20 (95%CI 0.05 to 0.35, p<0.01) at 12 months, 0.24 (95%CI 0.08 to 0.41, p<0.01 at 24 months and 0.27 at 36 months (95%CI 0.11 to 0.43, p<0.001) for the EHCF+LGG vs. the EHCF group.

Conclusion: Compared to EHCF, EHCF+LGG reduces the incidence of other allergic manifestations in children with IgE-mediated CMA. Moreover, the use of this hypoallergenic formula increases the rate of tolerance acquisition at 12, 24 and 36 months.

Disclosure of interest: This work was supported in part by an unrestricted grant from Mead Johnson Nutritionals.
Objectives and study: Interleukin-4 (IL-4) has a pivotal role in Th2 response. Tolerance acquisition in children with IgE-mediated cow’s milk allergy (CMA) is characterized by a different IL-4 DNA methylation pattern. We comparatively investigated the effect of two different dietary interventions on this epigenetic mechanism in children with IgE-mediated CMA.

Methods: Randomized, prospective study on naive IgE-mediated CMA children assigned to two groups of dietary intervention: 1. extensively hydrolyzed casein formula with the probiotic L.rhamnosus GG; 2. soy formula. DNA methylation of CpGs in the promoter region from peripheral blood mononuclear cells and respective serum concentration of IL-4 were assessed at baseline and after 6 months of exclusion diet.

Results: 16 children (10 male, aged 6-12 months) were enrolled: 8 in Group 1 and 8 in Group 2. Baseline DNA methylation profiles and serum levels of IL4 were similar in the 2 study groups. After 6 months of dietary treatment children receiving extensively hydrolyzed casein formula with L.rhamnosus GG showed significant higher DNA methylation rate and lower serum level rate of IL-4 if compared with patients treated with soy formula (p<0.05).

Conclusion: Dietary treatment with extensively hydrolyzed casein formula with L.rhamnosus GG induces a more pronounced epigenetic effect on IL-4 leading to decreased production of this cytokine. Dietary influence on epigenetic mechanisms might represents an innovative approach to target the development of oral tolerance.

Disclosure of interest: The study was supported by an unrestricted grant from Mead Johnson Nutrition, Evansville IN, USA devolved to CEINGE-Advanced Biotechnologies, University of Naples “Federico II” Naples, Italy.
Effect of different hydrolyzed formulas and soy formula on tolerance acquisition in children with cow’s milk allergy

Enza D’Auria\textsuperscript{1}, Benedetta Pietra\textsuperscript{2}, Marzia Mandelli\textsuperscript{2}, Giovanni Radaelli\textsuperscript{2}, Elvira Verduci\textsuperscript{2}, Giuseppe Banderali\textsuperscript{2}

\textsuperscript{1}San Paolo Hospital, Pediatrics, Milan, Italy
\textsuperscript{2}San Paolo Hospital-University of Milan, Department of Pediatrics-Department of Health Science, Milan, Italy

Objectives and study: To prospectively evaluate the effects of different hydrolyzed formulas vs soy formula on the rate of acquisition of tolerance in infants with cow’s milk allergy (CMA). Otherwise healthy infants with confirmed CMA were considered eligible for the study entry. Infants that would required an amino-acid based formula as first-line choice were excluded. One hundred forty infants, admitted at our Pediatric Department, Unit of Allergy, from January 2008 to December 2009 were included.

Methods: All infants were randomly assigned at six months of age or more to 4 different formulas (hydrolyzed casein formula ([eHCF], n = 35), extensively hydrolyzed whey formula (eHWF, n =35), hydrolyzed rice formula (HRF, n = 35) and soy formula (SF, n = 35) and prospectively evaluated. The study follow-up was 65 months. 28 subjects dropped out of the study. The acquisition of tolerance by oral challenge was periodically assessed every 12 months. Chi-square test or Fisher exact test were used for comparison among groups. The significance level was 0.05.

Results: One hundred twelve children (63 males, 56%; 49 females, 44%) completed the 65 months of follow-up and were distributed in the four groups as following: 33 SF (29.4%), 25 eHWF (22%) 25 eHCF (22%), 29 HRF (26%). Ninety two children successfully overcame the oral provocation test during the follow-up period. The median age of tolerance acquisition was 43.05 months (median 36; minimum 13, maximum 98; SD 23.19).

The median age at which tolerance was reached and the duration of the dietetic treatment with the formula was significantly different in the four groups (p = 0.004 and p = 0.003 respectively). The comparison among different formulas by a post hoc analysis showed that infants fed with both cow’s milk (CM) hydrolysed formula reached tolerance faster (eHWF: median age tolerance acquisition 26.88 months and diet treatment 19.55 months; eHCF: 30.6 months and 22.9 respectively) than those fed with SF (eHWF vs SF, eHCF vs SF; p = 0.002 and p = 0.004 respectively). Neither difference was observed between the CM hydrolysed (p = 0.683) nor between HRF vs SF (p = 0.105). Infants fed with eHF showed a trend towards a faster tolerance acquisition than RHF, without reaching the significance level (p = 0.075).

Conclusion: Infants with CMA fed with CM extensively hydrolyzed formulas reach tolerance faster than infants fed with vegetable-based formulas, probably due to the tolerogenic effect of residual CM peptides.

Disclosure of interest: None Declared
Pediatric intestinal failure patients dependent on parenteral nutrition are at risk of biochemical essential fatty acid deficiency

Josefine Paulaharju¹, Riikka Gunnar², Mirka Lumia³, Laura Merras-Salmio², Mikko Pakarinen⁴

¹Helsinki University Children’s Hospital, Dept. of Pediatric Gastroenterology, Helsinki, Finland
²Helsinki University Children’s Hospital, Dept. of Pediatric Gastroenterology, Pediatric Liver and Gut Research Group, Helsinki, Finland
³Helsinki University Children’s Hospital, Dept. of Neonatology, Helsinki, Finland
⁴Helsinki University Children’s Hospital, Dept. of Pediatric Surgery, Pediatric Liver and Gut Research Group, Helsinki, Finland

Objectives and study: Pediatric Intestinal Failure (IF) patients are at risk to develop essential fatty acid (EFA) deficiency because of the impaired enteral absorption of fatty acids from long-chain triglycerides and the modern parenteral lipid restriction employed to alleviate the IF associated liver disease (IFALD). Since EFAs are of major importance for CNS development, their deficiency may lead to neurodevelopmental problems, even in the absence of clinical symptoms.

Methods: We analyzed serum fatty acid fractions (FA-FR) in pediatric IF patients attending our IF clinic. We identified altogether 44 FA-FR analyses in 40 patients taken either during predominantly parenteral (> 50% of daily calories) nutrition (PN-group, n=24) or on full enteral nutrition (EN-group, n=20). In 4 patients FA-FR analyses were available in both groups. Remaining intestinal anatomy was recorded according to chart review. Median ages were 2.9 and 4.9 years, respectively. 77.5% of patients had short bowel syndrome, with average age-adjusted remaining small bowel at 26%. Dysmotility disorder was diagnosed in 22.5%.

Results: Results from FA-FR analyses are depicted in the table. Most importantly, in the PN group EFA fraction of linoleic acid was significantly low. Mead acid was comparable in both groups, whereas trien:tetraen ratios were elevated in the PN group, indicating paucity of EFAs. Arachidonic acid and α-linoleic acid fractions were smaller in the PN group, but within healthy individual ranges reported in literature. Eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) fractions were increased in the PN group, with EPA fractions clearly higher than those in healthy individuals. In the EN group trien:tetraen ratios correlated with remaining ileal length (r= -0.4436, p=0.0340), whereas bowel anatomy did not significantly affect the FA-FR in PN group. No patient developed clinical EFA deficiency symptoms.
Table: Median serum fatty acid (FA) fractions (%) in pediatric intestinal failure patients (n=40).

<table>
<thead>
<tr>
<th>FA</th>
<th>Fraction (%)</th>
<th>Fraction (%)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>EN group</td>
<td>PN group</td>
<td></td>
</tr>
<tr>
<td>Linoleic acid</td>
<td>25.50</td>
<td>13.90</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>α-linoleic acid</td>
<td>1.09</td>
<td>0.78</td>
<td>0.0017</td>
</tr>
<tr>
<td>Mead acid</td>
<td>0.16</td>
<td>0.17</td>
<td>0.3768</td>
</tr>
<tr>
<td>Arachidonic acid</td>
<td>5.36</td>
<td>3.78</td>
<td>0.0090</td>
</tr>
<tr>
<td>Eicosapentaenoic acid</td>
<td>1.01</td>
<td>3.34</td>
<td>0.0019</td>
</tr>
<tr>
<td>Docosahexaenoic acid</td>
<td>1.57</td>
<td>3.23</td>
<td>0.0134</td>
</tr>
<tr>
<td>Omega-6 FAs total</td>
<td>32.3</td>
<td>20.90</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Omega-3 FAs total</td>
<td>4.50</td>
<td>8.14</td>
<td>0.0702</td>
</tr>
<tr>
<td>Trien:tetraen ratio</td>
<td>0.03</td>
<td>0.04</td>
<td>0.0010</td>
</tr>
</tbody>
</table>

**Conclusion:** Employing PN lipid restriction is necessary for alleviating IFALD. Our current practice to limit PN plant-derived lipids to < 1 g/kg/day in cholestatic patients with gradual increase of dose when cholestasis resolves has proven effective in preventing progressive IFALD. We use fish oil based lipid emulsion to provide extra energy. Consequently, FA fractions reported here confirm that such practice does result in moderate or mild biochemical EFA deficiency during the PN phase. However, EN patients weaned off PN had no sign of EFA deficiency, even though EFA fractions were smaller with less remaining ileum.

**Disclosure of interest:** None declared for any of the authors.
The adhesion of S. pneumoniae to respiratory cells is reduced by bovine milk oligosaccharides

Joseph Thomas Ryan¹, Helen Slattery², Rita M. Hickey², Mariarosaria Marotta¹

¹Food for Health Ireland, Teagasc Food Research Centre Moorepark, Fermoy, Ireland
²Teagasc Food Research Centre Moorepark, Fermoy, Ireland

Objectives and study: Streptococcus pneumoniae is a Gram positive pathogen, which regularly colonises the upper respiratory tract (URT) of healthy individuals. However increased numbers of S. pneumoniae have been observed colonizing the URT of children affected by respiratory tract infections. Furthermore, S. pneumoniae is associated with ~30% of pneumonia related deaths. One of the epithelial receptors involved in S. pneumoniae adherence and translocation has been identified previously as Galβ1-4GlcNAcβ1-3Gal. This structure is similar to the milk oligosaccharide lacto-N-neoTetraose, Galβ1-4GlcNAcβ1-3Galβ1-4Glc (LNnT). For this reason, several studies have focused on demonstrating that free oligosaccharides (OS), such as LNnT and its sialylated ligands, inhibit S. pneumoniae adhesion to epithelial cells of the respiratory tract. Breast milk represents a rich source of OS and plays a major role in protecting infants from infections. Human Milk Oligosaccharides (HMO) have been shown to reduce adhesion of a range of pathogens. Thus, an attractive option would be to provide OS to not breast-fed infants. However, human milk due to its limited availability cannot be considered a commercial source of OS. Recent studies have shown that bovine milk and its processing streams contain OS with similar structures to HMO and may represent a commercially viable source for OS extraction.

In this study, demineralised whey was exploited as a source of free OS. The extracted OS were subsequently investigated for their ability to reduce S. pneumoniae adhesion to both pharynx and lung cells.

Methods: Demineralised whey was subjected to consecutive microfiltration, ultrafiltration and diafiltration steps to remove both protein and lactose. The final retentate containing OS was passed through a size-exclusion chromatography to further enrich for OS. The final OS-enriched fraction (OSF) was incubated with S. pneumoniae in the concentration range of 6 to 0.24 mg/mL. After 30 min incubation at 37°C with 5% CO₂, the bacteria were added to pharynx and lung cells, which were activated with 5 µg/mL interleukin 1β. After 30 min incubation, the non-adherent bacteria were removed by washing with PBS and the adherent bacteria were recovered by treating the human cells with triton X-100 and plating on sheep blood agar plates.

Results: The final OSF was found to contain 0.9% (w/w) lactose and 23% (w/w) sialyllactose. The sample was analysed by UPLC-Hydrophobic Interaction Liquid Chromatography coupled to mass spectrometry for structural assignment. This allowed the identification of 19 structures, ranging between 300 and 1200 Da. Five of the 19 structures are also found in breast milk. When OSF was tested for anti-adhesive properties, it was found to significantly reduce the adhesion of S. pneumoniae R6 to the pharynx cells by 78, 51 and 25% at concentrations of 6, 4 and 2 mg/mL, respectively. Also, OSF significantly reduced the adhesion of S. pneumoniae to the lung cells by 55, 34 and 17%, at concentrations of 2.4, 1.15 and 0.24 mg/mL, respectively.

Conclusion: A variety of sialylated and neutral OS were extracted from whey by employing a combination of membrane filtration and size-exclusion chromatography. The extracted OS were capable of reducing S. pneumoniae adhesion to pharynx and lung cells when tested at physiological concentrations. This study shows the potential of milk OS as functional ingredients aimed at lowering the incidence of infectious diseases.

Disclosure of interest: None Declared
IgG–binding Fc receptor (FcRn) expression in small intestine and brain in neonatal rats

Ester Arevalo Sureda1, Björn Weström1, Carolina Falini1, Kateryna Goncharova1, Olena Prykhodko1

1Lund University, Biology, Lund, Sweden

Objectives and study: The rat is an altricial species born with immature intestinal (IB) and blood-brain barriers (BBB). The intestine of the newborn is adapted for absorption of nutrients from the milk, but also to acquire passive maternal immunity, i.e., selective uptake of milk IgG mediated by the neonatal Fc-receptor (FcRn). At weaning, the intestinal barrier function increases, resulting in a cessation of macromolecular absorption. The BBB barrier is highly selective and protects the brain blocking most of blood-borne macromolecules to pass. Recently it has been shown that the uptake of maternal IgG from the intestine to blood circulation might have influence on synaptic maturation in newborn pigs (Pierzynowski, S. et al, Int. J. Dev. Neurosci 35:64–71, 2014). Hence, the aim of the study was to investigate macromolecular passage and expression of FcRn in the intestines and brain of neonatal and weaned rats in order to acquire further insight on this during development.

Methods: Suckling 14-d and weaned 28-d old Sprague-Dawley rats (n=10/age) were gavaged human serum albumin (HSA, 1.25 mg/g bwt) and i.p. injected with bovine serum albumin (BSA, 0.5 mg/g bwt) for testing the in vivo permeability of the IB and the BBB, respectively. After 3 h the rats were euthanized and blood was collected for measurement of marker HSA uptake and rat IgG (RIGG) in plasma while BSA was analyzed in brain homogenates by immunoassay. The proximal small intestine and brain were also collected for immunohistochemistry of FcRn.

Results: HSA marker absorption to blood had ceased in the weaned rats as compared to suckling rats (6.9±1.0 μg/ml; p<0.0001). This was reflected in the plasma level of IgG, that was decreased in the weaned (2.4±1.4 mg/ml) as compared to 14-d old suckling rats (5.7±1.0 mg/ml; p<0.0001). In contrast to the IB, the BBB in weaned rats showed increased permeability to BSA (11.9±1.6 μg/ml) compared to suckling rats (6.7±0.8 μg/ml; p<0.001). FcRn was highly expressed in the proximal small intestine in suckling rats, in the apical part of the epithelial cells along the villi, while it had markedly declined in weaned rats. In the brain, FcRn expression was found in cerebellum, cerebral cortex, mainly in endothelium, and in the choroid plexus (a part of the blood-cerebrospinal fluid barrier), at the basolateral side of the epithelium.

Conclusion: The ceased marker passage and decrease of FcRn expression in the small intestine correlates with the decreased plasma level of RIlG and increased IB function after weaning. In contrast, the BBB was found to be more permeable after weaning. We also found expression of FcRn in brain tissue, which appeared visually higher in weaned rats, suggesting that FcRn might be involved in a selective IgG uptake from blood to the brain in addition to its role in IgG passage in the intestines. We hypothesize that FcRn in brain has a role in selective IgG uptake that might influence brain maturation.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 732
Modulation of Serotonergic Stress Neurocircuitry by Dietary Prebiotics and Bioactive Milk Fractions

Brian Berg1, Robert Thompson2, Agnieszka Mika2, Maciej Chichlowski3, Monika Fleshner2

1Mead Johnson Pediatric Nutrition Institute, Evansville, United States
2University of Colorado-Boulder, Integrative Physiology, Boulder, United States
3Mead Johnson Nutrition, Discovery, Evansville, United States

Objectives and study: Early life nutrition impacts many aspects of physiology and behavior. In our previous studies, rats fed prebiotic diets exhibited reduced anxiety and depressive-like behavior produced by uncontrollable stress. The current study tested if 4 weeks of early life diet containing prebiotics (galactooligosaccharide, GOS + polydextrose, PDX), milk fat globule membrane protein (MFGM) and globular glycoprotein (lactoferrin, LAC) would change the activation of neurotransmitter system and cognition-related brain plasticity associated with the central stress response.

Methods: Male F344 rats (p24) were pair-housed in a barrier facility and fed experimental or control diet. After 4 weeks, rats were exposed to 100, 1.6mA, 5-s, unpredictable, inescapable tail shocks (100 IS) or remained in their home cages. Immediately after stressor termination, rats were rapidly decapitated and blood, brain and peripheral tissues were collected. The brain regions examined were the dorsal raphe nucleus (DRN), amygdala, hippocampus, dorsal striatum (DS), locus coeruleus (LC), nucleus of the solitary tract (NTS) and prefrontal cortex (PFC). Brains were processed for assessment of mRNA expression using in situ hybridization.

Results: Expected increases in food intake and body weight were observed over time but not affected by diets. Stress robustly increased cfos mRNA expression in the LC and DRN (dorsal, ventral and lateral) and diet did not modulate this effect. However, the test diet facilitated the stress-induced increase in cfos mRNA in the amygdala and DS when compared with the control diet. In addition, the test diet increased baseline cfos mRNA expression in the in the rostral NTS and PFC. Neither stress nor the diet affected the cfos expression in the hippocampus. We further tested if diet would impact the effect of stress on 5-HT1a and 5-HT2C receptors mRNA. The 5-HT1a receptor is a serotonergic inhibitory autoreceptor; prior work has demonstrated that enhanced stress resistance is associated with increased gene expression for the 5-HT1a receptor. Stress decreased 5-HT1a receptor mRNA in the rostral, mid and caudal DRN; however the diet had no impact on this effect. Interestingly, test diet decreased 5-HT2C mRNA in the DM striatum. Further, test diet attenuated the stress-induced decrease in BDNF mRNA in the DG of the hippocampus; the test diet also lessened the stress-induced increase in BDNF mRNA in the PFC.

Conclusion: These data suggest early life diets that contain prebiotics and bioactive milk fractions may selectively modulate the serotonergic stress neurocircuitry in a manner that supports behavioral stress resistance. Supported by Mead Johnson Nutrition.

Disclosure of interest: None Declared.
An Early Diet with Prebiotics and Bioactive Milk Fractions Modulates the Stress-Evoked Inflammatory Response

Maciej Chichlowski¹, Robert Thompson², Abby Hills², Lida Beninson², Brian Berg³, Monika Fleshner²

¹Mead Johnson Nutrition, Discovery, Evansville, United States
²University of Colorado-Boulder, Integrative Physiology, Boulder, United States
³Mead Johnson Pediatric Nutrition Institute, Evansville, United States

Objectives and study: The current study tested if 4 weeks of early life diet containing a complex blend of prebiotics (galactooligosaccharides, GOS + polydextrose, PDX) and bioactive whey fractions (milk fat globule membrane, MFGM and lactoferrin, Lf) would change basal concentrations and stress-evoked responses of the sympathetic nervous system and hypothalamic-pituitary-adrenal response in blood and tissues.

Methods: Male F344 rats (p24) were pair-housed in a barrier facility and fed test or control diet. Food consumption and body weight were monitored. After 4 weeks, rats were exposed to 100, 1.6mA, 5-s, unpredictable, inescapable tailshocks (100 IS) or remained in their home cages. Food intake and body weight increases were equal across diets. The basal concentrations and stress-evoked responses of the sympathetic nervous system (SNS), hypothalamic-pituitary-adrenal response (corticosterone and glucose), pro-inflammatory cytokines (IL1β, IL6, TNFα), anti-inflammatory cytokines (IL10, TGFβ), chemokines (CINC-1, MCP-1) and cellular stress marker (Hsp72) in blood and tissues were measured.

Results: Stressor exposure reduced spleen wt (a proxy for SNS activation), corticosterone and glucose and diet did not impact these responses. Stress increased plasma IL1β, IL6, IL10, CINC-1, MCP-1 and Hsp72. Test diet attenuated the stress-evoked increase in plasma IL6. Stress increased splenic concentrations of IL1β, CINC-1, and Hsp72 and reduced TNFα; test diet reduced the effect of stress on splenic CINC-1 and TNFα but not Hsp72. Test diet also increased basal concentrations of splenic IL1β and TNFα and reduced basal levels of CINC-1. Stress increased liver CINC-1 and Hsp72, and test diet reduced the stress-evoked increase in Hsp72. Test diet also reduced basal concentrations of liver IL10. Finally, stress increased subcutaneous white adipose tissue (sqWAT) concentrations of IL1β, CINC-1, and Hsp72. Test diet reduced the stress-evoked increase in IL1β and CINC-1, but not Hsp72. Test diet also elevated sqWAT IL1β and CINC-1.

Conclusion: Overall, these data demonstrate that an early life diet has little impact on hormonal stress responses and basal levels of inflammatory proteins, but does constrain some aspects of the sterile cytokine and chemokine stress response evoked by an intense acute stressor. Supported by Mead Johnson Nutrition.

Disclosure of interest: None Declared.
Lactobacillus rhamnosus GG (LGG) soluble mediators ameliorate visceral pain hypersensitivity induced by early life stress in rats

Rosaline Waworuntu¹, Karen-Anne McVey Neufeld², Siobhain M O’Mahony², Sarmauli Manurung¹, Gabriele Gross³, Brian Berg¹, Ted G Dinan², John F. Cryan²

¹Mead Johnson Pediatric Nutrition Institute, Evansville, United States
²Apc Microbiome Institute, Cork, Ireland
³Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands

Objectives and study: Visceral hypersensitivity plays an important role in the context of functional gastrointestinal disorders, colic and irritable bowel disease. Among the various underlying mechanisms, currently the microbiota-gut-brain axis receives particular attention. Early-life stress-induced visceral hypersensitivity can be studied in a maternal separation model of rat pups, in which probiotic feeding has been shown to ameliorate some of these stress-induced alterations. Biologically relevant products of probiotic metabolism may be involved in such effects, and therefore could deliver the required benefits without requiring the live organism to be present. In this study the effects of a specific preparation of soluble mediators from the probiotic Lactobacillus rhamnosus GG (LGG) were evaluated. Previously, immunomodulatory properties of this material have been demonstrated both in vitro and in vivo. Production conditions have been standardized with cultivation and downstream processing steps such as desalting, sterile filtration and lyophilization.

Methods: The maternal separation protocol was conducted as described in O’Mahony et al., 2009. Rats were separated from their mothers for 3 hrs/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 drinking water with or without supplementation of LGG soluble mediators. Supplementation of the lyophilized materials was benchmarked to the number of LGG viable cells at the end of cultivation to provide a dose equivalent to a range from 1.3x10⁸ to 4.3x10⁹ viable LGG/animal/day until PND 85. Visceral hypersensitivity was assessed using the colorectal distension test conducted at PND 79.

Results: There were no differences in body weight or water and food intake across groups. Early life stress resulted in visceral hypersensitivity to colorectal distension as reflected by a lower pain threshold in MS rats compared to NS rats. This effect was significantly ameliorated by supplementation with the LGG soluble mediator preparation (p=0.03). There were no differences in number of observed pain behaviors between treatment groups. Interestingly, the increased pain threshold in rats that received LGG soluble mediators was not observed in animals supplemented with unconditioned culture medium subjected to the same processing steps as the LGG soluble mediator preparation. This underpins the role of specific bioactives secreted by LGG present in the soluble mediator preparation.

Conclusion: Administration of LGG soluble mediators in rats reversed the altered visceral pain sensitivity induced by MS. Further studies are needed to elucidate specific mechanisms of action related to gut and brain neurochemistry.

Disclosure of interest: RV Waworuntu, S Manurung, G Gross, and BM Berg are employees of Mead Johnson Nutrition; KA McVey Neufeld, SM O’Mahony, and TG Dinan, None Declared; JF Cryan, Research funding: Mead Johnson Nutrition, Cremo, Suntory Wellness and 4D Pharma; Research Collaboration: Alimentary Health; Speaker’s Bureau: Yakult, Mead Johnson Nutrition, Janssen, Boeringer Ingelheim, Danone-Nutrita; Research Consultant: Alkermes and Mead Johnson Nutrition.
Free-living Glycemic Profiles of Children With Overweight and Obesity in Association With Cardiometabolic Risk

Jesse Rijks¹, Kylie Karnebeek¹, Jan-Willem van Dijk², Elke Dorenbos¹, Willem-Jan Gerver¹, Pauline Stouthart¹, Jogchum Plat³, Anita Vreugdenhil¹

¹Maastricht University Medical Centre, Paediatrics, Maastricht, Netherlands
²Han University of Applied Sciences, Institute of Sports and Exercise Studies, Nijmegen, Netherlands
³Maastricht University, Human Biology, Maastricht, Netherlands

Objectives and study: Insulin resistance is common among children with overweight and obesity, however it is unknown when subtle glucose dysregulation emerges. Moreover, the relevance of these early subtle glucose disturbances, especially in the context of future cardiovascular risk, remains unknown in this high-risk population. The aim of study was to evaluate glycaemic profiles of children with overweight and obesity in free-living conditions and to evaluate the associations of these profiles with insulin resistance and cardiovascular risk parameters.

Methods: 111 (40 boys; 71 girls) children with a mean age of 12.0 ± 3.0 years with overweight (19%), obesity (40%), and morbid obesity (41%), without type I and II diabetes were included in this cross-sectional study at Centre for Overweight Adolescent and Children’s Healthcare (COACH). 48 hours free-living sensor glucose concentrations, fasting plasma glucose concentrations, post-glucose load plasma glucose concentrations, serum lipid and lipoprotein concentrations, and blood pressure were evaluated. Insulin resistance was estimated by homeostatic model assessment of insulin resistance (HOMA-IR).

Results: In this group of children with overweight and obesity, high-normal glucose excursions (≥6.7 mmol/L) and hyperglycaemic glucose excursions (≥7.8 mmol/L) were frequently observed under free-living conditions (65%, n=72; 25%, n=28, respectively). The median free-living sensor glucose concentration was 5.0 (2.7 - 7.3) mmol/L. Median sensor glucose concentrations were positively correlated with fasting plasma glucose concentrations (r=0.190, p=0.046), fasting serum insulin concentrations (r=0.218, p=0.021), and HOMA-IR (r=0.230, p=0.015). Within the subgroup of children with hyperglycaemia, the hyperglycaemic area under the curve was positively correlated with known cardiovascular risk parameters, such as waist circumference (r=0.455, p=0.025), serum triacylglycerol concentrations (r=0.425, p=0.024), and HOMA-IR (r=0.616, p<0.001).

Conclusion: Hyperglycaemic glucose excursions are frequently observed in children with overweight and obesity under free-living conditions. Children with insulin resistance have higher median free-living glucose concentrations and a larger hyperglycaemic sensor glucose AUC. Most importantly, median free-living glucose concentrations and hyperglycaemic sensor glucose AUC demonstrated to be associated with increased cardiometabolic risk. Long-term longitudinal follow-up studies are necessary to investigate whether free-living glycaemic profiles can early identify children who have a high risk of developing type 2 diabetes and cardiovascular diseases.

Disclosure of interest: The authors have nothing to disclose
Direct effects of fermented rice with lactobacillus paracasei cba l74 on th1/th2 response in children with cow’s milk allergy

Rosita Aitoro¹, Lorella Paparo¹, Rita Nocerino¹, Antonio Amoruso¹, Viviana Granata¹, Linda Cosenza¹, Carmen Di Scala¹, Roberto Berni Canani²

¹University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
²University of Naples “federico ii”, Translational Medical Science-Elfid-Coinge Advanced Biotechnologies, Naples, Italy

Objectives and study: Probiotic fermented foods may modulate allergic response. We aimed to evaluate the effects of fermented rice with L. paracasei CBA L74 (RM-CBL74) on Th1 / Th2 cytokines response in peripheral blood mononuclear cells (PBMCs) from children affected by IgE-mediated cow’s milk allergy (CMA).

Methods: PBMCs from 3 children with sure diagnosis of IgE-mediated CMA (2 males, all Caucasian, mean age 3.5, range 1-5 years) were stimulated with beta-lactoglobulin (BLG, 100 μg/ml) in the absence or presence of RM- CBL74 at different doses (0.115- 115 mg/ml) for 48 hours. IL-4, IL-5, IL-10 and IFN-γ production was analyzed on cell supernatant, by ELISA.

Results: PBMCs stimulation with BLG resulted in a significant increase in IL-4 and IL-5 production, but not in IL-10 and IFN-γ production, that remained stable after stimulation. RM- CBL74 stimulated, in a dose-dependent manner (maximal effective dose 11.5 mg/ml), IL-10 and IFN-γ production and inhibited IL-4 and IL-5 production.

Conclusion: Through a direct interaction with the PBMCs from IgE-mediated CMA children, RM-CBAL74 regulates allergic response modulating Th1/Th2 cytokines production. These data suggest a potential use of probiotic fermented food for prevention and treatment of food allergies.

Disclosure of interest: None declared
**NUTRITION: Basic science**

N-P-008

**Pituitary hyperresponsiveness to thyrotropin releasing hormone in children with overweight and obesity**

Jesse Rijks¹, Bas Penders¹, Elke Dorenbos¹, Saartje Straetemans¹, Willem-Jan Gerver¹, Anita Vreugdenhil¹

¹Maastricht University Medical Centre, Paediatrics, Maastricht, Netherlands

**Objectives and study:*** High thyroid stimulating hormone (TSH) concentrations in combination with normal free thyroxin (fT4) concentrations are common in children with overweight and obesity, and have been associated with increased cardiovascular disease risk. Various mechanisms underlying the high TSH concentrations have been postulated. The TSH release of the pituitary in response to thyrotropin releasing hormone (TRH) was however not studied in children with overweight and obesity. This study aimed to evaluate TSH release of the pituitary in response to TRH in children with overweight and obesity.

**Methods:*** 77 (31 boys; 46 girls) children with a mean age of 12.8 ± 3.1 years with overweight (15%), obesity (38%), and morbid obesity (47%), without a history of thyroid diseases were included in this cross-sectional study at Centre for Overweight Adolescent and Children's Healthcare (COACH). Baseline TSH concentrations, fT4 concentrations, TSH concentrations and area under the curve (AUC) during TRH stimulation test, and pro-inflammatory markers were evaluated.

**Results:*** In 52% of the children with normal baseline TSH concentrations (n=73) a hyperresponsiveness of the pituitary to exogenous TRH was present. These children had significant higher baseline TSH concentrations (p<0.001) and were significantly younger (p=0.039) compared to the children with a normal response. Hyperresponsiveness of the pituitary to exogenous TRH was also found in all children with elevated baseline TSH concentrations (n=4). The TSH area under the curve during the TRH test was significantly negative associated with C-reactive protein concentrations (r=-0.290, p=0.011) and interleukin-6 concentrations (r=-0.239, p=0.042).

**Conclusion:** Hyperresponsiveness of the pituitary to exogenous TRH is common in the majority of children with overweight and obesity despite normal baseline TSH concentrations. This pituitary hyperresponsiveness in might contribute to TSH concentrations in the high normal range, which is a regular finding children with overweight and obesity.

**Disclosure of interest:** The authors have nothing to disclose
The influence of phospholipids derived fatty acids to circulating non-esterified fatty acids

Felicitas Maier1, Hans Demmelmaier1, Marina Fugmann2, Christian Hellmuth1, Andreas Lechner2, Berthold Koletzko1, Olaf Uhl1

1Dr. von Hauner Children’s Hospital, Munich, Germany
2Ludwig-Maximilians University, Munich, Germany

Objectives and study: The objective of this study was to explore the potential contributions of glycerophospholipid (GPL) and sphingomyelin (SM) fatty acids to the circulating non-esterified fatty acids (NEFA). NEFA are known to be associated with the development of insulin resistance and gestational diabetes, which is further known as a risk factor for increased fetal weight and later metabolic and cardiovascular diseases. A recent study found differences in the NEFA profile in women with history of gestational diabetes (postGDM) and healthy controls. Little is known about the NEFA sources in the postprandial state, which prevails most of the day.

Methods: Thirty-nine women were studied in mean nine months after the delivery after they gave informed consent. Serum samples of 19 postGDM women and 20 controls were obtained in fasting state (t0) and 90 minutes (t90) after an oral glucose tolerance test. Serum samples of each participant were separated and stored at -80 °C. After sample preparation fatty acid composition of GPL was analyzed by gas chromatography. The fatty acid composition of NEFA and SM was analyzed with liquid chromatography coupled to triple quadrupole mass spectrometry.

Results: PostGDM and controls differed significantly in their anthropometric data, insulin and glucose levels at t0 and t90. NEFA 10:0 showed significant lower concentrations at t0 and t90 in postGDM (0.5 µmol/l in postGDM and 1.13 µmol/l in controls at t0 with p<0.0009; 0.04 µmol/l for postGDM and 0.09 µmol/l in controls with p<0.0009). The concentrations of all other measured individual fatty acids showed no differences between postGDM and controls in NEFA, GPL or SM. The ratio of individual NEFA at t90 vs. t0 increased with the chain-length (7% for C16:1, 82% for C26:3). At t90, long-chain polyunsaturated fatty acids showed high correlations between NEFA and GPL in postGDM (r=0.889 for 20:5, r=0.704 for 22:4, r=0.868 for 22:5 and r=0.850 for 22:6) and in controls (r=0.642 for 20:3, r=0.647 for 20:4 and r=0.839 for 20:5). Very long-chain fatty acid 24:0 correlated significantly between NEFA and SM in postGDM and controls (r=0.528 and r=0.498 for 24:0, respectively). Saturated and monounsaturated as well as essential fatty acids correlated less between NEFA and GPL or SM.

Conclusion: PostGDM and controls differed significantly in their clinical data. No differences were found between the two groups in the individual fatty acid concentrations in NEFA, GPL and SM, except NEFA 10:0 with a higher amount in postGDM at t0 and t90. The NEFA composition varied highly between fasting and fed state in postGDM and controls, presumably due to a high variance in the relative contribution of individual fatty acids from adipose tissues and from other sources. Long-chain fatty acids seemed less influenced by glucose intake. An association was found for long-chain polyunsaturated fatty acids in GPL and NEFA and for very long-chain fatty acid 24:0 in SM and NEFA. GPL might therefore contribute long-chain polyunsaturated fatty acids to the NEFA pool. SM might contribute very long-chain fatty acids to the NEFA pool.

Disclosure of interest: The authors confirm that this article content has no conflicts of interest.
The sources of pediatric nurses knowledge and skills in children feeding

Ewa Winnicka

The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutrition Disorders and Pediatric, Warsaw, Poland

Objectives and study: Incorrect feeding technique is one of the factors leading to feeding disorders in child with poor feeding skills. Appropriate technique increase feeding efficacy and safety, it prevents deterioration of feeding disorder symptoms. Nurses duties comprise of feeding infants during their hospitalization as well as giving parents the instructions how properly feed their child. Nurses should be highly qualified in feeding techniques thus my aim was to assess their ways of acquiring the skills and knowledge concerning feeding technique.

Methods: 253 nurses answered the questions. 86% of them declared that they have feeded children currently or previously. 11% declared that they would possibly do it in the future, 3% said they would not feed children. The survey was performed among nurses who participated in the lectures in 5 different cities. The characteristic of feeding disorders and the ability of food intake as an activity based on child sensory-motor experiences were presented during the lectures. After this lectures participants were asked how they had learned feeding technique and weather the way of feeding depended on feeder skills.

Results: 93% of individuals declared that feeding technique depended on nurses skills. Only 3% said that it was irrelevant. 10% of participants had learned children feeding at university or professionals courses, 25% while practicing in hospitals and 8% during special courses. 24% relied on intuition, own experiences or a trial and error method. 33% had learned from more experiences colleagues. 74% declared they were not skilled enough to feed children, only 26% claimed they did not need-practical trainings.

Conclusion: The knowledge of pediatric nurses and their skills in children feeding are not sufficient. Most of them have learned how to feed children without considering systematic knowledge and techniques recommended by experts.

Disclosure of interest: None Declared.
Serum butyrate concentration in children affected by cow’s milk allergy

RITA NOCERINO¹, Lorella Paparo¹, Antonio Amoroso¹, Carmen Di Scala¹, Antonio Calignano², Diana Tronino², Roberto Berni Canani³

¹University of Naples “Federico II”, Department of Translational Medical Science, Naples, Italy
²University of Naples “Federico II”, Department of Pharmacology, Naples, Italy
³University of Naples “Federico II”, Department of Translational Medical Science, European Laboratory for the Investigation of Food-Induced Diseases (Elfid) and Ceinge, Naples, Italy

Objectives and study: Butyrate is a major short chain fatty acid involved in oral tolerance acquisition. We aimed to comparatively evaluate butyrate serum concentration in children affected by cow’s milk allergy (CMA) and in age-matched healthy controls.

Methods: A venous blood sample was collected after an overnight fast in patients with IgE-mediated CMA. Children were in stable clinical condition without symptoms of CMA, and already treated with a hypoallergenic formula for a period of at least 6 months with extensively hydrolyzed casein formula containing L.rhamnosus GG (group 1), rice hydrolyzed formula (group 2) or soy formula (group 3). Serum concentration of butyrate was determined by gas chromatography interfaced to a mass spectrometer.

Results: 28 subjects [85.7% male, mean (SD) age of 24.3 (6.9) months] were enrolled: 10 in group 1, 9 in group 2 and 9 in group 3. Subjects in group 1 showed significantly (p<0.05) higher serum concentration of butyrate (0.51 mM) compared with children in group 2 (0.36 mM) or group 3 (0.35 mM). There were no difference in serum concentration of butyrate between group 2 vs group 3.

Conclusion: Extensively hydrolyzed casein formula containing L.rhamnosus GG but neither rice hydrolyzed formula nor soy formula is able to increase butyrate serum concentration. This effect could be related to the previous demonstrated effect on oral tolerance acquisition in children with CMA.

Disclosure of interest: None Declared
Gestational protein restriction impacts bulk $^{15}$N natural isotopic abundance from birth in mice offspring

Karine Bernardo$^1$, Celine Jousse$^2$, Illa Tea$^3$, Pierre Fafournoux$^2$, Richard Robins$^3$, Regis Hankard$^4$, Arnaud De Luca$^1$

$^1$Inserm U1069, Tours, France
$^2$Umr Inra 1019, Univ. Clermont-Ferrand, France
$^3$Umr Cnrs 6230, Univ. Nantes, France
$^4$Inserm U1069, University of Tours, France

Objectives and study: Natural isotopic abundance (NIA) measurement of $^{15}$nitrogen ($^{15}$N) may be an index of protein metabolism. In a preliminary study in mice, we showed that offspring exposed to gestational protein restriction had a lower bulk hair $^{15}$N NIA at 16-month old despite eating the same diet since 15 months. Our aim was to determine if this imprinting is present from birth.

Methods: Pregnant Balb/c mice were fed an isocaloric, low protein diet (10% protein, LPD, n=5) or a normal diet (22% protein, ND, n=5) during gestation. Their offspring (F1) were sacrificed one day after birth, and liver and leg samples were frozen. Twenty-seven F1 mice were included in the LPD group and 30 in the ND group. Samples were lyophilised and weighed into tin capsules. Bulk $^{15}$N NIA values were measured using isotope ratio measurement mass spectrometry coupled with an elemental analyser. Results are expressed as mean ± SD and were compared using t-test.

Results: Weight at sacrifice was not different between groups: LPD 1.66±0.19g vs. ND 1.70±0.14g, $P=0.39$. Bulk $^{15}$N NIA in tissues were lower in the LPD group compared to control mice, both in the liver (6.42±0.37‰ vs. 7.28±0.29‰, $P<0.0001$) and in the leg (6.99±0.28‰ vs. 7.75±0.33‰, $P<0.0001$). Bulk $^{15}$N NIA in ND diet was higher than in LPD diet (3.78±0.17‰ vs. 2.59±0.10‰, $P<0.01$). ND diet included added casein, whose $^{15}$N NIA was higher than the reference diet.

Conclusion: These data suggest that the metabolic impact of a gestational exposition to protein restriction may alter bulk $^{15}$N NIA from birth. Then, bulk $^{15}$N NIA could be an index of the diet's impact on foetal protein metabolism. Isotopic content may serve as an imprinting of nutritional and metabolic environment over time.

Disclosure of interest: None Declared.
Protein Oxidation as a Relevant Factor for Determining Protein Status in Adults

Gerlof Reckman¹, Marion Priebe², Martijn Koehorst³, Theo Boer³, Henk Schierbeek⁴, Roel Vonk⁵

¹University Medical Center Groningen, Internal Medicine, Groningen, Netherlands
²Umcg, Pediatrics, Groningen, Netherlands
³Umcg, Clinical Medicine, Groningen, Netherlands
⁴Amc, Pediatrics, Amsterdam, Netherlands
⁵Umcg, Cell Biology, Groningen, Netherlands

Objectives and study: Defining optimal protein intake in various metabolic conditions like the newborn, aging and during exercise is highly relevant. Recently, it has been suggested that high protein intake in newborn could lead to excessive weight gain in later life (Kirchberg et al. 2014). Limited protein oxidation could be a relevant parameter directly related to this. To monitor protein oxidation we developed a non-invasive ¹³C-protein-derived breath test using naturally enriched milk protein (fractions). We validated and applied this technique in healthy adults under various metabolic conditions as a pilot study.

Methods: After baseline sampling, 30 g of naturally labelled ¹³C-milk protein were consumed. Breath samples were taken every 10 min and ¹³CO₂ was measured by isotope ratio mass spectrometry. The following variables were used to calculate the amount of substrate oxidized: administered dose, ¹³C enrichment of substrate, molecular weight of substrate, number of carbon atoms in a substrate molecule, estimated CO₂-production of the subject based on body surface area.

Results: Postprandial kinetics of oxidation of whey (rapidly digestible protein) and casein (slowly digestible protein) derived from our breath test were comparable to literature data regarding the kinetics of appearance of amino acids in blood (Boirie et al. 1997). Using this test we could demonstrate that in 255 min 20% ± 3% (mean ± SD) of the milk protein was oxidized compared to 18% ± 1% for 30 g glucose. Over 330 min 24% ± 3% of the milk protein was oxidized, which served as control (100%). Compared to control a decrease of 31% ± 18% in milk protein oxidation was observed after a 3 day protein restricted diet (~10 g of protein/day) compared to a normal diet and 30 minutes of cycling before protein consumption reduced protein oxidation by 39% ± 37%. A protein restricted diet plus exercise reduced oxidation by 52% ± 19%. Whey oxidation was increased (49% ± 12%) when 30 g glucose was administered simultaneously.

Conclusion: Protein oxidation, which can be monitored in breath, is a significant factor in protein metabolism. With our technique we are able to characterize changes in overall protein oxidation under various metabolic conditions such as a protein restricted diet, competitive substrates and exercise, which could be relevant for defining optimal protein intake under various metabolic conditions. Measuring protein oxidation in newborn might be relevant to establish its contribution to the protein status and its age-dependent development.

Disclosure of interest: First author: none declared; second author: none declared; third author: none declared; fourth author: none declared; fifth author: none declared; sixth author: CEO Hanze Nutrition B.V., the company which provided the substrates.
Glycoside-hydrolase activity in the human gut microbiome

Alicia Ruiz¹, Tomas Cerdo², Ascension Marcos³, Manuel Ferrer⁴, Cristina Campoy², Antonio Suarez¹

¹Department of Biochemistry and Molecular Biology II, University of Granada, Spain
²Euristikos Excellence Centre for Paediatric Research, University of Granada, Spain, Department of Paediatrics
³Institute of Science and Food Technology. Csic. Madrid, Spain
⁴Institute of Catalysis and Petrochemical. Csic. Madrid, Spain

Objectives and study: The gut microbiota has recently emerged as an important player in host physiology. Focused on obesity, many studies have been linked obesity with gut disbiosis. An increased ratio of Firmicutes/Bacteroidetes has been observed in the microbiota of genetically obese mice (ob/ob) that confer an obese phenotype in germ-free mice. However, a number of studies have failed to associate these microbial community changes with obesity in humans. Although it is clear that the gut microbiota is likely to play a role in obesity and metabolic disease, it is difficult to draw definite conclusions on the importance of any particular bacterial group.

A number of reports suggest that the relative contribution of glycoside-hydrolases (GH) is indicative of the capacity for sugar metabolism and energy production in the gut microbiota, and that its increase may stimulate weight gain. Our previous work showed that gut microbial GH activity is higher in obese and significantly correlated with fasting glucose, insulin resistance and body mass index (BMI) in obese. We hypothesized that a functional approach may relate gut microbial carbohydrate metabolism to obesity. Besides, we studied the dynamics of gut microbial functionality in response to calorie restriction.

Subjects and Methods: We systematically collected glycosidase activity data from faecal bacteria in obese (n = 13) that followed a dietary intervention for 1 year and in lean (n = 8) subjects. Glycosidase activity was represented by β-galactosidase and α-glucosidase. The variations in faecal bacterial glycosidase activities were complemented with a comparative analysis between activity levels and anthropometric and biochemical parameters to find presumptive correlation variables.

Results: All the significant correlations observed are represented in figure 1, panel A for β-galactosidase and panel B for α-glucosidase. Lean and obese communities showed significantly different levels of β-galactosidase and α-glucosidase activities (data not shown). Remarkably, we found a sigmoid association between BMI and β-galactosidase, BMI>24.5 acting as a functional frontier (panel A). Moreover, we found a positive correlation between insulin levels (Spearman Rho = 0.43, p<0.01), HOMA-IR (Spearman Rho = 0.36, p<0.05) and LDL (Spearman Rho = 0.35, p<0.05) with β-galactosidase activity, and, between BMI (Spearman Rho = 0.65, p<0.0001) and HOMA-IR (Spearman Rho = 0.34, p<0.05) with α-glucosidase activity.

*This research is part of the EVASYON Study Project funded by the Health Institute Carlos III
Figure 1. Microbial GH activities as metabolic markers positively correlated with insulin resistance and obesity.

**Conclusion:** All together, these results confirmed our previous evidences of the positive correlation between the anabolic capacity of gut microbiota, BMI and insulin resistance. Moreover we found a new association between this anabolic capacity and LDL plasma levels. Despite diet-induced weight loss, gut microbial functionality shows a bimodal phase depending on host's BMI.

**Disclosure of interest:**
"None Declared".
NUTRITION: Clinical nutrition

N-P-015

Simple dietary criteria to improve serum n-3 fatty acid levels of mothers and their infants one month after delivery

Ulla Hautero¹, Tuija Poussa², Kirsi Laitinen³

¹University of Turku, Turku University Hospital, Department of Paedics, Kaarina, Finland
²Stat-Consulting, Nokia, Finland
³University of Turku, Institute of Biomedicine, Turku, Finland

Objectives and study: Sufficient maternal dietary intake of n-3 fatty acids (FAs) supports offspring development. We aimed to construct simple criteria for dietary counselling to improve intake and nutritional status of n-3 FAs in mothers and their infants.

Methods: Serum phospholipid FAs from mothers (n=90) and infants (n=63) were analysed by gas chromatography one month after delivery. Dietary intake of foods during pregnancy and one month after delivery were recorded using 3-day food diaries and an index for healthy eating was calculated. Fish consumption was established by questionnaires. Dietary consumption of foods resulting in an increase in serum n-3 FAs was defined.

Results: After delivery, the mother’s consumption of fish at least three times per week resulted in an increase in total serum n-3 FAs [mean difference 1.7% of total FA (95% CI 0.7-2.8), p<0.001] and docosahexaenoic acid [1.1% (0.5-1.8), p<0.001] compared to non-consumers. Persistent fish intake once weekly throughout pregnancy increased total serum n-3 FAs (p=0.001) and docosahexaenoic acid (p<0.001). Overall, a healthy diet (middle and highest tertiles of healthy eating index score compared to the lowest tertile) resulted in higher total serum n-3 FAs (p=0.004) and docosahexaenoic acid (p=0.008). Mother’s diet along with higher serum levels of n-3 FAs were related serum FAs levels in one-month-old infants.

Conclusion: An overall healthy diet and persistent consumption of fish at least once weekly throughout pregnancy or more frequent fish intake three times per week increases n-3 FAs in serum phospholipids of both mothers and their infants.

Disclosure of interest: None Declared
Nutritional status of children with severe form of cerebral palsy fed by gastrostomy

Anija Orel¹, Nataša Fidler Mis², Matjaz Homan³, Rok Orel⁴

¹University of Ljubljana, Biotechnical Faculty, Ljubljana, Slovenia
²University Children's Hospital Ljubljana, Slovenia
³University Children's Hospital, Department of Gastroenterology, Hepatology and Nutrition, and Genius Group, Ljubljana, Slovenia
⁴University Children's Hospital Ljubljana, Department of Gastroenterology, Hepatology and Nutrition, Ljubljana, Slovenia

Objectives and study: Many patients with serious neurologic disabilities are malnourished. While feeding through gastrostomy overcomes problems such as swallowing difficulties and esophageal dismotility, other factors such as delayed gastric emptying, poor tolerance to sufficient amounts of food as well as parents/carers' aversion to feed their children entirely through gastrostomy and to follow dietary advices still put this children at increased risk of malnutrition. The aims of the research were to determine the proportion of malnourished patients in the group of gastrostomy fed children and adolescents with severe cerebral palsy (CP).

Methods: Body weight (BW), ulna length (to calculate the height (BH)), the thickness of skinfolds (biceps, triceps, subscapular and suprailliac) and bioimpedance (devices BIA 101 and STA, Akern, Italy) (BI) were measured in 53 patients (23 girls), all classified with Gross Motor Function Classification System (GMFCS) grade 5 disability, aged between 2 and 26 years (median 11 years). The proportion of body fat was calculated according to the formulas from skinfolds, body mass index (BMI) and BI measurement values.

Results: The proportions of patients with BW and BH beneath the 3rd percentile for healthy population were 83% and 58%, respectively. When compared with special norms for CP, 32% of the subjects had BW below the 10th percentile, but nobody's BH was below it. Weight for age index below -2 Z was found in 45% of patients (aged 2 to 10 years), weight for height index in 54% (aged 2 to 5 years), and BMI in 68% of patients (all ages). According to the body composition measured with various methods, the proportion of undernourished patients was between 27% and 58%.

Conclusion: The study confirmed that a large proportion of children and adolescents with severe cerebral palsy is malnourished despite gastrostomy feeding. Estimation of nutritional status depends on the methods and standards which are used.

Disclosure of interest: None Declared.
The role of Leptine Gene Polymorphisms 223 G/A in children's obesity

Marginean Cristina Oana¹, Banescu Claudia², Marginean Maria Oana², Duicu Carmen², Claudiu Marginean²

¹University of Medicine and Pharmacy Tirgu Mures, Pediatrics, Tirgu Mures, Romania  
²University of Medicine and Pharmacy Tirgu Mures, Tirgu Mures, Romania

Objectives and study: The aim of this study is to establish the role of LEPR 223 G/A gene polymorphisms in children's obesity. Obesity is caused by the combined effect of genes, environment, lifestyle, and the interactions of these factors. The most frequent polymorphisms of the leptin gene involved in obesity is LEPR 223 G/A gene.

Methods: We did a prospective study on 213 children admitted in a tertiary county hospital from Romania. The pediatric patients were divided into 2 groups: control group – 113 children and obese the group - 100 children.

Results: The groups were evaluated regarding LEPR 223 G/A gene polymorphisms, anthropometric parameters (BMI, MUAC, TST) and paraclinical results (protein, leptin, adiponectin and IL 8). The most frequent genotypes in obese children versus control group were GA+GG for LEPR 223 gene (p = 0.0001). Genotype GG of LEPR 223 gene was correlated with MUAC, TST, direct proportional with leptin and inversely with adiponectin (p = 0.001/0.002/0.001/0.02), while the GA genotype correlates only with serum IL 8 (p = 0.05). We did not find any correlations with the protein levels.

Conclusion: Obesity is more frequently in children with GG+GA genes for LEPR 223 gene. Genotype GG of LEPR 223 was correlated with anthropometric parameters like MUAC, TST and also with serum level of leptin and adiponectin. Further studies are needed on larger groups of children.

Disclosure of interest: “None Declared”.

Keywords: children, obesity, LEPR 223 G/A gene polymorphisms
Nutritional support is useful in infant with congenital heart disease

Ignacio Ros¹, Cristina Martínez-Faci², Lorenzo Jiménez-Montañés³, Ruth García-Romero¹, Gerardo Rodriguez⁴

¹Miguel Servet Children's Hospital, Gastroenterology and Nutrition Unit, Zaragoza, Spain
²Miguel Servet Children's Hospital, Zaragoza, Spain
³Miguel Servet Children's Hospital, Cardiology Unit, Zaragoza, Spain
⁴University of Zaragoza.Iis Aragon, Zaragoza, Spain

Objectives and study: Infants with congenital heart disease (CHD) are prone to malnutrition, which increases morbidity of their underlying disease. Our aim was to evaluate the nutritional support usefulness in congenital heart disease infants who required early surgical intervention, according to the routine clinical practice in a Paediatric Nutrition Unit

Methods: Retrospective review, collection and analysis of medical record information of patients younger than 3 years of age with CHD whom had been surgically corrected with extracorporeal circulation. Patients referred to the Nutrition Unit were compared to those who were not. Variables related to the nutritional status (weight, height and BMI z-score, weight for height, Waterlow index and Shukla index) were performed at different ages up to 18 months.

Results: 25 patients were included. 48% (12) were referred to the Nutrition Unit. All of them received nutritional support with a high-energy formula (1 kcal/ml) and nasogastric tube feeding was necessary in half of them. The kind of CHD, gender, weight and height at birth and the incidence of other conditions were statistically similar between the groups.

Referred patients had poorer nutritional indices than control group at the time of referral to the Nutrition Unit (average: 4.16 ± 2.03 months old) and during the first 18 months of life, although weight and height z-score were statically equaled at the time of surgery (average: 12.69 ± 8.21 months old). The patients' nutritional status in the group monitored in the Nutrition Unit didn't change between the time of referral and surgery, meanwhile a progressive statistical deterioration of the nutritional indices was found in the control group.

Conclusion: An early nutritional support in children with CHD who are expected to undergo surgery, is not able to improve their nutritional indices, but is useful to avoid the nutritional worsening associated to the disease that appear in children that are not referred to a Paediatric nutrition Unit.

Disclosure of interest: None Declared
Role of Nutrition Management of Chylous Ascites Post Pediatric Liver Transplantation, Single Center Experience

Sahar Madkhali¹, Kumar Kishwer², Mohamed Shagrani²

¹King Faisal Specialist Hospital & Research Center, Nutrition Services Department, Riyadh, Saudi Arabia
²King Faisal Specialist Hospital & Research Center, Department of Liver and Small Bowel Transplantation, Riyadh, Saudi Arabia

Objectives and study: The aim of this review is to outline the resolution rate of CA post pediatric liver transplantation treated by dietary modification including low fat diet supplemented with medium-chain triglycerides (MCT) based formula.

Methods: From January 2011 to September 2015, 191 Pediatric liver transplantation procedures have been performed in our Centre. Out of these 19 cases were confirmed to have CA. The age ranged between 4 months to 11 years old (11 girls and 8 boys). One case underwent cadaveric liver transplantation and 18 cases underwent living related liver transplant. CA in these 19 cases developed between day 4-5 post liver transplantation, which related to the time of oral intake. CA (Chylous ascites) was suspected because of milky or creamy peritoneal fluid drainage that began after oral intake or was found via ultrasonography for abdominal distension after drain removal, and it was diagnosed on the basis of the triglyceride, cholesterol, leukocyte, and lymphocyte contents of the liquid. In the laboratory diagnosis of chylous ascites, a drained liquid/serum triglyceride ratio > 1.0 and a cholesterol ratio < 1.0 were considered important.

Nutritional treatment is done by following low fat diet and using MCT-based formula for 4-6 weeks, No TPN (Total Parenteral Nutrition) or pharmacotherapy treatment were required. Drain was removed as per our regular protocol whenever the output is below 100 cc per day.

Results: The nutrition treatment resulted in resolution of the CA in all of our cases (100%) within 1-2 weeks. Resolution was confirmed by measurement of the chyle output via a drainage (< 2ml/kg/day) and normalization of the TG level in fluid (0.7-0.5 mmol/l). The diet was kept for a total of 4-6 weeks in spite of resolution to avoid the recurrence due to early cessation of the diet (as reported in some studies).

Conclusion: Chylous ascites may appear due to injury of the lymphatic system in the periportal and retrohepatic areas during hepatic resection and inadequate ligation of injured lymphatic vessels

Application of MCT-based formulae with low fat diet alone was effective in 100% of the cases. More invasive treatments like TPN, pharmacological treatments or surgery should not be thought of as first option. After resolution of CA, low-fat diet and MCT-based formulae can be converted to regular diet and

Disclosure of interest: “None Declared”.
NUTRITION: Clinical nutrition

N-P-020

Current issue of nutrition status assessment in hospitalized children with chronic heart failure

Natalia Zvonkova¹, Tatiana Borovik¹, Leila Gandaeva², Elena Basargina²
¹Scientific Center for Children's Health, Healthy and Sick Child Nutrition Department, Moscow, Russian Federation
²Scientific Center for Children's Health, Cardiology Department, Moscow, Russian Federation

Objectives and study: Congenital heart disease and cardiomyopathy are the main causes of heart failure in children, which leads to disability and mortality. Progress of heart failure results in an increase of energy expenditure, gastrointestinal malabsorption, chronically low dietary intake, psychological problems, that may lead to growth problems. The latter means further complications that may affect heart function. The aim of the study was to evaluate nutritional status and determine the prevalence of undernutrition in children with chronic heart failure hospitalized to cardiology department.

Methods: In 113 patients (57 girls) at the age from 1 month to 10 years (median 62.0 months) with chronic heart failure due to various cardiac diseases (congenital heart disease before and after surgery, dilated cardiomyopathy), clinical assessment, ultrasonic Doppler heart examination and anthropometric measures (height, weight; head, chest and upper arm circumferences) were performed during 48 hours after admission. Anthropometric analysis was accomplished through the calculation of Z-scores with the support of the WHO Anthroplus, 2009 software. Z-scores were calculated for the following parameters: weight-for-age, weight-for-height, height-for-age, body mass index (BMI)-for-age. Undernutrition was defined using anthropometric Z-scores (Table).

Results: Total prevalence of undernutrition in children with chronic heart failure on admission was 48.6%. Chronic undernutrition was observed in 55 (10.6%) patients; acute in 43 (23.9%) - acute mild in 16 (14.2%) patients, acute moderate in 14 (12.4%), acute severe in 13 (11.5%). In 41 patients with acute undernutrition most children (48.8%) were 0-2 years, 4 children (9.7%) from 2 to 5 years and 17 children (41.5%) from 5 to 10 years old.

Table: Classification of malnutrition using Z scores

<table>
<thead>
<tr>
<th>Nutritional status</th>
<th>Weight-for-height*</th>
<th>Height-for-age</th>
<th>Weight-for-age</th>
</tr>
</thead>
<tbody>
<tr>
<td>Adequate</td>
<td>&gt;-1.0</td>
<td>&gt;-1.0</td>
<td>&gt;-1.0</td>
</tr>
<tr>
<td>Mild</td>
<td>≤-1.0 to &gt;-2.0</td>
<td>≤-1.0 to &gt;-2.0</td>
<td>≤-1.0 to &gt;-2.0</td>
</tr>
<tr>
<td>Moderate</td>
<td>≤-2.0 to &gt;-3.0</td>
<td>≤-2.0 to &gt;-3.0</td>
<td>≤-2.0 to &gt;-3.0</td>
</tr>
<tr>
<td>Severe</td>
<td>≤-3.0**</td>
<td>≤-3.0</td>
<td>≤-3.0**</td>
</tr>
</tbody>
</table>

*Or BMI in children >2 years of age

**Or edema, regardless of weight

Conclusion: Undernutrition has high prevalence in hospitalized children with chronic heart failure, especially in young children. Evaluation of nutritional status in children with chronic heart failure is an important component of diagnostic approach which allows to determine undernutrition and to start nutritional support with specialized enteral nutrition formulas without delay. Approximately 50% of such patients need a dietitian’s supervision and individual nutritional support.
References:


Disclosure of interest: None Declared
Caffeine consumption in adolescents: from coffee to energy drinks and back again

Barbara Santangelo¹, Rosa Lapolla¹, Irene Rutigliano², Massimo Pettoello Mantovani¹, Angelo Campanozzi³

¹University of Foggia, Pediatrics, Foggia, Italy
²Irccs Casa Sollievo Della Sofferenza, Pediatrics, San Giovanni Rotondo, Foggia, Italy

Objectives and study: In recent years the interest of pediatricians, parents and legislators on caffeine consumption in children has increased. As caffeine has several negative effects on the pediatric population, caffeine intake should be always discouraged in all children. Particularly, caffeine consumption should not exceed 45-85 mg/day in children 6-12 years old and 2.5 mg/kg/day (up to a maximum of 100 mg/day) in subjects older than 12 years. Of course, the daily intake of caffeine should consider all sources of this substance, mainly coffee, Soft Drinks (SD) and Energy Drinks (ED). Since no data are currently available on caffeine intake among Italian children and adolescents we aimed: 1) to investigate the prevalence of pediatric subjects consuming caffeine on a daily basis; 2) to estimate the amount of caffeine ingested; 3) to identify which beverage is the main source of caffeine.

Methods: We analyzed caffeine intake in 1231 adolescents (578 boys) aged 12–23, recruited from two public middle schools and two public high schools in Foggia, Puglia, Italy. The partecipants fulfilled an anonymous questionnaire, consisting of multiple choice questions, designed to investigate the caffeine consumption by analyzing, among the most popular Italian drinks containing that substance, the type of beverage consumed, its amount (number of glasses or cans) and frequency (daily, weekly or monthly). All data were entered into a database and then analyzed. Statistical analysis was performed using the Statistical Package for Social Sciences software Version 22 (SPSS v.22, IBM®).

Results: Approximately 73% of children consumed caffeine on a given day, in the amount of approximately 128 mg/day. Among them, 53% declared a consumption below the maximum amount allowed for age (100 mg/day), 33% reported a consumption between 100 and 200 mg/day and 14% declared a consumption between 200 and 400 mg/day. Among those students who reported a daily consumption of caffeine, 91% reported to have at least one coffee per day, 21% declared a daily intake of SD and 3% of ED. A trend with increasing age was observed. Coffee and EDs were responsible for the biggest daily intake of caffeine (about 120 mg/day); soft drinks were responsible for 1/3. The percentage of caffeine consumers increased from middle school subjects to high school students; the difference was due mainly to the different daily consumption of coffee and SD, but not of ED. Boys were the largest consumers of caffeine, mainly in SD and ED, while coffee consumption was not different between males and females. A total of 254/1231 students (20.6%) stated that they usually consume more than a drink containing caffeine per day, with an average caffeine intake two times higher than the upper limits for age; from this group, seven students reported they daily drink all three types of caffeinated beverages, with a considerable increase in the amount of caffeine ingested each day.

Conclusion: To our knowledge, this is the first study that investigates the consumption of caffeine in Italian children and adolescents. Our data show that sometimes teenagers consume large amounts of caffeine, underestimating its health-related risks.
Disclosure of interest: “None Declared”.
Objectives and study: Parenteral nutrition (PN) may be defined as to maintain the nutrition support intravenously in case oral or enteral nutrition is not sufficient. Although it is an efficient and safe treatment method, it has many metabolic complications depending on the content of PN mixture and many complications associated with venous access. In this study the data that may increase the effectiveness and safety of PN was intended to achieve by investigating the data of patients who received PN in a two-year period in a university hospital.

Methods: The data of 178 patients who received 230 episodes of PN was investigated in terms of PN indications, content of PN mixture, PN duration and the body weight changes, complications, management and outcomes of the complications.

Results: PN was given to the patients most commonly with the diagnoses of hematological malignancies, surgical diseases of gastrointestinal system and to the patients who were undergone hematopoietic stem cell transplantation. It was found that body weight increased in about one third of the patients, the patients who gained weight received more energy than the ones who lost weight and most of targeted energy could be given via central venous catheters (CVCs) than peripheral venous accesses. Hypokalemia (40,4%), hypophosphatemia (39,8%), hypomagnesemia (40,9%), hypertriglyceridemia (35,6%), elevated liver enzymes (55,2%), CVC related thrombosis (4,1%), microbial growth in blood culture obtained from CVC (31,3%) were the striking complications. Most of the electrolyte and mineral imbalances were seen in the first three days. 56% of ursodeoxycolic acid-treated group of the patients with elevated liver enzymes, recovered with treatment without any adverse reaction. No deaths were directly associated with PN.

Conclusion: PN was given to the children effectively and safely, the efficiency could be increased with CVCs, and if the electrolyte and mineral tests are routinely performed in the first three days most of abnormalities can be detected.

Disclosure of interest: We have no conflict of interest.
Nutritional status assessment of children of SOS children’s villages Bata (Equatorial Guinea) regarding nutrition training program for cooperation team

Mar Tolín , Hernani Iñaki Erquicia , María Fanjul, Irene Hidalgo, Candela Villanueva, Elena de Tomás, Esther Molina, César Sánchez Sánchez

1. H. Materno Infantil. H.G.U. Gregorio Marañón, Pediatric Gastroenterology and Nutrition, Madrid, Spain
2. Hospital Universitario Príncipe de Asturias, Anesthesiology, Alcalá de Henares, Spain
5. H. Materno Infantil. H.G.U. Gregorio Marañón, Nursery Department, Madrid, Spain

Introduction: Since 2010, two workshops on child nutrition are performed by a pediatrician for staff responsible for the care of children in NGO SOS Villages of Equatorial Guinea (Bata). This village, built in an enclosed area, includes 10 “houses” in which live between 8 and 10 children under the care of a responsible (“Mom”) with the budget by NGO local administrators.

Objectives: As a first step to assess the effectiveness of the educational program, an assessment of the nutritional status of children living in the village at the time of the last intervention and analyze the nutritional status according to the length of stay under the care of the NGO.

Patients, material and methods: Descriptive, cross study for five consecutive days with nutritional assessment on the children. This assessment included weight, height, brachial and head circumference, and skinfold measurement. All data included in SEGHNP computer program to adjust for age and zscore according to WHO curves. Body density (DC) allometric indices (Waterloo index for weight and height (IWp, IW t) Suckla index (IS) and percentage of lean mass (LM) and fat (FM) according to formula Siri,. In addition to these measurements related to place of birth variables, time spent at village and associated diseases they were collected

Results: In October 2015, 84 children were included in the study (6 to 10 children per household), with a median age of 8 years (range: 2 and 15 years), 60% male. 78% come from Bata and 22% out from there. The average length of stay in the village was 34 ± 36 months (1-132 months). The average weight and zscore were 29.3 ± 11.2 kg (13.5 to 59.3 kg) and -0.17 ± 1 (range -2.72 to 3.5 ). The average length and zscore were 128.5 ± 19 cm (90-172 cm) and -0.5 ± 1.5 (range: -8 to 3.53). BMI means and zscore were 17 ± 2 kg / m2 (13 to 22.2) and 0.15 ± 1 (range: -1.93 to 4.6). The average IWp was 102 ± 11% (80-145%), with only 10.7% of children with mild malnutrition. The IW average size was 97 ± 6.7 (range 62-108%), mild chronic malnutrition by 21%, 7% moderate and severe in 2.4% of children. The MUAC zscore regardless of -0.9 ± 0.9 (-3.36 to 1.39), zscore of triceps skinfold of -0.78 ± 1.1 (range: -3.2 ± 2.9), subscapular fold zscore -1.5 ± 0.9 (-3.2 to 1.4), biceps zscore of -0.5 ± 1.5 fold (-3.2 and 3.4), and suprailliac -0.7 ± 0.8 (-2.7 and 1.6). According to these data, percentage of LM was 24 ± 8.5% (range: 11.2 -49%) and 5.4 ± 3.3 % of FM (range 0.76 to 15.4). Only 3 patients (1.5 %)showed edema, and only 6% showed perianal disease or erythema. Only one child was HIV positive treatment. When we correlate different variables, the longer time in SOS Children NGO children showed better nutritional parameters specially BMI (p <0.04), higher percentage of MM (p <0.001) and FM (p <0.001). No significant differences were observed according to place of birth.

Conclusions: In our sample, most of the inhabitants of SOS Children’s Villages children show a adequate nutritional status and no significant nutritional complications. The children with longer time in the village had better nutritional status especially in relation to lean and fat mass. Therefore it seems that nutritional training received by responsible staff in charge of the NGO has proven effective for nutritional development of children .

Acknowledgements: Responsible staff of NGO SOS Children’s Villages in Spain and Bata specially Gumersindo Ndong and all moms of the program and children.

Disclosure of interest: None Declared.
Validation of Tanita BC-418 in a population of 8 year old Caucasian children, using deuterium oxide dilution as a reference technique

Veronica Luque¹, Joaquin Escribano¹, Mariona Gispert-Llauradó¹, Natalia Ferre¹, Michelle Venables², Priya Singh², Les Bluck², Veit Grote³, Martina Weber⁴, Berthold Koletzko⁵, Ricardo Closa¹

¹Universitat Rovira i Virgili, ISPv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
²Human Nutrition Research Centre, Cambridge, United Kingdom
³Von Haunersches Kinderspital, University of Munich Medical Centre, München, Germany
⁴LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
⁵Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany

Objectives and study: Body mass index is the most widely used method to diagnose obesity in clinical practice. However, this method cannot distinguish between fat and fat-free mass, and is in fact highly correlated with both body components. Bioelectrical impedance analysis (BIA) is an accessible technique to estimate body composition, but its accuracy is still questioned. BIA relies on the dependence between body impedance and total body water (TBW). So that the prediction of fat mass (FM) and fat free mass (FFM) is based on algorithms implemented in BIA devices. This study was designed to validate the bioelectrical impedance device Tanita BC-418 in a population of 8 year old Caucasian children, using deuterium oxide dilution as a reference technique.

Methods: A subsample of sixty, 8 year old Spanish children from the EU Childhood Obesity Project took part in the study. All had weight and height measured and their body composition assessed by BIA and deuterium dilution (DD).

Results: Results from 59, 8 year-old Caucasian children (mean weight 27.9 kg (4.5), mean height 1.28cm (4.5)) were obtained. Table 1 shows the main outcome results for comparison of TBW, FM and FFM assessed by both techniques.

Mean differences between techniques were 5% for TBW, 9% for FFM and 23% for FM. So that, the bias was low for TBW but increased when applying internal algorithms of the device to estimate FM and FFM. With increasing fat mass, there was an increasing tendency to underestimate fat mass by BIA. The intraclass correlation coefficients ranged between 0.694 (for FFM) and 0.852 (for TBW) (Table 1).

Table 1. Fat Mass and Fat Free Mass comparison between techniques.

<table>
<thead>
<tr>
<th></th>
<th>BIA [kg] Mean (SD)</th>
<th>DD [kg] Mean (SD)</th>
<th>Difference in % Mean (SD)</th>
<th>Bias [kg] Mean (SD)</th>
<th>ICC (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBW</td>
<td>15.70 (1.98)</td>
<td>15.15 (1.80)*</td>
<td>3.7 (5.8)</td>
<td>0.54 (0.91)</td>
<td>0.852 (&lt;0.001)</td>
</tr>
<tr>
<td>FFM</td>
<td>21.43 (2.71)</td>
<td>19.61 (2.37)*</td>
<td>9.4 (6.5)</td>
<td>1.82 (1.30)</td>
<td>0.694 (&lt;0.001)</td>
</tr>
<tr>
<td>FM</td>
<td>6.61 (2.16)</td>
<td>8.36 (3.18)*</td>
<td>-17.6 (18.5)</td>
<td>-1.75 (1.31)</td>
<td>0.734 (&lt;0.001)</td>
</tr>
</tbody>
</table>

DD: deuterium dilution; BIA: bioelectrical impedance; TBW: total body water; FFM: fat free mass; FM: fat mass; *p<0.001 vs. BIA for Student’s T test for repeated measures; ICC = Intraclass Correlation Coefficient.

Conclusion: The BIA device Tanita BC-418 is an accurate method to assess TBW and FFM in 8 years olds. However, BIA underestimates FM with increasing FM content. In clinical settings, the assessments of TBW and FFM estimation is acceptable but the accuracy of FM estimation may not be sufficient to detect relevant changes in adipose tissue.

Disclosure of interest: Authors disclose no conflicts of interest.
Nutrition assessment in 126 hospitalized children with hepatic disease

Ronghua Yu¹, Lili Mo¹, Aishu Liu¹, Yizhong Wang¹, Yongmei Xiao¹, Ting Zhang¹

¹Children’s Hospital of Shanghai, Department of Gastroenterology, Hepatology, and Nutrition, Shanghai, China

Objectives and study: To investigate the nutritional status and to explore the malnutrition prevalence of hospitalized children with hepatic disease.

Methods: We prospectively surveyed a total of 126 hospitalized children with hepatic disease in Children’s hospital of Shanghai. Height for Z-score (HAZ), weight for age Z-score (WAZ), and weight for height Z-score (WHZ) were calculated.

Results: The prevalence of stunting (HAZ<−2), underweight (WAZ<−2), and wasting (WHZ<−2) was 9.6%, 13.5%, and 13.5%, while the nutritional risk (-2≤Z<-1) was 12.7%, 7.9%, and 19.8%, respectively. The children were divided into cholestatic group and noncholestatic group, the prevalence of stunting, underweight, and wasting was 13.3%/6.1%, 20.0%/7.6%, and 15.5%/13.1%, respectively. The differences in HAZ, WAZ, and WHZ were statistically significant (P<0.05).

Conclusion: The malnutrition prevalence in hospitalized children with hepatic disease is higher than the common population, especially with cholestasis. Nutrition assessment is recommended for hospitalized children with hepatic disease.

Disclosure of interest: The authors have declared that no conflict of interest exists.
Association amongst anthropometric status, micronutrients deficiencies and bone mineral density in neurologically impaired children

Elena Crehuá-Gaudiza¹, Monica García-Peris², Maria Antonia Moreno-Ruiz³, Carmen Jovani-Casano⁴, Ana Belén Navarro-Gallego¹, Cecilia Martínez-Costa⁵

¹Hospital Clínico Universitario, Pediatrics, Valencia, Spain
²Hospital Luis Alcanyís, Pediatrics, Xàtiva, Valencia, Spain
³Hospital de Manises, Pediatrics, Valencia, Spain
⁴Hospital General, Pediatrics, Castellón, Spain
⁵University of Valencia, Pediatrics, Valencia, Spain

Objectives and study: To analyze the association amongst anthropometric status, micronutrients deficiencies and bone mineral density in neurologically impaired children. A prospective observational multicenter study was designed.

Methods: A prospective observational multicenter study was conducted in children with moderate-to-severe neurological impairment (equivalent to Gross Motor Function System Classification, GMFCS III-V). Data collected included: medical records, anthropometric measures (transformed into z-score for age and sex according to WHO references), micronutrients status, and bone mineral density (BMD) measured with densitometry (measures were converted to age and gender normalized z-scores). The study protocol was approved by the Ethics Committee of each hospital in accordance with the Declaration of Helsinki of 1964.

Results: Fifty-eight children (36 male and 22 female, aged 2-16 years) were recruited. Primary diagnosis included 40 cases of cerebral palsy, 4 of genetic disorders, 3 of neuromuscular diseases and 11 other diagnoses. According to GMFCS, 2 patients were classified as grade III, 15 as grade IV and 41 as grade V. 17 patients (29%) received feeding by gastrostomy tube. 62% of cases were on anticonvulsant therapy and 55% were on antireflux medications. In 56% of children, the weight z-score was below 2SD; height z-score was below 2SD in 65% patients; and body mass index resulted below 2SD in 35% children, suggesting prevalence of chronic undernutrition. Height could not be adequately recorded for 18 patients due to skeletal deformities. Biochemical analysis showed low vitamin-D levels (<30 ng/mL) in 43% of cases, together with normal concentrations of calcium, phosphorous, magnesium and alkaline phosphatases. Five patients (9%) evidenced moderate iron deficiency. Vitamin B12 and folate levels were normal in all cases. Zinc levels resulted low in 22% of patients. Prealbumin values were low in 19% of cases, while albumin levels were normal. Osteoporosis was evidenced in 47% of patients. Positive correlation between BMD z-score and weight z-score, and inverse between BMD z-score and age was found. No correlation between vitamin D levels and osteoporosis was proven.

Conclusion: Undernutrition is frequently in disabled children with specific deficiencies as vitamin D and zinc. The prevalence of osteoporosis, probably multifactorial, is high and increases with age and severity of undernutrition.

Disclosure of interest: Authors declare no conflict of interest.
Accurate Estimation of Energy Requirements of Youth in Different Nutritional Status

Zhang Lin¹, Ran Chen¹, Xiaonan Li¹

¹Department 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 in childhood and evaluate the accuracy of predicted resting metabolic rate using the published standards and the meaning of indirect calorimetry.

Methods: Recruited children and adolescents were from the department of child healthcare in Nanjing children’s hospital during Jan, 2014 to Sept, 2015. There were 273 youth aged 7–14 years including obese (n=148), lean (n=44) and normal group (n=81) according to their body mass index (BMI) for age and gender. Measurements of anthropometric parameters and body composition were performed at the beginning of the study. MREE was measured via an indirect calorimeter (IC). Predicted Energy Expenditure (pEE) was estimated using 10 published equations including those commonly used in children. Comparisons between MREE and pEE were performed using mean percent accuracy.

Results: There are different MREE among obese group (29.06±5.74 Kcal/kg/d) and normal group (36.91±6.03 Kcal/kg/d) and lean group (42.01±7.21 Kcal/kg/d). Partial correlation analysis indicated that REE/kg was negatively related with weight (r=-0.692, p<0.011), fat mass (r=-0.671, p<0.001), free fat mass (r=-0.599, p<0.001), BMISDS (r=-0.684, p<0.001) and W/H (r=-0.379, p<0.001). Mean percent accuracy (%) of pEE to MREE varied with the different equations. The accuracy of pEE in total subjects used by Schofield, WHO, Harris-Benedict, Mifflin, Cunningham, Liu, Jiahong, IOM, Molar, Owen were 40.82%, 37.97%, 41.77%, 35.13%, 31.01%, 31.65%, 31.01%, 37.66%, 37.97% and 34.18% separately.

Conclusion: MREE levels are associated with children nutritional conditions and the accuracy of prediction formula was poor compared to IC. It is necessary to develop a new method to estimate of energy requirements during childhood, particular for obese or lean children.

Disclosure of interest: “None Declared”.
Nutritional intervention neurologically impaired children: a population-based study
Claudio Romano1, Maria Ausilia Catena1, Francesca Muraca1, Simona Valenti1
1University of Messina, Pediatrics Department, Messina, Italy

Objectives and study: malnutrition is a common condition among neurologically impaired children. Feeding difficulties and non-nutritional factors may influence growth, and nutritional factors such as insufficient caloric intake, excessive nutrient losses and abnormal energy metabolism can contribute to growth failure. Malnutrition is associated with significant morbidity, while nutritional rehabilitation improves overall health. Nutritional support should be an integral part of the management of neurologically impaired children, and should focus not only on improving nutritional status but also on improving quality of life for patients and their families. The objectives of this study were: identification of the prevalence of nutrition problems in neurologically impaired children, risk of malnutrition, predictors of poor nutritional status, the selection of the best nutritional intervention and the modalities to monitor response to nutritional intervention.

Methods: Using a neurologically impaired pediatric population-base, from December 2013 to June 2015, from among 110 patients, 38 (34%) patients (aged 2-8 years) needed nutritional support for malnutrition, associated with oral dysphagia (n° 20, 52%), and respiratory symptoms (n° 18, 47%), respectively. Malnutrition or undernourished was defined as failure to gain weight resulting in a falling weight centile, weight loss, in cerebral palsy growth charts and triceps skinfold thickness < 10th centile. Table 1 describes the clinical diagnoses. Enteral nutrition support was with gastrostomy (n° 30, 78%) and tube feeding (n° 8, 21%). Nutritional support was a normal-energy polymeric formula (Nutrini, Nutricia) with bolus administration, intermittently or continuous, using an enteral feeding pump.

Results: in one year of follow-up, exclusive enteral feeds in neurologically-impaired children was associated with rapid improvement of anthropometric parameters such as weight, height, and triceps skinfold thickness. At two months, 35 pts (92%) presented an increase in weight (average 1 kg in 36 pts), triceps skinfold thickness (0.62 mm) and disappearance of gastrointestinal symptoms, such as constipation (71%), respiratory infections (68%) and vomiting (70%).

Table 1

<table>
<thead>
<tr>
<th>Disability</th>
<th>Children</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cerebral Palsy</td>
<td>18 (47%)</td>
</tr>
<tr>
<td>Genetic Syndromes</td>
<td>10 (26%)</td>
</tr>
<tr>
<td>Chromosomal Syndromes</td>
<td>10 (26%)</td>
</tr>
</tbody>
</table>

Conclusion: A significant proportion of children with neurodevelopmental disabilities are undernourished. In our study, the screening programme has allowed early identification of malnutrition secondary to feeding problems. The association between oromotor dysfunctions, gastroesophageal reflux with emesis and esophagitis, with food refusal and pulmonary aspiration can be considered the most important predictors of malnutrition. Triceps skinfold thickness and mid-arm circumference are more accurate than weight-for-height in detecting malnutrition. The best intervention was enteral nutrition support with gastrostomy (in 78% of our population) without preliminary nasogastric feeds. A 1 kcal/mL polymeric formula is preferred to a 1.5 kcal/mL formula or fibre-containing formulas, for better tolerance. In conclusion, nutritional assessment and support must be an integral part of the care of neurologically impaired children with close monitoring of oral feeding problems, and early nutritional intervention.

Disclosure of interest: None Declared.
Diabetic Ketoacidosis: What is changing

Irene Rutigliano\textsuperscript{1}, Pasquale Maccarone\textsuperscript{2}, Anthea Bottoni\textsuperscript{2}, Anna Pacilio\textsuperscript{2}, Giuseppina D'Angelo\textsuperscript{2}, Salvatore Cringoli\textsuperscript{2}, Maria Pia Falcone\textsuperscript{2}, Luciana Romaniello\textsuperscript{2}, Mario Rocco d'Altilia\textsuperscript{1}, Maria Pastore\textsuperscript{1}, Filomena Frascolla\textsuperscript{1}, Massimo Pettoello Mantovani\textsuperscript{2}, Michele Carmine Sacco\textsuperscript{2}

\textsuperscript{1}Paediatrics, Ircss "Casa Sollievo Della Sofferenza", San Giovanni Rotondo, Italy
\textsuperscript{2}Paediatrics, University of Foggia, Foggia, Italy

**Objectives and study:** Diabetic ketoacidosis is a potentially life threatening complications in patients with type 1 diabetes (DM1). We analysed the epidemiology of KAD, reviewing the Diagnosis of KAD at onset of DM1, in the last 15 years.

**Methods:** We reviewed children admitted to our Pediatric Unit with diagnosis of KAD at onset of DM1, from 2000 to 2014. Our population was divided into four groups according quartiles for date of diagnosis. Collected data included: age at diagnosis, sex, anthropometric evaluation. Statistical analysis was performed with IBM SPSS v 22.

**Results:** Our population consisted of 66 patients (31 males and 35 females, \( p=0.622 \)) with KAD at DM1 diagnosis: 14 patients were admitted from 2000 to 2004, 16 patients from 2005 to 2009, 36 from 2010 to 2014 (\( p=0.001 \)). Mean age at diagnosis was 7.1±3.4 yrs (range 1.2-15.6 yrs); in first quartile the mean age at KAD diagnosis was 5.7±3 yrs (range 1.2-11.2 yrs, 9 males and 7 female), 7.6±3 yrs in second quartile (range 3.9-13.9 aa, 5 male and 12 female), 7.3±4.1 yrs in third one (range 1.27-14.1, 9 male 8 female), 7.8±2.9 yrs in the fourth (range 3.3±15.6 aa, 8 male and 8 female). This distribution was not statistically significant (\( p=0.272 \) for age, \( p=0.398 \) for sex). Mean BMI z-score in our population was \(-0.32±1.3\) : \(-0.6±1.3\) in male, \(-0.1±1.22\) in female (\( p=0.327 \)). No difference was recorded in BMI z-score calculated in children among the four quartile (\( p=0.327 \)).

**Conclusion:** Our findings highlight an increasing trend in incidence of KAD at DM1 presentation in the last years. No difference are recorded, instead, in the age at diagnosis, sex distribution and nutritional status. Moreover, even if current literature described alterations in epidemiological pattern at DM1 diagnosis, these do not seem to affect the principal diabetes comorbidity: KAD.

**Disclosure of interest:** “None Declared”. 
Acute metabolic complications and nutritional assessment in children and adolescents with anorexia nervosa
Matea Crnković¹, Orjena Žaja¹, Sandra Strelec²
¹Clinical Hospital Centre Sestre Milosrdnice, Department of Pediatric Gastroenterology, Hepatology and Nutrition, Zagreb, Croatia
²University of Medicine, Zagreb, Croatia

Objectives and study: Anorexia nervosa (AN) in children and adolescents is still a serious cause of morbidity and mortality which may result in premature death or life-long medical and psychosocial morbidity. Although many of the medical complications improve with nutritional rehabilitation and recovery from the disorder, some are potentially irreversible. Over the last decade the prevalence of AN is not only increasing but also starting to affect younger children. The aim of this study was to investigate the value of anthropometric parameters with possible electrolyte deviations, and to examine the duration and number of hospitalizations depending on the presence and the frequency of nutritional support, caloric value and duration of it.

Methods: Anthropometric measures and electrolyte concentrations were evaluated in 165 AN patients from 7 to 23 years old hospitalized in the Department of Pediatrics, Sestre milosrdnice, Clinical Hospital Centre Zagreb from 2005 to 2014.

Results: Some of the parameters such as body weight, percentage of ideal body weight and body mass index were significantly lower than expected regarding age, and as for the level of electrolytes-results were in accordance to previous studies. As expected 7,27 % of patients initially presented themselves with hypokalemia which can be due to both vomiting or misuse of laxatives. 14,55 % of admitted patients were hypoglycemic and 9,09% initially had hypophosphatemia. Hypercholesterolemia occurred in 33,94 % of the patients, 75% of whom had LDL level above 3 mmol/L (Table 1.). Girls who have received an average of 1096 ± 432.35 kcal nutritional support per day were hospitalized for a longer period of time, but fewer times.

Table: Serum electrolyte and cholesterol abnormalities

<table>
<thead>
<tr>
<th>Potassium</th>
<th>Sodium</th>
<th>Chloride</th>
<th>Phosphate</th>
<th>Magnesium</th>
<th>Total cholesterol</th>
<th>LDL</th>
<th>Triglycerides</th>
</tr>
</thead>
<tbody>
<tr>
<td>% of patients with values lower than reference interval</td>
<td>7,27</td>
<td>1,21</td>
<td>1,82</td>
<td>9,09</td>
<td>0</td>
<td>/</td>
<td>/</td>
</tr>
<tr>
<td>% of patients with values higher than reference interval</td>
<td>0,6</td>
<td>4,5</td>
<td>1,8</td>
<td>/</td>
<td>/</td>
<td>33,94</td>
<td>24,24</td>
</tr>
</tbody>
</table>
Conclusion: Our results confirm the high prevalence of acute metabolic complications in children and adolescents with AN. With timely and appropriate diagnostic approach, AN can be detected at an earlier stage, when prompt intervention, multidisciplinary approach (pediatrician, psychiatrist, psychologist, clinical nutritionist) and nutritional rehabilitation can prevent irreversible metabolic complications.

Disclosure of interest: “None Declared”.
Lean Body Mass Measurement as a Part of Dietitian Assessment in Infants with Cholestatic Liver Disease before Liver Transplantation.

Luba Marderfeld¹, Corina Hartman², Irit Poraz¹, Neta Biran¹, Yael Mozer-Glassberg², Raanan Shamir²

¹Schneider Children’s Medical Center of Israel, Nutrition and Dietetics Department, Petach Tikva, Israel
²Schneider Children’s Medical Center of Israel, Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel

Objectives and study: Children with cholestatic liver disease may suffer from chronic malnutrition. We aimed to evaluate body composition by air displacement plethysmography of infants with cholestatic liver disease as a part of nutritional and overall assessment before liver transplantation in a pediatric tertiary hospital.

Methods: Infants underwent full nutritional assessment by dietitian that included a number of anthropometry measurements: weight and height, mid upper arm circumference, skin fold thickness and air displacement plethysmography. Laboratory tests were extracted from medical records and PELD Score for End-Stage Liver Disease was calculated.

Results: 16 infants aged 21.6 (±13) weeks old, 45% boys were included in the analysis. 81% had biliary atresia, PELD score was 12.8 ±10. Mean z-score for height and weight was -2.4±1.8 and -2.4±1.2 respectively. Mean fat free mass and fat mass were 84.5%±5.6% and 15.5%±5.6%. Fat free mass correlated significantly (P<0.05) negatively and with PELD and bilirubin and positively with MUAC z-scores and albumin. PELD correlated significantly (P<0.05) negatively with MUAC.

Conclusion: In this population, measuring body composition is closely associated with disease level and important for identifying infants at higher risk for malnutrition.

Disclosure of interest: None Declared
Effect of cyproheptadine on growth velocity in children with Silver-Russell syndrome

Anaïs Lemoine¹, Salem Jennifer², Harbison Madeleine³, Tounian Patrick¹, Netchine Irène⁴, Dubern Béatrice⁵

¹Hôpital Trousseau - Aphp, Pediatric Nutrition and Gastroenterology Unit, Paris, France
²Magic Foundation, Rss/Sga Research and Education Fund, Oak Park, United States
³Ichan School of Medicine at Mount Sinai, Pediatrics, New York, United States
⁴Hôpital Trousseau - Aphp, Pediatric Endocrinology Unit, Paris, France

Objectives and study: Russell-Silver syndrome (RSS) is a rare syndrome, characterized by at least four of the following criteria: intrauterine growth restriction and/or failure to thrive below -2 SDS, relative macrocephaly, hemi-body asymmetry, feeding difficulties or body mass index (BMI) lower than -2 SDS, prominent forehead. Nutritional management is crucial during the first years of life before initiation of growth hormone (GH) treatment. Cyproheptadine (CYP) was previously described for its orexigenic effect in diseases such as cystic fibrosis or AIDS. However, no study described its effect in RSS patients. Our study aimed to evaluate the effect of CYP on weight and height evolution of RSS patients.

Methods: Anthropometric parameters (weight (W), height (H), ratio between W and expected W for H (W/H) and BMI) of 34 children with RSS were recorded at baseline (M0) and at 3, 6, 9 and 12 months (M3, M6, M9, M12) after starting treatment with CYP. Two groups were defined: group 1 including children treated with CYP alone (n = 23) and group 2 including children treated with CYP associated with previously introduced enteral nutrition (EN) and / or GH (n = 11).

Results: At baseline, the median age of RSS children was 2 years with median weight of 7.5 kg (-4.7 SDS), median height of 75.6 cm, (-3.2 SDS), median W/H to 77.3% and median BMI Zscore at -2.8 SDS. At T0, in group 1, children were significantly shorter and thinner when compared to group 2 (weight: -5.72 SDS vs -3.55 SDS, p = 0.015; height: -3.6 SDS vs -2.86 SDS, p = 0.034) and with a marked weight stagnation during the months preceding the start of CYP. Weight and height were significantly different from M0 and all other time, without significant difference between the two groups. After one year of treatment, the overall size and weight gain was significant (weight: + 1.06 SD, p <0.0001; height: + 0.31 SD, p = 0.027) as soon as 3 months of treatment. At M3, significant improvement of W/H and/or BMI were also noted (in group 1: W/H 74.9% vs 79.3% (p = 0.016), BMI Zscore: -3.4 vs. -2.4 SDS (p = 0.006); in group 2: W/H 79.3% vs 88.9% (p = 0.032)). 58.1% of patients were classified as responders or partial responders to CYP defined as weight gain of at least one SDS over the evaluation period. Responders were significantly thinner (weight: -5.63 SDS vs -3.55 SDS, p = 0.019) and younger (1.9 years vs 2.5 years, p = 0.04) when compared to non-responders and gained +1.5 SDS of weight over a period of one year. EN had no influence on the effect of CYP.

Conclusion: In our cohort, CYP was effective in approximately 60% of RSS patients and was associated to a significant improvement of growth velocity and nutritional status before GH treatment. Our results suggest that CYP can be used for the nutritional management of children with RSS. Further studies are necessary to confirm our results especially with control group.

Disclosure of interest: None Declared
Survey on dietary habits of a pediatric IBD population in Southern Italy: preliminary results.

Massimo Martinelli¹, Elena Scarpato¹, Caterina Strisciuglio², Maria Rosaria Serra¹, Erasmo Miele¹, Annamaria Staiano¹

¹Federico II University, Department of Translational Medical Science, Section of Pediatrics, Naples, Italy
²Second University of Naples, Department of Woman, Child and General and Specialized Surgery, and Genius Group, Naples, Italy

Objectives and study: It has been reported that patients with IBD consider dietary factors to be relevant to their disease and often claim to reduce their intake because of those beliefs. Indeed, some reports have demonstrated that inadequate caloric intake is the primary cause of growth retardation in pediatric IBD. Aim of this study was to characterize dietary habits of IBD pediatric patients in terms of macronutrients and micronutrients intakes through the administration of a Food Frequency Questionnaire.

Methods: We prospectively enrolled pediatric patients with a diagnosis of IBD coming to our referral center for routine visits between May and November 2015. Data regarding demographic characteristics, disease localization according to Paris classification, disease activity (PCDAI and PUCAI) and ongoing therapy were collected at the enrollment. In addition, a qualitative and quantitative assessment of nutritional intake was made through the administration of a validated food frequency questionnaire. Dietary intake was successively converted in micro and macronutrients determination through Winfood software. The adequacy of different nutrients’ intake was established through the use of Italian Recommended levels of intake of nutrients and energy (LARN).

Results: Forty children affected by IBD were consecutively enrolled [(CD:12 (30%), UC:28 (70%); median age: 13.5 yrs; range 5-18; M/F: 18/22)]. Median age at diagnosis was 12.3 yrs (range 3-16). Median PCDAI and PUCAI at the enrollment were 10 and 12.5 (range: 0-25 and 0-30, respectively). At the enrollment the ongoing therapies of IBD children were: mesalazine (n=19, 36.5%), azathioprine (n=16, 30.8%), methotrexate (n=2, 3.8%) and biologics (n=3, 5.8%). The total daily energy intake was lower than the expected value for age in 28 out of 40 patients (70%). No significant difference was observed among CD and UC patients (p=0.7). Among macronutrients, an inadequate intake of protein was identified in 7 out of 40 patients (23.2%), while 11 out of 40 patients (27.5%) made an excessive consumption of lipids. Conversely, 37 out of 40 patients (92.5%) had an inadequate fibers intake. Regarding micronutrients, among the enrolled patients there was a high prevalence of subjects with inadequate intake of vitamin A (54.2%), vitamin B6 (20%), vitamin C (40%), vitamin D (90%), calcium (40%), folate (80%), iron (55.5%), niacin (35%), phosphorous (50%), riboflavin (47.5%), thiamine (10%) and zinc (50%). There were no significant differences in the percentage of subjects consuming inadequate amount of micronutrients when compared by disease type or disease activity.

Conclusion: Our preliminary results suggest that IBD children are at increased risk of macro and micro-nutrients deficiencies regardless of disease type and disease activity. It is therefore warranted a nutritional surveillance and a multivitamin supplementation in order to avoid several nutrition deficiencies.

Indications for using the hydrolyzed protein industrial formula in infants treated with the Home Enteral Nutrition (HEN) - not only in case of allergy.

Małgorzata Matuszczyk¹, Michal Szczepanski¹, Anna Wiernicka¹, Olga Niewiadomska², Jarosław Kierkus³

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, Nutrition Disorders and Pediatrics, Warsaw, Poland

Objectives and study: The obvious reason for using the hydrolyzed protein industrial formula in enteral feed infants is undernutrition and/or age above six months in the combination with the cow’s milk allergy but there is no available data about usefulness of such diet in other clinical conditions. It is known that the most common indications for chronic enteral nutrition during infancy are prematurity, neurological problems and genetic birth defects. All of these medical conditions may be related with gastrointestinal disorders (gastro-oesophageal reflux, gastroparesis), malabsorption and maldigestion. As a result the symptoms of diet intolerance and the insufficient weight/growth gain are often observed. Based on our practice the replacement of polymeric diet by the hydrolyzed protein industrial formula may be benefit in such group of patients.

Methods: We retrospectively analyzed the data of 44 infants qualified to the HEN since the infant's hydrolyzed protein industrial formula (Infatrini Peptisorb) is available in Poland -01.01.2014- till 18.12.2015. The indications for enteral nutrition and additionally among the patients feed with Infatrini Peptisorb the reasons for using such diet and the nutritional status at baseline and 3 months after the start of therapy were analyzed.

Results: The indications for enteral nutrition in studied group were: genetic congenital malformations (n=14), prematurity (n=13), neurological disorders (n=11), gastrointestinal diseases (n=4) and congenital heart malformations (n=2). In 19 (43%) children in median age of 6.6 months (with the range of 1.7-11) the hydrolyzed protein industrial formula (Infatrini Peptisorb) was introduced, mainly in patients with genetic congenital malformations (n=8;40%), prematurely infants (n=5;25%) and children with neurological problems (n=3;23%). In the rest it was recommended occasionally, in 2 cases with gastroenterological diseases and in 1 infant with congenital heart malformation. The cow's milk allergy was indication for using the hydrolyzed formula only in 2 children. In the rest (n=17;89%) the decision was taken due to the observation of polymeric diet intolerance, demonstrated by vomiting after the increase of diet's volume (n=10), loose stools (n=7), flatulence (n=7) and anxiety during feeding (n=9). In this group among 15 (88%) of patients the undernutrition was stated based on BMI below 3 percentile on the WHO charts. In all 17 children the replacement of polymeric industrial diet by the Infatrini Peptisorb was effective and leads to the reduction of the intolerance's symptoms. The additional benefit was the improvement of the nutritional status. The increase of BMI was observed in all 11 infants who were seen after 3 months on the control visit (mean 1.8 kg/m²±1.6) and among 7 of them (64%) it met the normal value on the WHO growth charts. The rest 4 infants are newly qualified to HEN and expected on first control visit.

Conclusion: Our analysis show that among infants who needs chronic enteral nutrition the using of hydrolyzed protein industrial diet can be benefit in other than cow's milk allergy cases. The special attention should be paid to children with genetic congenital malformations, neurologic problems and prematurely infants. They may experience different gastrointestinal disorders and as a result the symptoms of standard polymeric diet's intolerance in the combination with the insufficient nutritional status are common problems.

Disclosure of interest: None Declared
The use of specialist medium chain triglyceride (MCT) formulas in infants with biliary atresia

Deepa Kamat¹, Sara Mancell¹, Serena Kyrana¹, Touqueer Fatima¹, Helen Mortimer¹, Kerryn Moolenschot¹, Anil Dhawan¹

¹King's College Hospital, Paediatric Liver, Gi & Nutrition Centre, London, United Kingdom

Objectives and study: Biliary atresia (BA) is often associated with malnutrition. In order to prevent this and maximise absorption, specialist formulas containing MCT are used and growth is monitored regularly. In addition, children frequently require nasogastric (NG) feeding to meet nutritional requirements. As MCTs are partially water soluble they do not require bile for emulsification and can be easily absorbed; this is essential where there is cholestasis. In our centre, specialist MCT feeds are used on all children until they are either transplanted or clear their jaundice (i.e. bilirubin of <34 μmol/L). In spite of intensive input, growth failure can still occur which is important to consider as it can be one of the indications for liver transplantation.

Our aim was to investigate growth and nutritional outcomes, in particular the use of MCT formulas in a group of patients diagnosed with biliary atresia.

Methods: Records of 88 patients (45 male) diagnosed with BA between 2010-2015 were retrospectively reviewed. Data was collected up to 12 months post Kasai portoenterostomy. Parameters assessed were use of MCT feeds, weight Z-score, presence of jaundice at 6 months (bilirubin <34 μmol/L), requirement for NG and need for liver transplant. SPSS was used for statistical analysis.

Results: 88 patients underwent a Kasai at a median age of 7.43 (2.29-40.43) weeks. 3 died and 39 (44%) patients underwent a liver transplant at a median age of 51 weeks (20.86-106.14) and then no longer required MCT formula. Of the 43 patients who did not require a transplant, 39 were able to wean off MCT feeds onto standard feeds after a median time of 29.79 (6.14-150.14) weeks. The mean (SD) bilirubin at time of weaning off was 11.53μmol/L (12.84μmol/L). 4 patients still require MCT formulas whilst listed for transplant and 4 patients of 43 remain on MCT despite having cleared their jaundice, because of parent preference. 32 of 88 patients required NG feeding, 24 of 32 patients who needed NG feeding went on to receive a transplant or are listed for transplant currently. Growth was initially poor with mean weight Z-score worsening from birth up to 6 weeks post Kasai (from -0.45 to -1.5); there was then an improvement from 6 weeks until 12 months (from -1.57 to -0.46). There was a significant difference in post Kasai weight Z-score at 6 months (p=0.0247), 9 months (p=0.0009) and 12 months (p=0.0108) between those children who had cleared their jaundice at 6 months compared to those who had not. At 6 months post Kasai, there was a significant difference in weight Z-score between those children who were subsequently transplanted compared to those not transplanted (p=0.0087).

Conclusion: MCT feeds were introduced in all patients with BA and continued for an average of 7 months in those patients not requiring a transplant. Despite all children having specialist MCT formulas, growth was poor initially but encouragingly it did gradually improve by 1 year for the group as a whole. Growth was significantly worse in those who failed to clear their jaundice at 6 months and for patients requiring a transplant. The patients requiring transplantation were much more likely to be fed MCT formulas via NG. Nutritional support should particularly target these children given their increased nutritional risk. In our experience, MCT feeds are an essential part of care for children with BA.
The Importance of Regional Body Composition when using DXA scan in Patients with End Stage Liver Disease (ESLD)

Eirini Kyrana 1, Jane E Williams 2, Jonathan CK Wells 3, Anil Dhawan 1
1 King’s College Hospital, Paediatric Liver, GI and Nutrition Centre, London, United Kingdom
2 UCL Institute of Child Health, Childhood Nutrition Research Centre, London, United Kingdom

Objectives and study: Children with ESLD suffer from poor growth and muscle wasting. Muscle wasting is identified as a predictor of poor outcome in many chronic diseases. Ten patients with end stage liver disease had a whole body DXA scan as part of their body composition assessment.

Methods: The children were in the process of being assessed for a liver transplant. They had a whole body DXA scan (Lunar Prodigy, software version 6.7, GE Medical Systems). As these patients are at risk of having growth issues, we report here indices corrected for height i.e. body mass index (BMI), fat mass index (FMI) and lean mass index (LMI) and the standard deviation scores (sds) were calculated from UK reference data 1.

Results: 6 patients were female. Ages varied from 4.7 to 17.2 years (median 9.9 years). Diagnoses were biliary atresia (pts 1, 5 and 10), Alagille syndrome (pts 3 and 7), re-transplantation (pts 4 and 6), neonatal sclerosing cholangitis (pt 2), cryptogenic cirrhosis (pt 9) and HCV cirrhosis (pt 8).

When assessing BMI and FMI only patient 2 is < -1.04 sds (<15th percentile), but with LMI 3 patients (patients 2, 3, 6) are identified to be with reduced lean mass and specifically < -1.64 sds (< 5th percentile). These patients frequently have organomegaly, and this is reflected in a relatively higher trunkLMIsds, which then confounds the totalLMIsds. Whereas when we look at segmental data e.g. armLMIsds and legLMIsds we see that 5 and 7 patients respectively have significantly reduced arm or leg lean mass.

Table:

<table>
<thead>
<tr>
<th>ID</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
<th>9</th>
<th>10</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI sds</td>
<td>1.18</td>
<td>-2.53</td>
<td>-0.52</td>
<td>0.34</td>
<td>0.88</td>
<td>-0.57</td>
<td>0.80</td>
<td>0.28</td>
<td>0.37</td>
<td>-0.41</td>
</tr>
<tr>
<td>totalFMI sds</td>
<td>0.36</td>
<td>-1.68</td>
<td>0.04</td>
<td>-0.13</td>
<td>-0.39</td>
<td>0.04</td>
<td>0.41</td>
<td>-0.11</td>
<td>0.39</td>
<td>-0.52</td>
</tr>
<tr>
<td>armFMI sds</td>
<td>-0.35</td>
<td>-1.79</td>
<td>0.08</td>
<td>-1.16</td>
<td>-0.54</td>
<td>-0.66</td>
<td>0.49</td>
<td>-0.24</td>
<td>0.39</td>
<td>-0.86</td>
</tr>
<tr>
<td>legFMI sds</td>
<td>0.26</td>
<td>-1.86</td>
<td>0.14</td>
<td>-0.34</td>
<td>-0.56</td>
<td>0.00</td>
<td>0.22</td>
<td>-0.23</td>
<td>0.60</td>
<td>-0.62</td>
</tr>
<tr>
<td>trunkFMI sds</td>
<td>0.51</td>
<td>-1.38</td>
<td>-0.15</td>
<td>0.34</td>
<td>-0.22</td>
<td>0.12</td>
<td>0.45</td>
<td>0.02</td>
<td>0.25</td>
<td>-0.36</td>
</tr>
<tr>
<td>totalLMIsds</td>
<td>1.04</td>
<td>-2.34</td>
<td>-1.79</td>
<td>0.28</td>
<td>1.92</td>
<td>-1.52</td>
<td>0.14</td>
<td>0.06</td>
<td>-0.82</td>
<td>-1.00</td>
</tr>
<tr>
<td>armLMIsds</td>
<td>-1.75</td>
<td>-4.05</td>
<td>0.03</td>
<td>-0.43</td>
<td>-0.89</td>
<td>-1.69</td>
<td>-0.98</td>
<td>-0.29</td>
<td>-4.42</td>
<td>-3.41</td>
</tr>
<tr>
<td>legLMIsds</td>
<td>-1.21</td>
<td>-3.51</td>
<td>-2.00</td>
<td>-1.42</td>
<td>0.33</td>
<td>-1.84</td>
<td>-0.77</td>
<td>-0.49</td>
<td>-2.53</td>
<td>-2.66</td>
</tr>
<tr>
<td>trunkLMIsds</td>
<td>3.92</td>
<td>0.01</td>
<td>-1.39</td>
<td>1.42</td>
<td>3.30</td>
<td>-0.62</td>
<td>0.93</td>
<td>0.70</td>
<td>1.40</td>
<td>0.94</td>
</tr>
</tbody>
</table>

Conclusion: Basic anthropometry is inadequate when used for body composition assessments in children with ESLD. Regional measurements like arm or leg LMI are more appropriate in identifying patients with muscle wasting.


Disclosure of interest: None declared
Pediatric Nutrition Week: The four editions – Colombia

Maria Bages¹

¹EL Bosque University, Bogota, Bogota, Colombia

Objectives and study: For the last four consecutive years (2012-2015), we conducted a systematic nutritional assessment survey in pediatric wards. Eight hospitals participated in this cross-sectional survey using a web-based tool: e-Pinut. We want to determinate the prevalence of malnutrition in hospitalized children.

Methods: All participating centers conformed to the Pediatric Nutrition Week guidelines for systematic nutritional assessment. Children admitted the same week were measured, weighed and their diagnoses recorded. Diagnostic procedure (clinical examination) was conducted only for children below the third centile of BMI for age and sex (World Health Organization Reference).

Results: Eight centers participated in this survey. On 528 observations collected, 528 were analyzed, totaling 528 patients (56.3% boys, median age: 3.2 years). Weight for height (WFH) < -2 Standard Deviation (acute malnutrition) was found in 18% of the whole population. Fifteen point one percent of children had a height for age < -2 Standard Deviation. Chronic diseases were present in a higher number of the children with a higher rate of malnutrition. All of the participating centers claimed to use e-Pinut as a tool to develop the awareness of malnutrition within their staff.

Conclusion: e-Pinut succeeded in mobilizing a growing number of pediatric wards in Colombia and contributed to standardize malnutrition diagnostic procedure. Frequency of malnutrition varied with centers and are in accordance with previous survey e-Pinut made in other countries. Next steps for 2016 are to widen the initiative and to extend it toward paramedical health professionals.

Disclosure of interest: None Declared.
Vitamin E deficiency in children with chronic liver disease

Juliana Roda¹, Patricia Rocha², Susana Nobre³, Sandra Ferreira³, Isabel Goncalves³

¹Hospital Pediátrico de Coimbra, Gastroenterology and Nutrition Unit, Coimbra, Portugal
²Centro Hospitalar de Leiria, Pediatric Department, Leiria, Portugal
³Hospital Pediátrico de Coimbra, Pediatric Liver Transplantation Unit, Coimbra, Portugal

Objectives and study: Children with chronic liver disease have fat-soluble vitamins mal-absorption. Vitamin E deficiency may cause irreversible lesions of the central and peripheral nervous system, particularly in the first two years of age. The aim of this study was to evaluate serum vitamin E concentrations in children with chronic liver disease.

Methods: All patients followed by the Liver Transplantation Unit of a Portuguese Tertiary Hospital that had their serum vitamin E concentrations measured from 2010 until 2014 were included in the study. The following variables were retrospectively analysed: demographic data, vitamin E /cholesterol ratio, total bilirubin, INR, platelets, type and dosing of vitamin E supplementation. Serum vitamin E /cholesterol ratio between 3.82 and 6.62 was considered normal.

Statistical analyses was performed using SPSS 20.

Results: One hundred and two patients were included in the study, corresponding to a total 181 serum vitamin E concentration measurements. Patients median age was 3 years old (1 month old to 18 years old). Female to male ratio was 1:1.

The most frequent diagnosis was biliary atresia (26%). Serum vitamin E/cholesterol ratio was low in 74 measurements (41%), normal in 85 (47%) and high in 22 (12%).

In the group with vitamin E deficiency, 69% was receiving vitamin E supplementation, most of them in the micellized formulation (55%).

No correlation was found between low serum vitamin E and total bilirubin values, INR or platelets count.

Conclusion: Vitamin E deficiency is frequent in children with chronic liver disease. Because of the potential neurocognitive consequences, serum vitamin E levels should be systematically measured in these patients, independently of the cholestasis severity. The frequency of these measurements should be adapted to each patient.

Disclosure of interest: None declared
The differences of food preference and physical fitness between children born low birth weight and children born normal birthweight are age- and gender-dependent

Muqing Cao¹, Yanna Zhu², Jin Jing², Yajun Chen², Wenhao Yang², Xiuhong Li², Li Cai¹, Jingjing Liang²

¹Sun Yat-Sen University, Maternal and Child Health, Guangzhou, China
²School of Public Health, Global Health Institute (Sghi), Sun Yat-Sen University, Department of Maternal and Child Health, Guangzhou, China

**Objectives and study:** There is limited information regarding health related behavior including food preference and physical fitness of low birth weight children in China. We hypothesis that children born low birth weight (LBW) have less preference of healthy food and less physical activity relative to children born normal birth weight (NBW).

**Methods:** The sample consisted of 11,380 children aged 6–18 years that were randomly selected from 13 schools in three urban districts of Guangzhou. All students received height and weight measurement which conducted by researchers, as well as a self-report questionnaire aimed to collect information including weekly food intake (vegetable, fruit, meat, sugar beverage) amounts and physical activity hours (high level physical activity, middle level physical activity, walking, sedentary time). A caretaker would answer the questionnaire on behalf of a child if he or she aged under nine years. Demographic information and birth weight were provided by the caretaker.

**Results:** A total of 8,860 students completed the study (aged 11.35± 3.45 years, 51.3% boys). The prevalence of low birth weight was 4.6% (5.0% in girls and 4.3% in boys). In each gender- age-group, child of LBW had lower height and body mass index (BMI) relative to their NBW counterparts (all p<0.05). For boys aged 6-12 years, those born LBW had less daily vegetable intake (1.94±0.15 vs. 1.55±0.22, NBW vs. LBW, serves/day, p=0.015), and fruit intake (1.47±0.12 vs. 1.25±0.17, NBW vs. LBW, serves/day, p=0.06). For boys aged 13-18 years, those born LBW had more daily walking hours (1.21±0.16 vs. 1.81±0.26, NBW vs. LBW, hours/day, p=0.005) and total physical activity hours (2.38±0.25 vs. 3.18±0.42, NBW vs. LBW, hours/day, p=0.026) relative to those born NBW. No food preference or physical fitness difference was found between NBW and LBW girls in either age group.

**Conclusion:** LBW boys aged 6-12 years tend to eat less vegetable and fruit, and LBW boys aged 13-18 years tend to have more walking hours and total physical activity hours. For girls, food preference and physical fitness seem not effected by low birth weight.

**Disclosure of interest:** None Declared.
Wilkie’s syndrome admitted with acute abdomen: a case presentation

Hasret Ayyildiz Civan1, Didem Gulcu1, tulay erkan1, Fugen Cullu Cokugras1, tufan kutlu1

1Istanbul University Cerrahpasa Medicine Faculty, Pediatric Gastroenterology Hepatology and Nutrition, Istanbul, Turkey

Objectives and study: Wilkie’s Syndrome (or superior mesenteric artery [SMA] syndrome) is a rare clinical entity which is caused by compression of duodenum by SMA as a result of decreased mesenteric fat tissue and narrowed angle between SMA and aorta. In this syndrome, progressive weight loss is accompanied by abdominal pain, distension, loss of appetite, nausea and vomiting after the meals. Radiography of barium passage and abdominal angio-tomography are useful for the diagnosis. We present a 16-year-old cachectic female patient admitted to the emergency department with abdominal distension, loss of appetite and vomiting for four days, which is eventually diagnosed with SMA syndrome.

Methods: Common acute abdomen etiologies were ruled out however abdominal ultrasonography reported a massive intraperitoneal fluid which was then regarded as the dilated stomach and its content. A barium passage radiography of duodenum confirmed the diagnosis.

Results: She was referred to our pediatric gastroenterology department after ruling out common acute abdomen etiologies, with a probable diagnosis of inflammatory bowel disease. From her history, she had a period of constipation four months ago. Loss of appetite and a temporary eating disorder emerged at that time and thus she ended up in a weight loss of 15 kg after three months. Her clinical presentation was not suggestive of an inflammatory bowel disease. In physical examination, there was no abdominal tenderness or organomegaly. As Wilkie’s syndrome was suspected, a barium passage radiograph of esophagus-stomach-duodenum was taken. In the horizontal part of duodenum, a delayed passage of barium was identified which was in consistency with the compression of SMA. Enteral feeding via nasojejunal tube was well tolerated and provided weight gain in a short time.

Conclusion: In patients presented with acute abdomen, Wilkie’s syndrome should be considered in differential diagnosis when there is an history of progressive weight loss.

Disclosure of interest: None declared.
NUTRITION: Nutrition and health outcomes

N-P-043

Family history of atopy in infants with cow’s milk protein allergy: a french real lifestyle study

Nicolas Kalach1, Marc Bellaiche2, Pascal Maigret3, Christophe Dupont4

1St Vincent de Paul Hospital, Lille, France
2Robert Debré Hospital, Paris, France
3Menarini, Rungis, France
4Necker Hospital, Paris, France

Objectives and study: In absence of data on the development of cow's milk protein allergy (CMPA) in atopic and non-atopic families in France, this study aimed to describe the family history of atopy (FHA) in a population of new-borns and infants with a suspected or documented CMPA (dCMPA).

Methods: HERITAGE was a non-interventional, cross-sectional, national multicentre study conducted in infants (0 - 18 months) with suspected or dCMPA, attending to private practice. Infants’ characteristics, environmental factors, evocative symptoms, CMPA diagnosis work-up, and FHA were collected by 466 randomly selected physicians, mainly paediatricians (N=452). The diagnosis of CMPA was left to physicians’ judgment to be the closest to the usual practice. Physicians’ initial diagnosis was then centrally reclassified according to the level of evidence into four sub-groups: dCMPA (n=260; 15.5%), highly probable CMPA (n=873; 52.2%), allergic sensitization (n=139; 8.3%), and undocumented CMPA (n=402; 24.0%).

Results: 1,674 evaluable infants were analysed (median age: 4.5 months, range: 0.1 - 18.0). First CMPA-evocative signs were reported within the first 6 months of life (95.8% of infants), and CMPA manifestations were mainly delayed (63.9%). FHA was reported in 1,413 infants (84.4%): first-degree relatives in 74.4% [95% CI: 72.3-76.5%] of the whole population and/or second-degree relatives in 57.3% [95% CI: 54.9% - 59.7%]. No significant differences were observed in infant characteristics between those with / without FHA, except the lower presence of pets in non-atopic families (14.2% vs. 25.4%, p<0.001). FHA infants were more likely to experience skin symptoms (62.9% vs. 47.9% in non-atopic families, p<0.001) and sleep disorders (44.7% vs. 36.4%; p=0.013). Infants with dCMPA had a significantly higher rate of first-degree FHA compared to those without dCMPA (81.2% vs. 73.1%, p=0.006). First-degree relatives’ most common atopies were allergic rhinitis or conjunctivitis (36.6%) and skin allergy (34.6%); these manifestations were significantly more frequent in first-degree relatives of dCMPA infants than in those of the other infants [respectively, 42.7% vs. 33.1%, p=0.003, and 43.5% vs. 35.3%, p=0.012]. Most common atopies of second-degree relatives were skin allergy (28.6%) and asthma (24.4%).

Conclusion: This study showed a high level of FHA in a large population of new-borns and infants with a suspected and particularly dCMPA, seen in private practice in France.

Pooled analysis of the Cow’s Milk Symptom Score (CoMiSS) as a predictor for the diagnosis of cow’s milk allergy

Yvan Vandenplas¹, Philippe Steenhout², Anette Jarvi², Anne-Sophie Garreau³, Rajat Mukherjee⁴

¹Uz Brussel, Department of Pediatrics, Brussels, Belgium
²Nestle Health Science, Vevey, Switzerland
³United Pharmaceuticals, Paris, France
⁴Cytel Consulting, Cambridge, United States

Objectives and study: The efficacy of an extensively hydrolyzed formula was evaluated in three separate clinical trials in terms of the results from a challenge test and the Cow Milk Symptom Score (CoMiSS) (Acta Paediatr 2013;102:990–8; Arch Dis Child 2014;99.933–6; Eur J Pediatr 2014;173:1209–16).

Methods: Data from the three studies were selected for the pooled analysis based on the following criteria: i) The challenge test result was available; ii) the CoMiSS total score was known both at baseline and after 1 month. Pooled analyses were conducted based on regressing the results of the 1-month challenge test on the month-1 CoMiSS, adjusting for baseline CoMiSS using a logistic regression model. In addition a logistic regression model was also fitted to the month-1 challenge test result with the change in CoMiSS from baseline as a predictor. Results are summarized in terms of Odds-Ratios (OR) with 95% confidence intervals and P-values.

Results: Results suggest that infants having a low CoMiSS after 1 month dietary treatment with an extensively hydrolyzed formula have a significant risk of having a positive challenge test (OR = 0.83, 95% CI: 0.75, 0.93, P-value = 0.002).

Conclusion: The results of the pooled data analysis suggest that the change in CoMiSS from baseline to month-1 can be used to predict CMPA as confirmed using the challenge test at month-1. However, in order to validate such a tool, infants without CMPA would also need to be enrolled in a validation trial. An obvious concern is that it may not be ethical to expose healthy infants to an extensive hydrolysate and to a challenge test.

Disclosure of interest. YVDP is consultant for United Pharmaceuticals, ASPEN, Nutricia Belgium. PS and AJ are Nestle employees. ASG is United Pharmaceuticals employee. RM is Cytel Consultancy employee.

Mark Hanson¹, Matthew Pretty²

¹University of Southampton, Academic Unit of Human Development and Health, Southampton, United Kingdom
²International Federation of Gynecology and Obstetrics, London, United Kingdom

Objectives and study: Malnutrition throughout women’s adolescence and reproductive years represents a major public health issue; nutrition and lifestyle can have lasting effects on a girl or woman’s long-term health, as well as influencing the future health of her offspring in terms of perinatal survival and risk of later non-communicable diseases. While there is global consensus on the need for girls and women to adopt optimal nutrition practices when planning a pregnancy, during a pregnancy and in the post-partum period, there has previously been no comprehensive resource setting out evidence-based guidance for health care professionals (HCPs) to assist them in advising their patients. The International Federation of Gynecology and Obstetrics (FIGO) endeavoured to create such a document and is now working towards its global implementation.

Methods: An international expert group was established, which met and consulted over an 18 month period. The group was concerned to address malnutrition, including under- and overnutrition, macro- and micronutrient balance and related lifestyle issues, and to present guidance on these using a life course approach. In addition to creating guidelines for HCPs, the group aimed to raise awareness of the links between maternal malnutrition and non-communicable diseases and emphasise the importance of nutrition to achieving the global health targets identified in the Sustainable Development Goals.

Results: FIGO recommendations on Adolescent, Preconception and Maternal Nutrition provide a comprehensive resource describing in detail the key nutritional issues HCPs need to observe and analyse in girls and women of reproductive age. It explains potential consequences to the woman and her offspring of malnutrition and the advised interventions. With the over-arching theme of ‘Thinking Nutrition First’ the document uses regional case studies to exemplify local situations and offer specialized solutions. These recommendations seek to empower and to provide opportunities for all levels of HCP to contribute to achieving improved nutrition in their communities.

Conclusion: FIGO’s recommendations create a framework for action to improve the nutritional care and support of girls and women through their pre-pregnancy, pregnancy, post-pregnancy, and inter-pregnancy periods of life. Regional differences create challenges as well as opportunities for translating the recommendations into practice. In order to implement the recommendations, regional and national guidelines must be developed along with training and capacity building activities. Advocacy at local and international level should focus on public health measures to improve nutritional education and literacy, particularly of adolescents and young women, and greater access to preconception services for women of reproductive age to aid planning and preparation for healthy pregnancies and healthy children. This is a future goal of the FIGO initiative.

Disclosure of interest: The authors have no conflict of interest.
Gluten: essential for wheat survival but detrimental to human health

Aaron Lerner¹, Torsten Matthias²

¹Technion-Israel Institute of Technology, B. Rappaport School of Medicine, Haifa, Israel
²Aesku.Kipp Institute, Research, Wendelsheim, Germany

Objectives and study: The ancient wild wheat Triticum species were genetically diploid, very fragile hard to harvest very low in gluten content and with low survival. Genetic variability was essential for the wheat species to adapt to changing environmental conditions. Due to changing environment and men-originated breeding manipulations, selective advantage of wheat toward improved grains number and wheat survival and adaptation, occurred. This process was accompanied by enrichment of gluten content in the wheat and today 80% of the proteins are gluten. Parallel, some unwanted effects induced by gluten consumption in non-celiac affected populations were recently described.

Aims: to summarize the medical literature for gluten consumption and withdrawal effects on autoimmune diseases

Methods: A systematic review was performed to identify Studies referred to wheat gliadin, survival, gluten, GFD, gliadin, effects, morbidity, mortality, pathogenicity and health, using Medline, Google, and Cochrane Library databases.

Results: The following conditions might respond to gluten free diet (GFD): Transaminasemia, type 1 diabetes, rheumatoid arthritis, dermatitis herpetiformis, thyroiditis, lymphocytic and non-specific deudenitis, irritable bowel syndrome and HIV enteropathy, gluten ataxia, multiple sclerosis, non-celiac gluten sensitivity, autism spectrum disorder, schizophrenia, attention deficit hyperactivity disorder, depressive disorders, headaches, fibromyalgia and epilepsy. Several pathophysiological avenues were described for the detrimental effects of gluten: breach of intestinal tight-junction integrity, decreased viability and apoptosis induction in human cell-lines, induction of neutrophil migration, decrease in NKG2D and ligand expression, increase Th17 population, affects regulatory T-cell subsets, change innate immunity and dendritic cell functions and change diversity of the microbiome.

Conclusions: multiple non-celiac autoimmune diseases and conditions respond, to a variable degree, to GFD. The protective mechanisms of GFD are constantly unraveled and involve multiple immunoregulatory pathways. Since transglutaminase 2 is pivotal in post translational modification of gluten and autoimmunogenesis, GFD might slow its progression. Several pathophysiological pathways can explain the detrimental health effects of gluten consumption in humans.

Disclosure of interest: T M, A L “none declared”.
A multi-component intervention programme for overweight and obese children

Milena Morano, Irene Rutigliano, Alfonso Rago, Massimo Pettoello-Mantovani, Angelo Campanozzi

1Parisi-De Sanctis Institute, Italian Ministry of Education, University and Research (Miur), Foggia, Italy
2Paediatrics, Ircss "Casa Sollievo Della Sofferenza", San Giovanni Rotondo, Italy
3Paediatrics, University of Foggia, Italy

Objectives and study: The increase of paediatric obesity is a social concern related to adverse physical and psychosocial consequences, and highlights the need for suitable interventions promoting healthy lifestyles in children. This study examined changes in nutritional status, physical fitness, physical activity (PA) and some psychosocial determinants of activity behaviour in a sample of overweight children involved in a multi-component programme.

Methods: After admission to the hospital outpatient clinic of the Paediatric University Centre of Foggia, Italy, 18 obese and overweight children (11.3 ± 0.4 years) followed a 6-month programme focused on nutritional education, fun-based skill-learning PA and exercise training (two 2h sessions/week). Before (T0) and after (T1) the intervention, participants were assessed with respect to body weight, height, circumferences, skinfold thickness and fat mass. The health-related fitness tests of Sargent vertical jump (SVJ), 2kg medicine-ball throw (MBT), 10×5m agility shuttle-run (ASR) and Harre's circuit (HCT) were also administered. PA levels and individuals' perceptions of strength, speed and agility were measured with the PA Questionnaire for Older Children and the Perceived Physical Ability Scale, respectively. Pleasant and unpleasant emotional states and attitudes towards PA were evaluated with an existing list of descriptors, while body image was measured using Collins' Child Figure Drawings.

Results: From T0 to T1, BMI z-score (1.85 ± 0.43 vs 1.56 ± 0.41; p = 0.001), body fat percentage (39.95 ± 6.07 vs 36.59 ± 6.81; p < 0.001), arm (28.91 ± 3.26 vs 27.14 ± 2.48; p = 0.003) and waist (90.25 ± 6.91 vs 85.48 ± 6.64; p = 0.004) circumferences decreased. Biceps (23.73 ± 7.35 vs 18.06 ± 8.24; p < 0.001), subscapular (23.61 ± 7.76 vs 19.83 ± 6.93; p = 0.008) and suprailiac (28.78 ± 8.36 vs 25.33 ± 7.05; p = 0.001) skinfolds also declined after treatment. With regard to physical fitness, there were significant changes over time in the SVJ (17.68 ± 7.33 vs 20.20 ± 6.98 cm; p = 0.029), MBT (3.81 ± 0.69 vs 4.28 ± 0.79 m; p < 0.001), ASR (24.49 ± 1.90 vs 23.53 ± 2.01 sec; p < 0.001) and HCT (33.15 ± 7.08 vs 29.51 ± 5.03 sec; p < 0.001), with children showing better performances at T1. For behavioural and psychosocial outcomes, significant time effects were found, with participants reporting higher PA and perceived physical ability scores (p < 0.001), and presenting lower values of unpleasant emotional states (p = 0.039) and body dissatisfaction (p = 0.002) from pre- to post-intervention (Table 1).
Table 1 - Descriptive statistics

<table>
<thead>
<tr>
<th>Variable</th>
<th>T0</th>
<th>T1</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(M ± SD)</td>
<td>(M ± SD)</td>
</tr>
<tr>
<td><strong>PA levels</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>1.75 ± 0.44</td>
<td>2.53 ± 0.70</td>
</tr>
<tr>
<td><strong>Perceived physical ability</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive scale</td>
<td>14.83 ± 1.95</td>
<td>18.67 ± 2.20</td>
</tr>
<tr>
<td>Negative scale*</td>
<td>16.72 ± 2.42</td>
<td>22.00 ± 2.91</td>
</tr>
<tr>
<td><strong>Emotional states</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pleasant states</td>
<td>34.06 ± 13.55</td>
<td>37.39 ± 7.81</td>
</tr>
<tr>
<td>Unpleasant states</td>
<td>13.94 ± 14.04</td>
<td>7.17 ± 6.96</td>
</tr>
<tr>
<td><strong>Body dissatisfaction</strong></td>
<td>1.61 ± 0.56</td>
<td>1.04 ± 0.53</td>
</tr>
</tbody>
</table>

* Items are reverse-scored

**Conclusion** Results indicate that a multi-component programme not based merely on a dose-effect approach to exercise, but focused on educational and behavioural interventions, has the potential to increase PA adherence and promote the health benefits associated with it. Such interventions should target factors that co-exist with obesity (e.g. poor physical fitness, low perceived physical ability, negative attitude towards PA, body image concerns) within a multidimensional perspective aimed at improving healthy lifestyles of obese children.

**Disclosure of interest:** None Declared
The relationship between nutrition and vitamin D sufficiency in infants and children under three years of age residing in the south of Russia

Victoria Kuryaninova¹, Irina Zakharova², Leonid Klimov¹, Svetlana Dolbnya¹, Ekaterina Evseeva²

¹Stavropol State Medical University, Stavropol, Russian Federation
²Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation

Objectives and study: was to evaluate the vitamin D (VD) levels in infants and children under three years of age residing in Stavropol (45° North), depending on the feeding pattern and dietary supplementation.

Methods: In the period from 11.2013 to 03.2014, 130 Stavropol infants and children aged from 1 month to 3 years were examined: 73 infants (56.1%) aged under 12 months, 29 (22.3%) 1 to 2 years, and 28 (21.6%) 2 to 3 years. 35 subjects (26.9%) were breast-fed, 38 infants (29.2%) were bottle-fed, while 57 study subjects (43.9%) were on a “common diet”. Adapted milk formulas were only given to infants under one year of age. Aqueous cholecalciferol preparations were given for prophylactic purposes to 44 infants under one year of age (60.3%); 24 of them (54.5%) were breast-fed and 20 infants (45.5%) were bottle-fed. The average prophylactic dose of VD was 677.4±52.5 IU/day. No VD was given to 29 infants (39.7%). No pharmacological prevention of VD insufficiency was used in children aged over one year. The VD sufficiency criterion was a 25(ОН)D concentration of over 30 ng/mL, levels in the range of 20 to 30 ng/mL - low, VD insufficiency - 10 to 20 ng/mL and VD deficiency - below 10 ng/mL.

Results: The average calcidiol concentration in the study group was found to be 23.3±1.2 ng/mL. Sufficient 25(OH)D levels in 30 subjects (23.1%), levels 20 to 30 ng/mL in 40 subjects (30.8%), VD insufficiency-41 individuals (31.5%), and VD deficiency in 19 subjects (14.6%). VD levels continuously decrease with age: the average 25(OH)D concentration is 27.7±1.8 ng/mL in the first year of life, 18.5±1.6 ng/mL in the second year (p<0.001), and 17.4±1.2 ng/mL in children aged from 2 to 3 years (p<0.001). An inverse correlation was observed between the vitamin D concentration and the child’s age (r = -0.3, p = 0.002). A VD sufficiency analysis conducted for infants under one year of age by feeding type revealed a deficiency in 10 breast-fed subjects (28.6%) and in no bottle-fed infants (p<0.01); an insufficiency was observed in 5 (14.3%) and 7 (18.4%) cases, respectively (p=0.05), low levels in 12 (34.3%) and 12 (31.6%) subjects, respectively (p=0.05), and sufficient levels in 8 (22.9%) and 19 (50.0%) subjects, respectively (p=0.05). The average calcidiol concentration was 23.0±2.7 ng/mL and 32.1±2.4 ng/mL for breast-feeding and bottle-feeding, respectively (p<0.05). A VD sufficiency analysis conducted for subjects receiving no cholecalciferol supplementation by feeding type demonstrated sufficient VD levels in 5 (27.8%) bottle-fed subjects and in no breast-fed infants (p<0.05), low levels in 6 subjects (33.3%) and in 2 individuals (18.2%), respectively, an insufficiency in 7 subjects (38.9%) and in 2 infants (18.2%), respectively, and a deficiency in 7 subjects (38.9%) of breast-fed subjects (p<0.001). The calcidiol concentration in children receiving cholecalciferol supplementation increases with statistical significance: from 11.4±2.4 ng/mL to 28.2±3.2 ng/mL (p<0.001) on breast-feeding and from 25.4±2.7 ng/mL to 38.2±3.2 ng/mL in bottle-fed.

Conclusion: Infants and children aged under three years residing in the South of Russia (45° North) have low VD levels; breast-fed patients receiving no VD supplementation and children in their second or third year of life are particularly affected.

Disclosure of interest: None Declared.
Features of early physical development of overweight children aged 7-10 years old

Vera Skvortsova¹, Tatyana Borovik², Leila Namazova-Baranova³, Malokhat Khodzhieva⁴, Elena Roslavtseva¹

¹Scientific Center for Children's Health, Healthy and Sick Child Nutrition Dep., Moscow, Russian Federation
²Scientific Centre of Child Health, Nutrition of Healthy and Sick Child, Moscow, Russian Federation
³Scientific Center of Child Health, Moscow, Russian Federation
⁴Scientific Center for Children's Health, Moscow, Russian Federation

Objectives and study: To examine the history and anthropometric features in early age of overweight children aged 7 - 10 years old.

Methods: The study involved 70 children (boys 37, girls 33) at the age of 7-10 years. The study ('overweight') group (n = 40) were children with overweight and obesity, the comparison ('healthy') group (n = 30) were healthy children with normal body weight. The history data, and weight and height of children, recorded according to standard methods and expressed as standard deviation scores (z-scores) adjusted for age and gender using WHOAnthroPlus program 2009, (weight-for-age, WAZ; height-for-age, HAZ; body mass index (BMI)-for-age, BAZ), were studied.

Results: Children in the ‘overweight’ and ‘healthy’ groups had significant differences (p, Mann-Whitney criterion) in weight, height, WAZ and BAZ indices (Table).

The family history revealed at least one of parents was overweight or obese in 30% in the ‘overweight’ group, while only in 3% in the ‘healthy’ group. Significant direct correlation between overweight/obesity of parents and overweight in children showed both WAZ (r = 0,466, p = 0,001), and BAZ (r = 0,403, p = 0,001). Children of both groups had no differences and had normal physical development at birth, but by the age of 12 months statistically significant differences in certain indices of physical development between the groups revealed. Children of the ‘overweight’ group had a significantly higher WAZ (p = 0.038) and BAZ (p = 0.017) than children in the ‘healthy’ group. We identified direct strong correlation between the overweight and obesity at the age of 7-10 years and the overweight at age of 12 months by WAZ index (r = 0.501, p = 0.001), and weak direct correlation between BAZ index at 7-10 years, and WAZ and BAZ at 12 months of age.

Table:
The anthropometric parameters of the examined children

<table>
<thead>
<tr>
<th>Index</th>
<th>'overweight' group (n=40)</th>
<th>'healthy' group (n=30)</th>
<th>p&lt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Me (Q₁–Q₃)</td>
<td>Me (Q₁–Q₃)</td>
<td></td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>50,0 (32,6 – 60,2)</td>
<td>36,2 (24,0-43,1)</td>
<td>0,000</td>
</tr>
<tr>
<td>Height, cm</td>
<td>149,1(128,0-154,4)</td>
<td>140,1(123,1-145,2)</td>
<td>0,001</td>
</tr>
<tr>
<td>WAZ</td>
<td>2,5 (1,87-3,2)</td>
<td>1,11 (0,07-1,51)</td>
<td>0,001</td>
</tr>
<tr>
<td>HAZ</td>
<td>1,26 (0,14-2,24)</td>
<td>1,03 (0,13-1,92)</td>
<td>0,385</td>
</tr>
<tr>
<td>BAZ</td>
<td>2,29 (1,96-2,9)</td>
<td>0,30 (-0.43-0.72)</td>
<td>0,001</td>
</tr>
</tbody>
</table>
**Conclusion:** Children with overweight and obesity at the age of 7 - 10 years were higher than their peers with normal weight. 'Overweight' children significantly more often had overweight parents. Higher values of weight-for-age (WAZ) and body mass index (BMI)-for-age (BAZ) Z-scores at the age of 12 months in the group of children being overweight or obese by the age of 7 – 10 years suggests the possibility of the early origin of obesity.

**Disclosure of interest:**
None Declared
**NUTRITION: Nutrition and health outcomes**

N-P-050

**Influence of calcium intake and of calcium intake adequacy to recommendations on bone mineral density.**

Marta Zaragoza-Jordana1, Veronica Luque1, Joaquin Escribano1, Natalia Ferre1, Carmen Rubio-Torrents1, Veit Grote2, Berthold Koletzko3, Ricardo Closa1

1Universitat Rovira I Virgili, lspsv, Paediatrics, Nutrition and Development Research Unit, Reus, Spain
2Von Haunersches Kinderspital, University of Munich Medical Centre, Munich, Germany
3Dr. von Hauner Children's Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany

**Aim:** To analyse the influence of calcium (Ca) intake and of Ca intake adequacy to recommendations on bone mineral density (BMD) at 7 years of age in European children.

**Methods:** We evaluated data of children participating in the prospective European Childhood Obesity Project (EU CHOP), into which formula and breastfed children were enrolled up to the age of two months (mean enrollment age 2 weeks). Dietary intake was collected with 3-day weighed/estimated food records periodically, and was converted into nutrient intakes using food composition tables from all participating countries. Ca, phosphorus, vitamin D and protein intakes at 4, 5 and 6 years were calculated. Ca intake adequacy to the recommendations was calculated following the American Institute of Medicine guidelines for individual assessment, and using FAO/WHO/UNU Estimated Average Requirements, subjects were categorized according their probability of adequate intake (PA). At 7 years, BMD was measured in the Spanish subsample by Dual-energy X-ray absorptiometry using a Lunar Prodigy Primo device, internal z-scores of BMD were calculated. Children with BMD z-scores below -1 SD were considered osteopenic.

**Results:** BMD was measured in 179 children in whom dietary intake data were available. Ca intake at 6 years was positively correlated with lumbar spine (LS) BMD at 7 years (R=0.205, p=0.030). In a linear regression analysis an increase of Ca intake by 100 mg/d explained 19.4% (p=0.011) of BMD z-score variation, and modified it by 0.089 (0.021, 0.157) units, when adjusting for body mass index (BMI). Probability of adequate intake (PA) of Ca, Ca intake adequacy >75% ranged from 60 to 90%, depending on age. Children with PA of Ca >95% showed a higher BMD z-score at both LS and whole body (WB) than children with PA of Ca <95% (Figure 1). Linear regression models adjusting by BMI and dietary intake of protein, phosphorus and vitamin D showed that having PA>95% maintained over 2 consecutive years (5 & 6 years) explained up to 26.3% of LS BMD z-score variation (p<0.001), increasing z-score by 0.669 (0.202, 1.137). PA>95% maintained over 3 years (4, 5 & 6) explained 24.9% of BMD z-score variation and increased z-score by 0.773 (0.282, 1.264). Effects of Ca adequacy on WB were 17.4 or 20%, and 0.559 (0.089, 1.028) or 0.668 (0.197, 1.140) when PA>95% was maintained 2 or 3 consecutive years, respectively. Logistic regression analysis determined that children with PA>95% maintained during 2 years had 13.84 fold reduced osteopenia risk at LS (p=0.001) adjusted by BMI and dietary factors. At WB, PA>95% reduced osteopenia risk 12 fold when adjusting by BMI and dietary factors.
**Figure 1.** BMD z-score according to probability of adequacy.

LS and WB BMD differences according to Ca probability of adequacy group (PA>95% vs PA<95%). *:p<0.05 and ***:p<0.001 vs children with PA <95%.

**Conclusions:** Ca intake adequacy in childhood, particularly if maintained over several years, increases LS and WB bone mineral density at 7 years and reduces the risk of osteopenia.

**Disclosure of interest:** Authors disclose no conflicts of interest. Financially supported in part by the European Commission.
NUTRITION: Nutrition and health outcomes

N-P-051

Nutritional status and motor function in cerebral palsy in spanish regional hospital

MCarmen Rivero de la Rosa¹, Victoria Molina Martínez¹, Paola Díaz Borrego², Raquel Barbosa Romero², Belén Romero Romero², Juan Andrés Conejero Casares², Federico Argüelles Martín¹

¹Hospital Universitario Virgen Macarena, Pediatric Gastroenterology and Nutrition, Seville, Spain
²Hospital Universitario Virgen Macarena, Rehabilitation Unit, Seville, Spain

Objectives and study: Cerebral palsy (CP) is a neurological syndrome secondary to a developing brain damage. Its effects are permanent. Growth and nutrition disorders are common secondary health conditions in children with CP. It merit study because of their impact on health, including psychological function, societal participation, motor function, and survival. Principal study aim is to describe the nutritional status, motor and presence of swallowing disorders in patients with PCI in our health area.

Methods: Prospective-descriptive study. We report data from evaluation CP patients from our Children Rehabilitation Unit, over 4 months. We collect demographic data (age, sex, CP type), nutritional data (weight, height, body mass index: BMI), malnutrition classification (Waterlow Index), Gross Motor Function Measure (GMFM) and monitoring data in Dysphagia and Child Nutrition Unit.

Results: Thirty-six patients are collected in child rehabilitation. Only 16 patients are followed in Infant Nutrition Unit of the Hospital. Most of them were males (51.6%) with an average age of 7.97 years old. Most common CP type was spastic tetraplegic (51.4%), which is the most common abnormality among patients followed at the Department of Nutrition (68.7%). 34% of patients had a percentile 50 for weight and height; this percentage drops to 25% in patients followed in Nutrition Unit; 22.9% of the total were classified according to the IW, had moderate to severe malnutrition (IW≤80 ). In Nutrition Unit, 50% had a normal IW, finding a 25% classified as moderate to severe malnutrition. 43.7% of patients were fed by percutaneous endoscopic gastrostomy. Of the total patients, 80.5% were being evaluated in consultation Dysphagia. Patiens in Nutrition Unit, 25% had swallowing disorders and dysphagia tracking, finding in these patients a better nutritional status according IW. 36.4% of all patients had five levels of Gross Motor. Only 18.7% in the Nutrition unit. A significant association (p <0.05) between the type of PC, GMFM, BMI, IW and monitoring in Dysphagia was observed.

Conclusion: Children with CP usually present nutritional disorders, so it seems beneficial to be evaluated in nutrition consultation. The children assessed in our Nutrition Unit at the beginning were those who had poorer nutritional status, benefiting from long-term monitoring, highlighting those fed primarily through percutaneous endoscopic gastrostomy. It seems important to monitor patients with swallowing disorders by the Dysphagia Unit. Since our sample of patients followed in nutrition highlights 25% of patients with improvement of nutritional status after being evaluated by the unit. Children with cerebral palsy with better BMI and nutritional status have better motor function.

Disclosure of interest: “None Declared”.
Sugarsweetened beverages intake positively associated with the risks of abdominal obesity and increased triglyceride concentration among children aged 7-18 in China

Baoting He¹, Yajun Chen¹, Jin Jing¹, Yanna Zhu¹

¹School of Public Health, Global Health Institute (Sghi), Sun Yat-Sen University, Department of Maternal and Child Health, Guangzhou, China

Objectives and study: Excessive consumption of sugarsweetened beverages (SSB) may related to the increasing incidence of obesity and other metabolic risk factors. However, data regarding the relationship between SSB intakes and the metabolic risk factors is insufficient in Chinese children. Thus, we aimed to explore the association between SSB intakes and the risks of several cardiometabolic risk factors in children aged 7-18 in China.

Methods: Based on a multistage cluster sampling, children aged 7-18 were enrolled in this cross-sectional study. Fasting blood glucose, lipids, and anthropometric characteristics were evaluated. Information of demography, dietary and physical activities were children-reported or parent-reported.

Results: Overall, an amount of 2,037 children, including 1,017 boys and 1,020 girls, participated in the study. A proportion of 21.6% participants in this study consumed more than 750ml SSB per week, of whom the body mass index (19.43±3.86kg/m², P<0.001) and triglyceride concentration (0.96±0.53mmol/L, P<0.001) were higher and high-density lipoprotein (HDL) concentration (1.32±0.31 mmol/L, P<0.001) were lower when compared with those who had a less consumption of SSB per week. Furthermore, adjusted odds ratio of SSB intake more than 750ml in contrast to SSB intake less than 250ml was 1.75 (1.19, 2.59) for abdominal obesity and 1.80 (95%CI: 1.23, 2.62) for increased triglyceride concentration.

Conclusion: A positive association between SSB intake and the risks of abdominal obesity and increased triglyceride concentration was revealed in 7-18 years old Chinese children, suggesting high SSB intake in children may elevate the risk of metabolic syndrome and consequent cardiometabolic disease in adulthood.

Disclosure of interest: None Declared.
Hepcidin and iron metabolism associated with cardiometabolic risk factors in children: a case-control study

Yanna Zhu¹, Baoting He¹, Jin Jing¹, Jun Ma², Xiuhong Li¹, Wenhan Yang¹, Yu Jin¹, Yajun Chen¹

¹School of Public Health, Global Health Institute (Sghi), Sun Yat-Sen University, Department of Maternal and Child Health, Guangzhou, China
²School of Public Health, Peking University., Institute of Child and Adolescent Health, Beijing, China

Objectives and study: Iron metabolism plays a crucial role in the development of cardiometabolic disease, however, the association between cardiometabolic risk factors and hepcidin as well as other iron parameters remains unclear in children. The aims of this study were to compare circulating hepcidin level and iron metabolism between children with and without cardiometabolic risk factors, and to explore the association between those iron parameters and cardiometabolic risk factors.

Methods: A case-control study was conducted among 1,126 children aged 7-14 in two groups: the case group (n=563) with cardiometabolic risk factors and the healthy control group (n=563). Iron parameters, lipids and anthropometric characteristics were evaluated. Information of demographics, diet and physical activities were collected by children-reported or parent-reported questionnaire.

Results: Compared with healthy controls, children with cardiometabolic risk factors had higher level of hepcidin and lower levels of serum iron, transferrin and soluble transferrin receptor (sTfR) (P<0.001). Besides, odds ratios for low high-density lipoprotein (HDL) were 2.03 (95%CI: 1.10, 3.74), 0.21 (95%CI: 0.10, 0.43) and 0.33 (95%CI: 0.18, 0.60) in children with higher hepcidin, transferrin and sTfR levels (P<0.05). Furthermore, odds ratios for cardiometabolic risk were 0.22 (95%CI: 0.12, 0.42) and 0.19 (95%CI: 0.10, 0.36) in children with higher tranferrin and sTfR levels, respectively.

Conclusion: The higher levels of hepcidin and the lower level of iron, transferrin and sTfR in children with cardiometabolic risk factors suggested that iron metabolism associated with cardiometabolic risk factors in children. Meanwhile, hepcidin positively associated with the risk of low HDL level, whereas transferrin and sTfR were negatively correlated with the risk of low HDL level. Additionally, serum iron, transferrin and sTfR level were negatively associated with cardiometabolic risk.

Disclosure of interest: None Declared.
Vitamin D Deficiency in Moscow Teenagers

Ekaterina Evseeva¹, Irina Zakharova¹, Sugyan Narine²

¹Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation
²Russian Medical Academy of Postgraduate Education, Pediatric, Moscow, Russian Federation

Objectives and study: to study vitamin D deficiency in prepubertal and pubertal children in Moscow as well as risks of low vitamin D supply.

Methods: Teenagers aged 10 to 17 living in Moscow have been examined. To assess seasonal change of vitamin D blood status the mean major vitamin D metabolite 25(OH)D₃ was detected throughout different months of the year. The inclusion criteria for children’s participation in the laboratory investigations was age (from 11 to 18 years old), absence of organic or genetic disorders, permanent Moscow residence, no current treatment either with calcium drugs or active vitamin D metabolites.

Results: 360 children aged 10 to 18 were enrolled (i.e. 30 children were examined every month). Analysis of the obtained data revealed diversity of vitamin D supply in children examined in winter, spring, summer, autumn months. Vitamin D serum concentration firmly proved to be higher in summer months versus winter period. The lowest level of 25(OH)D was detected in May since 80% of children suffered from vitamin D deficiency < 10 ng/ml and 20% of children had vitamin D concentration 10-20 ng/ml. The majority of the children (47-63%) experienced lack of vitamin D supply in winter, and practically none of them revealed adequate metabolite status. At the same time, as few as 3% of children were diagnosed with vitamin D deficiency in July which is 25(OH)D<10 ng/ml, and 67% had 20-40 ng/ml vitamin D serum concentration. The most frequent chronic diseases in the above given group of children were gastrointestinal tract disorders (50.6%) including chronic gastroduodenitis, gastric and duodenal ulcer, Gilbert’s syndrome, gastroesophageal reflux (GER), dyscholia. Sex differences in terms of vitamin D supply among Moscow teenagers were absent. Dietary estimation revealed that rate of fish consumption, the main source of vitamin D supply, was extremely low.

Conclusion: It is necessary to pay special attention to the development of effective ways of low vitamin D status correction and prophylaxis. Optimal level of vitamin D status is impossible to maintain within winter period due to insufficient solar insolation, short-lasting walks of children during the academic year as well as the absence of cholecalciferol rich products in children’s dietary. Half of the trial participants suffering from cholecalciferol deficiency have intestinal tract disorders which are apparently one of the reasons for the above mentioned condition, because vitamin D absorption takes place mainly in duodenum and jejunum at the presence of bile acids, consequently, biliary tract disorder, duodenum mucosa injury may affect normal calciferol metabolism in the organism.

Disclosure of interest
“None Declared”. 
Severe Vitamin D Deficiency Rickets in an infant Manifested as Hypocalcaemic Seizures a case report

Biljana Vuletic1, Nedeljko Radlovic2

1Pediatric Clinic CC Kragujevac, Gastroenterology, Kragujevac, Serbia
2University Children Hospital, Gastroenterology, Belgrade, Serbia

Objectives and study: Hypocalcaemic seizures are uncommon in the post-neonatal period. Herein, we report an infant with hypocalcaemic seizures caused by a severe deficiency of vitamin D.

Case outline: A 5-month-old male infant was admitted to hospital with recurrent generalized afebrile seizures resistant to clonazepam therapy in March 2013. At the clinical examination, the infant showed characteristic rachitic signs, so that after the blood sample was taken for laboratory testing, the infant was given infusion of 2 ml/kg of 10% of calcium gluconate at a rate of 0.5 ml/min. The treatment resulted in immediate termination of seizures and normalization of the consciousness of the infant.

Blood sample analysis showed extremely low levels of free and total calcium (0.36/1.24 mmol/L) and 25(OH)D (<3 ng/ml), elevated alkaline phosphatase (878 U/L) and parathyroid hormone (283 pg/ml), and low calcium/creatinine ratio (mg/mg) in a portion of urine (0.03), while the levels of serum phosphorus, pH, total protein, albumin and creatinine were within the reference range. Wrist X-ray showed typical signs of rickets. In order to fully stabilize calcium homeostasis, along with 2000 IU of vitamin D3 daily and standard cow's milk formula, calcium gluconate (80 mg/kg daily) was given orally over 2 weeks. The treatment resulted in complete stabilization of the infant’s condition and rapid improvement in laboratory, radiological and clinical findings of rickets.

Conclusion: Generalized convulsions in the afebrile infant represent a serious and highly heterogeneous problem of the etiopathogenesis. Extremely rarely, as in the case of our patient, it may be due to severe hypocalcaemia caused by vitamin D deficiency.

Keywords: vitamin D deficiency, hypocalcaemia, convulsions

Disclosure of interest: “None Declared”.
Liver disease and early vascular lesions in obese children

Manon Goisbault¹, Arnaud Legrand², Caroline Storey³, Damien Bonnet⁴, Patrick Tounian⁵, Béatrice Dubern⁵

¹Nantes University Hospital, Nantes, France
²Women’s & Children’s Clinical Investigation Center (Cic Fea 1413), Nantes University Hospital, Nantes, France
³Trousseau Hospital, Paris, Nutrition Department, Paris, France
⁴Necker-Enfants Malades Hospital, Cardiology Department, Paris, France
⁵Trousseau Hospital, Nutrition Department, Paris, France

Objectives and study: Non Alcoholic Fatty Liver Disease (NAFLD) is common among obese population, liver damage ranging from simple steatosis to steatohepatitis, with the risk of cirrhosis and hepatocellular carcinoma. In adults, NAFLD has been associated with metabolic syndrome and vascular alterations, independently of metabolic syndrome. To date, few studies have evaluated the link between NAFLD, endothelial dysfunction and cardiovascular risk factors in obese children. The main objective of our study was to assess the correlation between early vascular lesions and liver damage in a cohort of French obese children.

Methods: 207 obese children (122 F, mean age 11.6 ± 2.5 years, BMI Z-score 4.5 ± 1.0 SD) had phenotypic characterization including anthropometric data (weight, height, BMI, body composition using biphotonic absorptiometry) and metabolic parameters (blood pressure, hepatic enzymes, lipids, oral glucose tolerance). Ultrasound vascular study was performed to explore the arterial mechanical properties and endothelial function (intima-media thickness, incremental elastic modulus, flow mediated dilation and glyceryltrinitrate mediated dilation).

Results: Aspartate transaminase (AST) and alanine transaminase (ALT) were respectively > 35 IU/L in 4.6% and 16% of the patients. ALT were significantly higher in boys than in girls (29.2 IU/L vs 22.7 IU/L, p = 0.001). AST were significantly correlated to BMI Z-score (r = 0.19 ; p = 0.02). There was a positive correlation between ALT and both triglycerides (r = 0.23 ; p = 0.008) and android/gynoid fat mass ratio (r = 0.31 ; p = 0.002). Gamma-glutamyl transferase (GGT) were significantly correlated to BMI Z-score (r = 0.23 ; p = 0.01) and to systolic blood pressure (r=0.19 ; p=0.02). No correlation was found between liver enzymes and vascular markers. The crossing of 2 global composite criteria (liver test and vascular test) showed that the extreme terciles of the population were not associated (only 16.7% were in the 3rd tercile of each composite score, NS).

Conclusion: Our study did not establish a significant relationship between liver enzymes abnormalities and impaired vascular markers in obese children, despite the link described in adults. It may be due to the short time children are exposed to the risk or to factors unique to adults, such as tobacco or alcohol consumption. However, since transaminases underestimate liver damage, further studies are needed to confirm our results.

Disclosure of interest: none declared
Motivational aspects of alcohol consumption in sporting adolescents

Thierry De Vreker¹, Tine Decraene², Koen Huysentruyt³, Yvan Vandenplas⁴

¹Universitair Kindertziekenhuis Brussel, Kinder- en Jeugd-, Enterologie, Brussels, Belgium
²Universitair Kindertziekenhuis Brussel, Kindercardiologie, Brussels, Belgium
³Universitair Ziekenhuis Brussel, Vrije Universiteit Brussel (VUB), Pediatrics, Brussels, Belgium
⁴Uz Brussel, Department of Pediatrics, Brussels, Belgium

Objectives and study: Youths drinking behavior represents a major public health concern, including poor educational performance, risky sexual behavior, crime and disorder, and psychological harms. Alcohol consumption and sport are known to be linked since many years. Sporting adolescents, girls and boys, consume alcohol earlier, more frequently, and in larger quantity than non-sporting adolescents. Adolescent alcohol consumption is a predictor of future dependency with very long term effects on health. We confirmed previously the correlation between alcohol and sport in 476 Belgian adolescents and started a program to reverse this situation. In search for the best solution we wanted to explore the motivational aspects of this curious trend in adolescents.

Methods: Studies for this review were identified by electronic searches of online databases, including PsycINFO, MEDLINE, Web of Science, and Sociological Abstracts. We used the terms alcohol or drinking, and athlete or sport, limited to adolescents, to identify relevant articles and searched the reference sections of studies identified via these databases.

Results: Many hypothesis or possible explanations could be withheld.

1. The “work hard, play hard” hypothesis. The concept is that a subset of sporting adolescents are motivated to put forth maximum effort in all their activities: sport, school and drinking.
2. Extrinsic versus intrinsic motivation. This variable is suggested by recent findings that adolescent athletes who were extrinsically motivated to engage in sports drank more than those who were intrinsically motivated.
3. The “damage control” hypothesis in which individuals seek to control, by exercise, the damage done by alcohol consumption.
4. The personality-mood framework: it is possible that alcohol consumption and physical activity are linked via a personality trait. Research suggests that either extraversion or sensation seeking could be this trait. Susceptibility to perceived media images and rebelliousness self-image are positively linked to alcohol use.
5. External factors: sub-culture of a sport like peer norms, bonding and initiation rituals stimulate alcohol use. There is also an influence of perceived social norms, with overestimation of peer drinking. The time commitment to be involved in a particular sport, or coach expectations and tensions that are thought to be relieved by alcohol. Competitiveness among athletes may translate from the sporting arenas into activities like attempting to out-drink one’s peers. In field and team sport alcohol is more consumed compared to individual sports, probably linked to the social habits and pressure. In team sport the individual is influenced by the normative attitude of the group.
6. Stress: sporters in competition level drink more than recreational or top-sporting.

Conclusion: There is a clear correlation between sport and alcohol use in adolescents. As youth drinking represents a major health concern we explored online databases to understand the motivational framework. Many explanations and hypothesis are suggested but none was completely convincing. More research is absolutely needed to better understand this troublesome problem.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 792
Bone microarchitecture in children with long term parenteral nutrition: a prospective pilot study.

Typhaine Louazon¹, Lioara Restier¹, Belmalih Abdelouahed¹, Justine Bacchetta², Alain Lachaux³, Stephanie Bouttroy⁴, Noel Peretti⁵

¹Hôpital Femme Mère Enfant, Service de Gastroentérologie, Hépatologie et Nutrition Pédiatriques, Centre de Nutrition Parentérale À Domicile, Lyon, France
²Hôpital Femme Mère Enfant, Service de Néphrologie et Rhumatologie Pédiatriques, Inserm Umr 1033, Lyon, France
³Hôpital Femme Mère Enfant, Department of Pediatric Gastroenterology and Hepatology; Reference Centre for Wilson Disease, Lyon, France
⁴Hôpital Edouard Herriot, Inserm Umr 1033, Lyon, France
⁵Hcl Inserm, Université Claude Bernard Lyon 1, Faculté de Médecine Lyon-Est, Inserm U1060, Carmen Laboratory, Lyon, France

Objectives and study: Long time parenteral nutrition may induce bone complications, such as osteopenia, osteoporosis and increased risk of fracture. While Dual X-ray Absorptiometry (DXA) is the reference tool to evaluate bone density in adults, this exam has limitations in children. New tridimensional bone imaging techniques, such as High Resolution peripheral Quantitative Computed Tomography (HR-pQCT), may be more appropriate in children as it allows the assessment of compartmental volumetric densities and bone microarchitecture. The aim of this study was to evaluate bone status with HR-pQCT in children with long time parenteral nutrition in comparison with healthy children.

Methods: This prospective pilot cross-sectional single-centre study was performed between March 2014 and June 2015. Inclusion criteria were: age above 9 years old (due to technical limitations of HR-pQCT in younger children), and parenteral nutrition for more than 2 years (to have a sufficient delay of bone growth). The following biochemical parameters were evaluated: calcium, phosphorus, bicarbonates, osteocalcin, PTH, 25-OH vitamin D, alkaline phosphatase and urinary calcium/creatinine ratio. HR-pQCT (Scanco Medical AG®, Switzerland) evaluated total, cortical and trabecular volumetric bone mineral densities, and bone microarchitecture: cortical thickness and trabecular parameters at the ultradistal tibia and radius. Each patient was age-, gender- and puberty-matched with 2 healthy controls from a local cohort. Results are presented as median (min-max). Non-parametric Mann-Whitney tests were performed on SPSS 17.0.

Results: Eleven patients (3 girls) with a median age of 16 years (9-19) were included. Duration of parenteral nutrition was 122 months (84-220). Etiologies of intestinal failure were: 6 short bowel syndrome with median length of 90 cm (50-200) (3 Chronic Intestinal Pseudo Obstruction , 3 intestinal atresia), 3 congenital enteropathy, 1 immunodeficiency and 1 lymphangiectasia. Intravenous intakes were: phosphorus 0.55 mmol/kg/d, calcium 0.42 mmol/kg/d, vitamin D 7 UI/kg/d. Patients with parenteral nutrition were shorter (-1.5DS vs 0.8DS, p=0.001), weightless (-1.1DS vs 0.6DS, p<0.001) but had similar BMI (19.2 vs 19.4 kg/m², p NS) than controls. PTH was higher but normal in patients (46 vs 18µg/L, p=0.005). Conversely osteocalcin was lower but normal in patients (44 vs 74 µg/L, p=0.005). Plasmatic phosphorus, calcium, 25-OH vitamin D, ALP and urinary calcium/creatinine ratio were not different between groups. At the ultradistal radius, there were no significant differences with HR-pQCT for all parameters of densities and microarchitecture. However, patients had a trend towards decreased trabecular area at the tibia, and increased trabecular separation on tibia.

Conclusion: In this pilot single-centre study of children receiving long term parenteral nutrition we observed: 1/ quite reassuring results for bone status in children with long term parenteral nutrition and 2/ increased but normal PTH levels despite similar levels of vitamin D, thus raising the question of the adequacy of phosphate intake in patients with long time parenteral nutrition.

Disclosure of interest: Nonen Declared.
Food safety in Infancy: are the Italian paediatricians informed enough?

Michele di Toma1, Antonia Gentile1, Cinzia Ciullo1, Flavia Indrio2, Stefania Castellaneta3, Maria Stella2, Ruggiero Francavilla2, Fernanda Cristofori4

1Scuola DI Specializzazione in Pediatria, Università di Bari, Italy
2Dipartimento Interdisciplinare DI Medicina, Sezione di Pediatria, Università di Bari, Italy
3Dipartimento DI Pediatria P.O. San Paolo, Bari, Italy
4Uoc Pediatria. P.O. Centrale Santissima Annunziata, Taranto, Italy

Objectives and study: At present there are specific directives of the European Commission to assure a high level of food safety for infants and young children. The aim of this study is to evaluate the level of knowledge of Italian paediatricians on food safety in infancy (FSI).

Methods: We have developed and distributed to paediatricians [paediatric consultants (PC), paediatric general practitioners (PGP) and paediatric residents (PR)] a multiple-choice questionnaire investigating the knowledge about FSI.

Results: 144 pediatricians participated (14% PC, 53% PGP, 33% PR). Age distribution was: younger than 30 (24%), 30-50 (22%) and 50-70 years (54%). Overall 89% of participants is aware on the importance of FSI on the health of infants and children and 48% feels confident with this topic. Only 15% knows that during pregnancy all women have contaminants in their umbilical cord blood. 67% of paediatricians believes that “baby-food” may contain pesticides. 56% knows that mycotoxin patulin may contaminate apples, that mycotoxins may be present in cow’s milk (74%) and that arsenic may be present in rice (59%). 46% knows the maximum dose of deoxynivalenol (DON) in pasta for children and 12% believes that organic food give the same guarantees of baby food.

Conclusion: Significant differences in knowledge exist regarding FSI. Identification of knowledge gaps may be useful to develop educational materials to improve the current knowledge and allowing the best counselling for infant nutrition.

Disclosure of interest: None Declared.
The impact of nutritional status on oral health and lipid metabolism parameters in adolescents

Małgorzata Klichowska-Palonka¹, Paulina Krawiec², Elżbieta Pac-Kożuchowska²

¹Medical University of Lublin, Department of Conservative Dentistry, Lublin, Poland
²Medical University of Lublin, Department of Paediatrics, Lublin, Poland

Objectives and study: In adolescents during puberty there is an increased risk of dental caries due to unfinished mineralization of teeth, and increased incidence of gingivitis associated with hormonal changes. It has been shown that alterations in hormonal balance during puberty may affect lipid metabolism. The aim of the study was to determine the impact of nutritional status expressed as Body Mass Index on serum and salivary lipid profile and their relationship with the state of oral cavity.

Methods: A total of 160 healthy adolescents aged 11-16 were enrolled to the study. Nutritional status was determined using the Body Mass Index (BMI). We assessed lipid profile including total cholesterol, high-density lipoprotein-cholesterol (HDLC), low-density lipoprotein-cholesterol (LDLC) and triglyceride in the serum and total cholesterol and triglyceride in saliva. The examination of oral cavity assessed the condition of dentition and periodontium. Dental caries was determined by the Decayed, Missing, Filled Teeth Index (DMFT) and periodontal status by the Community Periodontal Index of Treatment Needs (CPITN). We noted separately advancement of dental caries, including teeth needing endodontic treatment or extraction.

Results: We observed a statistically significant increase of dental caries advancement in adolescents older than 14 years compared to those aged 11-14 years old. However, there were no statistically significant differences in total cholesterol, HDLC and triglycerides in serum between adolescents older than 14 years and those aged 11-14 years old. There were also no statistically significant differences in lipid parameters in saliva depending on the age and BMI of adolescents. In adolescents with lower BMI values, significantly more often the tartar and teeth needing endodontic treatment or extractions were found.

Conclusion: Nutritional status of adolescents affects the condition of teeth and periodontium, however has no impact on lipid parameters in saliva. Adolescents require intensive prevention and dental care.

Disclosure of interest: None Declared.
Chronic malnutrition in pediatric cancer patients: incidence, risk factors and complications

Amandine Rubio¹, Cécile Perret², Anne Pagnier², Dominique Plantaz²

¹Grenoble University Hospital, Pediatric Gastroenterology and Nutrition, Grenoble, France
²Onco-Hématologie Pédiatrique, Clinique Universitaire de Pédiatrie, Hôpital Couple Enfant, Chu Grenoble Alpes, Grenoble, France

Objectives and study: Malnutrition is a common problem in pediatric patients with cancer. Chronic undernutrition is deemed to be of poorer prognostic in these patients, but its incidence and consequences have never been explored. This study aimed to describe the occurrence and complications of chronic undernutrition in cancer patients during anticancer therapy.

Methods: In a retrospective cohort study of 204 patients, nutritional status was assessed at diagnosis and continuously throughout therapy. Malnutrition was defined as either the occurrence of major weight loss and/or a body mass index (BMI) Z-score < -2 standard deviation at any time during treatment. Chronic malnutrition was malnutrition of duration exceeding 3 successive months.

Results: In our cohort, 71 patients suffered from chronic malnutrition (35%). Mean duration of malnutrition was 4.4±0.2 months (range 1-17). Tumors with the highest nutritional risk were bone tumor and neuroblastoma. In a multivariate analysis, risk factors at diagnosis for chronic malnutrition were undernutrition at diagnosis (OR=11.11 [2.20-55.56]), metastasis (OR=7.13 [2.35-21.64]), requirement for surgery (OR=4.19 [1.43-12.31]). Complications of chronic malnutrition were occurrence of infections (OR=11.65 [3.43-39.58]), death (OR=5.56 [2.12-14.60]) and stunting (OR=6.11 [1.33-28.03]). Patients having suffered from chronic malnutrition at any time during treatment had significantly reduced height-for-age, weight-for-age and BMI z-scores at the end of therapy.

Conclusion: The high proportion of children developing chronic malnutrition and its consequences during anti-cancer therapy underlines the need to prioritize nutrition as part of patient care and to provide adequate nutritional support, in particular when undernutrition is already present at diagnosis.

Disclosure of interest: None declared for any of the others
Cow's milk allergy guidelines: the quality appraisal with the AGREE II instrument

Piotr Dziechciarz¹, Marek Ruszczynski¹, Andrea Horvath¹, Hania Szajewska¹

¹The Medical University of Warsaw, Dept of Pediatrics, Warsaw, Poland

Objectives and study:. The appropriate diagnosis and management of the cow's milk allergy (CMA) may be challenging. Thus, a number of organizations addressed the problem by publishing guidelines on the management of CMA. The aim of this study was to systematically review the quality of the existing guidelines on CMA.

Methods. The Cochrane Library, MEDLINE, and EMBASE databases were searched from 2010 to November 2015 for guidelines on the management of the CMA in children. The methodological rigor, quality and transparency of the guidelines was assed with the use of Appraisal of Guidelines for Research and Evaluation (AGREE II) tool which is a 23-item tool comprising six quality-related domains (scope and purpose, stakeholder involvement, rigor of development, clarity and presentation, applicability, and editorial independence), plus two overall assessment items (overall quality of the guideline, and whether the guideline would be recommended for use, recommended with modifications or not recommended for use).

Results: Out of 15 included guidelines, three guidelines, all developed by the recognized scientific organizations, were evaluated as of very high quality. Six others were considered high quality (i.e. scored >60%). The quality scores for each domain varied. Out of all domains, clarity and presentation (domain 4) had the highest scoring, and applicability (domain 5) had the lowest scoring. The scores (mean ± SD) for individual domains were as follows: domain 1 (score and purpose) 62% ± 36%; domain 2 (stakeholder involvement) 52% ± 34%; domain 3 (rigor of development) 55% ± 38%; domain 4 (clarity of presentation) 69% ± 32%; domain 5 (applicability) 44% ± 33%; domain 6 (editorial independence) 69% ± 27%. One guideline had the maximum possible score at 100% in all AGREE II domains.

Conclusion: While a number of guidelines on CMA is available, their quality varies. Overall, the guidelines developed by recognized professional/scientific organizations were of the highest quality. These guidelines should be recommended for use in clinical practice. Still, the methodological quality of the CMA guidelines may be improved and warranted by the use and incorporation of tool such as the AGREE II instrument.

Disclosure of interest: None declared
Italian pediatric nutrition day

Antonella Lezo 1, Antonella Diamanti 2, Teresa Capriati 3, Paolo Gandullia 4, Paolo Fiore 5, Laura Laclitignola 6, Simona Gatti 7, Maria Immacolata Spagnuolo 8, Nicola Cecchi 9, Giovanna Verlato 9, Sara Borodani 10, Luisa Forchielli 11, Roberto Panceri 12, Brunori Elena 13, Maria Pastore 14, Sergio Amarri 15, SIGENP Nutrition Day Group 16

1 Regina Margherita” Children’s Hospital, Dietetics and Clinical Nutrition, Turin, Italy
2 Bambino Gesù Hospital, Dietetics and Clinical Nutrition, Rome, Italy
3 G. Gaslini Institution, Gastroenterology and Clinical Nutrition, Genoa, Italy
4 G. Gaslini Institution, Dietetics and Clinical Nutrition, Genoa, Italy
5 Meyer Children’s Hospital, Gastroenterology, Florence, Italy
6 Salesi Hospital, Marche University, Pediatrics, Ancona, Italy
7 Federico II University of Naples, Pediatrics, Naples, Italy
8 Santobono-Pausilipon Hospital, Pediatrics, Naples, Italy
9 Padua Hospital, Pediatric Dietetics and Clinical Nutrition, Padua, Italy
10 Turin University, Turin, Italy
11 Bologna University, Pediatrics, Bologna, Italy
12 San Gerardo Hospital, Pediatrics, Monza, Italy
13 Stella Maris Institute, Pediatric Neuropsychiatry, Pisa, Italy
14 Casa Sollievo Della Sofferenza, Pediatrics, San Giovanni Rotondo, Italy
15 Santa Maria Nuova Hospital, Pediatrics, Reggio Emilia, Italy
16 Italian Society of Pediatric Gastroenterology and Nutrition, Milan, Italy

Objectives and study: the prevalence of malnutrition and its impact on outcomes in children is under recognized by clinicians in Italy as well as worldwide. A novel definition of paediatric malnutrition has been recently proposed by the A.S.P.E.N. working group based on the correlation with illness and the use of z-score of anthropometric parameters. The aim of the study was to investigate the prevalence of malnutrition and related nutritional support among hospitalized children in Italy, in a nation-wide survey performed in a single day observation (16/4/2015).

Methods: an open access website (http://nday.biomedia.net) collected data from 73 hospitals distributed in 14 Italian regions (1,994 patients). Anonymous information were gathered on hospitals’ characteristics, patient’s anthropometric data, admission diagnosis (16 choices), presence of chronic diseases (none or one of 17 choices) and use of nutritional support: oral nutritional supplements (ONS), enteral nutrition (EN) or parenteral nutrition (PN). Z-scores of anthropometric parameters, calculated with Epi Info 7.1.5, defined nutritional status: wasting was identified by BMI and Weight-for-Length z-score (<-1 mild, <-2 moderate, <-3 severe), stunting by Height-for-Age z-score <-2. In absence of height or length, Weight-for-Age z-score was utilised to define wasting. WHO and CDC 2000 growth charts were used respectively for children younger and older than 2 years old.

Results: 1790 valid records were obtained for hospitalized patients aged 0-20 years old (53.3% males). For other 141 patients, only weight was available. More than 50% of children (52.9%) were aged 0-6 years. 58.8% of children suffered from chronic diseases. Wasting was detected in 28.7% being more represented in the age range 0-6 and 14-20 years while 17.3% of patients showed stunting; surprisingly almost 27% of them were aged 0-2 yrs (table 1). The admission diagnosis correlated with higher malnutrition rate were psychiatric (eating disorders), infective, pulmonary, gastrointestinal and cardiological pathologies, with >30% of malnourished patients. The prevalence of wasting was higher amongst children with chronic diseases (34.1% vs. 27.1%); stunting prevalence tripled in chronic disease patients (24.5% vs. 8.3%). Nutritional support (any kind) was given only to 23.5% of malnourished children (17%, 25.6% and 36.7%, respectively mild, moderate and severe malnutrition), see figure 1. Furthermore 12.1% of non malnourished and 14% of obese patients (BMI or Weight-for-Length z-score>2) received some nutritional support. Nutritional support: 11.7% of malnourished children received ONS (modular or complete), 11.5% enteral nutrition (6.4% via NG tube, 5.1% via gastrostomy) and 6.8 % received PN; in some patients a combination of two. Nutritional support is better represented among stunting patients with 39.5% of treated children. In the category
of only weight available patients, 77% of those having Weight-for-Age z-score <-2 receive nutritional support: 32.3% ONS, 58% EN and 6.5% PN (one or a combination of two). 23.4% of the patients in this category have neurological diseases; clinical reasons impeded to detect height or length in the rest of patients.

**Conclusion:** Malnutrition of any grade was observed in nearly 1/3 and stunting in 17% of the reported hospitalized children; it is likely to be under-recognised as the nutritional support reached only a small part of the malnourished children.

**Disclosure of interest:** None Declared
Systematic review: early infant feeding and the prevention of type 1 diabetes

Małgorzata Pieścik-Lech¹, Ania Chmielewska¹, Raanan Shamir², Hania Szajewska³

¹Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
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
³University of Warsaw, Pediatrics, Warsaw, Poland

Objectives and study: The European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) recommended in 2008, based on observational data, to avoid both early (less than 4 months) and late (7 or more months) introduction of gluten and to introduce gluten while the infant is still being breastfed as this may reduce not only the risk of CD, but also type 1 diabetes (T1D) and wheat allergy. Recently, it has been documented that infant feeding practices (breastfeeding, time of gluten introduction) have no effect on the risk of developing coeliac disease during childhood (at least at specific timeframes evaluated in the included studies).¹ In addition, with regard to T1D, recent individual patient data meta-analysis suggested weak protective associations between exclusive breast-feeding and T1D.² OBJECTIVE. To up-date current knowledge on the possible relationship between early feeding practices and the risk of T1D as this may affect European recommendations formulated for early feeding practices.

Methods: The protocol for this systematic review was registered with PROSPERO (CRD42015024310). In brief, the Cochrane Library, MEDLINE, EMBASE, CINAHL, LILACS, Maternity and Infant Care, MEDLINE and Science Citation Index were search for studies of any design up to July 2015. The primary outcome measure was the development of T1D or the development of T1D-related autoimmunity (T1DA).

Results: After screening on 2591 potential studies, six publications reporting 3 cohorts (BABYDIET, BABYDIAB, and DAISY) met the inclusion criteria. Breastfeeding at the time of gluten introduction, as compared to gluten introduction after weaning, has not been shown to reduce the risk of developing T1DA or T1D (Figure 1a). In children at high risk of T1D, except for gluten introduction at <3 mo compared with gluten introduction at >3 mo of age which increased the risk of T1DA, the age of gluten introduction in infants does not seem to influence the risk of developing T1DA (Figure 1b).
Table: Figure 1. Effect of early feeding practices on T1DA and T1D.

a. Effect of breastfeeding at the time of gluten introduction on the T1DA or T1D (observational studies).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Cases</th>
<th>Controls</th>
<th>Odds Ratio M--H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.1.1 T1DA</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cooper 2009</td>
<td>21</td>
<td>13</td>
<td>42.8% 1.13 [0.55, 2.33]</td>
</tr>
<tr>
<td>Norris 2003</td>
<td>15</td>
<td>585</td>
<td>1149 0.76 [0.38, 1.51]</td>
</tr>
<tr>
<td>Subtotal (95% CI)</td>
<td>283</td>
<td>1322</td>
<td>100.0% 0.92 [0.56, 1.51]</td>
</tr>
<tr>
<td>Total events</td>
<td>36</td>
<td>598</td>
<td></td>
</tr>
<tr>
<td>Heterogeneity: Chi² = 0.62, df = 1 (P = 0.43); I² = 0%</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Test for overall effect: Z = 0.33 (P = 0.74)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| 2.1.2 T1D         |       |          |                                |
| Frederiksen 2013  | 17    | 765      | 1782 0.63 [0.35, 1.13]         |
| Subtotal (95% CI) | 53    | 1782     | 100.0% 0.63 [0.35, 1.13]       |
| Total events      | 17    | 765      |                                |
| Heterogeneity: Not applicable |
| Test for overall effect: Z = 1.56 (P = 0.12) |

Test for subgroup differences: Chi² = 0.96, df = 1 (P = 0.33); I² = 0%

b. Effect of timing of gluten introduction on the T1DA (observational studies).

<table>
<thead>
<tr>
<th>Study or Subgroup</th>
<th>Cases</th>
<th>Controls</th>
<th>Risk Ratio M--H, Fixed, 95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>2.3.1 Gluten at &lt;3 mo vs &gt;3 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ziegler 2003</td>
<td>4</td>
<td>61</td>
<td>1136 4.38 [1.80, 10.68]</td>
</tr>
<tr>
<td>Norris 2003</td>
<td>4</td>
<td>19</td>
<td>485 1.31 [0.46, 3.75]</td>
</tr>
<tr>
<td>2.3.2 Gluten at &lt;3 mo vs &gt;7 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norris 2003</td>
<td>4</td>
<td>586</td>
<td>11 2.73 [0.89, 8.37]</td>
</tr>
<tr>
<td>Norris 2003</td>
<td>4</td>
<td>11</td>
<td>586 2.73 [0.89, 8.37]</td>
</tr>
<tr>
<td>2.3.4 Gluten at &lt;3 mo vs 4–6 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norris 2003</td>
<td>4</td>
<td>30</td>
<td>59 0.96 [0.39, 2.38]</td>
</tr>
<tr>
<td>Cooper 2009</td>
<td>5</td>
<td>30</td>
<td>59 0.96 [0.39, 2.38]</td>
</tr>
<tr>
<td>2.3.5 Gluten &lt;4 mo vs &gt;4 mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Norris 2003</td>
<td>4</td>
<td>34</td>
<td>124 1.49 [0.64, 3.48]</td>
</tr>
<tr>
<td>Frederiksen 2013</td>
<td>6</td>
<td>34</td>
<td>124 1.49 [0.64, 3.48]</td>
</tr>
<tr>
<td>2.3.6 Gluten &lt;4 mo vs &gt;6mo</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Frederiksen 2013</td>
<td>6</td>
<td>34</td>
<td>1049 1.49 [0.64, 3.48]</td>
</tr>
<tr>
<td>Hummel 2011</td>
<td>8</td>
<td>8</td>
<td>73 0.95 [0.38, 2.39]</td>
</tr>
</tbody>
</table>

Conclusion: Current observational data suggest that breastfeeding at the time of gluten introduction and timing of gluten introduction at specific timeframes evaluated in the included studies have no effect on the risk of developing TID or T1DA.

Disclosure of interest:
All authors: None Declared
Development of Urinary Adiponectin and Fibroblast Growth Factor-21 Assay Tool for the Population-based Screening of Pediatric Metabolic Syndrome

Ahlee Kim, Jin Soo Moon, Jae Sung Ko, Ju Young Chang, Young Won Nam, Kyoung Hoon Lee, Sang Hoon Song, Jung Han Song

1Seoul National University Hospital, Pediatrics, Seoul, Korea, Rep. of South
2Seoul National University Boramae Medical Center, Pediatrics, Seoul, Korea, Rep. of South
3Seoul National University, Laboratory Medicine, Seoul, Korea, Rep. of South

Objectives and study: Obesity is one of the most important metabolic syndrome in current society, and the prevalence of obesity is rapidly increasing. Although there are well-known evaluating values of obesity such as body mass index (BMI) and waist circumference, we need more accurate and noninvasive biomarkers for early screening and evaluation of the pediatric obesity and metabolic syndrome. The purpose of this study is to develop new biomarkers to clarify the risk stratification and treatment plan for the obese children by analyzing urinary adiponectin and fibroblast growth factor-21 (FGF-21).

Methods: We used the data from the cohort database of pediatric obesity biomarker project of Ministry of Science, Information & communication technology and Future Planning, South Korea. We selected 93 obese group whose BMI values were > 99 percentile of the population, and 92 controls whose BMI values were between 25 and 75 percentile. The physical information of all individuals such as height, body weight, waist circumference, and blood pressures were collected. A total of 184 serum and urine samples were obtained from the medical examination. Urinary adiponectin and FGF-21 were measured by ELISA method. The diagnosis of metabolic syndrome was made using the International Diabetes Federation criteria for children and adolescents, using 2007 Korean National Growth Chart.

Results: Urinary adiponectin and FGF-21 level were significantly higher in obese group than normal control (P=0.021, 0.006). When comparing metabolic syndrome group and normal control, urinary adiponectin and FGF-21 level were higher in children with metabolic syndrome, though they were not statistically significant (P=0.068, 0.065). When adjusted with creatinine or albumin, urinary adiponectin and FGF-21 were significantly higher in children with metabolic syndrome (P=0.013, 0.037). When comparing metabolic syndrome group and non-metabolic syndrome, only creatinine-adjusted urinary adiponectin was statistically significant (P=0.037). The receiver operating characteristic curve analysis was used to compare the obesity and normal group. The highest area under the curve (AUC) value was observed in albumin-adjusted urinary adiponectin (0.703). In comparison between metabolic syndrome and normal group, AUC was slightly lower than former analysis. The highest AUC value was also observed in albumin-adjusted urinary adiponectin (0.686). We determined cutoff level of each biomarkers by Maxstat software. Among all cutoffs, creatinine- and albumin-adjusted cutoffs were determined as statistically significant (P<0.001). In logistic regression analysis for the diagnosis of metabolic syndrome using all biomarkers and adjusted levels, albumin-adjusted urinary adiponectin (Odds ratio 1.192, P=0.004) and FGF-21 (Odds ratio 1.007, P=0.01) showed positive effect on the diagnosis of metabolic syndrome.

Conclusion: Urinary adiponectin and FGF-21 assays can be useful screening biomarkers for screening pediatric obesity and metabolic syndrome due to simple and noninvasive sampling method. Creatinine-adjusted urinary adiponectin may be a reliable biomarker for screening pediatric metabolic syndrome.

Disclosure of interest: This research was supported by the Civil research projects for solving social problems through the National Research Foundation of Korea (NRF) funded by the Ministry of Science, ICT & Future Planning (grant number NRF-2013M3C8A2075911, NRF-2013M3C8A2A01078732).
A comparative study of the course and outcome of pregnancy and delivery, and the blood and colostrum content of hormones regulating energy homeostasis in Moscow women with normal and excessive body weight

Nataliya Shilina¹, Galina Selivanova², Svetlana Braginskaya², Maria Gmoshinskaya¹, Igor Kon¹

¹Institute of Nutrition, Age-Related Nutritiology, Moscow, Russian Federation
²Maternity Hospital №6, Moscow, Russian Federation

Objectives and study: The statistical data show that the occurrence of obesity in general population has doubled in the past 30 years. The prevalence of overweight and obesity in Russia is smaller than in the developed countries but the rate of these conditions growth becomes higher in all population groups, and in the obstetric population as well. However, there is a limited number of studies in Russia on the impact of overweight and obesity in pregnant women on the course and outcome of pregnancy and labor, their level of hormones regulating energy homeostasis, and the condition of newborns.

The aim was a comparative study of the course and outcome of pregnancy and delivery, anthropometric indices and state of newborns health, the level of leptin, grelin, adiponectin and insulin-like growth factor 1 (IGF-1) in blood and colostrum of Moscow women with normal and excessive body weight.

Methods: The study was performed at Moscow maternity hospital and outpatient clinic women's consultation. All participants gave their informed consent. The design of the study was approved by local ethical committee. The course and outcome of pregnancy and delivery, anthropometric indices and state of newborns health were evaluated in 83 overweight and obese pregnant women (BMI>24.9 kg/m²) and 51 pregnant women with normal body weight (BMI 18.5-24.9 kg/m²). The levels of leptin, grelin, adiponectin and IGF-1 were determined in serum blood and colostrum by ELISA. Statistical analysis was performed by the SPSS 20. The differences were considered statistically significant at p<0.05.

Results: The average weight gain during pregnancy in women with overweight and obesity amounted to 13.8 ± 5.2 kg, which was higher than the weight gain in women with normal body weight (11.7 ± 4.5 kg). In women with overweight and obesity there was an increased risk of complications during pregnancy (preeclampsia, anemia), delivery (more frequent operational, premature, and delayed delivery), as well as 2-3 times more frequent birth of infants with significantly enhanced birthweight, including macrosomia. In the blood of overweight and obese women we observed increased levels of hormones compared with the blood of women with normal body weight (M±SEM, 97±22 vs 18±7ng/ml, p<0.05, for leptin; 492±42 vs 420±130 ng/ml for IGF-1). Analogous increase was observed in colostrum as well (6.2±0.9 vs 2.6±0.7 ng/ml, p<0.05, for IGF-1; 3.7±0.7 vs 1.3±0.9 ng/ml for leptin and 1.6±1.2 vs 0.3±0.1 ng/ml for grelin). There were no notable differences in blood and colostrum adiponectin levels.

Conclusion: The overweight and obesity increase the risk of pregnancy and delivery complications and have negative effects for mother and infants health. The increased levels of hormones regulating energy homeostasis in overweight and obese mother’s blood and colostrum, in particular, IGF-1, can possibly lead to enhanced risk of obesity in these women’s infants. In fact, it was shown that the increased level of these hormones in breast milk correlates with infants' high growth rate [Kon et al., 2014], a recognized risk factor of obesity [Dennison et al., 2006].

Disclosure of interest: None Declared.
NUTRITION: Nutrition and health outcomes

N-P-068

Obesity, but not metabolic syndrome, is associated with decreased trace elements in adolescents

Szu-Ta Chen¹, Yu-Hsien Lin², Hsueh-Yi Lu³, Yen-Hsuan Ni³

¹National Taiwan University Hospital Yun-Lin Branch, Dept. of Pediatrics, Dou-Liu City, Taiwan
²Graduate Institute of Industrial Engineering and Management, National Yunlin University of Science and Technology, Dou-Liu City, Taiwan
³National Taiwan University Hospital, Dept. of Pediatrics, Taipei, Taiwan

Objectives and study: Obesity and metabolic syndrome (MS) have been important public health concerns in children. Trace elements (TEs) are essential nutrients involved in various roles in development and metabolism. This study aimed to examine the associations between the levels of TEs and the status of obesity and metabolic syndrome (MS) in adolescent participants in the National Health and Nutrition Examination Survey (NHANES 2007-1010).

Methods: Among 2,577 aged 12 – 19 years subjects out of 20,686 participants, we studied 2,174 adolescents and 403 participants with missing variables were excluded. The overweight and obesity were defined as body mass index (BMI) ≥ 85th percentile and 95th percentile for age respectively. MS was determined in children with ≥ 3 of 5 major criteria based on the waist circumference, high-density lipoprotein (HDL) cholesterol, triglyceride, blood pressure and fasting glucose levels. Iron deficiency (ID) was determined according to serum iron, ferritin, and transferrin receptor levels. We analyzed the biochemical variables and the levels of TEs (lead, iron, cadmium, mercury, thallium, and platinum) and the associations with the status of obesity and MS.

Results: Among the 2,174 participants, 398 (18.3%) subjects were overweight and 482 (22.2%) were obese, otherwise were control cases. Regarding metabolic factors, children with obesity had significantly higher low-density lipoprotein cholesterol (94.9 ± 28.3 versus 85.5 ± 24.1 mg/dL, P < 0.0001), triglyceride (101.8 ± 52.4 versus 75.5 ± 41.8 mg/dL, P < 0.0001), fasting glucose (96.8 ± 7.8 versus 95.6 ± 25.5 mg/dL, P < 0.0001) and insulin levels (161.5 ± 99.3 versus 68.2 ± 45.2 pmol/L, P < 0.0001) than control subjects. Interestingly, the blood cadmium (0.230 ± 0.233 versus 0.285 ± 0.395 µg/L, P < 0.0001), lead (0.843 ± 0.516 versus 0.943 ± 0.767 µg/L, P = 0.0089), and iron levels (72.7 ± 32.3 versus 91.6 ± 38.5 µg/L, P < 0.0001) were significantly lower in obese participants than control cases. The blood mercury, urine thallium and platinum levels revealed no significant differences between obese and control subjects. Besides, obese participants had significantly higher ferritin (40.9 ± 32.4 versus 34.5 ± 26.9 mg/mL, P < 0.0259) and transferrin receptor (3.78 ± 1.35 versus 3.42 ± 1.69 mg/L, P < 0.0001) than those control cases. The prevalence rate of ID was also significantly higher in children with obesity than control cases (9.13% versus 4.25%, P < 0.001). The prevalence rate of MS in control, overweight and obesity groups were 2.3%, 2.5%, and 11.0% respectively. Among 482 obese cases, the blood cadmium, lead, iron, ferritin, and transferrin receptor levels revealed no differences between subjects with and without MS.

Conclusion: We found the associations between low blood TEs levels (cadmium, lead, and iron) and the status of obesity, but not MS, in adolescents. ID is also associated with obesity in adolescents, instead of MS. Obesity and metabolic syndrome might have different influences on the metabolism of TEs and ID in adolescents.

Disclosure of interest: None Declared.
Are gluten free products available in Europe and in USA comparable?

Paula Crespo Escobar1, Jaoquim Calvo Lerma2, David Hervas3, A. Pamela Cureton4, Carmen Ribes Koninckx5

1Hospital Universitari i Politècnic La Fe, Valencia, Spain
2Instituto de Investigación Sanitaria La Fe, Valencia, Spain
3Instituto de Investigación Sanitaria La Fe, U. Bioestadística, Valencia, Spain
4Massachusetts General Hospital, Boston, United States
5La Fe University Hospital, Department of Pediatric Gastroenterology and Hepatology, Valencia, Spain

Objectives and study: To compare the nutritional composition of gluten-free products (GFP) consumed in Europe and USA regarding the main macronutrients: energy, proteins, carbohydrates, sugar, fatty acids, saturated fatty acids and fiber.

Methods: A prospective observational study collecting, from the labels, the nutritional composition of different GFP available for celiac patients in Spain (Valencia) and USA (Boston). We compared the average of several brands of the same type of GFP in each country according to a mixed effect linear regression model adjusted for type of product. Also, we compared in each country the different brands for each type of GFP.

Results: The following 14 types of GFP from 13 brands in Spain and 46 in Boston were analyzed: bread, toasts, flour, bread crumbs, sandwich bread, hamburger bread, pizza dough, pasta, cereals, biscuits, cream-filled cookies, brioche, muffins, cakes and crackers. Overall the Spanish GFP have statistically significant more energy (7%), fats (20%) and saturated fatty acids (45%) than the American GFP (p<0.001). The quantity of carbohydrates, sugar and fiber is similar in both countries (p=0.13, 0.66 and 0.38 respectively). However, the American GFP contain overall 50% of protein content more than Spanish GFP. If we look into the variation of macronutrients product by product in each country we found the following similarities: cream-filled cookies are the product with the highest energy (100 kcal more than the average of GFP) whereas bread has the lowest amount (90 kcal less). Regarding proteins, cereals have the highest content and brioche the lowest but with less variation than in energy. Cereals and flour have the maximum amount of carbohydrates (15 grams more than the average of GFP) while the different types of bread have a similar quantity of this macronutrient and the lowest amount (18 grams less). In case of sugar, fatty acids and saturated fatty acids biscuits show a high and significant content of these macronutrients (20, 12 and 8 grams more than the average of GFP respectively) as compared to other types of products whereas pasta displays the lowest amount. Finally, the highest fiber content is found in cereals and the lowest in biscuits and muffins but with minor differences as compared to the rest of the products. The additional analysis show that there is also a high variability in the nutritional profile for the same GFP among different brands, this being more relevant in brioche, cereals, crackers, biscuits, cakes and muffins.

Conclusion: True differences are observed between Spanish and American GFP in the macronutrients content, the first ones containing an overall significant higher amount of saturated fatty acids. It can be asserted that Spanish celiac children consuming special GFP, are at risk of a higher fat intake and saturated fatty acids as compared with American celiac children. These differences plus the variability detected among different brands for each type of product leads to the need of implementing nutritional education to celiac disease (CD) patients so as to enable them to successfully self-manage the large variety of brands and options offered and to choose the best nutritional composition profile in order to ensure these children carry a balanced diet. Moreover, dietitians should be actively involved as dietary advisors in the management of CD patients. These results could be of value to further assess the impact of other comorbidities of CD.

Disclosure of interest: No conflict of interest to declare.
Dietary fiber intake in children with inflammatory bowel disease

Aleksandra Pituch-Zdanowska¹, Aleksandra Banaszkiewicz², Piotr Albrecht²

¹Medical University of Warsaw, Warsaw, Poland
²The Medical University of Warsaw, Dept. of Pediatric Gastroenterology and Nutrition, Warsaw, Poland

Objectives and study: Although available data suggest that patients with inflammatory bowel disease (IBD) in clinical remission or mild disease activity should not limit dietary fiber intake, many of them are on a low-fiber diet. The aim of the study was to estimate intake of dietary fiber and its fractions, by children with IBD in remission or mild disease activity compare with healthy controls.

Methods: This was a prospective controlled study on children with IBD. Food consumption data were collected by using the 3-day dietary dairy. The mean intake was calculated using computer program Diet 5.0; for intake of soluble and insoluble fibers author’s questionnaire was used.

Results: The study included 50 children with IBD (median age, 13.63 ± 2.6 years) and 50 healthy children (median age, 14.03 ± 2.4 years). There were no statistically significant differences between both groups (age, weight, height, BMI percentiles). In the study group 80% of children were in clinical remission. The mean disease duration was 3.5 ± 2.5 years. The differences in energy, fat, protein and carbohydrates intakes between both groups were not statistically significant (p = 0.5716). There was a high compliance of dietary fiber intakes obtained by using both methods (p = 0.6028). The average intake of dietary fiber in the study group was higher than in the control group (15.34 g/d vs 14.06 g/d) but the differences were not statistically significant (p = 0.3396). The average intake of soluble fiber in the study group was 4.99 g/d and in controls 4.69 g/d (approx. 34% of total dietary fiber). Whereas the intake of insoluble fraction was 10.18 g/d vs 9.69 g/d (approx. 66% of total dietary fiber). Age (p = 0.0098) and gender (p <0.0001) were significantly associated with dietary fiber intake and its fractions. The intake increased with age and it was higher among boys in each age group. The main source of dietary fiber in both groups were grains (44.8% vs 49.5%), vegetables (15.9% vs 16.9%), fruit (14.7% vs 14.3%) and potatoes (12.2% vs 14.1%). In both groups, the boys better achieved adequate intake AI recommendations than girls (p = 0.0033).

Conclusion: Children in clinical remission or mild IBD consumed more dietary fiber and its fractions than healthy children, but these differences were not statistically significant.

Disclosure of interest: “None Declared”.
Iron deficiency - potential risk factor for febrile seizures

Raluca Maria Costea¹, Neamtu Mihai Leonida²

¹Pediatric Clinical Hospital, Ceforaten, Sibiu, Romania
²Lucian Blaga University, Pediatric Clinic Hospital, Ceforaten, Sibiu, Romania

Objective and study: Febrile seizures (FS) have an impact on the psychological status because of the potential for recurrence and development as epilepsy. Iron, essential element in the homeostasis, is also involved in neurotransmission and neuromodulation, dopamine receptors D1 and D2 being down regulated in iron deficiency anemia (IDA). Its protective role by upregulating the seizure threshold or as a risk factor for FS is on debate. The aim of the study is to determine the role of iron status in FS.

Methods: A case-control study conducted between January 2012 - September 2014. The inclusion criteria were: age 1 month - 5 years, admittance in Pediatric ward due to current febrile conditions, including FS. The exclusion criteria were: current CNS infection and past afebrile seizures. The study subjects were grouped in: study (seizure) group - subjects with FS (less than 1 year, 1-2 years and more than 2 years old subgroups) and control group - subjects with other current febrile conditions. For both groups we followed: plasma iron, hemoglobin concentration (Hb), mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH). For study group we followed: type, number and magnitude of FS.

Results: 96 patients with FS and 96 controls were enrolled; mean age of 26.75 months for FS and 24.48 for control group. The two groups were homogeneous as belonging to gender (p 0.53), provenience (p 0.28) and age >2 years (p 0.58). The least seizure exposed age group is <1 year (p 0.0006), concluding a protective role for this age [RR = 0.312 95% CI (0.142-0.645)]. With a double risk of FS [RR= 1.986 95% CI (1.256-3.211)] the age group 1-2 years is the most exposed. This results respect the literature data: peak incidence of FS is 14-18 months which overlaps with that of IDA (6-24 months). Patients with IDA are more exposed to FS (p 0.01). No statistical significance was found between: low VEM (p 0.99), Hb (0.96) or HEM (0.56) value and FS risk, not even for low values for all erythrocytic indices (p 0.28). This global low parameters seem to have a minimal protective role [RR = 0.689 95% CI (0.358-1.303)]. Among the patients with IDA the group age under 2 is more exposed to FS (p 0.05). A high statistic significant correlation was noticed with the FS number (more) indicating a possible risk for recurrence in patients with FS and IDA (p 0.01). A statistical significance was found between low sideremia and atonic seizure (p 0.02) but disregarding non epileptic events from atonic seizures is sometimes difficult. No statistical significance was attained between IDA and seizure type-simple or complex (p 0.96), gender (p 0.41) or magnitude of the FS (complex FS, more episodes, tonic-clonic).

Conclusion: The study suggests that iron status screening should be considered to determine which children with FS may be at risk for recurrence. An adequate nutritional status might reduce FS risk, especially in high risk patients. Iron status and not hypochromic microcytic anemia should be considered as a possible risk factor for FS.

Disclosure of interest: None Declared.
Early feeding practices influence weight gain and gastrointestinal health in the STRONG Kids 2 cohort.

Sharon Donovan¹, Salma Musaad²

¹University of Illinois, Urbana, Food Science & Human Nutrition, Urbana, United States
²University of Illinois, Urbana, Human Development & Family Studies, Urbana, United States

Objectives and study: Human milk is the ideal nutrition for the developing infant and contains components that shape the microbiome and reduce infections. Herein, the impact of feeding mode in the first 3 months (mos) of life on health status and stool characteristics at 3 and 12 mos was investigated.

Methods: Infants were recruited into the ongoing STRONG Kids 2 (SK2) birth cohort of 400 families in Champaign, Illinois. Analyses were restricted to those who have data at 12 months (n=230). Feeding mode (exclusive breastfeeding, BF; exclusive formula feeding, FF; or combined feeding, CF), stool frequency and characteristics, and infant health outcomes were obtained by parental report. Infant weight and length were measured at 3 and 12 mos by researcher staff and weight-for-length Z-score (WLZ) was calculated using the 2006 WHO growth charts. Breastmilk and stool samples were collected at 3 and 12 mos. Data are expressed as mean±SD.

Results: Mean gestational age, birthweight and length were 39.6±1.2 wks, 3.48±0.43 kg and 51.1±2.9 cm, respectively, and 28% were delivered by C-section. In terms of race and ethnicity, 83% of the infants are White, 4% are Hispanic or Latino and 5% are Black and 49% are male. The percentage of infants that were BF, FF or CF was 64, 23 and 13% at 3 mos and 44, 31, and 10% at 12 mos, respectively. At 12 mos, 15% of infants were no longer BF or FF. WLZ change from birth to 12 mos differed by feeding at 3 mos, being 0.84±1.58 for BF, 1.11±1.06 for CF, and 1.99±1.53 for FF (P<0.05). At 3 mos, BF infants (2.9±1.9) had greater stool frequency per day than FF (1.8±1.0) or CF (1.9±1.3) infants (P=0.015). By 12 mos, stool frequency was similar in all groups. In terms of stool consistency at 3 mos, FF (62.5%) and CF (58.5%) infants were more likely (P=0.008) to have soft stools than BF (34.7%), and less likely (P<0.001) to have semi-watery stools: FF (33.3%) and CF (41.6%) vs. BF (72.6%). At 12 mos, FF (17.6%) and CF (25%) infants were more likely (P=0.033) to have soft stools than BF (43.7%). In terms of illnesses, FF were 4.5-fold and 2.8-fold more likely (P=0.024) to have had diarrhea in the previous 2 wks than BF and CF and were 6.4-fold and 2.8-fold more likely (P=0.009) to have vomited in the previous 2 wks than BF and CF.

Conclusion: FF infants were more likely to be overweight at 12 mos than BF; whereas CF was intermediate. FF infants had poorer GI health at 3 mos of age, as evidenced by reduced stool frequency, more solid stool and greater vomiting and diarrhea. Milk composition and gut microbiome analyses are on-going. (This work was supported by grants from the Dairy Research Institute and the Gerber Foundation).

Disclosure of interest: None Declared
Obesity prevention project in preschool-age: the 3P-Project effectiveness in short- and medium-term

Marco Poeta¹, Dario Di Salvio¹, Nives Torsiello¹, Grazia Massa¹, Salvatore Guercio Nuzio¹, Riccardo Savastano¹, Giovanna Alfano¹, Luca Pierrí¹, Marina Tripodi¹, Maria Anna Siano¹, Maria Rosaria Terminiello², Pierluigi Mottola³, Pietro Vajro¹

¹Pediatric Section, University of Salerno, Department of Medicine and Surgery, Baronissi, Italy
²Salerno Municipality, Schools Canteens Nutrition Section, Salerno, Italy
³Italian National Olympic Committee (Coni), Local Division, Salerno, Italy

Objectives and study: Obesity pandemics is very recalcitrant to school-based prevention strategies, probably because they start too late. We therefore investigated the short and medium term efficacy of a controlled, early, healthy lifestyle intervention aimed to improve motor and nutritional knowledge and preferences, and Mediterranean Diet (MD) adherence in 3-6 y.o. preschoolers.

Methods: A multicomponent 15 month prevention intervention (the 3P-Project). Eighty preschoolers (intervention group) and 35 controls of middle income Southern Italy families were characterized at baseline, at 7 and 15-mos after the start of intervention. Evaluations consisted of auxologic measurements [body mass index (BMI), waist circumference (WC), waist-to-height ratio (WtHR) adjusted for sex and age], family questionnaire (KidMed, Food Neophobia, Screen-time, Sleep debt, Visual body weight, Preschool-Age Physical Activity scores) and photo-panels based game-interviews assessing children’s knowledge/preferences. Classroom activities (a coloring book illustrating healthy foods and activities, seminars for parents and teachers, weekly yogurt and fruit snacks, monthly school MD-based lunches extended to families, daily physical activity sessions monitored by an expert) were performed only by the intervention group.

Results: At baseline overweight(OW)/OB prevalence was present in 1 out of 3 preschoolers (37%, 29% and 40% by considering BMI, WC and WtHR, respectively). High blood pressure values (>90th percentile) were already present in 6%. At short term FU (end of the school year =7-mo) anthropometrics, screen-time, sleep duration and body misperception remained stable in both groups (p>0.05), whereas food neophobia, physical activity and nutrition knowledge/preferences significantly improved in the intervention group (p<0.001) as compared to controls (p>0.05). This positive changes were maintained at a longer-term FU (15-mo), when visceral obesity prevalence (p<0.001) and MD adherence (p<0.01) also improved (table).
Table:

<table>
<thead>
<tr>
<th></th>
<th>Intervention group (n=85)</th>
<th>Control group (n=35)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>T0</td>
<td>T1</td>
</tr>
<tr>
<td><strong>BMI (%ile)</strong></td>
<td>61.2 ± 27.7</td>
<td>61.2 ± 29.2</td>
</tr>
<tr>
<td><strong>WC (%ile)</strong></td>
<td>69.6 ± 20.8</td>
<td>67.8 ± 19.6</td>
</tr>
<tr>
<td><strong>Food knowledge</strong></td>
<td>3.9 ± 1.7</td>
<td>5.0 ± 1.7</td>
</tr>
<tr>
<td><strong>Food preferences</strong></td>
<td>3.0 ± 1.8</td>
<td>4.6 ± 1.9</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>3.6 ± 1.7</td>
<td>4.0 ± 1.5</td>
</tr>
<tr>
<td><strong>Physical activity</strong></td>
<td>3.4 ± 1.6</td>
<td>4.0 ± 1.5</td>
</tr>
<tr>
<td><strong>KidMed</strong></td>
<td>5.7 ± 2.2</td>
<td>5.7 ± 2.1</td>
</tr>
<tr>
<td><strong>Food Neophobia</strong></td>
<td>9.4 ± 3.0</td>
<td>8.4 ± 3.3</td>
</tr>
</tbody>
</table>

**Abbreviations:** T0=Basal time; T1=7-mos follow-up; T2=15-mos follow-up; * p<0.05 compared with T0; ° p<0.05 compared with T1; %ile = percentile; BMI = Body Mass Index; WC = Waist circumference.

**Conclusion:** This type of intervention appears to determine rapid and persisting improvements of healthy eating and lifestyle habits in preschoolers. Further and larger -but similarly measurable-controlled studies are needed to verify the longer-term effectiveness. Being relatively inexpensive, it warrants consideration as a model exportable to other contexts integrated with their own regional preventive programs.

**Disclosure of interest:** None Declared.
BMI and food behavior in a cohort of Russian young children aged 12-35 months.

Aleksandra Surzhik¹, Tatyana Borovik², Irina Zakharova³, Leila Namazova-Baranova⁴
¹Scientific Center of Child Health, Danone Nutricia ELN (Nutricia Russia), Moscow, Russian Federation
²Scientific Centre of Child Health, Nutrition of Healthy and Sick Child, Moscow, Russian Federation
³Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation
⁴Scientific Center of Child Health, Moscow, Russian Federation

Objectives and study: Obesity is one of the most prevalent nutritional disorder among children in the world. And overweight among toddlers is the first step to overweight. Critical factors for prevention of obesity is healthy lifestyle included physical activities and food behavior. Unfortunately health care professionals don’t spent enough time to overweight prevention during their day-by-day work. The aim of this study was to define prevalence of overweight among young children and to clear the main and common food misbehavior, which should be improved for prevention of obesity in future.

Methods: A regionally diverse cohort (n=1420) based on official birth data was recruited. This was made up of 720 children 12-23 months (group I) and 700 children of 24-35 months (group II). A 3-day estimated diet diary undertook dietary assessment and additional questionnaire for mothers included questions about nutrition habits of their children was used for database. The physical development was estimated by the WHO Child growth standards and WHOAnthro (2011) program.

Results: The average BMI in I group was 16.79±1.81, in II group 16.29±2.61. Calculation of z-score (BAZ) showed that 67.4% children of 12-23 mo and 52.3% children of 24-36 mo had BMI within the age norm (from -2 till +1). Malnutrition with z-score less than -2 was detected for 1.5% children in I group and 11.9% in II group. Overweight with z-score from +1 till +2 was found in 22.5% (I group) and 19.1% (II group). Z-score higher than +2 was detected in 8.5% in group I and in 16.7% in group II. The next main food misbehavior was detected in the study: low consumption of vegetables and fruits, intake of “inappropriate” or ‘non-core’ foods including mayonnaise, chips, sausages, soft beverage, intake of “fat food” with saturated fatty acid. 255 children (35.4%) in group I continued night feeding, mothers of 14% children of 12-23 mo and 20.8% of 24-35 mo used sugar regular for cooking. The results of the detailed analysis of the potential interrelation between food habits and body weight presents in table 1. A lot of children had more than one mistake in there food behavior and it was difficult to find simple correlation between one and BMI.

Table: Table 1. The interrelation between food habits and body weight.

<table>
<thead>
<tr>
<th>Food habits</th>
<th>BMI</th>
<th>Unpaired Mann-Whitney test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Regular night feeding</td>
<td>16.97±2.07</td>
<td>p=0.03</td>
</tr>
<tr>
<td>No night feeding</td>
<td>16.70±1.65</td>
<td></td>
</tr>
<tr>
<td>High consumption of “fatty food” (&gt;4 times per week)</td>
<td>17.73±3.95</td>
<td>p=0.04</td>
</tr>
<tr>
<td>Seldom consumption of “fatty food” (&lt;2 times per week)</td>
<td>16.25±2.55</td>
<td></td>
</tr>
<tr>
<td>Additional sugar as regular practice</td>
<td>16.38±2.26</td>
<td>p=0.07</td>
</tr>
<tr>
<td>No additional sugar</td>
<td>15.96±2.37</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Apparently prevalence of overweight among young children 12-35 months is too high in Russia and it is very important to draw attention of health care professionals and parents to this problem. The interrelation between some food habits and body weight was detected. But no single food habit has been connected with overweight. Mother behavior during cooking and feeding to make child’s food habits. Education program for parents appear important to improve the dietary practices and more work is required for this for children over 12 months.

Disclosure of interest: A. Surzhik Conflict with: Employed by 2Danone Nutricia ELN (Nutricia LTD, Russia), T. Borovik None Declared, I. Zakharova None Declared, L. Namazova-Baranova None Declared
The effect of breastfeeding and complementary feeding on growth and later health: a systematic review of systematic reviews

Bartłomiej Zalewski¹, Bernadeta Patro-Gołąb¹, Maciej Kołodziej¹, Berthold Koletzko², Hans van Goudoever³, Stefanie Kouwenhoven³, Hania Szajewska⁴

¹Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
²Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
³Vu University Medical Center Amsterdam, Department of Pediatrics, Amsterdam, Netherlands
⁴University of Warsaw, Pediatrics, Warsaw, Poland

Objectives and study: The EarlyNutrition Project, currently the largest research project worldwide in the area of developmental origins of health, aims to develop new, improved strategies and recommendations on nutrition in infants and young children, which take into account the effect of early nutrition on later health. To achieve this we performed systematic review of systematic reviews on the effects of specific nutritional interventions or exposures in children (up to 3 years of age). Here we report on the effects of breastfeeding (BF) and complementary foods (CF) on growth, and the risk of overweight, obesity or adiposity in later life.

Methods: The Cochrane Database of Systematic Reviews, the Database of Abstracts of Reviews of Effects, Ovid MEDLINE, EMBASE, and some additional sources were searched up to September 2015. The methodological quality was assessed with the use of a modified AMSTAR tool.

Results: Ten systematic reviews, clinically and methodologically heterogeneous, focused on BF. One review found higher fat free mass in most assessment time points in the first year of life and higher fat mass only in the assessment at 12 mo of age in formula-fed infants compared to exclusively breastfed infants (eBF). A recent high-quality Cochrane review failed to show protective effect of eBF for 6 mo versus 4 mo against childhood overweight and obesity. Another review showed that any BF compared with formula feeding was associated with significant reduction of overweight/obesity (OR 0.88; 95%CI 0.83 to 0.93; high quality studies only). Five systematic reviews demonstrated that longer BF duration was associated with greater protective effect against obesity.

Five systematic reviews focused on CF. Two of these reviews suggested that there is a link between early (at 4 mo) introduction of CF and the risk of childhood obesity. In contrast, the only review of high methodological quality found that introduction of CF at 4 mo compared with 6 mo had no effect on weight change in infancy. One review found that children fed ‘healthy diet’ had a higher lean mass at 4 years of age, but not BMI, and there was no difference in other body composition measures.

Conclusions: Current evidence shows some protective effect of BF against obesity. The effect of the age of CF introduction on the risk of overweight and obesity remains uncertain.

Disclosure of interest: None declared. 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].
A new approach to home artificial nutrition in children: a multidisciplinary process between a university hospital and local health authority (ASL-NA1) in Campania region

Fabrizia Chiatto¹, Daniela Mambretti², Diana Cerullo², Andrea Lo Vecchio³, Maria Immacolata Spagnuolo⁴, Alfredo Guarino²

¹Federico II University, Department of Translational Medical Science – Section of Pediatrics, Naples, Italy
²Federico II University, Naples, Italy
³Federico II University, Pediatrics, Naples, Italy
⁴Federico II University, Pediatrics, Naples, Italy

Objectives and study: The transition to home of children on artificial nutrition (AN) requires an optimized coordination of a multidisciplinary team. Caregivers usually receive a training on the management of AN from two different teams (in hospital and at home respectively). The aim of our study was to evaluate the efficacy of a new-established multidisciplinary protocol for an optimum continuum healthcare process for patient on AN discharged from hospital to home.

Methods: From January 2013 to date, all patients followed at the Local Health Authority in the area of Naples city (ASL-NA1) attended a training course carried out by nurses from both University Federico II and ASL-NA1 (cases). A control group of patients followed in the previous six months with standard procedure was identified. Our centre had a coordinating role and provided human and professional resources, while the ASL-NA1 provided nurses, a pharmacy service and the materials required for Domiciliary Assistance Nutrition (DAN). We used protocols and procedures in accordance to the guidelines for the management of Central Venous Catheter (CVC). Efficacy parameters were identified: the time spent by each caregiver for the training, the number of days of hospitalization, the number of days needed to activate the home care service, the number of hospitalizations and Day-Hospital (DH) after discharge.

Results: After 21 months from the beginning of the project, we found that 65 hours of theoretical and practical training on nursing home care of children in home AN were needed, and 3 out of 5 nurses have completed the whole program. A total of 8 children were enrolled, 4 (2 males; median age 21 ± 34 months) represented the cases and 4 (2 males; median age 3.5 ± 0.7 months) were the controls. In comparison to controls, the first group showed a mean number of days of hospitalization (8.75 ± 13:25 vs 58.25 ± 38.79, p = 0.052), of days of caregivers’ training (1.75 ± 3.5 vs 15 ± 0; p <0.001) and of days required for the activation of the home care service (0 ± 0 vs 60 ± 26; p = 0.005) significantly lower. There was no significant difference between the two groups in relation to the number of hospitalizations (1.50 ± 1; p = 0.79) and number of DH (3.50 ± 2.88; p = 0.28).

Conclusion: Although these are preliminary data, they showed that the integration between the third-level center of reference and the local health facilities globally improves the training of caregivers. Supply of specific materials required for DAN from the pharmacy and the individuation of a dedicated nurse were the major barriers. Even if these results show high level of satisfaction, this care plan needs to be intensified.

Disclosure of interest: None Declared.
Aetiology and outcome of long term hospital intestinal failure in 2015

Vinod Sharma¹, Abhishek Singh¹, Jutta Koeglmeier¹, Mark Cowles¹, Susan Hill¹

¹Great Ormond Street Hospital, Paediatric Gastroenterology, London, United Kingdom

Objectives and study: Parenteral nutrition is an essential supportive treatment for severe intestinal failure. However long-term parenteral nutrition 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 and outcome of intestinal failure-associated liver disease (IFALD).

Methods: All paediatric 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 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 diagnosis; commonest diagnosis was NEC in 11 (18%) children followed by gastroschisis in 2 (3%), hirschsprung disease in 2 (3%) and atresia in 2 (3%) children. Thirty (49%) children had Primary non-digestive disorder; the commonest group was oncology children 20 (36%) followed by cardiology 4 (6%), Immunology 2 (3%) and other 4 (6%). Thirty eight children (62%) were fully established on feeds and their PN was stopped. 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 less than 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. No death was reported.

Conclusion: IFALD incidence was lower than previously reported even when children with similar aetiologies were compared. Surgical neonates are at the greatest risk of developing IFALD.

Disclosure of interest: Conflict of interest “None Declared.”
Is the actual trend of eating habits among 5-12 years old children going in the right direction?

Cristina Becheanu¹, Andreia Florina Nita², Mircea Purcaru³, Iulia Tincu⁴

¹“Grigore Alexandrescu” Emergency Children Hospital, Gastroenterology, Bucharest, Romania
²“Carol Davila” University of Medicine and Pharmacy and “Grigore Alexandrescu” Emergency Hospital for Children, Gastroenterology, Bucharest, Romania
³Elias University Clinical Hospital, Bucharest, Romania
⁴“Grigore Alexandrescu” Emergency Children Hospital, Emergency Department, Bucharest, Romania

Objectives and study: Nutritional status of children aged 5-12 years influences their whole achievements and activity, starting from cognitive functions to well-being. Moreover, future health status of children in this age group is directly dependent on nutrition habits. Romania, an Eastern European country with a democratic political regimen since 1989, had rapidly imported all the social “trademarks” of democracy including food consumption habits. In the light of these facts, we consider that there is a clear need for assessment of nutritional status and habits of Romanian children. This study was aimed to provide an evaluation of the nutritional status and eating habits of healthy children aged 5-12 and to determine if any intervention is needed.

Methods: We conducted a prospective study that included healthy children aged 5-12 attending swimming classes in a specific swimming pool in Bucharest. Nutritional assessment by measurements of anthropometrics was performed at the beginning of the classes. Information about their nutritional habits, medical history, and daily rest schedule was collected from parents using a questionnaire. Data was interpreted using WHO growth reference charts and body mass index (BMI) was evaluated according to International Obesity Task Force (IOTF) criteria for children and adolescents. Statistical analysis was performed with Microsoft Excel 97-2003 and EpiInfo3.5.4.

Results: A total of 106 children aged 5-12 were included in the study; 94.69% were from urban area and 85.84% came from families with a high education level (bachelor). The BMI-for-age was computed and the values plotted on Z-score charts indicated the following: for 32.06% of the children the Z score is shifted to the right; out of them, 13.20% were obese. Median age for overweight children is 6 years (STDEV=2.1) and 5 years (STDEV=1.2) for obese children. Regarding their eating habits, almost 30% eat junk food 1-3 times/week; fast food is consumed with a frequency of 1-2 times/month by 40.71% of children and once in 2-3 months by 47.79% children. Lower meals frequency and breakfast skipping were directly associated with obesity (p< 0.05). The interaction between hyper caloric carbohydrate juices consumption and level of knowledge in nutrition was found to be highly associated to obesity, indicating that children with less knowledge and frequent hyper caloric carbohydrate juices consumption were 4 times more likely to be obese (OR=4.3; 1.1-24.9).

Conclusion: Eating habits of children aged 5-12 years, coming from families with a good socio-economic status that enables access to all of the food diversity of an European capital, do not promote health and wellbeing. The present study highlights an important gap between affordability of a healthy lifestyle and the actual practice in a peculiar area of the society. Action is needed in order to prevent the evolution to obesity, a disease with a great impact on the future adult and modern society.

Disclosure of interest: Nothing to declare.
Protein and fat intake in children up to 3 years and their effect on growth and later risk of overweight/obesity: a systematic review of systematic reviews

Maciej Kołodziej, Bernadeta Patro-Gołąb, Bartlomiej Zalewski, Hans van Goudoever, Berthold Koletzko, Stefanie Kouwenhoven, Hania Szajewska

1Medical University of Warsaw, Department of Paediatrics, Warsaw, Poland
2Vu University Medical Centre, Paediatrics, Amsterdam, Netherlands
3Dr. von Hauner Children’s Hospital, LMU Munich, Division of Metabolic and Nutritional Medicine, Munich, Germany
4Vu University Medical Center Amsterdam, Department of Pediatrics, Amsterdam, Netherlands
5University of Warsaw, Pediatrics, Warsaw, Poland

Objectives and study: The Early Nutrition Project (www.project-earlynutrition.eu) aims to investigate the effects of developmental programming on later health outcomes, with a focus on obesity and adiposity in later life. We performed a systematic review of systematic reviews to assess the effects of protein and fat intake in children (up to 3 years of age) on growth and subsequent risk of obesity, overweight or adiposity.

Methods: The Cochrane Database of Systematic Reviews (CDSR); the Database of Abstracts of Reviews of Effects (DARE); Ovid MEDLINE; EMBASE (Biomedical and pharmacological bibliographic database), and some additional sources of data were screened up until September 2015 for eligible systematic reviews.

Results: Two systematic reviews assessed protein intake (PI). Both reviews found that higher protein intake was positively associated with increased growth and higher body mass index (BMI) later in life. However, important methodological limitations such as inclusion of studies in which the exposures/interventions were assessed not only during early childhood but also during later childhood call for caution when interpreting these results.

Four systematic reviews evaluated fat intake. Among them, one review which assessed reduction in fat intake and changes to fat profiles in children’s diets starting from 8 months to 10 years of life resulted in non-significant changes in anthropometric measures. The remaining systematic reviews found that reduction of total fat intake resulted in consistent, stable, but small, effect on body fatness (lower weight, BMI, and waist circumference). Based on the findings from one systematic review there is no sufficient evidence to assess the role of long-chain polyunsaturated fatty acids supplementation, lasting an average of from 0 till 5 year of age, on the risk obesity in early childhood.

Conclusions: More research is needed to investigate both protein and fat intake in early childhood on long-term health outcomes.

Disclosure of interest: None Declared
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].
Profile of hypernatremic dehydration due to inadequate breastfeeding in a referral NICU in India: review of 76 cases

Deepa Hariharan1, Lavanya Balasubramanian1, Ganesh Veluswami1, Velmurugan Kannappan1
1Sooriya Hospital, Neonatology, Chennai, India

Objectives and study: There is widespread media promotion of the benefits of breastfeeding and legislation to support exclusive breastfeeding in infancy the past few years. The aim of this prospective case-control study was to study the profile of hypernatremic dehydration due to inadequate breastfeeding in this scenario in a referral NICU in India.

Methods: Exclusively breastfed term or near-term (>35 weeks gestation) infants with serum sodium >150mEq/l, and weight loss >15% after day 4 till day 29, with the diagnosis of dehydration due to inadequate breastfeeding were included in the 22-month study period (cases, n=76 out of 1894 admissions, 4%). [incidence 3.3% in 2013]. Infants with anomalies, sepsis or other major problems were excluded. Appropriately matched exclusively breastfed infants in a well-baby follow-up clinic were used as controls for demographic and clinical parameters. Clinical features and risk factors in the 2 groups were studied.

Results: Presenting symptoms of cases were fever (65), poor feed (70), lethargy (59), less urine (38), jaundice (33), red urine (5), seizures (11). Diagnosis of lactation failure as etiology before referral by primary paediatrician was made only in 11 cases. Summary of infant / mother characteristics follows:

<table>
<thead>
<tr>
<th></th>
<th>Cases n=76</th>
<th>Controls n=76</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean birth weight, gestation</td>
<td>2.54kg, 38.1 weeks</td>
<td>2.67kg, 39.1 weeks</td>
</tr>
<tr>
<td>Mean maternal age, parity</td>
<td>29.6 (19–42 years), 1.6 (1-3)</td>
<td>26.4 (20-43 years), 2.1 (1-4)</td>
</tr>
<tr>
<td>Adequate knowledge of benefits of breastfeeding, major sources of info (validated questionnaire)</td>
<td>7/0</td>
<td>63</td>
</tr>
<tr>
<td>Adequate knowledge of technique of breastfeeding, major sources of info (validated questionnaire)</td>
<td>1/8</td>
<td>60*</td>
</tr>
<tr>
<td>Early discharge (&lt;24h in vaginal delivery, &lt;72h in Caesarean)</td>
<td>25</td>
<td>18**</td>
</tr>
<tr>
<td>Mean Weight loss %</td>
<td>25.4 (17 – 42%)</td>
<td>9.6 (7 – 13.2%)*</td>
</tr>
<tr>
<td>Mean serum sodium mEq/L</td>
<td>166.3 (152 – 188)</td>
<td>-</td>
</tr>
<tr>
<td>Mean blood urea (mg%)</td>
<td>99.8 (67 – 313)</td>
<td>-</td>
</tr>
<tr>
<td>Major complications: seizures/ exchange transfusion/ dialysis</td>
<td>19/3/4</td>
<td>-</td>
</tr>
</tbody>
</table>
There was positive correlation between weight loss and serum sodium and blood urea levels and major medical complications (p<0.01). Maternal age, delivery route, and medical complications were similar in the 2 groups. Primiparity, late prematurity and early discharge correlated positively with weight loss in the cases. Breast or nipple problems and poor latching on were higher in the cases. Interestingly, higher maternal education, greater knowledge of benefits of exclusive breastfeeding and use of media /internet / family / friends as the main sources of information correlated positively with lactation failure (p=0.01). Subjectively, there was greater anxiety about breastfeeding in this group. Knowledge of technique of breastfeeding and counseling by medical personnel correlated negatively with weight loss (p<0.01).

Conclusion: Hypernatremic dehydration due to inadequate breastfeeding continues to be prevalent. Enthusiastic promotion of breastfeeding benefits must be matched by greater support systems for individualized lactation counseling. Paediatricians need to be aware of need for early follow up of neonates and high index of suspicion for complications of lactation failure in the era of early discharge.

Disclosure of interest: none
The early-life nutritional status and progress in nutritional support strategy of extremely low birth weight infants in China

Meiying Quan¹, Danhua Wang¹

¹Peking Union Medical College Hospital, Pediatric Department, Beijing, China

Objective and study: To evaluate the nutritional status of extremely low birth weight infants and the progress in nutritional support policies during last decade in China.

Methods: Retrospectively analyzed the enteral and parental nutritional support data, growth velocity and complications of extremely low birth weight infants during hospitalization in the neonatal intensive care unit (NICU) from 2005 to 2014.

Results: ① From January 1st of 2005 to December 31st of 2014, a total of 74 extremely low birth weight premature infants were admitted to our NICU, but 16 of them died before discharge. Fifty-eight cases of premature infants including 35 males and 23 females were discharged alive. ② The eighteen extremely low birth weight infants admitted to NICU from 2005 to 2009 were defined as group A and the 40 counterparts admitted from 2010 to 2014 were defined as the group B. There was no statistical difference between Group A and Group B when comparing the gestational age (28.6±1.9w vs 28.1±2.0w, p=0.461), birth weight (881.1±80.9g vs 850.6±118.6g, p=0.327) and head circumference (25.2±0.9cm vs 24.8±1.4cm, p=0.241). Group A had more SGA than group B (88.9% vs 62.5%, p=0.037), while the EUGR ratio at discharge (77.8% vs 52.5%, p=0.061) was similar. When compared with group A, infants in group B had larger amount of initial enteral feeding (3.0±2.0ml/kg/d vs 5.6±4.4ml/kg/d, p=0.004) and feeding volume at the end of the first week (12.2±9.5ml/kg/d vs 19.8±16.0ml/kg/d, p=0.036). Similarly, the starting dose of amino acids in parenteral nutrition (1.0±0.2g/kg/d vs 1.8±0.5g/kg/d, p=0.000), the maximum dose of amino acids (3.3±0.4g/kg/d vs 4.0±0.4g/kg/d, p=0.000), the total calories at the end of the first week (71.1±15.2kcal/kg/d vs 82.6±12.6kcal/kg/d, p=0.004) and the second week (92.3±17.9kcal/kg/d vs 103.7±19.8kcal/kg/d, p=0.041), the weight gain velocity from birth to discharge (16.9±2.8g/kg/d vs 18.7±2.9g/kg/d, p=0.031) and Z scores of weight at discharge (-2.2±1.2vs-1.5±1.1, p=0.031) were statistically different between the two groups, with better outcome in group B. However, the duration of parenteral nutrition, the total amount of amino acids, the total amount of fat, the ratio of protein to calories from the first to the fourth week, the time to full enteral feeding, the length of hospital stay were similar between two groups. ③ Ten cases of infants in group A were breastfed, accounting for 61.1%, and four of them were fortified with human milk fortifier (HMF) (fortified rate was 22%). Breastfeeding cases in group B was 32 (80%), exclusive breastfeeding with human milk fortifier was 23 cases (fortified rate was 57.5%). The time to initiate HMF was at 30.2±13.2 days, and human milk amount was 89.9±34.5ml/kg, fortified duration was 32.8±15.7 days.

Conclusion: The nutritional support strategy for extremely low birth weight infant in China has improved during the past ten years. We can see the initial amount of enteral feeding and the feeding volume of the first week had increased dramatically. The starting dose and maximum dose of amino acids in parenteral nutrition also increased. Human milk and human milk fortification of preterm infants was preferred as routine. Above nutritional management accelerated the weight gain velocity of extremely low birth weight infants and result in higher Z scores of weight at discharge.

Disclosure of interest: None Declared
The clinical study of growth retardation of 50 extremely low birth weight infants

Meiying Quan¹, Danhua Wang¹

¹Peking Union Medical College Hospital, Pediatric Department, Beijing, China

Objectives and study: To study the growth retardation of extremely low birth weight (ELBW) infants during hospitalization and after discharge.

Methods: Retrospectively analyzed the clinical data of ELBW infants in our hospital from 2005 to 2014 and evaluated growth retardation rate.

Results: Fifty ELBW infants were followed up for over 6 months. The average weight gain was 17.9±2.8g/kg/d during hospitalization. Z scores for weight, length and head circumference at discharge were lower than that at birth. The period with the lowest growth retardation rate was at 0~3 months of corrected age (CA), which was respectively 20%, 26% and 22% by weight, length and head circumference. By the time of 24 months of CA, the rate of growth retardation showed a little increase. These infants were divided into groups according to SGA or not, the gestational age at birth (≤28 weeks and >28 weeks), birth weight (≤750g and >750g) and the period at birth (2004~2009 and 2010~2014), and the growth retardation rates were compared between groups at 6 and 24 months of corrected age. The SGA group and >28 weeks group had higher growth retardation rate at 6 months of corrected age. By the time of 24 months of CA, growth retardation rate (by head circumference) was higher in the group with birth weights ≤750g.

Table: None

Conclusion: ELBW infants showed high rate of intrauterine growth retardation and with even higher rates of extra-uterine growth retardation. With more aggressive nutritional support recent years, the majority of preterm infants accomplished catch up growth by 3 months of CA. ELBW infants who were SGA at birth or with birth weight ≤750g may be more prone to show growth retardation.

Disclosure of interest: None Declared
Successful management of neonatal chylous ascites in extremely preterm infants a report on three cases and a literature review

Meiying Quan¹, Zhenghong Li¹

¹Peking Union Medical College Hospital, Pediatric Department, Beijing, China

Objectives and study: Chylous ascites is rare in preterm infants. We aim to summarize the clinical features and treating strategies of chylous ascites in preterm infants.

Methods: Retrospectively analyze the clinical characteristics, treatment protocol of three very low and extremely low birth weight preterm infants with chylous ascites who were admitted to Peking Union Medical College Hospital. Search case reports of neonatal chylous ascites in PUBMED to summarize the clinical features and of this disease.

Results: ① The gestational age of the three preterm infants was 26+2, 28+3 and 28+6 weeks respectively and corresponding birth weight 685g, 1200g and 1220g. The onset time of chylous ascites was on the fourth day, eighth day and tenth day after birth. All of them had started enteral feeding and catheterized through umbilical vein. The clinical manifestations included abdominal distension with red skin and weakened bowel sounds. All the three cases resolved by conservative treatment of fasting with total parenteral nutrition for 3 weeks. Formula containing 50% medium chain fatty acids was fed sequentially and no feeding intolerance or abdominal distension was observed. Follow-up for 35~48 months with no recurrence. ② There were 22 case reports of neonatal congenital chylous ascites retrieved in PUBMED, including only 6 cases of preterm infants. Eleven infants was diagnosed by prenatal ultrasonography. Lymphoscintigraphy revealed lymphatic obstruction or lymphatic leakage in 8 infants out of 11 cases. Twelve infants required an octreotide infusion, and 11 cases ultimately underwent exploratory laparotomy or laparoscopic operation after conservative treatment failed.

Conclusion: Fasting, total parenteral nutrition, and sequential enteral feeding using a high medium chain triglyceride-based formula achieved good outcomes for treating preterm infants with chylous ascites. However, octreotide and surgery may be effective in intractable cases of neonatal congenital chylous ascites.

Disclosure of interest: None Declared.
Quality Initiative to Improve Expressed Breast Milk Use in Very Low Birth Weight Infants

Anup Thakur¹, Neelam Kler¹, Pankaj Garg¹, Satish Saluja¹, Manoj Modi¹, Arun Soni¹

¹Sir Ganga Ram Hospital, Neonatology, New Delhi, India

Objectives and study: Background: Human milk is the preferred nutrition for very low birth weight (VLBW) infants; however the usage of expressed breast milk (EBM) is low if donor human milk is not available. There is a need for quality initiative interventions to improve EBM usage in VLBW infants.

Aims and objectives: To improve the usage of EBM in VLBW infants admitted in the NICU of Sir Ganga Ram Hospital, New Delhi by January 2016.

Methods: This quality initiative (QI) project is being conducted in India as part of improvement advisor (IA) professional development programme conducted by Institute of healthcare Improvement (IHI, Massachusetts, U.S.A) in collaboration with ACCESS health international (Indian School of Business) between April 2015 to Jan 2016. IA training was conducted at three intensive workshops in India, each lasting 4 days and by a web based program called Extranet designed by IHI. Gaps in existing system of lactation counseling were identified. Project charter, driver diagram, change ideas, process and outcome measures were chalked out after various “all teach all learn sessions”. Various plan-do-act-study (PDSA) cycles were conducted to test change ideas like antenatal counseling including help of brochure and video, post-natal telephonic reminders within 6 hours of birth, standardization of kangaroo mother care and Non-nutritive sucking protocol etc. Implementation of changes was started from June 2015. Data was analyzed using statistical process control software and QI charts. The initial results of the impact of this QI program till September 2015 in a Level III B NICU in India is being reported.

Results: A total of forty six of VLBW infants were admitted to the NICU from April 2015 to September 2015. The median (IQR) time of availability of first EBM in the NICU decreased from 50 (37-64) hours to 27 (24-47) hours. The median (IQR) volume of EBM available in first 24 hours after birth increased from 0 (0-6.5) ml to 5 (2-10) ml. The proportion of EBM once infant reached a feed volume of 100 ml/kg/day increased from 70 (33-95) % to 99 (81.5-100) %. Shewhart’s chart (I Chart) constructed for these changes showed significant special cause variations.

Conclusion: QI interventions have shown promising early results of increase EBM usage in VLBW infants.

Disclosure of interest: None of the authors have any conflict of interest to declare.
In vivo Assessment of Lipophilic Nutrients Absorption Mechanisms using Human Milk and Infant Formula With Novel Mono- and Di-glycerides Based Emulsification Technologies

Mustafa Vurma¹, Stephen DeMichele², Dana Lee³, Fei Wang³, Patrick Tso³

¹Abbott Nutrition, Global Product Research & Development, Columbus, Ohio, United States
²Abbott Nutrition, Global Discovery Research & Development, Columbus, Ohio, United States
³University of Cincinnati, Department of Pathology, Metabolic Disease Institute, Cincinnati, Ohio, United States

Objectives and Study: Previous research has shown that a mixture of mono- and di-glycerides (MDG) helps solubilize lutein and facilitates gastrointestinal (GI) micelle formation – thus improving lymphatic lutein absorption compared to triglyceride oils. The primary goals of this study were to understand the mechanisms behind the absorption enhancing properties of MDG emulsification technology on lipophilic nutrient absorption and compare these results with human milk (HM), the gold standard for infant nutrition.

Methods: We compared using a conscious lymph fistula rat model, the number of lymphatic chylomicrons transported [apolipoprotein (apo) B48], characterization of chylomicron size distribution, GI mucosal bound lipophilic nutrients (lutein, zeaxanthin and tocopherol), and lymphatic tocopherol output in four different liquid infant formula prototypes. Five groups of male adult Sprague Dawley rats (n= 6-12/group) were randomized to receive via the stomach infusion tube (~6.0 µg lutein per animal) one of the following infant formula prototypes containing ~2 mg/L lutein: (AET-Control) lutein is premixed with safflower oil and then added to the oil phase; (AET-1) lutein premixed with MDG and lecithin, and then added to the oil phase; (AET-4-4) lutein is premixed with MDG and choline chloride, and then added to the water phase; (AET-9-1) lutein is premixed with MDG and mixed with lecithin and choline, and then added to the water phase. Fresh, non-pasteurized, non-frozen HM was analyzed for triglyceride content and gastrically infused (with matching triglyceride dose as in infant formula prototypes) to animals for comparison of apo B48 outputs. Aliquots of lymph were taken at fasting and hourly for 6 hours for chylomicron and tocopherol analyses. GI mucosa was also harvested at the end of the 6 hour infusion period for carotenoid and tocopherol analyses.

Results: Similar to HM, gastric delivery of AET-1 and AET-4-4 significantly increased lymphatic apo B48 output (2.5 to 4 fold; p<0.05) 2-6 hours after formula feeding versus AET-Control. Chylomicron size distribution was not affected by MDG emulsification technology. GI mucosal bound lutein, zeaxanthin and tocopherol were all increased significantly after feeding AET-1 and AET-4-4 versus AET-Control. Lymphatic tocopherol output was significantly higher for AET-1 versus AET-Control.

Conclusion: Similar to HM, this novel MDG based emulsification technology has the unique ability to increase the number of chylomicrons that are produced during the digestion and absorption process (since there is one apo B48 per chylomicron particle, the relative output of apo B48 in lymph reflects the relative number of chylomicron particles secreted). The increase in the number of chylomicrons secreted will enhance the lymphatic transport of lipophilic nutrients in the GI mucosa. This study helps to explain the previously observed lutein absorption enhancements.

Disclosure of Interest: Mustafa Vurma and Stephen DeMichele are employees at Abbott Nutrition, Dana Lee: None Declared, Fei Wang: None Declared, Patrick Tso: None Declared.
Recommended intakes of protein for infants in Russian Federation: a debating point.

Olga Lukoyanova¹, Tatyana Borovik²

¹Scientific Centre of Children's Health, Nutrition Department, Moscow, Russian Federation
²Scientific Centre of Child Health, Nutrition of Healthy and Sick Child, Moscow, Russian Federation

Objectives and study: Human milk composition is not constant and varies among lactating women. The protein level of human milk is strongly higher during early lactation than later on which apparently reflects decreasing infant’s requirements for protein with age. The recommended intakes of protein are based on an adequate intake (AI) that reflects the mean protein intake of infants fed human milk. In Russia, recommended dietary allowances (RDA) of protein for infants aged 0-3 months, 4-6 months and 7-12 months are 2.2, 2.6 and 2.9 g/kg/day respectively.

We assessed the level of protein in 186 milk samples from 74 healthy well-nourished mothers. Human milk samples were collected in 1, 4 and 6 months of lactation. All samples were stored in a freezer at -80°C.

Methods: The protein analysis was based on the Kjeldahl method. Protein content was calculated as total nitrogen x 6.38.

Results: Our study showed that the protein level in human milk in 1 month of lactation was 13.7±1.9 g/L, in 4 months – 11.6±2.1 and in 6 months – 11.2±2.4 g/L (p=0.0134).

Considering that the common breast milk intake in 1, 4 and 6 months old infants is 790, 780 and 880 milliliters per day and the average weight of these infants is 4.6, 6.7 and 7.5 kg (taken from Table 29 of the 1985 FAO/WHO/UNU report on energy and protein requirement) the AI of protein for these infants is 2.4, 1.4 and 1.3 g/kg/day respectively.

It was interesting to compare our data with the reference protein intake values recommended by WHO/FAO/UNU, adopted in Russia and other countries. We calculated that the AI of protein in 6 months old exclusively breastfed infant was 9.9 g/day which corresponded the US and Australia recommended standards (9.1 and 10 g/day respectively), was close to the United Kingdom and the WHO standards (12.7 and 13 g/day respectively) but was 2 times lower than the standards adopted in Russia (19.5 g/day). We found that in most countries the recommended protein intake (g/kg/day) decreased as the child grew older while in Russia recommended protein intake increased with age and was 1.5-2 times greater than the internationally recommended values.

Conclusion: This finding may indirectly indicate the excessive recommended intakes of protein in our country. The question of protein RDA in Russia requires is to be reviewed considering the adverse long term health outcomes of high protein intake.

Disclosure of interest: None Declared.
Nutritional Antioxidant Composition of Donor Milk

Corrine Hanson¹, Ann Anderson Berry², Elizabeth Lyden³, Jeremy Furtado⁴, Laura Dugick⁵, Matthew Van Ormer³, Clara Hageman⁵, Elizabeth Elliott³
¹University of Nebraska Medical Center, Medical Nutrition Education, Omaha, United States
²University of Nebraska Medical Center, Pediatrics, Omaha, United States
³University of Nebraska Medical Center, Omaha, United States
⁴Harvard University, Boston, United States
⁵Nebraska Medicine, Omaha, United States

Objectives and study: Human milk is the optimal food for human infants, including infants born prematurely. In the event that a mother of a hospitalized infant cannot provide breast milk, donor milk is considered an acceptable alternative. It is known that the macronutrient composition of donor milk is different than human milk, with variable fat content and protein content lower than mature milk. However, much less is known about the micronutrient content of donor milk, including nutritional antioxidants.

There is increasing evidence that links early exposure to oxidative stress with potentially lifelong consequences. The premature infant is especially susceptible to damage from oxidative stress for two reasons: 1) Adequate concentrations of antioxidants may be absent at birth; 2) The ability to increase synthesis of antioxidants is impaired. This can lead to an increased risk for the development of oxidative stress-induced diseases such as bronchopulmonary dysplasia, retinopathy of prematurity, necrotizing enterocolitis, and periventricular leukomalacia. Therefore, it is critical in premature infants to ensure an adequate supply of dietary antioxidants. The objective of this analysis was to compare the nutritional antioxidant profile of different types of feedings for premature infants, including samples of maternal breast milk collected during neonatal hospitalization and pasteurized pooled donor milk.

Methods: Samples of breast milk from 12 mothers of infants hospitalized in the Newborn Intensive care until were collected and analyzed for concentrations of nutritional antioxidants, including alpha-carotene, beta-carotene, beta-cryptoxanthin, lycopene, lutein+zeaxanthin, retinol, and α-tocopherol. Additionally, a homogenized sample of donor milk available from a commercial milk bank, a premature infant formula, and a transitional infant formula were also analyzed. Concentrations of nutritional antioxidants were measured using high-performance liquid chromatography. Descriptive statistics were calculated for all variables.

Results: Mean concentrations of the nutritional antioxidants are shown in the following table:

<table>
<thead>
<tr>
<th>Nutritional Antioxidant (mean mg/L)</th>
<th>Premature Formula</th>
<th>Transitional Formula</th>
<th>Maternal Breast Milk (n=12)</th>
<th>Donor Milk</th>
<th>Donor milk/breast milk (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alpha-carotene</td>
<td>0.51</td>
<td>1.40</td>
<td>7.7</td>
<td>3.6</td>
<td>47</td>
</tr>
<tr>
<td>Beta-carotene</td>
<td>71.1</td>
<td>63.9</td>
<td>49.1</td>
<td>13.7</td>
<td>28</td>
</tr>
<tr>
<td>Beta-cryptoxanthin</td>
<td>0.93</td>
<td>0.91</td>
<td>21.7</td>
<td>3.8</td>
<td>18</td>
</tr>
<tr>
<td>Lycopene</td>
<td>1.47</td>
<td>5.84</td>
<td>66.1</td>
<td>11.9</td>
<td>18</td>
</tr>
<tr>
<td>Lutein+zeaxanthin</td>
<td>65.5</td>
<td>56.9</td>
<td>40.1</td>
<td>21.4</td>
<td>53</td>
</tr>
<tr>
<td>Retinol</td>
<td>3,086.2</td>
<td>911.8</td>
<td>401.6</td>
<td>185.8</td>
<td>46</td>
</tr>
<tr>
<td>Alpha-tocopherol</td>
<td>20,109.1</td>
<td>13,360.2</td>
<td>5,880.8</td>
<td>1,381.9</td>
<td>23</td>
</tr>
</tbody>
</table>

Conclusion: Compared to breast milk collected from mothers of hospitalized infants, commercially available donor milk had 18-53% of the nutritional antioxidant content of maternal breast milk. As donor milk is becoming a common nutritional intervention for the high risk preterm infant, the nutritional antioxidant status of donor milk fed premature infants and their adverse outcomes related to oxidative stress, may merit further investigation.

Disclosure of interest: None Declared
Serum Concentrations and Ratios of Alpha and Gamma Tocopherol in Newborn, Hospitalized Infants

Corrine Hanson, Melissa Thoene, Elizabeth Lyden, Jeremy Furtado, Laura Dugick, Matthew Van Ormer, Clara Hageman, Elizabeth Elliott, Ann Anderson Berry

1University of Nebraska Medical Center, Medical Nutrition Education, Omaha, United States
2Nebraska Medicine, Omaha, United States
3University of Nebraska Medical Center, Omaha, United States
4Harvard University, Boston, United States
5University of Nebraska Medical Center, Pediatrics, Omaha, United States

Objectives and study: Vitamin E occurs naturally in several different isoforms, including alpha and gamma tocopherol. New evidence indicates that vitamin E isoforms have different roles in influencing inflammation. In contrast to the anti-inflammatory properties of the alpha-tocopherol isoform, the gamma-tocopherol isoform has been shown to demonstrate pro-inflammatory properties. Importantly, serum gamma-tocopherol isoforms at as little as 10% of the concentration of alpha-tocopherol have been shown to ablate the anti-inflammatory benefit of alpha-tocopherol. Infants admitted to Newborn Intensive Care Units (NICU) are at risk for increased inflammation due to stress caused by such factors as mechanical ventilation and infection. Inflammation is associated with long-term negative outcomes in the preterm infant, making an understanding of the relationships between modifiable pro-inflammatory mediators such as vitamin E tocopherols essential. Therefore the objective of this study was to assess maternal intake of tocopherols and the concentrations of alpha and gamma tocopherols in the serum of maternal and cord blood samples, and samples of breast fed, formula fed, and parentally fed infants during NICU hospitalization.

Methods: Samples of maternal and infant cord blood were collected on 34 mother-infant pairs at delivery for infants admitted to the NICU, and during NICU hospitalization after 3 consecutive days of exposure to maternal breast milk, formula, or parenteral nutrition. Concentrations of alpha and gamma tocopherol in mcg/L were measured using high-performance liquid chromatography. Maternal intake of tocopherols was assessed using a Food Frequency Questionnaire. Descriptive statistics were calculated and the concentration of gamma tocopherol as a percentage of the total alpha tocopherol was calculated. Spearman correlations coefficients were used to look at the association of maternal intake and serum tocopherol measurements. P<0.05 was considered statistically significant.

Results: Maternal intake of tocopherols was positively associated with cord concentrations of alpha tocopherol (r=0.47, p=0.04). Alpha and gamma tocopherol concentrations, and gamma tocopherol as a percentage of the total alpha tocopherol concentrations were:

<table>
<thead>
<tr>
<th>Serum sample</th>
<th>Alpha Tocopherol</th>
<th>Gamma Tocopherol</th>
<th>Gamma tocopherol: % concentration of alpha</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal (n=31):</td>
<td>12528.1</td>
<td>1743.7</td>
<td>14%</td>
</tr>
<tr>
<td>Cord (n=23):</td>
<td>2214.0</td>
<td>232.3</td>
<td>10%</td>
</tr>
<tr>
<td>Breast Fed Infants (n=23)</td>
<td>8463.5</td>
<td>1545.7</td>
<td>18%</td>
</tr>
<tr>
<td>Formula Fed Infants (n=9)</td>
<td>11368.5</td>
<td>595.5</td>
<td>5%</td>
</tr>
<tr>
<td>Parenterally Fed Infants (n=5)</td>
<td>9021.6</td>
<td>1031.5</td>
<td>11%</td>
</tr>
</tbody>
</table>

Conclusion: Infants receiving maternal breast milk had increased levels of gamma tocopherol relative to alpha tocopherol. It is possible that a typical Western diet, which is extremely high in gamma tocopherol and low in alpha tocopherol, is impacting maternal factors which influence a newborns tocopherol profile. Increased proportion of gamma tocopherol as compared to alpha tocopherol may increase risk for adverse outcomes in a NICU patient population. Nutrition interventions geared at increasing alpha tocopherol intake in a population of pregnancy mothers may merit evaluation.

Disclosure of interest: None Declared
The Impact of Maternal Intake of Sources of Vitamin A on Newborn Concentrations

Corrine Hanson¹, Melissa Thoene², Elizabeth Lyden³, Jeremy Furtado⁴, Laura Dugick², Matthew Van Ormer³, Clara Hageman³, Elizabeth Elliott³, Ann Anderson Berry⁵

¹University of Nebraska Medical Center, Medical Nutrition Education, Omaha, United States
²Nebraska Medicine, Omaha, United States
³University of Nebraska Medical Center, Omaha, United States
⁴Harvard University, Boston, United States
⁵University of Nebraska Medical Center, Pediatrics, Omaha, United States

Objectives and study: It is well documented that preterm infants have low vitamin A (retinol) stores at birth. Vitamin A in the form of retinol is provided to the fetus through a tightly controlled placental transfer, however there are other potential sources of vitamin A, including the pro-vitamin A compounds alpha and beta-carotene. In addition to providing a possible source of vitamin A for the newborn infant, recent evidence has shown that these compounds may have unique roles in eye and brain development, independent of retinol. However, very little is known about the influence of maternal intake on carotene concentrations in the newborn hospitalized infant. Therefore, the objective of this analysis was to evaluate the impact of maternal intake of alpha and beta carotene concentrations in cord blood, and in the serum of breast fed infants.

Methods: Samples of blood were collected from the umbilical cord at delivery and after 3 consecutive days of exposure to maternal breast milk in 19 infants after admission to a Newborn Intensive Care Nursery. Concentrations of alpha and beta carotene in μg/L were measured using high-performance liquid chromatography. Maternal intake of vitamin A compounds was assessed using a Food Frequency Questionnaire. Descriptive statistics were calculated and Spearman correlations coefficients were used to look at the association of maternal and cord measurements. P<0.05 was considered statistically significant.

Results: The mean gestational age at birth was 36.7 weeks; mean birth weight was 2685.5 grams. Cord blood levels of alpha carotene were associated with maternal intakes of total carotene (r=0.59, p=0.01), vitamin A (r=0.57, p=0.01), beta carotene (r=0.060, p=0.007) and lutein (r=0.52, p=0.01). Serum concentrations of alpha carotene levels in the breast fed infants were associated with maternal intakes of alpha carotene (r=0.44, p=0.05), beta carotene (r=0.52, p=0.02), lycopene (r=0.44, p=0.05) and lutein. Serum concentrations of beta carotene were associated with maternal intakes of lutein (r=0.48, p=0.04).

Conclusion: Maternal intake of vitamin A related compounds demonstrated an impact on the serum concentrations of alpha and beta carotene of the infant at birth, and during breastfeeding. Maternal nutrition education interventions regarding carotenes may provide a mechanism for improving infant vitamin A status and subsequent outcomes in hospitalized infants.

Disclosure of interest: None Declared
Cow’s milk fat in infant nutrition; the importance of lipid structure

Jeske Hageman¹, Stefanie Oude Elferink¹, Jeroen Heck¹, Laurien Ulfman¹

¹Frieslandcampina Innovation, Wageningen, Netherlands

Objectives and study: Without doubt breastfeeding is the best nutrition for an infant. However, breastfeeding is not always an option. In such case, infant formulas can satisfy the nutritional requirements of infants during the first months of life (EU Directive 2006/141). Breast-milk substitutes should be designed to create similar nutritional and physiological effects as breast-milk. In the past, for the fat content of the infant formula the focus was mostly on obtaining the right fatty acid composition. Little attention was paid to structure of fat globules or to the structure of triglycerides. Emerging evidence shows that this structure might contribute to better digestibility and absorption.

Methods: The lipolysis of fresh and processed cow’s milk was studied using an in vitro two-phase digestion model, consisting of a stomach and duodenal phase, set at term infant conditions. The level of triglycerides, diglycerides, monoglycerides and free fatty acids at different time points were determined by TLC-FID. The globule size distributions of the fresh and processed cow milk were investigated by a Malvern Mastersizer, and compared to human milk. Furthermore, a literature search was performed to study the difference in stereo-specificity between human milk fat, cow’s milk fat and vegetable fat, and the related health effects.

Results: The globule size distribution of fresh cow’s milk and pasteurized cow’s milk were similar, and also comparable to the globule size distribution of human milk. Homogenization of cow’s milk resulted in smaller particles and a higher lipolysis level in the gastric phase and a faster lipolysis in the duodenal phase compared to fresh and pasteurized cow’s milk. Literature shows the importance of triglyceride structure. The placement of long-chain saturated fatty acids (LC-SAFA) on sn-2 position of the glycerol backbone seems favorable for absorption. In human milk and cow’s milk a substantial part of the LC-SAFA are placed at the sn-2 position. In vegetable fat the LC-SAFA are mainly positioned at sn-1 and sn-3 sites of the glycerol backbone. Studies investigating the effect of structured triglycerides, where the LC-SAFA are present at the sn-2 position, versus standard vegetable fats show that indeed the efficiency of fat absorption is higher for the structured triglycerides; less fatty acids are found in the feces. Additionally, structured triglycerides resulted in less calcium soaps of LC-SAFA in the stools and softer stools.

Conclusion: The structure of fat is an important factor for the digestion and absorption of lipids in infants. Fat globule sizes influence the rate of digestion. The triglyceride structure influences the absorption of lipids. It is recommended to optimize the digestion and absorption of lipids in infant formulas by optimizing the fat globule and triglyceride structure while maintaining an adequate fatty acid composition.

Prevalence of Laboratory-Defined Malnutrition in Maternal-Infant Dyads During NICU Hospitalization in the United States

Corrine Hanson1, Elizabeth Lyden2, Jeremy Furtado3, Melissa Thoene4, Laura Dugick4, Matthew Van Ormer2, Elizabeth Elliott2, Clara Hageman2, Ann Anderson Berry5

1University of Nebraska Medical Center, Medical Nutrition Education, Omaha, United States
2University of Nebraska Medical Center, Omaha, United States
3Harvard University, Boston, United States
4Nebraska Medicine, Omaha, United States
5University of Nebraska Medical Center, Pediatrics, Omaha, United States

Objectives and study: Retinol is the predominant circulating form of vitamin A in the blood. Deficiency of vitamin A is associated with significant infectious morbidity and mortality in infants and children. The World Health Organization (WHO) has defined criteria for malnutrition based on vitamin A status, as measured by retinol concentrations. Serum concentrations of ≤0.7 nmol/L are considered vitamin A deficient, and a cutoff value of ≤1.05 nmol/L has been used to identify those with inadequate vitamin A stores. While vitamin A deficiency is a known public health issue in developing countries, less consideration is given to vitamin A status in developed countries such as the United States. As newborns are dependent on a maternal supply of vitamin A, they represent a population who may be susceptible to vitamin A deficiency. Therefore, the objective of this study was to evaluate the vitamin A status of maternal-infant pairs after admission to a Newborn Intensive Care Nursery.

Methods: Samples of maternal and infant cord blood were collected on 33 mother-infant pairs at delivery for infants admitted to the Newborn Intensive Care Nursery. A second blood sample was collected after 72 hours of stable administration of either human breast milk or formula feeding. Concentrations of retinols were measured using high-performance liquid chromatography.

Results: Mean retinol concentrations in maternal samples was 1.1 nmol/L; mean cord retinol concentrations were 0.60 nmol/L. Ten percent of mothers met the criteria for vitamin A deficiency and malnutrition, while 57% met the criteria for inadequate vitamin A status. Due to the infant’s dependence on a maternal supply of vitamin A, at birth 73% of infants were born with serum retinol concentrations that place them in the malnourished and vitamin A deficient category, with all of the remaining infants meeting the criteria for inadequate vitamin A status. Breast feeding in the NICU was ineffective at raising serum retinol concentrations, while all infant receiving formula had retinol levels above the WHO thresholds.

Table:

<table>
<thead>
<tr>
<th></th>
<th>Serum Retinol ≤1.05 nmol/L</th>
<th>Serum Retinol ≤0.7 nmol/L</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maternal serum samples</td>
<td>17/30 (57%)</td>
<td>3/30 (10%)</td>
</tr>
<tr>
<td>Cord blood samples</td>
<td>33/33 (100%)</td>
<td>24/33 (73%)</td>
</tr>
<tr>
<td>Breast-fed infant serum samples</td>
<td>23/23 (100%)</td>
<td>16/23 (70%)</td>
</tr>
<tr>
<td>Formula-fed infant serum samples</td>
<td>0/9 (0%)</td>
<td>0/0 (0%)</td>
</tr>
</tbody>
</table>

Conclusion: Vitamin A deficiency was common in newborns and did not improve in breast fed infants. Breast feeding remains the optimal food for all infants, however poor maternal nutrition may be reflected in the nutrient profile of breast milk. Education on dietary sources of vitamin A to pregnant and nursing mothers may be a possible mechanism for improving vitamin A status in both pregnant mothers and their infants.

Disclosure of interest: None Declared
NUTRITION: Neonatal and infant nutrition

Estimating the contribution on the reduction of the burden of Iron Deficiency Anemia from the current fortification strategy for commercial foods targeted to infants and toddlers in India

Alberto Prieto Patron¹, Patrick Detzel¹, Zsuzsa Hutton¹

¹Nestle Research Center, Public Health Nutrition, Lausanne 26, Switzerland

Objectives and study: Iron deficiency anemia (IDA) among infants and toddlers is still a considerable public health concern in India. After the exclusive breastfeeding period of 6 months, when children transit to mixed diets, their iron intake frequently is below the requirements. The Indian National Health Survey 2005/06 reports that over 80% of children between the ages of 6-23 months are anemic, and approximately 60% among these children is attributable to iron deficiency. A previous study [Prieto et al] has identified commercial fortified baby food as the complementary food that has the strongest significant association hemoglobin concentration in Indian children in this the most vulnerable age window. The objective of this study is to estimate the contribution on the reduction of the burden in IDA of fortified infant food using standard health economic models.

Methods: The estimated annual social cost of IDA in children 6-23 months in India in 2010 [Plessow et al 2015] was 23.8 billion US dollars and 6.9 million Disability Adjusted Life Years (DALYs). Using the same standard health economic model for a burden of a disease we estimate the contribution of the current fortification strategy on the reduction using estimates of efficacy from systematic review of clinical trials of fortified versus not fortified infant cereals [Eichler et al 2012] and effectiveness from national health survey association [Prieto et al 2015].

Results: Preliminary results suggest that current consumption already reduces the annual burden of iron deficiency anemia by 1,401 million USD and 569 thousand DALYs. Focusing only on current consumers this represent around 50% reduction of the health burden (in DALYs) and 36% reduction of the monetary losses.

Conclusion: This analysis can usefully to evaluate how scaling up consumption of fortified foods could contribute further to alleviate the burden of IDA. It equally helps to formulate effective public health nutrition interventions responsive to mothers’ needs and awareness on micronutrient deficiencies.

Disclosure of interest: All authors are employees of Nestle Research Center. Nestle is a company leader in Nutrition, Health and Wellness.
Dairy lipids in infant formula: impact on growth and gastrointestinal tolerance in healthy infants

Maria Lorella Gianni1, Paola Roggero1, Charlotte Baudry2, Pascale le Ruyet2, Fabio Mosca1

1Neonatal Intensive Care Unit (Nicu), Department of Clinical Science and Community Health, Fondazione Ircs “ca’ Granda” Ospedale Maggiore Policlinico, University of Milan, Italy
2Lactalis R&d, Nutrition, Retiers, France

Objectives and study: When breastfeeding is not possible, infants are fed formulas in which lipids are usually of plant origin. Blends of plant oils are used in formulas to provide the two essential fatty acids (FA): linoleic (LA) and α-linolenic acids (ALA). However, the use of dairy fat in combination with plant oils enables a lipid profile in formula closer to breast milk in terms of FA composition, triglyceride structure and cholesterol content. Moreover, experimental data in rats suggest that a mix of dairy fat and plant oils could stimulate the endogenous conversion of ALA to long chain polyunsaturated FA, resulting in higher brain levels of docosahexaenoic acid (DHA) (Du et al., 2012). The objectives of this study were to investigate the impact on growth and gastrointestinal (GI) tolerance of a formula containing a mix of dairy lipids and plant oils in healthy infants.

Methods: This monocentric, double-blind, controlled, randomized trial was approved by the Ethical Committee of the Fondazione IRCCS of Milan, Italy (Giannì et al., 2012; NCT01611649). After delivery, healthy term infants whose mothers decided not to breastfeed were randomly allocated to be fed for 4 months with a formula containing either: a mix of dairy fat and plant oils (D; ALA 2.3% of total FA (TFA), LA/ALA=6), only plant oils (P; ALA 1.8% TFA, LA/ALA=10) or plant oils supplemented with AA (arachidonic) and DHA (PDHA; ALA 1.8% TFA, LA/ALA=10, DHA 0.2%, ARA/DHA=2). Breastfed infants were included in a reference group (BF). Anthropological parameters (weight, height, cranial circumference) and body composition were measured after 2 and 4 months. GI tolerance was evaluated during a 2 day-period after 1 and 3 months thanks to descriptive parameters reported by parents (frequency, color and consistency of stools; frequencies of colics, flatulence, sleeping disturbances; frequency and description of regurgitations). Differences between groups were assessed using an analysis of covariance with sex as covariate.

Results: 88 formula-fed and 29 BF infants were enrolled in this study. At baseline, patients’ characteristics (gestational age, sex ratio, morphological parameters) were similar between groups, except for weight and cranial circumference in group P, which were significantly lower than BF. Gains of weight, height, cranial circumference and fat mass were similar between the 3 formula-fed groups at 2 and 4 months. Gains of weight and height of formula-fed infants were comparable to BF. Gains of cranial circumference were higher at 2 and 4 months in groups D and PDHA than in BF. Also, fat mass gain was significantly higher in group PDHA than in BF at 4 months. No difference was observed between the 3 formula-fed groups for stool frequency, consistency and color. However, formula-fed infants were different from BF for stool consistency and color. Frequencies of colics, flatulence and sleeping disturbances were similar in all groups. Finally, regurgitations of small amounts were frequently observed without differences between groups.

Conclusion: A formula containing a mix of dairy lipids and plant oils enables a normal growth in healthy newborns. This formula is well tolerated and does not lead to abnormal GI symptoms. Consequently, reintroduction of dairy lipids could represent an interesting strategy to improve lipid quality in infant formulas.

Disclosure of interest: This study was supported by Lactalis. C. Baudry and P. le Ruyet are employees of Lactalis.
Sodium, Potassium, Calcium, and Phosphorus Content of Human Milk over the First Year of Lactation: a GEHM Study of Three Global Cohorts

Michael Gray 1, Sarah Maria 1, Shay Phillips 1, Christina Valentine 1, Robert McMahon 1, Ardythe Morrow 2

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: Minerals in human milk are critical to infant growth and development; however, multiple factors, e.g. maternal genetics, body mass index, and diet, may introduce variability into the elemental composition of human milk. This study expands the longitudinal and geographic resolution for sodium, potassium, calcium, and phosphorus content in human milk through the first 12 months of breastfeeding by characterization of samples collected from three distinct geographies.

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 (U.S.). A total of 435 milk samples from 90 mothers at 2, 4, 13, 26 and 52 wks were analyzed by inductively coupled plasma-mass spectrometry.

Results: Human milk exhibited similar mineral concentrations and temporal patterns by geographic site over the first year of lactation. Mean calcium concentration remained stable between 2 and 13 wks at 0.29 g/L before decreasing to 0.22 g/L through 52 wks (p<0.001). From 2 to 52 wks postpartum, mean potassium and phosphorus content of human milk decreased ~30% across lactation, ranging from 0.59 to 0.41 g/L for potassium (p<0.001) and 0.17 to 0.12 g/L for phosphorus (p<0.001). Sodium displayed a high level of interindividual variability throughout lactation with a resulting mean concentration of 0.26 g/L at 2 wks, dipping to 0.10 g/L at 26 wks, and then increasing through 52 wks to 0.17 g/L (p<0.001). Characterization of mineral ratios demonstrated the Na:K ratio of human milk to have a modestly U-shaped, significant trend (p<0.001) over the first year of lactation with ratios of 0.47 at 2 wks, 0.23 at 26 wks, and 0.38 at 52 wks postpartum. Human milk Ca:P ratio also showed longitudinal trending increasing from 1.7 at 2 wks to 2.1 at 13 wks, then decreasing to 1.9 at 52 wks; however, the Ca:P ratio did not demonstrate statistical significance across lactation.

Conclusion: This study offers a global perspective of sodium, potassium, calcium, and phosphorus content in human milk including similarity in concentrations over lactation between mothers with diverse genetic, dietary, and geographic influences. The demonstration of distinct concentration patterns for sodium, potassium, calcium, and phosphorus over lactation may also offer insight into infant intake of minerals provided via human milk during infant growth and development.

Impacts of the structure of infant formulas on their digestive behaviour and hydrolysis: insights from in vitro studies and comparison with human milk

Claire Bourlieu\textsuperscript{1}, De Oliveira S.C.\textsuperscript{2}, Mousties C.\textsuperscript{2}, Chever S.\textsuperscript{2}, Ménard O.\textsuperscript{2}, Cuinet I.\textsuperscript{3}, Le Ruyet P.\textsuperscript{3}, Bonhomme C.\textsuperscript{4}, Le Huërou-Luron I.\textsuperscript{5}, Dupont D.\textsuperscript{2}, Deglaire A.\textsuperscript{2}

\textsuperscript{1}Umr Stlo 1253 Inra-Agrocampus Ouest, Bioactivity and Nutrition, Rennes, France
\textsuperscript{2}Inra-Agrocampus Ouest, Umr 1253 Stlo, Rennes, France
\textsuperscript{3}Lactalis, R&d, Rétiers, France
\textsuperscript{4}Lactalis, Nutrition, Torcé, France
\textsuperscript{5}Inra, Ur 1341 Adnc, Saint-Gilles, France

Objectives and study: Human milk lipids are the major source of calories to support infant growth and are delivered under the very specific form of milk fat globules. These micronic droplets (3-5 µm) are based on an apolar core enclosing specifically structured triglycerides. The core is enveloped by a membrane of Milk Polar Lipids (MPL) and proteins. This specific structure is shared by many mammalian milk, including cow’s milk. In comparison, infant formulas are submicronic emulsions of vegetable lipids optimized in terms of total fatty acids composition but not biomimetic of human milk structure which may impact their digestive behavior and kinetics of lipolysis. The reintroduction of some cow’s milk lipid fractions (MPL or triglycerides) seems a clever approach to mimic human milk natural structure. And yet, very few infant formulas use milk lipids more expensive than vegetable lipids. To assess the benefits of such reintroduction, the structure, digestive behaviour and kinetics of lipolysis of commercial or model infant formulas with or without cow’s MPL were determined using an in vitro dynamic model of neonatal digestion (DIDGI\textsuperscript{®}) and compared with data obtained on human milks.

Methods: The dynamic digester parameters were based on an exhaustive literature review to mimic the digestion of a 1 month old term newborn. First age infant formulas (IFs) of close compositions but with variable droplet sizes (0.2 to 0.7 µm), all based on vegetable fats versus a model IF stabilized by MPL (size 2 µm) were digested. Lipolysis, released fatty acids (FA), lipid classes and the microstructure of the matrices were evaluated before and along digestion. These digestion data were compared with the ones obtained on raw or pasteurized pooled human milks (HMs) (De Oliveira et al., 2016, FRI).

Results: Commercial IFs differed from HMs in terms of chemical composition (specifically regiodistribution), prehydrolysis state and emulsion structure. These initial differences impacted lipolysis kinetics and deconstruction. Model IF with MPL had a structure and interfacial composition closer to HM. Lipolysis was lower in IFs than in raw HM, before digestion and during gastric phase, and on the contrary higher at the beginning of the intestinal phase, due to the important surface developed by the lipid droplets in commercial or model IFs (14 to 32 m\textsuperscript{2}/g of lipid) compared to HMs (4 m\textsuperscript{2}/g of lipid). The profile in released FA from HMs was rich in quickly metabolizable, i.e. medium chain and oleic FA, in relation with their specific external distribution on triglycerides. Conversely, palmitic free FA was depleted in HM but remained dominant in IFs (based on vegetable fat). A profile closer to HMs can be obtained in IFs including cow’s milk triglycerides.

HMs and model IF with MPL had closer digestive disintegration with the persistence of large entities (droplets or globules) over the digestion underlining the paradoxical metabolic fate of dairy lipids (Bourlieu et al., 2015, EJLST): rapid conveyor of energy through their triglyceride core, but containing some low digestible bioactive complex lipids and proteins in their stabilizing membrane.

Conclusion: The specific structure of HM at several scale levels is a key parameter modulating the profiles of liberated FA, kinetics of lipolysis and colloidal behaviour in gastric phase. The reintroduction of some cow’s milk lipids in IFs could help making them more biomimetic of HM digestive behaviour.

Disclosure of interest: This project was partially funded by Lactalis.
Impact of L. fermentum CECT 5716 and dairy lipids in maternal diet on fatty acid composition of cerebral and peripheral tissue in pups’ mice

Corinne Joffre1, Anne-Laure Dinel1, Agnès Aubert1, Catherine Fressange-Mazda2, Pascale le Ruyet3, Sophie Layé1

1Inra, Nutrineuro, Bordeaux, France
2Lactalis, Nutrition Europe, Torce, France
3Lactalis R&d, Nutrition, Retiers, France

Objectives and study: During the perinatal period, maternal diet plays a crucial role in the pups brain growth and development. Docosahexaenoic acid (DHA) accretion in brain is becoming a real challenge since DHA can prevent neuroinflammation and reduce the cognitive deficits at adulthood. Instead of dietary supplementation, increasing the bioavailability of the food nutrients may be an alternative strategy. Probiotics are of interest since some bacterial strains may increase n-3 polyunsaturated fatty acids (PUFA) in brain.

This project aimed at evaluating the impact of maternal diets (different n-6/n-3 ratio, different matrix, ± L. fermentum) on the fatty acid composition of cerebral tissues (prefrontal cortex PFC) and hippocampus (HC) and peripheral tissues (adipose tissue and liver) in 14-days pups.

Methods: Pregnant CD1 mice were fed since day 1 of gestation with different diets: 1) vegetable lipids (VEG), 2) vegetable lipids deficient in n-3 PUFA (DEF), 3) vegetable lipids deficient in n-3 PUFA with L. fermentum CECT 5716 in drinking water (PRO); 4) dairy lipids (DL). As it has been previously showed that the composition of maternal milk reflect most of the differences between pregnancy feeding, at postnatal day 14, pups were sacrificed and fatty acid composition of gastric content, PFC, HC, adipose tissue and liver was analyzed.

Results: PUFA composition of PFC and HC, involved in memory, was modified by probiotics. DHA was significantly increased in PRO as compared to DEF (5.7% versus 4.3% in PFC and 5.7% versus 4.5% in HC) whereas n-6 PUFA were not changed. DHA was the highest in the PFC and HC of the DL group (12.9% versus 4.3-10.6%) as compared to the other groups. The same trends were observed in adipose tissue and liver phospholipids. A decrease in the Δ6 desaturase index and an increase of Δ5 desaturase index were observed in liver of PRO as compared to DEF. These changes may be associated to a positive correlation between 18:3 n-3 in the maternal milk and DHA in brain structures and peripheral tissues.

Conclusion: Our results showed that probiotics impacted peripheral but also cerebral PUFA composition. Protecting the brain against n-3 PUFA deficiency is critical during the perinatal period to limit the risk of developing mnesic disorders at adulthood. L fermentum CECT 5716 may have a role by increasing the bioavailability of n-3 PUFA.

Disclosure of interest: None Declared.
NUTRITION: Neonatal and infant nutrition

N-P-097

Dairy lipids during the perinatal period impact microglial phenotype and neuronal plasticity in CD1 mice

Dinel Anne-Laure, Charlotte Rey, Cecile Bonhomme, Pascale Le Ruyet, Corinne Joffre, Sophie Layé

Nutrineuro Laboratory, Inra 1286, Bordeaux, France
Nutrineuro Laboratory, Bordeaux, France
Lactalis Nutrition, Recherche et Developpement, Retiers, France

Objectives and study: Increasing docosahexaenoic acid (DHA) level during perinatal development is a major objective of neonatal nutrition. Postnatal period is a critical time window during which brain DHA accretion is the highest. DHA is highly present in the brain since it constitutes about 15% of the fatty acids in the human frontal cortex. Its accumulation in the central nervous system during the developmental period depends on its availability. Mimicking the breast milk composition appears to be necessary for infant formula to maintain DHA level and to have comparable effect. This study aimed at evaluating the short and long term impact of partial replacement of vegetable oil in infant formula by dairy fat on brain development.

Methods: Pregnant C57Bl/6 mice were fed with balanced vegetable lipids or balanced dairy lipids supplemented or not in DHA (0.2%) and ARA (0.4%). At postnatal day (PND) 14, DHA accretion and microglial activity were explored by flow cytometry. Neurogenesis (doublecortin-positive cell numbers in the hippocampus) and HPA axis activity (plasma corticosterone and glucocorticoid receptors in the hippocampus) were evaluated at PND14 and PND90 to characterize neurodevelopmental consequences of lipid quality in infant formula.

Results: Our results showed that at PND14 accretion of DHA in prefrontal cortex was increased by balanced dairy lipid diet. Microglial number was also increased by dairy lipid diet. This was accompanied by an increase of neurogenesis and BDNF protein activity. HPA axis was also modulated with a decrease of the phosphorylation of the glucocorticoid receptor in the hippocampus with no effect on corticosterone level. At adulthood, the number of immature DCX-positive cells was decreased by the consumption of dairy lipid supplemented in DHA and ARA. HPA axis activity was also affected since corticosterone level and phosphorylation of glucocorticoid receptor were increased in animals fed with balanced dairy lipids. A supplementation in DHA and ARA in DL group brought back the PGR/GR ratio and corticosterone concentration to a level similar to results obtained in VL animals.

Conclusion: The present study confirmed the importance of dairy lipids for DHA accretion in the brain and demonstrated that the quality of lipids in the diet impacted neurodevelopmental period.

Disclosure of interest: “None Declared”.

Vol. 62, Supplement 1, May 2016 835
Dairy fat matrix diet could prevent cognitive decline at adulthood induced by lipopolysaccharide injection during perinatal period

Dinel Anne-Laure¹, Charlotte Rey¹, Cecile Bonhomme², Pascale Le Ruyet², Corinne Joffre¹, Sophie Layé¹

¹Nutrineuro Laboratory, Inra 1286, Bordeaux, France
²Lactalis Nutrition, Recherche et Développement, Retiers, France

Objectives and study: The innate immune system of the brain is principally composed of microglial cells, which, once activated, protect neurons against insults (infectious agents, lesions etc.). Activated microglial cells produce inflammatory cytokines that act specifically through receptors expressed by the brain. The functional consequences of chronic brain cytokine action are the alteration in cognition, affect and behaviour, a hallmark of altered well-being. Limiting synthesis of inflammatory cytokines in brain could be crucial during perinatal period to prevent cognitive alteration in adulthood. Polyunsaturated fatty acids of the n-3 family (n-3 PUFA), in particular docosahexaenoic acid (DHA), are very potent anti-inflammatory agents. Dairy lipids are important for DHA accretion during perinatal period since DHA are highly incorporated in the brain. The present project aimed at evaluating the impact of different dietary fat matrix (vegetable or dairy lipids) with or without supplementation in DHA/arachidonic acid (ARA) or deficient in n-3 PUFA on neurophysiological alterations (neuroinflammation, microglial phenotype) induced by a postnatal inflammation.

Methods: Pregnant CD1 mice and their offspring were fed since day 1 of gestation with different diets: 1) equilibrated with dairy lipids (dairy lipids, sunflower, rapeseed oil) with or without DHA (0.2%) and ARA (0.5%), 2) equilibrated with vegetable lipids (palm, sunflower, rapeseed oil) with or without DHA (0.2%) and ARA (0.5%), 3) diet with vegetable lipids deficient in PUFA n-3. At postnatal day (PND) 14, pups were injected intraperitoneally with lipopolysaccharide (LPS, 100µg/kg) from E.coli. At PND 21, animals fed with deficient diet received equilibrated diet with dairy lipids. Animals were euthanatized at PND 90.

Results: Our results showed that microglial phenotype depends on dietary fat matrix. The number of CD11b+/CD45 low cells at PND 14 is modulated by the diet. In this population of microglial cell, the number of CD206 cells (anti-inflammatory phenotype) is significantly decreased in animals supplemented in DHA and ARA. Moreover cytokine expression 3h post-LPS are modulated by diet, suggesting a priming of microglia by diet during perinatal period. At adulthood, consumption of dairy lipids protect against cognitive deficit induced by LPS injection during perinatal period. Consumption of dairy lipid after PND21 rescue alteration induced by deficient diet.

Conclusion: To conclude, our results showed that consumption of dairy lipids diet protect from neuroinflammation and its consequences after a postnatal inflammation.

Disclosure of interest: “None Declared”. 
Are current ESPGHAN recommendations for enteral nutrient supply for preterm infants also applicable for late preterm infants?

Ralitsa Wilson Georgieva¹, Monique Van de Lagemaat², Harrie N. Lafeber², Anne Schaafsma³

¹Specialized Hospital for Active Treatment of Children’s Disease, Neonatology, Sofia, Bulgaria
²VU University Medical Centre, Neonatology, Amsterdam, Netherlands
³Frieslandcampina, Research & Development, Leeuwarden, Netherlands

Objectives and study: ESPGHAN recommendations for vitamin and iron fortification in formulae for preterm infants are often applied to late preterm infants. We studied different concentrations of iron (0.98 vs 1.67 mg), vitamin A (280 vs 360 µg-RE), folic acid (60 vs 45 µg) and vitamin D₃ (3.0 vs 6.7 µg) all per 100 kcal preterm formula (A vs B) in healthy Bulgarian late preterm infants (n=29, 32-34 weeks of gestation). Study participants (aged 14±2 days) were at random allocated to formula A or B, aiming to provide 120 kcal/kg/day during a period of 8 weeks. The study protocol was approved by the Medical Ethical Committee of the hospitals involved.

Methods: Hb, ferritin (ECLIA), serum retinol (all-trans) (HPLC), serum folate (competitive IA), and homocysteine (tHcy, competitive IA) were studied in venous blood samples at 14±2 days and 75±2 days postnatal age. Non parametric distributions were tested with the Wilcoxon matched pair Signed–rank test for changes within groups, and the Independent Samples Mann-Whitney U test for changes between groups. Normal distributions were tested with Paired Samples T test for changes within groups and with one-way ANOVA for changes between groups.

Results: In both groups blood Hb and ferritin concentrations decreased over time but were still within reference ranges (Hb: 100-140 g/L, ferritin >12 µg/L). Vitamin A increased in both groups from about 0.70 to 1.04 µM/L. Folic acid increased in both groups during the study period being borderline (p=0.076) higher in group A. For both groups, the median folate concentrations at the end of the study were considerably higher than the maximum of the references range (15-72 nmol/L). Total serum homocysteine only significantly decreased in group A (p = 0.003), being lower after 8 weeks (p = 0.02) than in group B. Both median concentrations are within the reference range (4.7-11.7 µmol/L). Final concentrations of serum 25OHD were normal to high in most infants. Median (range) intakes of both formulae were 197 (158-262) (A) and 194 (168-252) (B) ml/kg/day at around 8 weeks.

Table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Group A (n=)</th>
<th>Group B (n=)</th>
<th>P between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hb start (g/L)</td>
<td>132.7±15.2 (15)</td>
<td>147.6±22.1 (14)</td>
<td>0.430</td>
</tr>
<tr>
<td>Hb end(g/L)</td>
<td>106.6±15.7 (15)</td>
<td>107.5±11.3 (14)</td>
<td>0.851</td>
</tr>
<tr>
<td>Ferritin start (µg/L)</td>
<td>318 (126 - 533) (15)</td>
<td>353 (182 - 884) (12)</td>
<td>0.526</td>
</tr>
<tr>
<td>Ferritin end(µg/L)</td>
<td>91 (36 - 239) (15)</td>
<td>104 (44 - 543) (12)</td>
<td>0.760</td>
</tr>
<tr>
<td>Serum folate start (nmol/L)</td>
<td>43.8 (26.3-110.6) (14)</td>
<td>42.25 (32.3-166.8) (12)</td>
<td>0.961</td>
</tr>
<tr>
<td>Serum folate end (nmol/L)</td>
<td>189.7 (89.1-241.9) (14)</td>
<td>168.3 (37.7-227.7) (12)</td>
<td>0.270</td>
</tr>
<tr>
<td>Serum retinol (all-trans) start (µmol/L)</td>
<td>0.70±0.18 (15)</td>
<td>0.70±0.16 (12)</td>
<td>0.994</td>
</tr>
<tr>
<td>Serum retinol (all-)</td>
<td>1.04±0.20 (15)</td>
<td>1.00±0.24 (12)</td>
<td>0.418</td>
</tr>
</tbody>
</table>
### Conclusion

This study shows that for healthy late preterm infants, the current ESPGHAN recommendations do not entirely match with requirements. Based on the parameters studied, recommendations should be more close to: iron 1 mg/100 kcal, vitamin A 280 µg-RE/100 kcal, and for vitamin D 10 µg/day. For folic acid 45 µg/100 kcal seems to be more than enough. Furthermore, formula intakes per kg of bodyweight should be restricted to about 120 kcal/kg/day, and additional supplements should be discouraged.

### Disclosure of interest

A. Schaafsma is employed by Friesland Campina who sponsored this study. For the other authors: none declared.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Start Value (Mean ± SD)</th>
<th>End Value (Mean ± SD)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum 25OHD</td>
<td>73.80±17.93 (15)</td>
<td>79.09±16.98 (11)</td>
<td>0.601</td>
</tr>
<tr>
<td>25OHD</td>
<td>165.33±50.544 (15)</td>
<td>202.73±76.57 (11)</td>
<td>0.259</td>
</tr>
</tbody>
</table>

1 non-parametric distribution: median (range)
Tolerance and efficacy of extensively hydrolyzed formula for infants with IgE-mediated cow’s milk Protein Allergy (CMPA) JUNGLO study – PART 2: Extensively hydrolyzed rice protein formula

Alfonso Solar, Mª Dolores Ibañez, Jose Maldonado, Santiago Nevot, Ana Maria Plaza, Francisco Cañabate, Pilar Codoner-Franch, Beatriz Espin, Alfonso Rodriguez-Herrera, Carmelo Escudero, Silvia Sanchez, Jacqueline BRASY, Federico Lara, Catherine Fressange-Mazda, Cécile Bonhomme, Jose Manuel Moreno

Objectives and study: As part of a randomized and blinded study, the aim of this trial was to evaluate tolerance and efficacy of a new extensively hydrolyzed rice protein formula (Lactalis, France) during a 3-months consumption period, by infants with IgE-mediated cow’s milk Protein Allergy (CMPA).

Methods: Infants with suspected CMPA were pre-screened in 15 hospitals in Spain. All infants were full term, healthy and weighing over 2.5 kg at birth, and aged up to 9 months at inclusion. CMPA was confirmed by a specific IgE dosage before inclusion. An oral food challenge (OFC) was then conducted with 2, 5, 10, 25, 50 and 100 ml of formula given, at 10-minute intervals. The main outcome criterion was tolerance of formula at introduction by 97% infants. Forty three infants were necessary to evaluate this level of tolerance (88% power). Primary outcome was evaluated with a binomial test of proportion (5% significance). Descriptive statistics of all variables were also made. Over a 3-months follow-up period, evolution of the severity of clinical signs was evaluated by symptom-based scores, and growth measured by World Health Organization (WHO) charts, using z-scores of anthropometric data (weight, length, body mass index, head circumference).

Results: One out of 58 randomized patients had a protocol deviation and 7 a non-IgE-mediated CMPA. The 50 remaining children joined the trial; 31 boys and 19 girls, aged 22.7 (+/-8.4) weeks. They all tolerated the study formula at introduction, experiencing no adverse effect on the first day of formula intake. It Allows to affirm that over 97% of infants tolerated the study formula at introduction (p=0.0092). Only one adverse event was reported 8 days later. Cough and diarrhoea ceased after switching to an amino acid-based formula. A delayed tolerance was observed in more than 98% of the infants.

After one month follow up, infant’s condition showed great improvement; 34% cutaneous symptoms (urticaria, angioedema) reported at inclusion, felt to 4% only. Digestive symptoms (regurgitations, abdominal pains abnormal stools), atopic dermatitis and other symptoms (general condition, respiratory), respectively 24%, 24% and 22 % at inclusion felt to 0 %. At inclusion, severity of the cutaneous symptoms was mostly light (35%) to moderate (35%), light for atopic dermatitis (66.7%), severe for digestive symptoms (66.7%) and moderate for other symptoms (81.9%).

Growth for the 3-months follow-up showed a normal pattern, in agreement with WHO's growth charts; there was a significant evolution for weight-, length- and head circumference-for-age z-scores (p<0.006).
Conclusion: In the JUNGLO study the rice protein hydrolyzed formula is well tolerated at introduction with more than 97% of tolerance. It is also efficient to rapidly improve clinical symptoms and allows a normal growth pattern in infants with CMPA.

Disclosure of interest: A. Solar, no conflict; Mª D. Ibañez, no conflict; J. Maldonado, no conflict; S. Nevot, no conflict; E. Alonso, no conflict; A. Maria Plaza, no conflict; F. Cañabate, no conflict; P. Codoñer, no conflict; B. Espin, no conflict; A. H. Rodríguez, no conflict; C. Escudero, no conflict; S. Sanchez, no conflict; J. M. Moreno, no conflict; J. Brasy, Lactalis employee; F. Lara-Villoslada, Lactalis employee; C. Fressange-Mazda, Lactalis employee; C. Bonhomme, Lactalis employee.


**NUTRITION: Neonatal and infant nutrition**

N-P-101

**ESPGHAN recommendations for DHA in preterm formulae do not seem to be sufficient for healthy late preterm infants to reach optimal DHA status within 8 postnatal weeks.**

Ralitsa Wilson Georgieva¹, Frits A.J. Muskiet², Anne Schaafsma³

¹Specialized Hospital for Active Treatment of Children’s Disease, Neonatology, Sofia, Bulgaria
²University Medical Center Groningen, Laboratory Medicine, Groningen, Netherlands
³Frieslandcampina, Research & Development, Leeuwarden, Netherlands

**Objectives and study:** ESPGHAN recommendations for docosahexaenoic acid (DHA) in formulae for preterm infants range from 11-27 mg/100 kcal. An erythrocyte (RBC) DHA content of 8 g per 100 g fatty acids (g%) confers optimal cardiovascular health in adults. Mothers exhibiting this status produce breast milk with DHA contents close to 1 g% of total fatty acids, while their exclusively breastfed infants reach RBC-DHA contents of 7-8 g% within 3 months. In this partly blinded study we studied whether the maximum ESPGHAN recommendation for DHA is able to increase RBC-DHA to 7-8 g% in formula-fed healthy Bulgarian late preterm infants (n=29; 32-34 gestational weeks). The infants (aged 14±2 days) were randomly allocated to formula A or B, providing almost the same amount of DHA (25 vs. 26.5 mg/100 kcal), but different amounts of arachidonic acid (AA: 25 vs. 18 mg/100 kcal). The study protocol was approved by the Medical Ethical Committee of the participating hospitals. The trial was registered in the Netherlands Trial Registry (NTR 3373).

**Methods:** Venous blood samples were collected at 14±2 and 75±2 postnatal days, respectively. RBC fatty acids were measured by capillary gas chromatography/flame ionization detection. RBC-DHA outcomes were evaluated using the Wilcoxon matched pair Signed-rank test for changes within groups, and the Independent Samples Mann-Whitney U-test for between-group differences. Changes in AA concentrations were evaluated using Paired Samples T test for changes within groups and with one-way ANOVA for between-group differences.

**Results:** The slightly different formula DHA- and particularly AA-concentrations did not cause between-group differences in RBC-DHA and RBC-AA contents. In both groups, RBC-DHA increased (with 36.8-39.3%), while RBC-AA decreased (with 10.4-12.4%) (Table). RBC-DHA did not reach the 7-8 g% target, while RBC-AA was close to the 14.5-15.0 g% target.

**Table:**

<table>
<thead>
<tr>
<th>Fatty acid</th>
<th>All participants (n=29)</th>
<th>Group A (n=15) 25 mg DHA/100 kcal</th>
<th>Group B (n=14) 26.5 mg DHA/100 kcal</th>
<th>25 mg AA/100 kcal</th>
<th>18 mg AA/100 kcal</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>AA start</td>
<td>16.45±1.04</td>
<td>16.41±0.83</td>
<td>16.50±1.27</td>
<td>0.840</td>
<td></td>
<td></td>
</tr>
<tr>
<td>AA end</td>
<td>14.57±0.86</td>
<td>14.37±0.70</td>
<td>14.77±0.99</td>
<td>0.213</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target</td>
<td>14.5-15</td>
<td>14.5-15</td>
<td>14.5-15</td>
<td>0.000</td>
<td>0.002</td>
<td></td>
</tr>
<tr>
<td>p</td>
<td>0.000</td>
<td>0.002</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHA start</td>
<td>3.66 (2.57-6.08)</td>
<td>3.72 (2.57-6.08)</td>
<td>3.55 (2.64-4.89)</td>
<td>0.616</td>
<td></td>
<td></td>
</tr>
<tr>
<td>DHA end</td>
<td>5.24 (3.57-6.57)</td>
<td>5.26 (4.02-6.57)</td>
<td>5.04 (3.57-6.14)</td>
<td>0.266</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Target</td>
<td>7-8</td>
<td>7-8</td>
<td>7-8</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Data are presented as g% of total fatty acids in RBC. AA is presented as mean ± SD, DHA as median (range). Target values are derived from Kuipers et al. J Nutr 2011;141:418-427.

**Conclusion:** This study with healthy late preterm infants with poor DHA status at 2 postnatal weeks shows that 8 weeks feeding with the ESPGHAN recommended maximum amount for DHA in formulae is unable to increase RBC-DHA content to the optimum of 7-8 g%. We hypothesize that preterm formulae (and breast milk) DHA contents should be at least 0.7 g%. For AA the lower range of the ESPGHAN recommendations seems appropriate.

**Disclosure of interest:** A. Schaafsma is employed by FrieslandCampina who sponsored this study. For the other authors: none declared.
Tolerance and efficacy of extensively hydrolyzed formula for infants with IgE-mediated cow’s milk Protein Allergy (CMPA) JUNGLO Study – PART 1 : Extensively hydrolyzed casein formula

Ibañez Mª Dolores 1, Alfonso Solar 2, Jose Maldonado 2, Santiago Nevot 3, Elena Alonso 4, Ana Maria Plaza 5, Francisco Cañabate 6, Pilar Codoner-Franch 7, Beatriz Espin 8, Alfonso Rodríguez-Herrera 9, Carmelo Escudero 10, Silvia Sanchez 10, Jacqueline BRASY 11, Federico Lara 12, Catherine Fressange-Mazda 13, Cécile Bonhomme 13, Jose Manuel Moreno 10

1Hospital Infantil Universitario Niño Jesús, Madrid, Spain
2Hospital Materno Infantil Teresa Herrera, A Coruña, Spain
3Hospital Sant Joan de Déu, Manresa, Spain
4Hospital Materno Infantil Gregorio Marañón, Madrid, Spain
5Hospital Sant Joan de Déu, Barcelona, Spain
6Hospital de Poniente, El Ejido (Almeria), Spain
7Dr. Peset University Hospital, Valencia, Spain
8Hospital Infantil Virgen del Roció, Sevilla, Spain
9Instituto Hispalense de Pediatría, Unidad de Gastroenterología Y Nutrición, Sevilla, Spain
10Hospital 12 de Octubre, Madrid, Spain
11Lactalis, Retiers, France
12Lactalis, Granada, Spain
13Lactalis, Nutrition Europe, Torcé, France

Objectives and study: As part of a randomized and blinded study, the aim of this trial was to evaluate tolerance and efficacy of a new extensively hydrolyzed casein formula (Damira 2000®, Lactalis, France) along a 3-month consumption period, by infants with IgE-mediated cow’s milk Protein Allergy (CMPA).

Methods: Infants with suspected CMPA were pre-screened in 15 hospitals in Spain. All infants were full term, healthy, weighing over 2.5 kg at birth, and aged up to 9 months at inclusion. CMPA was confirmed by a specific IgE dosage before inclusion. An oral food challenge (OFC) was then conducted with 2, 5, 10, 25, 50 and 100 ml of formula, given at 10-minute intervals. The main outcome criterion was formula tolerance at introduction by 97% infants. 40 infants were necessary to evaluate this level of tolerance (88% power). Primary outcome was analyzed by a binomial test of proportion (5% significance). Descriptive statistics of all variables were also made. Over a 3-month follow-up period, evolution of the severity of clinical signs was evaluated by symptom-based scores, and growth measured and referenced to the World Health Organization (WHO) charts, using z-scores of the anthropometric data (weight, length, body mass index, head circumference).

Results: One out of 54 randomized patients had a protocol deviation and 6 a non-IgE-mediated CMPA. The 47 remaining children participated in the trial; 25 boys and 22 girls, aged 22.4 ± 7.9 weeks. They all tolerated the formula at introduction, experiencing no adverse reaction on the first day of formula intake. It allows to affirm that over 97% of the infants tolerated the formula at introduction (p=0.0112). Three adverse events were reported 4, 6 and 10 days later and were considered possibly or probably related to the study formula indicating an effective delayed tolerance of more than 93% of infants.

After one month follow-up infant’s condition showed great improvement; in fact, the rate of 40.4% digestive symptoms (regurgitations, abdominal pain, abnormal stools) reported at inclusion felt dramatically to 13%. Cutaneous symptoms (urticaria, angioedema), atopic dermatitis and other symptoms (general condition, respiratory) rated 38%, 19% and 27.6%, respectively at inclusion, felt to 0 at 1 month. At inclusion, severity of clinical signs was moderate in more than 50% of the different symptoms, and lightly severe in atopic dermatitis. The rates of severe symptoms were; 47.4% digestive, 27.8% cutaneous and 7.7% other symptoms.
Growth for the 3 months follow-up showed a normal pattern in agreement with WHO growth charts; there was a significant evolution for weight- and length-for-age z-scores throughout the different visits (p<0.05).

**Conclusion:** In JUNGLO study the new casein hydrolyzate formula is well tolerated at introduction with more than 97% tolerance in infants with CMPA. It is also efficient to rapidly improve clinical symptoms, and allows a normal growth pattern.

**Disclosure of interest:** Mª D. Ibañez, no conflict; A. Solar, no conflict; J. Maldonado, no conflict; S. Nevot, no conflict; E. Alonso, no conflict; A. Maria Plaza, no conflict; F. Cañabate, no conflict; P. Codoñer, no conflict; B. Espin, no conflict; A. H. Rodríguez, no conflict; C. Escudero, no conflict; S. Sanchez, no conflict; J. M. Moreno, no conflict; J. Brasy, Lactalis employee; F. Lara-Villoslada, Lactalis employee; C. Fressange-Mazda, Lactalis employee; C. Bonhomme, Lactalis employee.
Gender effect on brain DHA level of 1.5%ALA-pure-vegetal formula can be abolished by 1.5%ALA-dairy fat incorporation which induces simultaneously a better increase of brain DHA level compared to DHA-supplemented vegetal formula

Bernadette Delplanque¹, DU Qin², MARTIN Jean-Charles², Pascale le Ruyet³

¹Nmpa, Cnps, Universite Paris-Sud, Orsay, France
²Inra1260/Inserm1025, Nutrition, Marseille, France
³Lactalis R&d, Nutrition, Retiers, France

Background: Achieving an appropriate docosahexaenoic-acid (DHA) status in the neonatal brain is an important goal of neonatal nutrition. Infant formulas have been gradually replacing mother's milk and are usually prepared with vegetal oils. The essential fatty acids (EFA) composition of these formulas are controlled (ALA, LA) and DHA supplementation has been more recently proposed to mimic mother-milk. The bioconversion of ALA to LCn-3 (ie DHA) is depending on the Delta-6-Desaturase activity linked to a proper ratio n-6/n-3 (LA/ALA). Furthermore, it has been shown that gender is modulating the bioconversion, females being more prone to increase the levels of LCn3.

Objectives and study: In an attempt to validate the potential replacement of vegetal fat with dairy fat in infant formulas, we used the brain DHA level of rats as a nutritional model to compare the effects of blends based on dairy fat instead of palm oil providing the same EFA quantities: ALA and LA levels in these experimental diets followed the commonly recommended values for commercial vegetal fat formulas (1.5%, 15% respectively). We evaluated how introduction of dairy fat in the formula, improved DHA content in the brain of both male and female rats.

Methods: Three groups of rats (10 males and 10 females), born from dams fed over gestation and lactation with a low ALA-diet (0.4%FA), were fed, for 6 weeks after weaning, with diets providing similar levels of ALA (1.5%, from rapeseed source), blended with (i) anhydrous dairy fat, (ii) palm oil or (iii) palm oil supplemented with DHA (0.12%). Brain FA were determined by gas chromatography at weaning and after the post-weaning diets

Results: -The 1.5%ALA-palm diet (pure vegetal) induced a better restoration of brain DHA in females compared to males (+16%, p<0.001).

-Dietary supplementation with DHA corrected this difference by increasing the brain DHA level in males (+17%, p<0.0001) who reached the levels obtained in females supplemented or not with DHA (ns).

-Restoration of brain DHA levels was superior with the 1.5%ALA-dairy-fat diet compared to both 1.5%ALA-palm-blends: without DHA supplementation (+23%p<0.0001 for males and +7.5% p<0.006 for females) – or with DHA supplementation (+5% for male and females p<0.05.)

The gender/diet interaction which showed lower levels of brain DHA of males with the 1.5%ALA-palm diet, was abolished by the 1.5%ALA-dairy-fat diet so that brain DHA levels were similarly restored in males and females (13.5%of total FA). Dairy fat diet induced higher brain DHA levels compared to those obtained by DHA supplementation of palm diet (males +5.6%p<0.0024, females+5%p<0.048).

Conclusion: Restoration of brain DHA levels of young deficient rats is more efficient with a 1.5%ALA dairy fat blend diet compared to 1.5%ALA pure vegetal blend, despite similar dietary ALA levels. Furthermore, dairy fat blend smoothed positively the gender differences observed with pure vegetal blend (male DHA<female DHA levels). Supplementation of pure vegetal blends formula with DHA seems to be less efficient than dairy fat for brain DHA restoration. Human application for infant formulas should be considered.

Total protein, amino acids, and bioactive proteins in breast milk: a developmental perspective

Bo Lonnerdal¹, Peter Erdmann², Sagar Thakkar³, Frederic Destaillats²

¹University of California, Nutrition, Davis, United States
²Nestlé Nutrition, Vevey, Switzerland
³Nestlé Research Center, Lausanne, Switzerland

Objectives and study: Reliable information on the true protein and amino acid content of breast milk is important as it serves as a guideline for estimating protein requirements of infants and how they vary with age. It is also essential when designing the composition of infant formulas, particularly when a “staging” approach is used, i.e. the composition of the formula is modified in stages to reflect changes in breast milk and changing requirements as the infant gets older. Bioactive milk proteins can partially survive digestion and are capable of exerting activities in the infant gut, making them potentially beneficial additives to infant formula. We therefore performed a meta-analysis of total protein, amino acids and bioactive proteins in breast milk and their changes during lactation.

Methods: We did literature searches using PubMed, Scopus, EMBASE, and Google Scholar using the keywords: “breast milk”, “human milk”, “protein”, “true protein”, “total nitrogen”, “bioactive proteins”, “whey to casein ratio”, “lactoferrin”, “α-lactalbumin”, “IgA”, “lysozyme”, “IgG”, “IgM” and “amino acid”. Reference lists of the retrieved articles were also reviewed to identify references not found using electronic search methods. Only data from “normal” or “healthy” mothers who delivered healthy term infants were included. Selected studies provided sufficient information regarding geographic location, study design, sampling time and procedure, nature of sample, analytical methods and units.

Results: The true protein content in human milk declines over time. Median true protein content in milk expressed 16-30 days after delivery was 30% lower compared with 0-5 days after delivery (1.57 g/100 mL vs 2.06 g/100 mL). It decreased throughout the first year, but at much lower rates than in the first weeks. By 90-360 days, true protein content was 47% lower compared to 0-5 days after delivery (1.10 g/100 mL). Changes in true protein closely parallel changes in infant protein requirements. Total, essential, and non-essential amino acids also decrease over time. The largest decreases in amino acid content occurred between milk expressed 0-5 days and milk expressed 6-15 days after delivery, whereas it stabilized after 2 weeks after delivery. Ratios of essential amino acids to total amino acids were stable over time. Whey:casein ratios were highest the first 5 days after delivery and declined over time. In colostrum, it was 89:11, it then dropped to 65:35 at 6-15 days after delivery. After that, the ratio ranged from 61:39 to 59:41. Concentrations of bioactive proteins were highest in colostrum and then declined, with lysozyme being the exception showing a reverse trend.

Conclusion: Human milk contains a wide array of proteins with biological activities ranging from antimicrobial protection to immunomodulation and facilitation of nutrient absorption. The proteins in human milk also provide adequate amounts of essential amino acids to support the growth of maturing infants. This highly adapted system likely is responsible for providing many of the benefits of breast milk over infant formula. Our results provide a useful dataset for evaluation of protein quantity and quality in efforts to narrow the nutritional and immunological gap between breast milk and currently available infant formulas, particularly when using a staged approach.

Disclosure of interest: This work was sponsored in part by a grant from Nestlé Nutrition to BL. PE, ST and FD are Nestlé employees.
Gestation Specific Reference Growth Chart for North Indian Infants

Anup Thakur¹, Neelam Kler¹, Pankaj Garg¹, Melina S. Magsumbol², Thomas Wilson³, Arpita Ghosh², Archana Singh¹, Arun Soni¹, Manoj Modi¹, Satish Saluja¹

¹Sir Ganga Ram Hospital, Neonatology, New Delhi, India
²Public Health Foundation of India, Gurgaon, India
³Harvard T. H. Chan School of Public Health, Department of Biostatistics, Boston, United States
⁴All India Institute of Medical Sciences, New Delhi, India

Objectives and study:

Background: India specific growth reference curves across various gestation are few and include small number of infants <32 weeks. Updated population-level reference curves reflect advances in obstetric, socio-economic change, and help detect growth and nutritional discrepancies at the earliest opportunity.

Objectives:
1. To construct centile charts for birth weight, length and head circumference for infants born from 23 weeks to 41 weeks.
2. To compare our institutional centile charts with other national and international growth charts.

Methods:

Study Design: Observational study

Subject: All consecutively live born singleton infants from 23-41 weeks of gestation.

Methods: Electronic data was retrieved from hospital information system for birth weight, length and head circumference of infants born from January 2006-December 2014. Smoothened percentile curves for 3rd, 10th, 25th, 50th, 75th, 90th and 97th were created for weight separately for male and female infants using the Lambda Mu Sigma (LMS) method. We evaluated the quality of the newly estimated centiles using cross-validation. We planned to use chi-square goodness-of-fit tests to determine whether the weight, length and head circumference of infants in the cohort are consistent with two recent western and one national growth chart.

Results: Raw and smoothened curves for weight were created for 12,680 infants (6847 males and 5833 females) that met all inclusion criteria. Females were lighter than the males. On comparing the study curve with Fenton and Kim (2013, BMC Pediatrics) and Olsen et al. (2010, Pediatrics), our weight centiles across all gestation and in all major centiles were lower. The difference was largest among full term babies (37 weeks and above). On applying goodness-of-fit test, our weight centiles were closest to South Indian growth charts (Kandraju et al. 2011, Indian Pediatrics). The centile curves for length and head circumference are yet to be constructed.

Conclusion: We constructed a new sex-specific birth weight chart and confirm that it accurately classifies the cohort. The “North Indian” cohort tend to have lower weight for gestational age than would be expected based on the other charts. The updated weight curve is representative of our local (including very prematurely born) population and will avoid erroneous classification of our infants into SGA or LGA based on currently utilized western growth charts.

Disclosure of interest: None of the authors have any COI to declare.
Use of partially hydrolyzed whey formula in the general infant population: effect on growth and allergy prevention

Dunjin Chen1, Wen Sun1, Zhijian Wang2, Mei Zhong2, Qiao Xue3, Hongwu Chen3, Ping He3, Xiulan Wen4, Meizhen Tan5, Qianjun Liu5, Qiwei Li6, Yunxia Liu7, Chenguang Xu8, Huiqing Xu9, Zengyou Liu10, Wei Wang11, Yangping Yan12, Ruichun Lin13, Jingran He14, Ping Li15, Nanda de Groot11, Sophie Pecquet16, Evelyn Spivey-Krobath11, Carine Blanchard12, Sophie Nutten12

1The Third Affiliated Hospital of Guangzhou Medical University, Obstetrics and Gynecology, Guangzhou, China
2Southern Medical University Nan Fang Hospital, Obstetrics and Gynecology, Guangzhou, China
3Southern Medical University Nan Fang Hospital, Pediatrics, Guangzhou, China
4Guangzhou Women and Children's Medical Center, Obstetrics, Guangzhou, China
5Guangzhou Women and Children's Medical Center, Child Health Department, Guangzhou, China
6The First Affiliated Hospital of Sun Yat-Sen University, Obstetrics and Gynecology, Guangzhou, China
7The First Affiliated Hospital of Sun Yat-Sen University, Neonatology, Guangzhou, China
8Shenzhen Sixth People's Hospital, Obstetrics and Gynecology, Shenzhen, China
9Shenzhen Sixth People's Hospital, Pediatrics, Shenzhen, China
10The Third Affiliated Hospital of Guangzhou Medical University, Pediatrics, Guangzhou, China
11Nestlé Nutrition, Vevey, Switzerland
12Nestlé Research Center, Lausanne, Switzerland

Objectives and study: Numerous clinical studies have demonstrated that specific partially hydrolyzed whey based infant formulas (pHF-W) significantly reduce the risk of developing atopic dermatitis, when given in the first months of life, in infants with a positive family history of allergic diseases who cannot be exclusively breastfed (Szajewska H et al., 2010). While evidence of this benefit is demonstrated in this population, only few data are available in the general infant population regarding allergy prevention.

Methods: A prospective cohort study was performed in China, including a total of 1773 healthy term infants. During pregnancy, mothers were educated on the importance of maternal diet, on breastfeeding benefit and on the possibility and benefit to use pHF-W when breastfeeding is not possible. At 4 months, infants were classified into 3 groups depending on their feeding regimens within the first 4 months of life: pHF-W group who received pHF-W (Nestlé NAN H.A.1) alone or in combination with breastmilk, intact cow’s milk protein formula group (CMF) who received CMF (Nestlé NAN 1) alone or in combination with breastmilk, and exclusively breastfed group. Infants were followed up to 12 months of age. Infant growth and the incidence of atopic dermatitis were assessed during this period.

Results: Mother’s infant feeding choice repartition were exclusive breastfeeding n = 874 (49.3%), pHF-W n = 653 (36.8%) and CMF n = 246 (13.8%). Growth parameters (height, weight and head circumference) at 1, 3, 6, 9, 12 months after birth were not statistically different among the three groups. Eczema occurrences in the exclusive breastfeeding group and pHF-W group (27.00 vs. 27.26%) were similar and significantly lower than that of CMF group (34.96%). These results have confirmed the findings of three other studies involving general infant population (in Switzerland (Exl BM et al., 2000), Thailand (Ngamphaiboon J et al., 2006) and the United States (Hertman TC et al., 1994)) showing a reduction of atopic manifestations using pHF-W vs. intact cow’s milk protein formula, while supporting age-appropriate normal infant growth.

Conclusion: This study confirms that a specific pHF-W supports adequate growth comparable to that of breastfed infants, and significantly reduces the risk of developing atopic dermatitis in the general infant population as compared to intact cow’s milk formula. Taken together, it places this pHF-W as a nutritionally adequate and safe routine infant formula with the additional benefit for prevention of atopic dermatitis for infants who are unable to be exclusively breastfed.

Disclosure of interest: The study was sponsored by Nestlé CHINA. CB, SN, NdG, SP and ESK are Nestec employees.
L. fermentum CECT 5716 protects and prevents from intestinal epithelial barrier hyperpermeability in a newborn rat model

Tiphaine Vanhaecke1, Pierre-Antoine Grohard1, Philippe Aubert1, Julie Jaulin1, Julien Chevalier1, Tony Durand1, Hélène Boudin1, Philippe Naveilhan1, Amandine Ligneul2, Pascale le Ruyet2, Michel Neunlist3

1School of Medicine, University of Nantes, Inserm Umr 913, Nantes, France
2Lactalis R&d, Nutrition, Retiers, France
3University Hospital of Nantes, Inserm U913, Nantes, France

Objectives and study: Intestinal epithelial barrier (IEB) dysfunction plays a critical role in various pathologies and intestinal disorders affecting infant and children, including the development of food allergies and colitis. Recent studies highlighted the crucial role of intestinal microbiota in promoting postnatal maturation of the IEB. Therefore, probiotics may be useful in reducing allergy-associated dysfunction of the IEB in children. For this purpose, we characterized, in an immature rat pup model, the impact of oral administration of Lactobacillus fermentum CECT 5716 (LF) on the IEB function, and identified molecular targets responsible for these effects.

Methods: Healthy newborn rats received by gavage once a day, from postnatal day (PND) 7 to 10 or PND 7 to 24, either 2 dosages of LF (10^8 or 10^9 CFU/100g body weight/day) or water (controls). At the end of the supplementation period (basal condition), morpho-anatomical parameters and gut motility (total transit time (TTT)) were assessed. Paracellular (parac.) and transcellular (transc.) gut permeability were measured both in vivo and ex vivo in 3 intestinal segments. LF effects were also characterized on the IEB function in response to 2 different stressors (maternal separation (MS) and water avoidance stress (WAS)). Relative expression levels of tight junction proteins and inflammatory mediators were analyzed by Western blot and RT-qPCR.

Results: Whatever the dosage, daily administration of LF did not alter the morpho-anatomical parameters compared to control group. In basal condition, as well as stressed condition, only the higher LF dosage led to a reduction of IEB permeability. LF administration for 17 days induced a 21% decrease in in vivo parac. permeability (n=30, p=0.016), without altering TTT, compared to controls. A 2 hours-WAS applied once at PND24 enhanced in vivo parac. permeability in controls (+70 %, n=6, p<0.05) but not in the LF group (+31 %, n=6, p=0.05). In addition, ex vivo para/trans-cellular permeability in ileal and jejunal tissues of animals subjected to WAS decreased markedly in the LF group compared to controls (n=18, Parac. : -33 % p<0.0001 ; -18 % p<0.05 ; Transc. : -31 % p=0.01 ; -30 % p<0.05, respectively). A 4 hours-MS applied once at PND10 enhanced in vivo parac. permeability in controls (+44 %, n=6, p<0.05) but not in the LF group (+13 %, n=6, p>0.05). Interestingly, LF administration did not affect the increase in blood of corticosterone levels following WAS nor altered mRNA expression of IL-1β, TNFα, IL-10 and IFNγ in ileum compared to controls. Western blots of ileal tissues demonstrated increased expression of ZO-2 (+106 %, n=18, p<0.05), JAM-A (+66 %, n=18, p<0.05) and cingulin (+64 %, n=18, p<0.05) but no change in that of occludin, ZO-1 and claudin1-2-3 in LF group compared to controls.

Conclusion: These results show the ability of Lactobacillus fermentum CECT 5716, daily and orally administered, to rapidly strengthen the IEB not only in basal conditions but also in response to stress, in a rat model. The main site of action was in the upper digestive tract, partly via the modulation of the expression of tight junctions molecules in the small intestine. The use of this probiotic strain may therefore provide a new approach in the prevention and/or treatment of functional intestinal abnormalities and food allergies.

Disclosure of interest: The authors whose names are listed immediately below report a conflict with Lactalis : T. Vanhaecke, A. Ligneul, P. Le Ruyet.
Fat absorption of a new infant milk formula concept with large fat globules coated with phospholipids is comparable to the high fat absorption of current infant milk formula

Eefje Engels¹, Martin Balvers¹, Dennis Acton¹, Bert van de Heijning¹
¹Nutricia Research, Early Life Nutrition, Utrecht, Netherlands

Objectives and study: Fats in infant nutrition provide up to 60% of total energy. Fat absorption of human milk and infant milk formula (IMF) is highly efficient. Fat globules in human milk are on average 4 µm in diameter and are surrounded by a native biological membrane. We developed a new IMF concept (Nuturis®) with large (3-5 µm) fat globules coated with milk phospholipids. This results in an IMF more similar to human milk than current IMFs with small (~0.5 µm), uncoated fat globules¹. As a first preclinical safety assessment the absorptive equality the new IMF concept was tested in a fat balance experiment using adult rats.

Methods: IMFs containing new concept to be used for clinical safety studies were tested in a fat balance experiment versus an IMF containing the current lipid format. IMF powders were supplemented to AIN93G-compliant rodent diets, resulting in an entirely IMF-derived fat moiety (7%). Diets were supplied to single-housed, male, adult Wistar rats (n=10; 180-200 g) as freshly prepared dough balls (20% water). Apart from a control diet (C) containing about 95% vegetable oils, two diets comprising the new concept (Nuturis®) were tested: diet A with an oil blend and fatty acid (FA) composition identical to diet C, and diet B containing a fat blend in which palm oil was fully replaced by milk fat (~50% of total fat), resulting in a 6.3% β-palmitate content. Rats received each diet for 14 days in random order; during the last 72 h of each intervention period food intake was monitored and faeces collected and dried. Both quantity and quality of fat intake (diet) and output (faeces) were assessed.

Results: Diets were well accepted and the rats thrived equally well on each of them and no differences in animal health and wellbeing were observed. Dietary fat absorption was equally very high for each diet: average fat absorption (% ± s.d.) was highest (98.48 ± 0.56) with diet B (containing milk fat), but very similar to the other two diets tested: 97.85 ± 0.95 for diet A, and 97.59 ± 0.89 for diet C. Faecal levels of medium chain FAs (C6-C12) and n-3 long chain-poly unsaturated FAs (LC-PUFAs; EPA and DHA) were below detection limits, and hence assumed to be entirely absorbed. Absorption levels of mono unsaturated FAs and PUFAs were >98.5% for all diets. Palmitate (C16:0) absorption was highest for diet B: faecal palmitate content (% ± s.d.) was 0.43 ± 0.17, and 0.75 ± 0.40 and 0.83 ± 0.36 for diet A and C, respectively.

Conclusion: Adult rats proved to be a suitable model to test fat absorption. The fat absorption of all diets tested was very high (>97.5%) and in general no differences between diets tested were observed. Hence, the new lipid concept (Nuturis®) does not seem to affect overall fat absorption. These preclinical data support a safe clinical use of the new IMF concept. In addition, the data show that the presence of β-palmitate (in diet B) improves palmitate absorption. These preclinical safety data remain to be confirmed in well-designed clinical studies.

Disclosure of interest: All authors are employees of Nutricia Research.
¹ Gallier et al. 2015
NUTRITION: Neonatal and infant nutrition

N-P-109

Influence of nutritional variables on the onset of necrotizing enterocolitis in preterm infants: A case-control study

Laura Martínez-Rodríguez1, Javier Estañ1, Jose Domingo Bermúdez2, Jaime Fons1, Agustin Molina1, Cecilia Martínez-Costa3

1Hospital Clínico Universitario, Pediatrics, Valencia, Spain
2University of Valencia, Statistics, Valencia, Spain
3University of Valencia, Pediatrics, Valencia, Spain

Objectives and design: To analyze early nutritional variables that could influence the onset of necrotizing enterocolitis (NEC). Observational and case-control design

Methods: In 485 preterm infants, a two-phase study was undertaken: 1) Global analysis of epidemiological and clinical variables of all preterm infants admitted to a neonatal intensive care unit of a tertiary hospital since 2008-2010, divided in 3 different gestational age (GA) groups; 2) Case-control study (38 infants with NEC stage II or higher according to modified Bell’s classification, and 38 GA-matched controls) to analyze nutritional variables 4 days prior to disease onset.

Results: Feeding began at 2-5 days of age in all infants. A trend between delayed onset of feeding and lower GA was found (p<0.001). Compared to controls, cases exhibited a shorter period of minimal enteral feeding (that reached statistical significance in the most immature neonates (GA<28) (p=0.039)) and began enteral nutrition earlier (p=0.023). Volume increases were faster in cases 4 days prior NEC (p=0.022), Table I. Parenteral nutrition was used in 74% of cases and 87% of controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Cases (n=38)</th>
<th>Controls (n=38)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>X ± SD</td>
<td>Med</td>
</tr>
<tr>
<td>PN onset (hours of life)</td>
<td>20 ± 7</td>
<td>21</td>
</tr>
<tr>
<td>PN duration (days)*</td>
<td>36 ± 37</td>
<td>18</td>
</tr>
<tr>
<td>NPO duration (hours)</td>
<td>47 ± 34</td>
<td>42</td>
</tr>
<tr>
<td>MEF duration (GA&lt; 28 w) (hours) **</td>
<td>89 ± 72</td>
<td>58</td>
</tr>
<tr>
<td>Start of the EN (hours) ***</td>
<td>90 ± 71</td>
<td>73</td>
</tr>
<tr>
<td>Timing &gt;20 mL/Kg/d among 4 days before NEC start n (%)****</td>
<td>17 (45)</td>
<td>8 (21)</td>
</tr>
</tbody>
</table>

PN, parenteral nutrition; NPO, Nil Per Os, MEF, minimal enteral feeding (or trophic feeding); GA, gestational age; w, weeks; EN, enteral nutrition; NEC, necrotizing enterocolitis. *p 0.001, **p 0.039, ***p 0.023, ****p 0.022

Conclusions: Early but gradual establishment of minimal enteral feeding avoiding rapid volume increases can diminish the incidence of NEC.

Disclosure of interest: Authors declare no conflict of interest.
NUTRITION: Neonatal and infant nutrition

N-P-110

**Formula feeding by gastric port in preterm pigs as a model of enteral feeding in preterm infants**

Anna Socha-Banasiak¹, Danica Grujic², Kateryna Goncharova², Jaroslaw Wolinski³, Maria Boryczka³, Paulina Grzesiak¹, Galyna Ushakova⁴, Tatiana Kovalenko⁵, Iryna Osadchenko⁵, Julia Vasylyk⁶, Olesia Semchysyn⁶, Ruslana Vasylkovska⁶, Siarhei Kirko⁷, Andrea Donatelli⁸, Elzbieta Czkwianianc¹, Stefan Pierzynowski²

¹Polish Mother’s Memorial Hospital Research Institute, Dept Gastroenterology, Allergology and Pediatrics, Lodz, Poland
²Lund University, Biology, Lund, Sweden
³The Kielanowski Institute of Animal Physiology and Nutrition of the Polish Academy of Science, Dept Endocrinology, Jablonna, Poland
⁴Oles Honchar Dnipropetrovsk National University, Dept Biochemistry and Biophysics, Dnipropetrovsk, Ukraine
⁵Bogomoletz Institute of Physiology, Dept Cytology, Kiev, Ukraine
⁶Vasyl Stefanyk Prycarpathian National University, Dept Biochemistry and Biotechnology, Ivano-Frankivsk, Ukraine
⁷Institute of Biochemistry of Biologically Active Compounds, Dept Biochemical Pharmacology, Grodno, Belarus
⁸Perugia University, Dept Agricultural Sciences and Animal Nutrition, Perugia, Italy

**Objectives and study:** The pre-term porcine model which mimics human neonates of >30 weeks of gestational age is used to study the gut and lungs development. (Sangild et al, 2013; Merwe et al, 2014). The key similarities between preterm piglets and preterm human infants include their size, the immaturity of the gastrointestinal tract, as well as the impaired respiratory, nutritional, immunological and metabolic status after birth. It is well-known that the absorption of both fat and protein in newborns, especially preterm neonates formula fed, is not optimal due to the lack of pancreatic enzymes. Formula producers are trying to mimic mother’s milk, however, all formulas are missing lipase presented obviously in human mother milk. An adequate animal model for longer term enteral feeding of preterm neonates, which can also be used to test new formulas, is lacking. Thus, the main aim of study was to develop a preterm porcine model that can be used over a longer period of time to test the efficiency of enteral feeding with regular and pre-hydrolysed formulas via gastric port of the piglets.

**Methods:** 16 male and female piglets from 2 litters were born by Caesarean section, 7 days before full gestation (115 days) that mimic human neonates of approximately 32 weeks gestational age. In order to prevent infection as well as ensure proper brain/behaviour development (Pierzynowski et al, 2014), piglets were infused with pig immunoglobulins via umbilical vessel than orogastric tubes were inserted for the formula feeding. Twenty-four hours later the orogastric tubes were removed and specially designed gastric port catheters (Silastic, Laboratory Tubing 508-002) were inserted under iso-fluranaesthesia. During the same surgical procedure jugular venous catheters (Silastic, Laboratory Tubing 508-001) were also inserted for blood sampling and infusions. After surgery all piglets were fed parentally for 6 hours with 0.9% NaCl and 10% glucose, than they were switched to the gastric tube feeding with the pre-term infant formula (Similac, Abott), at a dose of 5mL/kg every 1h (24xd) or 2h (12xd). Three days following surgery the formula volume was increased by 5%/d and than increased by 5% each second day to adjust for the body weight gain. Piglet’s body weigh was measured daily from birth.

**Results:** Four days after surgery a mean body weight gain of 22.6g/day from an initial of 1144.7g (SD 208.3) was observed, indicating good nutrient absorption. At the same time the piglets also started passing stools, which is suggestive of normal gut motility. The piglets were playful and alert. Frequent feeding (24xd) with small volumes was found to be the best for the piglets, based on their behaviour after feeding. Some piglets tolerated better than others 2h feeding intervals with bigger volumes. One piglet died after switching to 2 h feeding interval with volume (10 mL/kg every 2h). At the abduction stomach atonia was found.
Conclusion: The feeding of formula via gastric tube/ports was well tolerated. The piglets did not vomit or had diarrhoea. They were alert and active between the feeding intervals. This new pre-term porcine model which mimics the pre-term human neonates on enteral feeding can help in the development of novel infant formulas with hydrolysed nutrients and other additional supplements for improved growth and development.

Disclosure of interest: None Declared.
**NUTRITION: Neonatal and infant nutrition**

N-P-111

**Importance of accumulated protein intake for growth rate improvement**

Masahiko Murase¹, Kozue Kobayashi², Manabu Suzuki¹, Nobuo Ooyama², Yuuya Nakano², Tokuo Miyazawa², Kazuo Itabashi²

¹Showa University, Pediatrics, Tokyo, Japan
²Showa University, Tokyo, Japan

**Objectives and study:** Commercially prepared fortifier added human milk to meet the nutritional requirements of very low birth weight infants (VLBWI). However, postnatal growth rates for VLBWI have a wide variation despite fortification. Since the nutritional content of human milk varies with the duration of lactation and between individuals, each VLBWI could be receiving a different accumulative level of human milk nutrition.

We conducted this study to confirm the relationship between accumulative human milk nutrition content and growth rate.

**Methods:** This retrospective study was conducted at the neonatal intensive care unit of Showa University Hospital and was approved by the Showa University ethical committee. We extracted medical record data for VLBWI who were single births and exclusively fed on human milk from June 2010 to March 2015. The analysis of human milk contents were initiated within 14 days postpartum using a Human Milk Analyzer (HMA, Miris, Sweden). We calculated the standard deviation (SD) of the VLBWI using the Japanese neonatal anthropometric chart. Growth rates were estimated using SD changes from the minimal SD to 36 weeks CA (ΔSD). Single regression analysis was used to examine the relationship between ΔSD and accumulated protein and energy intake. We performed multiple linear regressions adjusted for chronic lung disease and ligation of patent ductus arterious.

**Results:** Twenty three VLBWI were enrolled this study, and their characteristics are shown in Table. Accumulated protein and energy intakes were correlated with ΔSD ($r^2 = 0.611$, $p < 0.01$), and ($r^2 = 0.38$, $p < 0.01$), respectively. Multiple linear regression analyses revealed that there were significant correlations between ΔSD and accumulated protein intake ($p < 0.01$), but there were no correlations between ΔSD and accumulated energy intake ($p = 0.11$). These results indicated that 41 g/kg of protein intake was required to improve one SD.

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>Median (interquartile range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight (g)</td>
<td>1117 (952, 1312)</td>
</tr>
<tr>
<td>Gestational age (weeks)</td>
<td>29.4 (28.4, 30.5)</td>
</tr>
<tr>
<td>SD at birth</td>
<td>-0.7 (-1.5, -0.3)</td>
</tr>
<tr>
<td>Minimum SD during NICU hospitalization</td>
<td>-2.0 (-2.7, -1.7)</td>
</tr>
<tr>
<td>The day of minimum SD (day postpartum)</td>
<td>8 (6, 15)</td>
</tr>
<tr>
<td>Human milk protein content (g/dL)</td>
<td>1.1 (0.9, 1.3)</td>
</tr>
<tr>
<td>Human milk energy content (Kcal/dL)</td>
<td>61 (57, 65)</td>
</tr>
</tbody>
</table>

**Conclusion:** Accumulated protein intake has a positive relationship with ΔSD. Since the protein content of breast milk varies greatly, the individual fortification of human milk is recommended to improve the protein intake.

**Disclosure of interest:** The authors have no conflict of interests to declare in this study.
Dairy fat for infant formula: history and new evaluation of impact on tissue DHA levels in animals

Bernadette Delplanque¹

¹Nmpa, Cnps, Université Paris-Sud, Orsay, France

Background: Till the 20th century, full fat cow’s milk has been used to manufacture formulas to feed infant when breast feeding was not possible. Later, infant formulas were based on cow’s milk proteins but were associated to pure vegetal oil blends as lipid providers. This became the usual rule in most countries. Recommendations for infant formulas had been established on the basis of human breast milk composition, still considered as the gold standard.

However, infant formulas based on blends of vegetal oils mimic quite well the 20th century human breast milk composition in terms of essential fatty acids, but, they missed numerous other components of human milk such as cholesterol, fatty acids, triglycerides and globule fat structure. From this point of view, cow’s milk fat is naturally closer to human breast milk fat composition than vegetal blends.

Objectives: In an attempt to validate the re-introduction of milk fat in infant formulas, we recently studied, in an animal model, the impact of partial substitution of vegetal oils by dairy fat on lipid composition of blood and organs.

Methods: Formulas tested in rats complied with the lipid recommendations in use for infant formula: equivalent levels of palmitic acid (15%-25%), linoleic acid (LA15% -12%) and linolenic acid (ALA1.7%-2.3%). Three groups of young rats were fed for 6 weeks after weaning, with diets providing either1.7% of ALA (from rapeseed source), blended with (i) anhydrous dairy fat, (ii) palm oil or (iii) an increase to 2.3% of ALA of the diet blended with anhydrous dairy fat. Plasma, RBC and brain FA were determined by gas chromatography at weaning and after the post-weaning diets

Results: It appeared that, compared to pure vegetal blends, the use of dairy fat was beneficial in terms of Long-Chains-n-3 PUFA (LC-n-3) status of young rats. We observed in blood an increased amount of all LC-n-3, in brain an increase of docosahexaenoic-acid (DHA), and interestingly the brain DHA level was correlated with the blood n3-docosapentaenoic acid (DPAn-3) level. We also verified with dairy fat blends that an increase of dietary ALA from 1.7% to 2.3% (reduction of LA/ALA ratio from 10 to 5), induced a further increase of brain DHA levels in this model.

Conclusions: Dairy fat presents naturally some similarities with human breast milk, which are not simply available with pure vegetal blends, and may explain in part these effects. Consequently, the use of dairy fat in infant formulas should be reconsidered, as well as the absolute amount of polyunsaturated LA and ALA.

Disclosure of interest: B Delplanque Partially granted by Lactalis
Use of vitamin D and probiotics supplements in young children with genetic risk of type 1 diabetes

Jimin Yang1, Roy Tamura1, Carin Andrén Aronsson2, Katherine Silvis3, Anne Riikonen4, Nicole Frank5, Gesa Joslowski6, Christiane Winkler6, Ulla Uusitalo1, Jill Norris7, Suvi Virtanen4

1Health Informatics Institute, Morsani College of Medicine, University of South Florida, Tampa, United States
2Department of Clinical Sciences, Lund University, Malmö, Sweden
3Medical College of Georgia, Georgia Regents University, Augusta, United States
4National Institute for Health and Welfare; University of Tampere, Helsinki; Tampere, Finland
5Barbara Davis Center for Childhood Diabetes, University of Colorado School of Medicine, Aurora, United States
6Institute of Diabetes Research, Helmholtz Zentrum München and Forschergruppe Diabetes, Klinikum Rechts der Isar, Technische Universität München and Forschergruppe Diabetes e.V., Munich, Germany
7Department of Epidemiology, University of Colorado Denver, Colorado School of Public Health, Aurora, United States

Objectives and study: Vitamin D and probiotics have been associated with the risk of type 1 diabetes and islet autoimmunity (IA). This study aimed to document the prevalence of and factors associated with vitamin D and probiotics supplementation among young children with genetic risk of type 1 diabetes and whether the use changed after parents received notification of the development of IA in their children.

Methods: Use of dietary supplements between 0-2 years of age was reported every three months in 8674 at-risk children who participated in The Environmental Determinants of Diabetes in the Young (TEDDY) study. Logistic regression identified factors predicting supplement use. McNemar test was used to compare usage among children with IA before and after their parents were notified of IA development.

Results: Most of the children received at least one single or multivitamin/mineral (MVM) supplements during the first two years of life, as indicated in data as of June 30, 2015. More than 97% in Finland, Germany and Sweden, and 50% of the US children received supplemental vitamin D. Vitamin D supplementation was started in the first year of life in >90% of the users and at least half of the users in every country took vitamin D longer than a year. The use of probiotics supplements varied from 6% in the US to 7% in Germany, 15% in Sweden, and 60% in Finland. Probiotics supplementation was initiated within the first year of life in >80% of the users and lasted longer than one year in more than half of the users. The average total duration of consumption over the first two years was 81±32 weeks for vitamin D and 61±36 weeks for probiotics across all countries. Vitamin D supplementation was associated with being the first child (OR=1.26, 95% CI 1.08, 1.46), longer duration of breastfeeding (OR=1.06, 95% CI 1.05, 1.07), and three maternal factors (older age (OR=1.03, 95% CI 1.01, 1.04), higher education level (OR=1.66, 95% CI 1.34, 2.06), and no smoking during pregnancy (OR=0.77, 95% CI 0.60, 0.99)). Probiotics supplementation was associated with being the first child (OR=1.56, 95% CI 1.36, 1.79), longer duration of breastfeeding (OR=1.02, 95% CI 1.01, 1.03), shorter gestational age (OR=0.95, 95% CI 0.92, 0.99), and three maternal factors (older age (OR=1.03, 95% CI 1.01, 1.04), higher education level (OR=1.47, 95% CI 1.21, 1.78), and no smoking during pregnancy (OR=0.70, 95% CI 0.56, 0.87)). The use of probiotics supplements, but not the vitamin D supplements, increased slightly after parents received IA notification (McNemar test p=0.008).

Conclusion: The use of vitamin D supplements was common among 0-2 year old participants in every TEDDY country. The prevalence of probiotics supplementation varied across the countries. Most of the vitamin D and probiotics users started taking supplements in the first year of life. Several demographic and behavioral factors were associated with vitamin D and probiotics supplementation. Parental notification of IA development appeared to affect only the use of probiotics supplements.

Disclosure of interest: None declared.
Tolerance and growth in children with cow’s milk allergy fed a thickened extensively hydrolyzed casein-based formula

Christophe Dupont1, Bradatan Elena2, Soulaines Pascale1, Nocerino Rita3, Berni Canani Roberto3

1Necker Children’s Hospital, Pediatric Gastroenterology, Hepatology and Nutrition Department, Paris, France
2Regional Hospital, Department of Pediatrics, Namur, Belgium
3University of Naples “federico II”, Department of Translational Medicine – Pediatric Section, Naples, Italy

Objectives and study: In case of cow’s milk allergy (CMA), pediatric guidelines recommend for children the use of extensively hydrolyzed formulas (eHFs) as elimination diet. According to the American Academy of Pediatrics, the hypoallergenicity of each specific eHF should be tested in subjects with CMA.

Methods: A prospective, multicenter trial was performed to assess the tolerance/hypoallergenicity of a thickened casein-based eHF (eHCF, “Allernova AR®”, Novalac / United Pharmaceuticals, France) in infants aged <12 months with CMA proven by a double-blind placebo-controlled food challenge. Its efficacy, measured through allergy symptoms monitoring and Cow’s Milk-related Symptom Score (CoMiSS) calculation, and safety were evaluated during a 4-month feeding period. Growth z-scores were computed based on WHO anthropometric data.

Results: 30 infants (mean age: 4.8±3.0 months) with CMA proven by a DBPCFC tolerated the eHCF during the 4-month study. The CoMiSS, crying and regurgitation scores significantly decreased by 4.2±4.0, 0.9 (±1.2) and 0.7±1.1 respectively, after 14 days of feeding (p<0.001). The Scoring Atopic Dermatitis index, of 33.2 ±14.8 at inclusion in 9 patients, significantly decreased by 15.5±6.7 and 21.1±11.2, after 14 and 45 days of feeding, respectively (p<0.001). The percentage of infants having normal stool consistency (soft or formed stools) significantly improved from 66.7% (20/30) at inclusion to 90.0% (27/30) after 14 days of feeding (p=0.020). The growth z-scores, negative at study inclusion, significantly improved over the 4-month study. No adverse event was related to the eHCF.

Conclusion: The thickened eHCF was tolerated by more than 90% of included allergic infants with 95% confidence interval and can therefore be considered as hypoallergenic in accordance with current guidelines. The improvement of growth indices and absence of related adverse events confirmed its safety. Results of this trial back the use of the tested thickened eHCF as an efficient and safe alternative in children with CMA.

Disclosure of interest: The authors (or their institutions) received honoraria from United Pharmaceuticals, Paris, France for their work in this study. This study was funded by United Pharmaceuticals, Paris, France.
Microbiota can be affected by the lipid composition of infant formulas

Isabelle Le Huërou-Luron¹, Ferret-Bernard Stephanie², Le Bourgot Cindy², Bouzerzour Karima², Claire Bourlieu³, Olivia Ménard⁴, Carton Thomas⁵, Cuinet Isabelle⁶, Cécile Bonhomme⁷, Pascale le Ruyet⁸, Didier Dupont⁴

¹Inra, Human Nutrition Division, Saint-Gilles, France
²Inra, Nutrition & Digestive, Nervous and Behavioural Adaptations, Saint-Gilles, France
³Umr Stlo 1253 Inra-Agrocampus Ouest, Bioactivity and Nutrition, Rennes, France
⁴Inra - Agrocampus Ouest, Umr1253 Science et Technologie du Lait et de L'œuf, Rennes, France
⁵Biofortis, Nantes, France
⁶Lactalis, Research and Development, Retiers, France
⁷Lactalis, Nutrition, Torcé, France
⁸Lactalis R&d, Nutrition, Retiers, France

Objectives and study: Microbiota is known to be positively influenced by breastfeeding. Differences in the quality and structure of dietary lipids between maternal milk and infant formulas may contribute to microbiota modification. Incorporation of milk fat in infant formulas is a promising way to get closer to the composition and structure of human milk fat globules. However, little is known on the consequences of such addition on gut microbiota and physiology.

Methods: Two formulas were processed containing either vegetable lipids (VL) or a mixture of milk and vegetable lipids (ML) including milk fat globule membrane fragments. Formulas were automatically distributed to newborn piglets until 28 days of age. Feces and ileal tissue were sampled at slaughter at 28 days. The bacterial composition expressed as the percentage of assigned sequences at each taxonomic level as well as Shannon diversity and Chao richness indices were determined. Weight and mucosal density of empty ileum were measured. Ileal barrier function was evaluated ex vivo using Ussing chamber. Mononuclear immune cells isolated from mesenteric lymph nodes were cultured to evaluate their secretory cytokine profiles.

Results: No difference in bacterial diversity indices was observed between VL and ML groups. The analysis of dominant phyla revealed a greater proportion of Proteobacteria in ML than in VL microbiota (13.4 % vs. 5.4 % respectively) at the expense of Firmicutes that were reduced L (62.1 % vs. 74.5 % respectively). No difference in sub-dominant phyla was significant. Abundance of five bacterial families and genus was modulated with the dietary treatment. Increased Porphyromonadaceae family (Bacteroides phylum) consisted of a higher proportion of Parabacteroides, and increased Enterobacteriaceae family (Proteobacteria phylum) consisted of greater number of Escherichia/Shigella and Klebsiella genus in feces of ML piglets compared to VL piglets. In addition, Clostridiales Family XIII and Veillonellaceae family explained the decrease of Firmicutes in ML piglets. Interestingly, significant correlations between microbiota composition and gut physiological and immunological parameters were highlighted. Relative abundance of Klebsiella and Parabacteroides was negatively correlated with ileal pH (rho value = -0.56, P<0.01 and -0.45, P<0.04, respectively). Relative Escherichia/Shigella and Klebsiella abundances were correlated with the higher mucosal density observed in ML ileum (rho value = 0.44, P<0.03). Those bacteria were also correlated with IL-10 cytokine secretion of immune cells (rho value = -0.49, P<0.02, -0.45, P<0.03, respectively).

Conclusion: Incorporation of milk fat in infant formula changed the microbiota composition in feces. These changes were associated with modifications in ileal physiology and secretory activity of mesenteric lymph node immune cells. Long-term effects of these early physiological and bacterial modifications on health warrant further investigations.

Disclosure of interest: This project was funded by Lactalis.
Feeding of very preterm infants: the results application of modern standardized approaches in the practices

Marina Narogan 1, Irina Ryumina 1, Elena Grosheva 1

1 Scientific Center for Obstetrics, Gynecology and Perinatology Named after Academician VI Kulakov, Pathology Newborn and Premature Babies, Moscow, Russian Federation

Objectives and study: The definition of strategies of feeding of preterm infants with very low and extremely low birth weight (VLBW and ELBV) is a very important issue due to the fact that their application reduces the incidence of necrotizing enterocolitis (NEC) and the postnatal growth retardation in this group of patients. Since 2015 the Federal Perinatal Center has adopted new national clinical guidelines for feeding of infants with VLBW and ELBW. From the 1st day of life the dose of parenteral introduction of amino acids was 3 g/kg/day, of fats – 2-3 g/kg/day, of glucose – 5-6 mg/kg/min. The priority was an early enteral nutrition with breast milk/colostrum. The volume of enteral nutrition was increased by 20-30 ml/kg/day in infants with VLBW and by 10-20 ml/kg day in infants with ELBW. The objective is to evaluate the clinical effectiveness of the new standardized approaches to feeding of very preterm infants.

Methods: The infants born before 32 weeks of gestation and with weight less than 1500 g were included in the study. The babies with diseases requiring surgery not associated with necrotizing enterocolitis (NEC), genetic diseases and severe hemolytic diseases were excluded. Group I included 52 infants born in 2015 (27 - with VLBW, 25 - with ELBW), group II included 45 infants born in 2014 (26 - with VLBW, 19 - with ELBW). The gestational age was 28.8 ± 0.2 (Group I) and 29.3 ± 0.3 weeks (Group II), birth weight 1117 ± 41 g and 1134 ± 42 g, respectively.

Results: In 2015 the start with enteral nutrition was earlier, the median was 7.5 hours (3.5-23) versus 12 hours (6-48) in 2014 (p<0.05). The dose of 150 ml/kg/day of enteral nutrition also was reached significantly earlier: 12 days (6-48) in group I versus 17 days (13-44) - in group II (p<0.05). In 2015 NEC 1-2 according to Bell’s stages developed in 15% of cases, NEC 3 – 0%. In 2014 the incidence of NEC was 1.8 times higher: NEC 1-2 - in 24% of cases, NEC 3 – in 2% (p>0.05). But the frequency of gastrointestinal dysfunction was 54% in the group I and 31% in group II (p<0.05).

The majority of babies (96%) lost less than 15% of initial birth weight in both groups. Recovery of the birth weight up to 14 days occurred slightly more often in 2015 (96%) than in 2014 (89%). The frequency of formula feeding was 23% in 2015 and 27% in 2014. However "lack of milk" was not observed in 2015, whereas this reason for cessation of lactation was registered in 16% of cases in 2014. The feeding only with fortified breast milk (without formula) before discharge was 2.5 times higher in 2015 (27% vs. 11%, p<0.05). Significant improvement of postnatal growth was observed in 2015 in infants with VLBW, who did not have intrauterine growth restriction (Table.)

Table: The number of infants with weight below 10th percentile at 36 weeks of postmenstrual age, (%).

<table>
<thead>
<tr>
<th>Birth weight</th>
<th>2014</th>
<th>2015</th>
</tr>
</thead>
<tbody>
<tr>
<td>small for gestational age infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 1000 g</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>appropriate for gestational age infants</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 750 g</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>750-999 g</td>
<td>63</td>
<td>64</td>
</tr>
<tr>
<td>1000-1499 g</td>
<td>54</td>
<td>15*</td>
</tr>
</tbody>
</table>

* p<0.05
**Conclusion:** The application of current standardized protocols of feeding very preterm infants based on early introduction of nutrients for parenteral nutrition and early start of enteral nutrition with priority breast feeding allows to achieve earlier full enteral nutrition, to reduce the incidence of NEC, to increase the amount of breastfeed infants and to improve their postnatal growth. The problem of gastrointestinal dysfunction of babies with VLBW and ELBW is still very actual and requires further studies.

**Disclosure of interest:** None Declared
Applying TWORKAM methodology among medical staff to gain new skills of premature newborns' oral feeding

Ewa Winnicka¹, Joanna Smogorzewska², Grzegorz Szumski²

¹The Children’s Memorial Health Institute, Department of Gastroenterology, Hepatology, Nutrition Disorders and Pediatric, Warsaw, Poland
²The Maria Grzegorzewska Academy of Special Education, Warsaw, Poland

Objectives and study: Preterm newborns require special support to develop oral feeding function. They are at higher risk of feeding disorders due to their immaturity. Special technique increases feeding efficacy and safety, prevents deterioration of feeding disorder symptoms and supports infants' development. Unfortunately, medical knowledge is not sufficient in this field. It is widely believed that infants’ feeding requires neither special skills nor certain mental predispositions. This opinion is incorrect, caused mainly by ignorance and cultural beliefs. This may result in refusing new knowledge and sustaining old working schemes, which are insufficient for specific preterm newborns needs. Based on these deliberations, trainings should enable both gaining new skills and creating transformative learning, which changes thinking and perceptive schemes concerning preterm newborns oral feeding techniques and role of person who feeds premature newborns. The aim of this study is to verify the effectiveness of training based on transformative learning assumptions (TWORKAM methodology).

Methods: 31 nurses in 5 different Neonatal Intensive Care Units in Poland participated in trainings according to TWORKAM methodology prepared special for this study. These trainings were focused on changing old habits and cognitive schemes concerning preterm newborn feeding and developing feeding skills such as: working with infant’s body, selecting feeding accessories, a selection of oral control and dynamic stabilization and recognizing the signs of baby's readiness to start and to finish feeding. The level of transformative learning and feeding skills of nurses were examined at the beginning and at the end of training. The level of transformative learning was determined by 10 Precursor Steps of Transformative Learning⁴. The level of feeding skills was assessed by a checklist prepared for this study. Results were analyzed with ANOVA.

Results: Analysis has shown a significant difference in the level of transformative learning between pre- and posttest: F(3,90)=13.96; p<0.0001; $\eta^2=0.32$. Significant differences were also identified in the case of the level of feeding skills: working with infant body $F(1,28)=219.73; \ p<0.001, \ h^2=0.89$; selecting feeding accessories $F(1,28)=35.88; \ p<0.001, \ h^2=0.64$; a selection of oral control and dynamic stabilization $F(1,28)=232.96; \ p<0.001, \ h^2=0.89$, recognizing the signs of baby's readiness to start and to finish feeding $F(1,28)=183.74; \ p<0.001, \ h^2=0.87$.

Conclusion: Training based on TWORKAM methodology is effective in developing transformative learning and in gaining new skills in preterm newborns’ feeding.

Disclosure of interest: Non Declared
Early life exposure of the developing fetus and newborn to the mycotoxin deoxynivalenol

Saskia Braber1, Prescilla Jeurink2, Suzan Thijssen1, Arash Alizadeh1, Johanna Fink-Gremmels1, Johan Garssen3, Astrid Hogenkamp1

1Utrecht University, Utrecht, Netherlands
2Nutricia Research, Utrecht, Netherlands
3Utrecht University & Nutricia Research, Utrecht, Netherlands

Objectives and study: It is obvious that early life exposure to detrimental compounds can have significant effects on development. To what extent any compound can be deemed detrimental is a matter of impact on the entire course of growth and differentiation of organ systems. We have previously shown that the trichothecene deoxynivalenol (DON), a fungal metabolite found in grain-based human diets, acts as a specific disruptor of the intestinal tight junction network and hence might contribute to gastrointestinal disorders. As food antigens are transmitted through the placenta and breastmilk, we hypothesized that the developing fetus and/or newborn would be exposed to DON through these pathways, resulting in a negative impact on gastrointestinal development in the offspring. This, in turn, could lead to increased susceptibility to develop gastrointestinal disorders, such as food allergies.

Methods: Upon arrival, C3H/HeOuJ mice were fed the control AIN93G diet and after two weeks of acclimatization, breeding pairs were formed. Upon assessment of a sperm plug, females were either kept on the control diet or a control diet containing 10 mg DON/kg feed, until 15 days after delivery of the pups. The offspring of the control and the DON-treated dams were divided into three groups (1) sham-group, (2) oral tolerance-group and (3) food allergy group. Mice in group 1 were given oral gavages with PBS, mice in group 2 received PBS with 40 mg/ml OVA and group 3 was given 40 mg/ml OVA and 20 µg/ml Cholera toxin (CT). After weaning, offspring were fed the control diet and were sensitized orally once a week for four weeks with OVA + CT. Acute allergic skin responses, shock symptoms, body temperature, and specific plasma immunoglobulins were measured upon intradermal ovalbumin challenge. Th1, Th2, Th17 and regulatory T cells were analyzed with use of flow cytometric analysis in spleen and mesenteric lymph nodes.

Results: Increased intestinal permeability in the dams as a result of DON exposure was observed by increased translocation of FITC dextran across the intestinal interfaces. However, in the offspring there were no significant differences in the acute allergic skin responses, and body temperature of the mice did not appear to be significantly affected by maternal exposure to DON. Flow cytometric analysis of the mesenteric lymph nodes and the spleen revealed no clear effect of maternal DON exposure on the effector responses in the offspring. OVA-specific and total immunoglobulin levels were similar between offspring of control dams and DON-treated dams.

Conclusion: Our study suggests that maternal DON exposure in the current experimental setup does not affect the outcome of the OVA-specific food allergy in the offspring. It is possible that the DON-content of the diet was not sufficient to affect immune development in the offspring. Current research focuses on early life exposure of the developing fetus and/or newborn to different detrimental compounds in the maternal diet.

Disclosure of interest: None Declared
**Objectives and study:** It’s important for the neurodevelopmental of fetus that pregnant women consume adequate amounts of essential fatty acids (EFAs). Access to the Argentine population foods rich in these fatty acids is reduced both by habits as cost. Objective: To determine the consumption of food reach in EFAs, in the third trimester of pregnancy and the reasons for not eating fish and / or supplements.

**Methods:** Descriptive observational transversal study of 108 pregnant women attending control at the Private Hospital of the City of Córdoba, Argentina. The level of consumption of AGE was studied during the last trimester of pregnancy determined by a quantitative questionnaire. A descriptive analysis of the data was performed. Continuous variables were described in ± SD and expressed in %.

**Results:** The average age of women was 31.6 and its weight at 8 months of pregnancy was 68kg. As for supplements, 99% reported not eating. The fish they consume daily were: hake and mackerel in oil 3%, the most consumed weekly natural tuna (16%). Among the consumed 2 or 3 times a month and include shrimp fried calamari (26%). The seeds are consumed in greater amounts are daily linen (7%), chia (6%) and quinoa (5%). Half of pregnant consumed daily sunflower oil and 20 and 11% respectively, corn oil and olive. The reasons for the low consumption of fish are not pleasing odor (19%) and taste (17%) and not always available fresh (13%) is located.

**Conclusion:** The low consumption of food sources of EFAs is vital for the health team to conduct awareness campaigns and health education and improve the quality of the diet of pregnant and promote proper growth and development in the fetus.

**Disclosure of interest:** None Declared.
**NUTRITION: Neonatal and infant nutrition**

Amino acids’ $^{15}$N natural isotopic abundance in the umbilical artery and vein and in the venous blood of the mother at birth

Arnaud De Luca$^1$, Kuster Alice$^2$, Illa Tea$^3$, Dominique Darmaun$^4$, Jean-Christophe Roze$^5$, Richard Robins$^3$, Regis Hankard$^6$

$^1$Inserm U1069, Tours, France
$^2$Nantes University Hospital, Intensive Care Unit, Nantes, France
$^3$Umr Cnrs 6230, Univ. Nantes, Nantes, France
$^4$Nantes University, Inra, Umr 1280, Imad, Crnh Ouest, Nantes, France
$^5$Chu Nantes, Intensive Care Unit, Nantes, France
$^6$Inserm U1069, University of Tours, Tours, France

**Objectives and study:** We have shown that $^{15}$N natural isotopic abundance (NIA) was higher in infant’s hair than in their mothers at birth. This occurred although the primary pool of amino acids was the same, that of the mother. Present study aimed at measuring $^{15}$N NIA on the venous and arterial side of the umbilical cord and in the venous plasma of the mother at birth.

**Methods:** Seven mother and infant dyads with enough remaining material to get measurements on the 3 sites were selected from a larger study NCT00607061. Four were premature delivery. Plasma proteins were hydrolyzed and amino acids were separated using gas chromatography. NIA was measured using isotope ratio measurement by mass spectrometry. Two ways ANOVA with site, term and amino acid as fixed effects.

**Results:** Full model found a significant effect of sampling site ($P=0.02$) and amino acid ($P<10^{-5}$) on $^{15}$N NIA. Gestational age had no effect on $^{15}$N NIA. $^{15}$N NIA was 0.73 ‰ higher (10.40±0.78 vs. 9.68±0.80 ‰, $P=0.01$) in maternal venous plasma than in the arterial side of the umbilical cord and no difference between venous and arterial side of the umbilical cord, respectively 9.68±0.80 vs. 9.88±0.81 ‰. Non-essential, branched chain and transaminable amino acids had a higher $^{15}$N NIA with no interaction with site and gestational age.

**Conclusion:** This is the first study reporting simultaneously amino acids $^{15}$N NIA in mother and on the arterial and venous side of the umbilical cord in infants born at term and prematurely. Results suggest an uptake of $^{15}$N by the fetal-placental unit. A trophic effect, i.e. a change in $^{15}$N abundance between the alimentary source and proteins, may occur during the protein anabolic processes.

**Disclosure of interest:**
None Declared for any of the authors
Iron status at age 6 months in Colombian infants exclusively breast-fed for 4-6 versus 6 months

Gilma Olaya1, Margaret Lawson2, Mary Fewtrell2

1Nutrition and Biochemistry Department, Faculty of Sciences, Pontificia Universidad Javariana, Bogota, Colombia
2Ucl Institute of Child Health, Childhood Nutrition Research Centre, London, United Kingdom

Objectives and study: Prolonged exclusive breastfeeding (EBF) protects against infection but may increase the risk of iron deficiency/anaemia in vulnerable infants. The aim of this study was to compare iron status at 6 months of age in infants exclusively breast-fed (EBF) for 4-6 versus 6 months (EBF4-6 versus EBF6), from deprived areas of Bogota, Colombia; and to determine predictors of iron status.

Methods: Healthy term infants (birth weight>2500g) EBF for at least 4 months were recruited from baby clinics. At 6 months, infant feeding was recorded using a semi-quantitative food frequency questionnaire (FFQ) and a 24 hour recall. EBF was defined as the infant having received only breast milk without other food, liquids or supplements. Anthropometry was performed and results converted to SD scores using WHO 2006 growth standard data. Blood was obtained for haemoglobin (Hb) and ferritin (SF). Cut-offs recommended by WHO were used. Anaemia was defined as Hb<11g/dL and iron depletion as serum ferritin (SF)<12μg/L. Infants were grouped by the duration of EBF: 4-6 months (EBF4-6) or ≥6 months EBF (EBF6) and indicators of iron status and growth were compared between groups using t-test, Mann-Whitney or chi-square test. Secondary analyses explored predictors of iron status at 6 months, adjusting for potential confounders.

Results: 108 infants (54% boys) were recruited; 46% EBF for 4-6mo and 54% EBF at 6mo. There was no significant difference between groups in gestational age, type of delivery, birth weight or socioeconomic characteristics. EBF6 mothers were significantly older whilst there were a significantly higher proportion of boys in the EBF4-6 group. EBF6 infants had a significantly higher number of breastfeeds/day (7 (2) versus 6 (2), p=0.02) and higher estimated breast milk intake/day (830 ml (143) versus 714 ml (136), p<0.001) than EBF4-6 infants. Overall, 20% of infants had Hb<11g/l and iron depletion as serum ferritin (SF)<12μg/L. Infants were grouped by the duration of EBF: 4-6 months (EBF4-6) or ≥6 months EBF (EBF6) and indicators of iron status and growth were compared between groups using t-test, Mann-Whitney or chi-square test. Secondary analyses explored predictors of iron status at 6 months, adjusting for potential confounders.

Conclusion: Poor iron status and anaemia were common in this population despite normal birth weight but were not affected by EBF for 4 versus 6 months. Modifiable predictors in this population were the intake of cows’ milk, highlighting the need to strengthen the recommendation to avoid cow’s milk in the first year of life and to make sure this message is delivered before 6 months; and caesarean delivery, highlighting the potential importance of the timing of cord clamping.

Disclosure of interest: The authors have no conflict of interest to declare with regard to this study.
Frequency of feeding problems in infants with congenital diaphragmatic hernia

Alexandra Li¹, Kate Tavener², Kamal Ali¹, Ann Hickey³

¹King's College Hospital, Paediatrics, London, United Kingdom
²King's College Hospital, Nutrition and Dietetics, London, United Kingdom
³King’s College Hospital, Neon, London, United Kingdom

Objectives and study: Feeding difficulties are observed in infants following congenital diaphragmatic hernia (CDH) repair. These may persist beyond the neonatal period and often relate to reflux, contributing to respiratory morbidity. Fetoscopic tracheal occlusion (FETO) is an antenatal intervention offered within our centre to infants with a poor fetal prognosis. This study aimed to describe the frequency and severity of feeding difficulties observed within this population during the first two years of life and to investigate whether antenatal FETO treatment influenced feeding outcomes.

Methods: Infants born between January 2009 and June 2014 in a single surgical referral centre in the UK, who survived to discharge, were included in the study. Electronic medical notes were reviewed retrospectively to obtain data on gestation, whether the infant underwent FETO and the type of repair performed. Route of feeding (oral/nasogastric/gastrostomy) at 6, 12, 18 and 24 months of age was collated. Data on current feeding behaviour was collected using the Behavioural Pediatrics Feeding Assessment tool (BPFAS) (Crist et al, 2001). A frequency score of >84 correlates with maladaptive feeding behaviour. A problem score of >9 indicates that this behaviour is perceived negatively by parents. Parents were interviewed either when they attended clinic with their child or by telephone.

Results: 41 infants were included (63% male). Median gestational age at birth was 38.5 weeks (range 32.2-41.6 weeks). 41% underwent FETO antenatally. Gestational age was significantly lower in the FETO group (median 35.6 weeks vs 39.1 weeks, p<0.001). 54% underwent patch repair with the remaining 46% undergoing primary repair.

7 infants (17%) continued to require supplementary feeding via nasogastric or gastrostomy tube at 6 months of age (3 non-FETO, 4 FETO). One (FETO) infant required supplementary nasogastric tube feeding to be recommenced at 8 months of age due to poor weight gain. By 24 months, two infants continued to require supplementary feeding (one FETO, one non-FETO).

Parents of 25 (61%) participants completed the questionnaire. 36% (n=9) of this group had undergone FETO procedure. Median age at the time of questionnaire was 29 months (range 14-76 months). 24% (n=6) were classified as having a frequency score consistent with maladaptive feeding behaviours greater than the normative mean. 3 of these infants were on supplementary tube feeding at the time of the assessment. There was no significant difference in frequency scores between the FETO and non-FETO group. Median gestation for this subgroup was not significantly different from that of the group as a whole. In addition, 8% (n=2) of the above 6 parents interviewed scored higher than the normative mean for the problem score suggesting that they perceived their child’s feeding as challenging.

Conclusion: Our data supports the well-recognised occurrence of feeding problems post CDH repair but does not demonstrate an increased incidence in those problems in infants following antenatal FETO procedure. 24% of infants displayed a maladaptive feeding behaviour score greater than the normative mean, suggesting a significant behavioural component to morbidity that has previously been largely attributed to organic causes.

Disclosure of interest: None Declared
An innovative infant formula with large, phospholipid-coated lipid droplets supports an adequate growth in healthy, term infants


1Erasmus University Medical Centre/Sophia Children’s Hospital, Rotterdam, Netherlands
2Universitair Ziekenhuis, Brussel, Belgium
3Clinique et Maternité Sainte-Elisabeth, Namur, Belgium
4Albert Schweitzer Ziekenhuis, Dordrecht, Netherlands
5Kk Women’s and Children’s Hospital, Singapore, Singapore
6Centre Hospitalier Régional de la Citadelle, Liege, Belgium
7Algemeen Stedelijk Ziekenhuis, Aalst, Netherlands
8Amphia Ziekenhuis, Breda, Netherlands
9Isala Zwolle, Zwolle, Netherlands
10Nutricia Research, Utrecht, Netherlands

Objectives and study: Breastfeeding is the preferred nutrition for all term newborn infants. In case human milk feeding is not possible, human milk substitutes should provide nutritional and functional properties as close as possible to those of human milk. Lipid droplets in human milk are on average 4 μm in diameter and surrounded by a native biological phospholipid containing membrane. In contrast, infant formulae contain smaller lipid droplets (0.3 – 0.5 μm in diameter) without such natural membrane. An innovative infant formula has been developed containing large, phospholipid coated lipid droplets (NUTURIS®) with bovine milk phospholipids. The objective of the MERCURIUS study was to evaluate safety of this newly developed formula in infants compared to a standard formula and a breastfed reference group.

Methods: In a randomized, multi-country, double-blinded, prospective, controlled clinical trial, full formula-fed infants were enrolled up to 35 days of age and assigned to receive one of two formulas until 17 weeks of age: 1) CONTROL: a standard infant milk formula with 100% of its lipid moiety comprising of vegetable oils, or 2) NUTURIS®, an infant formula with larger phospholipid-coated lipid droplets (mode diameter of 3-5 μm; 1.6% milk phospholipids) and with 48% of its vegetable lipid moiety replaced by bovine milk fat. Apart from lipid quality, the formula compositions were identical (66 kcal, 1.3 g protein, 7.3 g carbohydrates and 3.4 g fat per 100 ml). A group of infants exclusively breastfed until at least 13 weeks of age served as reference. Safety was evaluated by equivalence analysis of weight gain per day during the intervention period (primary outcome) using equivalence margins of ± 0.5 SD within a predefined clinically relevant upper and lower margin of 3 and 5 g/d, respectively. Additionally, number and type of (serious) adverse events and other growth parameters (secondary outcomes) were monitored monthly.

Results: After enrollment, infants were allocated to CONTROL (n = 108) or NUTURIS group (n = 115) or were part of the breastfed reference group (n = 88). Equivalence of weight gain per day between formula groups was demonstrated, i.e. the difference in means for CONTROL vs. NUTURIS lay well within the pre-defined equivalence margins of ± 0.5 SD, in the per-protocol (PP) population (1.37 g/d; 90%CI [0.03; 2.71]) as well as the intention-to-treat (ITT) population. In addition, subgroup analyses of the PP population only including infants enrolled up to 14 days of age (n = 129), confirmed equivalence. The comparison to the breastfed reference group revealed equivalence in weight gain per day for the ITT populations in both formula groups and for the PP population of the NUTURIS group. The 90% CI of the difference in means of the CONTROL PP population compared to the breastfed reference only just crossed the upper equivalence margin. Secondary outcomes, including other growth parameters and number, severity or type of (serious) adverse events, were not different between the formula groups.
**Conclusion:** This study in newborn infants suggests that a newly developed infant formula comprising large, phospholipid coated lipid droplets (NUTURIS®) is safe and supports an adequate growth.

Growth and nutritional sequelae in infants with congenital diaphragmatic hernia

Alexandra Li¹, Kate Tavener², Kamal Ali¹, Ann Hickey³

¹King's College Hospital, Paediatrics, London, United Kingdom
²King's College Hospital, Nutrition and Dietetics, London, United Kingdom
³King's College Hospital, Neon, London, United Kingdom

Objectives and study: Following congenital diaphragmatic hernia (CDH), infants can experience faltering growth and feeding difficulties which contribute to overall morbidity. Fetoscopic tracheal occlusion (FETO) is an antenatal procedure offered within our centre to infants with poor fetal prognosis. This study aimed to describe long-term nutritional outcomes in infants following CDH repair and to compare the outcomes of those who underwent antenatal FETO versus those who did not.

Methods: Infants born between January 2009 and June 2014 in a single surgical referral centre in the UK, who survived to discharge, were included in the study. Electronic medical notes were reviewed retrospectively to obtain data on gestation, FETO intervention and the type of repair performed. Weight Z-score, feeding method (oral/nasogastric/gastrostomy) and use of anti-reflux medications were also collected at birth, discharge, and then at 6, 12, 18 and 24 months of age.

Results: 41 infants were included (63% male). Median gestational age at birth was 38.5 weeks (range 32.2-41.6 weeks). 41% underwent FETO procedure antenatally. Gestational age was significantly lower in the FETO group (median 35.6 weeks vs 39.1 weeks, p <0.001). 54% underwent patch repair with 46% undergoing primary repair. Infants who underwent FETO were significantly more likely to have a patch repair (88%) than those who did not have FETO (29%) (p<0.001).

Mean birth weight Z-score was similar in the FETO and non-FETO group at birth and both decreased by 6 months of age. The drop was significantly greater in the FETO group (p=0.02). Weight Z-score improved in both FETO and non-FETO groups after 6 months but remained lower at all time points in the FETO group, although this was not statistically significant.

Full enteral feeding was attained significantly later in the FETO group (p= 0.001). 59% of infants were prescribed medication for gastro-oesophageal reflux at hospital discharge. This number decreased over the first two years of life to 14%.

7 infants (17%) continued to require supplementary feeding via nasogastric or gastrostomy tube at 6 months of age (3 non-FETO, 4 FETO). By 24 months, two infants continued to require supplementary tube feeding (one FETO, one non-FETO).
Table:

Mean weight Z-score

**Conclusion:** Following repair of CDH, poor growth was demonstrated by a significant fall off in weight Z-score, most pronounced at 6 months of age with some recovery noted by 2 years age. Infants undergoing FETO antenatally are more at risk of growth failure. Gastro-oesophageal reflux is also more common in this group of infants. A subgroup of children following CDH repair may continue to require supplementary tube feeding over the first 24 months of life, which constitutes an important treatment burden for families and healthcare professionals.
Maternal body mass index (BMI) and leptin, ghrelin in human milk

Lorenza Rossi¹, Allegra Sardo¹, Silvio Fiorio², Francesco Savino³

¹University of Turin, Pedriatria 1 U, Turin, Italy
²University of Milan, Pedriatria 1 U Children Hospital Regina Margherita, Turin, Italy
³University of Turin, Pedriatria 1 U Childen Hospital Regina Margherita, Turin, Italy

Objectives and study: Body mass index is associated with increased risk of infant obesity. Hormones involved in food intakes, such as leptin and ghrelin are present in human milk and these could affect appetite behavior or pathway influencing obesity later in life. A positive association has been found between BMI and leptin values, but data on ghrelin are lacking. The aim of this study was to investigate correlations between maternal BMI and Leptin or Ghrelin concentrations in human milk.

Methods: Setting: Mothers were recruited from patients admitted at “Pediatria 1U Lattanti” University Division - Regina Margherita Children’s Hospital, Città della Salute e della Scienza di Torino, Turin, Italy. Breast milk samples were collected from mothers who want participate. Mothers who smoked, had multiple births, or had diabetes were excluded. We recruited 40 healthy, primiparous, breastfeeding mothers, over 20 years old at three months postpartum. We recorded maternal anthropometric measurements (weight, length), calculated BMI at sample collection and measured hormone concentrations using a multiplex assay (RIA test). Statistical analysis was performed setting the statistical significance at p< 0.05.

Results: The concentration of leptin in breast milk was 1.7 ng/ml (media, DS 1.17) and correlated with maternal BMI (r=0.36, p=0.004). Breast milk ghrelin was 828.17 pg/ml (media, DS 323.32) and did not correlate with maternal BMI.

Conclusion: Our data showed a positive correlation between maternal BMI and milk leptin concentration, in accordance with previous data in literature. These findings may have implications for infant appetite regulation and obesity risk later in life.

References:


Disclosure of interest: “None Declared”.
Complementary feeding practices in a group of Romanian mothers: physician recommendations versus maternal preferences

Corina Pienar¹, Pop Liviu Laurentiu¹

¹"Victor Babes" University of Medicine and Pharmacy, Pediatrics, Timisoara, Romania

Objectives and study: To compare the complementary feeding practices as recommended by physicians versus mothers’ preferences, in a group of Romanian mothers.

Methods: We developed a 17 questions questionnaire and submitted it for completion on a social media group. The group has more than 10,000 members (only mothers due to privacy issues), national coverage, promotes breastfeeding and offers breastfeeding support. We used the Wilcoxon signed-rank test (95% confidence interval) to evaluate the differences between physicians’ recommendation and mothers’ preference, for age at weaning, type and form of introduced foods.

Results: We examined a total of 570 completed questionnaires. The mean age of the mothers that completed the questionnaire was 30.54 ± 4.12 years. The vast majority resided in an urban setting (84.4%) and graduated or were enrolled in a form of higher education (89.9%). 72.5% of the mothers exclusively breastfed their babies until weaning, 71.2% researched baby-led weaning and 29.3% have adopted it a weaning method. Although 77% thought the physician’s role in infant weaning was important, 69.6% got their complementary feeding information from the internet or specialized books, and just 25.8% from their physician. We found significant differences between what physicians recommended and what mothers put in practice, in terms of age of weaning (p<0.001), type (p<0.001) and form of introduced foods (p<0.001). Physicians recommended initiation of weaning more frequent after 4 months (32.8%) or at 6 months (49.1%) and were less likely to delay weaning after 6 months (12.1%). Mothers started introducing complementary foods more frequently at 6 months (51.8%) or after 6 months (33.9%), and were less likely to start weaning after 4 months (13%). A worrisome 6% of physicians recommended weaning before 4 months and 1.4% of mothers started introducing solids before this age. Physicians recommended vegetables in 61.1%, fruits in 21.6% and cereal in 10.2% of cases, while mothers preferred vegetables (72.58%), fruits (20.91%) and to a lesser degree, cereals (2.81%), when starting weaning. Physicians recommended more frequently purees (52.6%) and soups/juices at the beginning of weaning (37.5%). Mothers introduced complementary foods more frequent as purees (41.93%) or a combination of purees and finger foods (26.32%), and were less likely to introduce foods as soups/juices (14.04%).

Conclusion: We found discrepancies between physicians’ recommendations and mothers’ preferences in our study group. Physicians tended to recommend an earlier age for weaning, while mothers preferred to delay introducing solid foods. Thus, physicians recommended introducing foods in a more liquid form (soups/juices and purees). Vegetables were the preferred type of foods when starting weaning. Mothers were receptive to newer weaning practices, like baby-led weaning.

Disclosure of interest: Corina Pienar: This work was supported by an internal grant of “Victor Babes” University of Medicine and Pharmacy, PII-C4-TC-2016-08. Liviu Laurentiu Pop “None Declared”
Adequate iron supply in infants fed according to dietary guidelines?

Hermann Kalhoff¹, Mathilde Kersting²

¹Westfälisches Kinderzentrum, Klinikum Dortmund, Pediatrics, Dortmund, Germany
²Research Institute of Child Nutrition, Dortmund, Germany

Objectives and study: Infants in the second 6 months of life are at a high risk of iron deficiency (ID: ferritin<12ng/ml) and iron deficiency anemia (IDA: ID and Hb<10.5 g/dl), because of extraordinary requirements for growth. In infancy, ID is known to be associated with weakness, but furthermore is suggested to impair development of neuronal structures. An earlier randomized controlled study (Dortmund Intervention Trial for Optimization of Infant Nutrition, DINO) suggested that the risk of ID and IDA in the second half of infancy while fed in accordance with German pediatric food based dietary guidelines might be higher in infants fully breastfed for 4-6 months compared to formula fed infants. To further clarify the adequacy of the current recommendations, we undertook a secondary analysis of dietary intake and markers of iron status in the dietary intervention study PINGU.

Methods: Starting at the age of 8 weeks, parents, after being advised on the food based guidelines, daily recorded type and weighed amounts of all foods (except for breast milk) consumed by their infants. At 4 and at 10 months of age, the infants were assessed by a pediatrician and non-fasting venous blood samples were analyzed for indicators of iron status. For the secondary analysis we considered only those n=83 infants with complete information on dietary intake and iron status at 4 and 10 months and without signs of inflammatory processes.

Results: The iron intake was considerably below German and even more below the latest EFSA iron intake reference values. Up to 30% of infants presented with ID at the age of 10 months. The multivariate statistical analysis showed no general effects of the mode of milk feeding in the first 4 months or the time of CF introduction (within the age window 4-6 months) on most markers of iron status. However, in infants with mainly breastfeeding new functional markers like the range of variation of erythrocyte volume (RDW-CV) possibly indicated incipient iron depletion.

Conclusion: In infants, the interpretation of iron status and the identification of valid markers are still difficult. However, iron intake of healthy infants fed according to German food based dietary guidelines, probably does not sufficiently meet the iron needs of a considerable proportion of these infants. Several strategies, e.g. optimized dietary choices, fortification of milk or complementary foods, or supplements could be discussed as options to enhance iron intake during infancy. Nevertheless, it remains open, how far a transiently marginal low iron status in some infants might alternatively be interpreted as a physiological phenomenon accompanying the protection against iron overload during a critical developmental period due to low iron content of breast milk.

Disclosure of interest: None Declared
NUTRITION: Neonatal and infant nutrition

N-P-128

The change from a soybean based to a mixed source lipid as first line parenteral lipid in infants born with gastroschisis improves bilirubin and enteral feeding outcomes

Perraju Bendapudi, Cheryl Battersby, Jonathan Hind, Ann Hickey

1 Kings College Hospital, Neonatal Unit, London, United Kingdom
2 Kings College Hospital, Paediatric Hepatology, London, United Kingdom
3 King’s College Hospital, Neon, London, United Kingdom

Objectives and study: Gastroschisis is increasingly prevalent and complex cases who can develop IFALD (intestinal failure associated liver disease) place an increasing burden on resources. Soya based lipids, high in omega 6 have been implicated in IFALD.

In August 2010, a mixed Soya, MCT, Olive and Fish-oil based lipid emulsion was introduced as the first line parenteral lipid in our unit for all babies with abdominal wall defects. Prior to that first line lipid was soy-bean based. We hypothesized that the change to a mixed source lipid containing omega-3 fatty acids would decrease incidence of IFALD and consequently reduce length of stay. The incidence of IFALD, length of stay and mode of discharge feeding between 2 groups of infants born pre and post the introduction of mixed source lipid as first line were compared.

Methods: A historical cohort study of all infants with gastroschisis born in a single centre between 1st January 2003 and 31st December 2014 was carried out. Retrospective case note and laboratory result review was performed for the demographic details, gastrointestinal and surgical outcomes, length of stay, and mode of discharge feeding. Data was analysed using SPSS 20. Differences were assessed for statistical significance using Mann-Whitney U test for continuous data and the chi-square test for binomial data. Z scores for weight were calculated using the LMS growth programme.

Results: 117 patients were identified of which 63 were in the soybean lipid era and 54 were in the mixed-source lipid era. There were no deaths. No demographic variations identified between the patients.

The median length of stay, in days, was lower in the mixed source lipid group 34.5 (18-277) Vs 39 (14-191) in soya based lipid group but this did not achieve statistical significance (p=0.79).

A subgroup analysis of 51 patients with IF (intestinal failure), defined as need for parenteral nutrition for 28 days or more was conducted.

Table: Comparison of outcomes in the Soya bean lipid group and mixed source lipid group

<table>
<thead>
<tr>
<th></th>
<th>Soya bean lipid (63)</th>
<th>Mixed source lipid (54)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Days to full enteral feeds</td>
<td>27.5 (9-123)</td>
<td>23 (8-266)</td>
<td>0.04</td>
</tr>
<tr>
<td>Median (Range)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Maximum conjugated bilirubin</td>
<td>42 (0-206)</td>
<td>22 (0-373)</td>
<td>0.008</td>
</tr>
<tr>
<td>Median (range) in µmol/L</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cholestasis</td>
<td>25/63 (39.6%)</td>
<td>10/54 (18.5%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Discharge feed (MEBM)</td>
<td>34/63 (53.9%)</td>
<td>22/54 (40.7%)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Intestinal failure sub group (51)

<table>
<thead>
<tr>
<th></th>
<th>Soya bean lipid (24)</th>
<th>Mixed source lipid (27)</th>
<th>P value</th>
</tr>
</thead>
</table>

Vol. 62, Supplement 1, May 2016 874
Maximum Bilirubin
Median ( range) in µmol/L  110 (38-238)  50.5 (9-441)  0.01

Maximum conjugated bilirubin
Median ( range) in µmol/L  60 (11-206)  34 (0-373)  0.02

Maximum bilirubin (discharge)
Median ( range) in µmol/L  72.5 (5-238)  11.5 (2-200)  <0.001

**Conclusion:** Infants with gastroschisis treated with mixed source lipid were less likely to develop cholestasis, had lower maximum bilirubins, reached full enteral feeds earlier, and were more likely to be discharged home on maternal breast milk. We were unable to demonstrate any positive influence on length of stay in the mixed source lipid group.

In infants who developed intestinal failure in our group, maximum conjugated bilirubin observed with mixed source lipid treatment was less than half that observed in those who received soya bean lipid as first line p=0.01

No adverse events were observed.

The study is limited by being a historical cohort study performed in a single centre, and confounded by the implementation on multi professional nutrition rounds in 2008.

**Disclosure of interest:** “None Declared”.

---

Vol. 62, Supplement 1, May 2016  
875
Effects of postnatal overfeeding and fish oil diet on energy expenditure in rats

Yanyan Dai1, Nan Zhou2, Fan Yan1, Shanshan Zhou1, Lijun Sha1, Jianping Wang1, Xiaonan Li3

1Nanjing Medical University, Nanjing, China
2Departments of Child Health Care, Nanjing Medical University, Nanjing Children's Hospital, Nanjing, China, Nanjing, China
3Department of Children Healthcare, Nanjing Children's Hospital Affiliated to Nanjing Medical University, Nanjing, China

Objectives and study: Obesity is the result of energy imbalance over a long period of time, which represents a major health challenge in the world. Early life nutrition is important in the regulation of metabolism in adulthood.

Methods: The present study aimed to evaluate the effects of postnatal overfeeding and polyunsaturated fatty acid diet given after weaning on energy expenditure. On postnatal day 3, rat litters were adjusted to a litter size of three (small litters, SLs) or ten (normal litters, NLs) to imitate lactation overfeeding or normal feeding of human respectively. After weaning, SLs were fed the standard diet or fish oil diet enriched with polyunsaturated fatty acids for 10 weeks. We monitored the metabolic parameters of rats using the TSE LabMaster at W3 and W13.

Results: The weight gain, O2 consumption and heat production of SLs were less than those of NLs at W3(\(P<0.05\)) and W13 (\(P<0.05\)) due to the postnatal overfeeding. Moreover, the postnatal overfeeding could increase the level of respiratory exchange ration (RER) in SLs at W3(\(P<0.05\)). Compared to standard diet, fish oil diet in SLs not only reduced weight gain, improved serum lipid levels and insulin sensitivity, but also increased O2 consumption(\(P<0.05\)), CO2 production (\(P<0.05\)) , heat production (\(P<0.05\)) and reduced the level of RER (\(P<0.05\)) in adulthood.

Conclusion: Postnatal overfeeding could decrease the level of body energy expenditure and induce obesity, but fish oil diet can increase energy expenditure and prevent the development of metabolic dysregulation in adults effectively.

Disclosure of interest: None Declared.
Milk feeding and first complementary foods during the first year of life in an international prospective TEDDY cohort study

Anne Riikonen1, David Hadley2, Ulla Uusitalo3, Nicole Miller4, Sibylle Koletzko5, Jimin Yang6, Carin Andrén Aronsson7, Sandra Hummel8, Jill M. Norris9, Suvi M. Virtanen1

1National Institute for Health and Welfare, Helsinki, Finland
2Transmed Systems, Inc., Cupertino, United States
3University of South Florida, Tampa, United States
4University of Massachusetts Amherst Mph in Nutrition Graduate, Amherst, Massachusetts, United States
5Ludwig Maximilian's University Munich Medical Center, Dr. von Hauner Children's Hospital, Munich, Germany
6Health Informatics Institute, Morsani College of Medicine, University of South Florida, Tampa, United States
7Lund University, Department of Clinical Sciences, Malmö, Sweden
8Helmholtz Zentrum München, Institute of Diabetes Research, Munich, Germany
9Colorado School of Public Health, Department of Epidemiology, Aurora, Co, United States

Objectives and study: The aim was to describe milk feeding patterns and first complementary foods of infants during the first year of life by maternal type 1 diabetes (T1D) status.

Methods: The Environmental Determinants of Diabetes in the Young (TEDDY) study, a birth cohort of 8,676 infants with genetically increased risk for T1D born in 2004-2010 in the U.S., Finland, Germany, and Sweden.

All children with complete dietary information (n=8,673) in the TEDDY study were included in the present study, with 1,307 (15%) children excluded from those analyses in which follow-up data at the age of 1 year was needed, or dietary information was missing. Detailed infant feeding data were initially collected by questionnaire at the 3 month clinic visit, and then were prospectively recorded by the parents (or primary caretakers) using a TEDDY notebook, from which data were extracted at the 6, 9, and 12 month visits.

Results: Giving supplementary milk to the infant during the first 3 days was common in all countries, although the type of the supplementary milk differed by country and by maternal T1D. Donated human milk was commonly used only in Finland, with significantly higher frequency in infants of women with T1D, than others (91% vs. 68%, respectively, p<0.001). Extensively hydrolysed formulas were commonly used in Finland and partially hydrolysed ones in Germany during the first 3 days. The use of cow’s milk based infant formula in the first 3 days was more common in the U.S or Sweden, compared to Finland and Germany. It was used more often in children of women with T1D, than without, in the U.S. and Sweden (p<0.001). The median duration of exclusive breastfeeding was relatively short in all the countries: in the U.S. 1 week, in Finland 3 weeks, in Germany 4 weeks and in Sweden 4 weeks. Overall breastfeeding duration (exclusive and partial) was 5.6 months in the U.S., 8.0 months in Finland, 6.3 months in Germany and 6.9 months in Sweden. Infants who received only breast milk (including donated human milk) during the first 3 days of life were overall breastfed longer than other infants in all the countries: in the U.S. 8.3 vs. 2.8 months; in Finland 9.0 vs. 6.5 months; in Germany 7.4 vs. 1.8 months; and in Sweden 7.0 vs. 5.3 months, respectively. The most common first complementary food was cow’s milk based infant formula in all the countries, especially among infants whose mothers had T1D. Root vegetables were common first complementary solid foods in European countries whereas in the U.S. fruits and rice were often given as first solid foods to children. Children received various types of formulas during the first year of life and there were notable differences in the use of different types of infant formulas between countries: extensively hydrolysed formulas were popular in Finland, partially hydrolysed ones in the U.S. and in Germany and soy formulas only in the U.S. By the end of the first year, most of the infants had received cow’s milk or cow’s milk products (not via infant formula) regardless of country.
**Conclusion:** The frequent infant formula use during the first days varied between the TEDDY countries and seemed to affect the length of breastfeeding.

**Disclosure of interest:** None declared.
Effect of high beta-palmitate infant formula supplemented with galacto-oligosaccharides on stool fatty acid soaps

Maroula Lambidou¹, Birgit Alteheld¹, Frank Jochum², Antonia Nomayo², Peter Stehle¹

¹University of Bonn, Department of Nutrition and Food Sciences, Bonn, Germany
²Evangelisches Waldkrankenhaus Spandau, Department of Pediatrics, Berlin, Germany

Objectives and study: Human milk is important for the nutritional needs of newborns for optimal development due to its special composition of all essential nutrients. Most saturated fatty acids in human milk, especially palmitic acid, are esterified to the sn-2 (beta-) position of the glycerol molecule. In regular infant formulas palmitic acid is esterified to the external sn-1 and sn-3 positions, which are rapidly hydrolyzed leading to substantial fecal extraction of fatty acid soaps. This might be reduced by formulas containing palmitic acid in sn-2 position.

The aim of our study was to compare the fecal excretion of fatty acid soaps from infants fed a high-beta-palmitate formula supplemented with 5 g/L galacto-oligosaccharides (GOS) versus a regular infant formula. It was hypothesized that high-beta-palmitate formula reduces stool soaps.

Methods: Healthy infants were randomly assigned to receive high-beta-palmitate formula based on cow’s milk fat (>40 % of the palmitic acid is esterified to the beta position of the glycerol backbone), vegetable and fish oils resulting in 20-25 % of the palmitic acid in beta position supplemented with 5 g/L GOS (verum, n=17) or standard formula based on vegetable oils (<10 % of the palmitic acid is esterified to the beta position of the glycerol backbone) (control, n=23). A non-randomized human milk-fed group (HM, n=10) was studied in parallel. The stool samples were collected at the age of 6 weeks and freeze-dried. After lipid extraction, the fatty acid methyl esters were analyzed by gas chromatography. ANOVA was applied to assess the difference among groups.

Results: Formula intake was comparable between verum (154.9 ± 29.5 mL/kg body weight*day) and control group (164.2 ± 29.8 mL/kg body weight*day). There was no significant difference for the stool total fatty acid (FA) soaps, palmitate (PA) soaps, and total FA between verum and control. The HM-fed group had significantly lower stool total FA soaps, PA soaps, and total FA than the verum and control group (Table).

The results for the safety parameters body weight and head circumference showed no differences among the groups.

Table: Stool fatty acid soaps and total fatty acids [µmol/g dry weight stool]

<table>
<thead>
<tr>
<th></th>
<th>Verum</th>
<th>Control</th>
<th>HM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total FA soaps</td>
<td>1080 ± 282.3</td>
<td>1083.8 ± 345.3</td>
<td>461.1 ± 274.9</td>
</tr>
<tr>
<td>PA soaps</td>
<td>739.6 ± 227</td>
<td>792.7 ± 254.6</td>
<td>203.8 ± 138.6</td>
</tr>
<tr>
<td>Total FA</td>
<td>1309.2 ± 224.6</td>
<td>1309.3 ± 360.9</td>
<td>667.5 ± 311.5</td>
</tr>
</tbody>
</table>

Mean ± SD; FA, fatty acid; PA, palmitic acid

Conclusion: As expected, breast-fed infants showed lower fecal excretion of stool fatty acid soaps and total fatty acids than infants fed with regular infant formula. However, increasing sn-2 palmitate in infant formula did not reduce stool total fatty acid soaps, palmitate soaps and total fatty acids after six weeks.

Disclosure of interest: None declared
Nutritional status in premature neonates fed with extensively hydrolyzed protein formula

Yi Feng¹, Li Hong¹, Li-ya Pan¹, Pan-pan Chang¹

¹Shanghai Children's Medical Center, Clinical Nutrition, Shanghai, China

Objectives and study: To analyze the nutritional status in premature neonates with extensively hydrolyzed protein formula feeding.

Methods: From Jan. 2013 to Oct. 2015, 448 premature neonates hospitalized in NICU, Shanghai Children's Medical Center, with extensively hydrolyzed protein formula fed were enrolled. Clinical data were recorded including related diseases, birth weight and gestational age, nutrients intake, and growth charts. Two groups were divided according to with or without feeding intolerance (feeding intolerance group, FI; feeding tolerance group, FT), and three groups were divided for birth weight (<1500 g, 1500~2500 g, and≥2500 g group).

Results: A total of 177 (39.5%) premature infants had feeding intolerance, and the less birth weight and gestational age, the more feeding intolerance, and the incidence of feeding intolerance in <1500 g group was 74.3%. The birth weight, gestational age, head circumference and length were significantly smaller in the feeding intolerance group, while the day of transfer formula and reaching to full feeding were longer than that of the feeding tolerance group (24.5±13.4 vs 13.4±5.6, P=0.000). The day of first feeding, transfer formula and reaching to full feeding were longer in those lower birth weight and smaller gestational age babies (P<0.01). The incidence of PN administrated in the feeding intolerance group and <1500 g group was higher with more calorie intake and longer duration (P<0.01).

Table: Table Nutrients intakes and growth in premature neonates with different birth weight

<table>
<thead>
<tr>
<th>Nutrients intake</th>
<th>&lt;1500 g (N=109)</th>
<th>1500~2500 g (N=286)</th>
<th>≥2500 g (N=53)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>First feeding day (d)</td>
<td>5.9±4.4</td>
<td>3.8±2.3</td>
<td>3.8±2.8</td>
<td>0.002</td>
</tr>
<tr>
<td>Feeding intolerance (%)</td>
<td>81(74.3%)</td>
<td>87(30.4%)</td>
<td>9(17.0%)</td>
<td>0.000</td>
</tr>
<tr>
<td>Transfer formula day (d)</td>
<td>25.4±18.5</td>
<td>9.5±6.0</td>
<td>6.5±3.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Reaching to full feeding day (d)</td>
<td>29.2±14.5</td>
<td>14.7±6.0</td>
<td>11.5±6.0</td>
<td>0.000</td>
</tr>
<tr>
<td>EN calorie (kcal/kg/d)</td>
<td>119.3±11.6</td>
<td>118.8±12.1</td>
<td>114.3±13.3</td>
<td>0.128</td>
</tr>
<tr>
<td>PN calorie (kcal/kg/d)</td>
<td>77.9±15.6</td>
<td>63.5±18.5</td>
<td>52.7±21.3</td>
<td>0.001</td>
</tr>
<tr>
<td>PN duration (d)</td>
<td>25.9±13.2</td>
<td>12.6±6.3</td>
<td>9.4±4.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Growth</td>
<td>Weight growth (g/d)</td>
<td>19.4±3.7</td>
<td>17.9±14.9</td>
<td>8.1±7.5</td>
</tr>
<tr>
<td>Head circumference growth (cm/w)</td>
<td>0.7±0.6</td>
<td>0.5±0.4</td>
<td>0.4±0.6</td>
<td>0.005</td>
</tr>
</tbody>
</table>

Conclusion: The growth in feeding intolerance group was similar to those feeding tolerance infant in our study with extensively hydrolyzed protein formula fed, which was associated with PN support. The less gestational age, birth weight and head circumference, the better for extensively hydrolyzed protein formula feeding.

Disclosure of interest: None Declared.
Social Factors Affecting Breastfeeding Rates: Mother’s Perception of Grandmother’s Attitude and Doctor Advices In East Delta of Egypt

Usama El Safy¹, Manar Abdel Karium¹, Eman El Safy²

¹Zagazig University, Pediatrics, Zagazig, Egypt
²Zagazig University, Psychiatry, Zagazig, Egypt

Objectives and study: Objective. To study of social factors affecting of breast feeding rates as regards of mother’s perception of grandmother’s attitude as well as doctor advices

Setting. Outpatient clinic of follow up of newborn at Zagazig university hospital

Participants. All mothers whose infants received well-child care from birth to 2 year of age.

Methods:. A survey of 21 questions in Arabic Language was developed and directed to 300 mothers. The survey assessed: 1) demographics and type of delivery, 2) prenatal and postnatal grandmother’s advices 3) sources of breastfeeding information, 4) timing of decision, 5) preference, 6) type of feeding selected, 7) duration of breastfeeding, 8) Advices of Pediatrician for feeding and 9) factors that would have encouraged bottle-feeding mothers to breastfeed.

Results: The breastfeeding initiation rate was 59 % By the time the infant was 6 months old, only 24% of these were still on breastfeeding for 2 years. The decision to breastfeed or to bottle-feed was most often made after delivery. The increased rate of cesarean section affected decision of breast feeding and increase bottle feeding. The Pediatrician advice to start bottle feeding after delivery because of his believes of small amount of colostrum presented 47 % of cause of bottle feeding. The second medical advice increased rate of bottle feeding, crying of newborn and infants related to insufficient breast milk. Grandmothers attitudes affected rate of breast feeding: first , their believes that white breast milk was diluted, second believes was that the continuous crying due to insufficient breast milk , third believes was that regurge in newborn and infant was due to allergy to breast milk One of common believes of grandmothers that the breast feeding affect the health of their daughters.

Conclusion: To overcome obstacles, issues surrounding perceived barriers, such as Grandmother’s attitude, quantity of milk, and time constraints, need to be discussed with each parent and Grandmother’s. To achieve the goal of 70% of breastfeeding mothers, extensive education regarding the benefits must be provided for both parents , optimally the grandmother and physicians as well as nurses by well-educated Pediatrician before pregnancy or within the first trimester.

Disclosure of interest: No conflict of interest for Authors

Usama R El Safy*, Manar F Abdel Karim*, and Eman R El Safy**

Pediatrics * and Psychiatry** Departments Zagazig University Egypt
Impact of an infant formula supplemented with Nutriexpert® factor regarding infections during the first 12 months of life

Florian Herrmann¹, Ana Nieto Ruiz², Marta Guarra Riba³, Mireia Moreras³, Maria Teresa Miranda⁴, Cristina Campoy⁵

¹University of Granada, Spain, Euristikos Excellence Centre for Paediatric Research, Granada, Spain
²University of Granada, Euristikos Excellence Centre for Paediatric Research; Brain, Mind and Behavior International Centre, Granada, Spain
³Ordesa S.L., Scientific Laboratory, Sant Boi de Llobregat, Spain
⁴University of Granada, Department of Biostatistics, Granada, Spain
⁵University of Granada, Centre of Excellence for Paediatric Research Euristikos, Granada, Spain

Objectives and study: The impact of early nutrition on the infectious diseases prevention in infants has been widely recognized, especially for breastfeeding. This study investigates the effect of a new infant formula supplemented with functional ingredients, usually present in human milk, such as LC-PUFAs, milk fat globule membrane and symbiotics on the incidence of infections.

Methods: 170 healthy term babies aged between 0-2 months were enrolled in a prospective double-blind control study. Infants were randomized to receive either an infant formula supplemented with Nutriexpert® factor (NF) or a standard formula (SF). Number of infections, pediatric and emergency visits and hospitalizations were registered during the first 12 months of life.

Results: At 6 months infants fed with NF presented a tendency of fewer infectious episodes without reaching statistical signification compared to SF. NF fed infants showed fewer pediatrician consultations than SF (p=0.049). SF children had more nonspecific febrile episodes than NF (p=0.025). At 12 months of life, the SF-group compared to the NF-group showed more infants with infectious episodes (p=0.044) while the NF-group presented less respiratory tract infections (p=0.046) and less gastroenteritis episodes (p=0.033).

Conclusion: Infant formula supplemented with Nutriexpert® Factor consumption is associated to fewer infections and reduced medical care needs.

Disclosure of interest: This work has been funded by Ordesa Laboratories-University of Granada General Fundation, COGNIS Research Project Contract nº3349.
Nutritional intervention in early life influences the head circumference in healthy male children at 2.5 years

Cristina Campoy1, Ana Nieto Ruiz2

1Euristikos Excellence Centre for Paediatric Research, Granada, Spain
2University of Granada, Euristikos Excellence Centre for Paediatric Research; Brain, Mind and Behavior International Centre, Granada, Spain

Objectives and study: During childhood, head circumference (HC) it is associated with the overall volume of grey and white matter and predicts brain growth and children neurocognitive development. This study aim to analyse the effect of a new infant formula supplemented with Nutriexpert® factor on the HC growth in healthy children up to 2.5 years of age.

Methods: 170 healthy term infants, with adequate birth weight for gestational age, were enrolled to a randomized double-blind study to receive a standard infant formula (F1: n=85) or a new one supplemented with Nutriexpert® factor (F2: n=85). HC was obtained at birth, 6, 18 months and at 2.5 years, using an inextensible tape (SECA212®); percentiles and Z-score HC/age was calculated, following WHO recommendations. Normal distribution was assumed using Kolmogorov-Smirnov test and Student t-test was performed using SPSS version 22.0.

Results: At 2.5 years, 75 children attended the follow-up call (40 males/35 females). There were no differences between the two study groups in HC measurements at any of the timepoint performed. However, male children fed F2 (n=27) showed a larger HC (p=0.019), higher percentile HC/age (p=0.006) and Z-Score HC/age (p=0.011), compared to those fed F1 (n=13). No such differences were found in the case of girls.

Conclusion: Early nutritional intervention with Nutriexpert® factor shows long-term effects by determining the further growth of HC at 2.5 years of age in male infants. These results suggest the need of neuroimaging studies to evaluate the extent of the effect on the brain and the consequences on cognitive function.

Disclosure of interest: This study has been funded by Ordesa Laboratories, SL Contract General Foundation of University of Granada, No. 3349.
**NUTRITION: Nutrition in intestinal failure**

N-P-136

**TauroLock is effective in preventing catheter related bloodstream infection in post-surgical infants on HPN**

Kajsa Waldenvik¹, Heléne Schurer Örden¹, Helen Lilja Engstrand¹, Ilektra Athiana¹, Mattias Paulsson¹, Yigael Finkel¹, Niklas Nyström¹

¹Akademiska Barnsjukhuset, Uppsala, Sweden

**Objectives and study:** TauroLock (TL) is a catheter lock solution for tunneled and nontunneled CVCs and port systems. It contains taurolidine (2%) as an antimicrobial and antifungal ingredient and citrate (4%) to prevent clot formation. Taurolidine acts by irreversibly binding to the cell walls of organisms resulting in the prevention of bacterial adhesion to biological surfaces. Taurolidine has proven to have a broad spectrum of antimicrobial activity against Gram-positive, Gram-negative bacterial and fungi infection with no bacterial resistance reported.

In our tertiary care pediatric hospital we introduced TL as a routine prophylactic treatment in 2012 and today TL is routine from the time when potential long-term PN > 29 d is expected, and started when the children are disconnected from PN for at least two hours. We retrospectively reviewed in our tertiary care pediatric hospital children, who were discharged home on parenteral nutrition (HPN) and the incidence of catheter related bloodstream infection (CRBSI) during their first year on HPN, to study whether taurolidine lock had any effect on the incidence of CRBSI.

**Methods:** We studied HPN during the first year in 16 post-surgical infants, divided into one group (TL+), who started and maintained TL and one group (TL-) who did not receive TL during their first year on HPN. 9/10 in TL+ and 2/6 in TL- were premature/VLBW. All children had single lumen tunneled central venous catheters. TL was started at discharge from the NICU/PICU to the surgical ward. PN solutions with all additives were compounded in the hospital pharmacy on individualised prescriptions. All infants were discharged home after the care-takers had completed the HPN training and had taken over all aspects of HPN care, which usually was 6-10 weeks postnatally.

**Results:** Please copy and paste the corresponding text here.

**Table:**

<table>
<thead>
<tr>
<th></th>
<th>Birth Weight kg (median)</th>
<th>Median age (m) PN &gt; 29d</th>
<th>CRBSI /1000days</th>
<th>Koag neg Staph CRBSI</th>
<th>Other bacterial CRBSI</th>
<th>Fungal CRBSI</th>
</tr>
</thead>
<tbody>
<tr>
<td>TauroLock</td>
<td>0.78</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>No TauroLock</td>
<td>3.45</td>
<td>1</td>
<td>5.93</td>
<td>6</td>
<td>7</td>
<td>-</td>
</tr>
</tbody>
</table>

**Conclusion:** TauroLock solution seems effective in preventing CRBSI in post-surgical neonates on long-term PN in hospital and during following HPN treatment.

**Disclosure of interest:** None Declared
Case Report: Complicated D-Lactic Acidosis in Short Bowel Syndrome

Lynette Forsythe¹, Valentina Le Thanh¹, Valeria Solari¹, Riccardo Coletta¹, Antonino Morabito¹

¹Royal Manchester Childrens Hospital Central Manchester University Hospitals NHS Foundation Trust, Paediatric Surgery, Manchester, United Kingdom

Objectives and study: D-lactic acidosis is a rare complication of short bowel syndrome (SBS). It is caused by the incomplete digestion of carbohydrates which are then fermented in the colon, producing a variety of acids including D-lactate. Since mammals lack D-lactate dehydrogenase, this acid is metabolised more slowly than its enantiomer (L-lactate) and it therefore accumulates causing a variety of neurological symptoms. No standard management has yet been formulated. The treatment of this complication usually relies on the acute treatment of acidosis, followed by a maintenance phase by decreasing the carbohydrates intake. This study reports a complex case of recurrent D-lactic acidosis in a paediatric patient with ultra SBS (<20 cm) due to complicated gastroschisis.

Methods: In October 2014, a 2-year old girl was admitted to hospital with neurological symptoms, namely confusion, lethargy and unsteadiness, together with abdominal distension and tachypnoea. Because of her ultra short bowel, she had undergone a bowel lengthening procedure achieving 33 cm in length. She required full parenteral nutrition (PN) which was gradually reduced as intestinal adaptation occurred. On this admission, a diagnosis of D-lactic acidosis was made through blood tests showing high levels of D-lactate (667umol/L, RefR<19). She started gut decontamination and her enteral feeds were stopped for 48 hours. She was discharged with antibiotics for gut decontamination, continued on parenteral nutrition with slow introduction of a low carbohydrate diet in addition to her peptide-based milk. The ultimate aim was to gradually wean her off PN which was achieved in mid-August 2015. Nevertheless, she continued to present with recurrent symptomatic episodes of D-lactic acidosis that required further carbohydrate restrictions, several changes in her gut decontamination treatment (courses of gentamycin, erythromycin, tobramycin, metronidazole and rifaximin were used) and reintroduction of PN (in October 2015) which represented a serious challenge to her enteral autonomy.

Results: In spite of several courses of antibiotics for gut decontamination and dietary restrictions, the child still showed recurrent episodes of neurological symptoms and acidosis (D-lactate >6000umol/L). However, her medical condition significantly improved with dietary manipulation to a carbohydrate free milk, low carbohydrate food intake and D-lactate free probiotics. She has now been free from recurrences for 12 weeks with continued reduction in PN to 2 nights per week and she has stopped all antibiotic therapy.

Conclusion: Our case report highlights the need in considering D-lactic acidosis in paediatric patients with a history of SBS manifesting neurological symptoms and it also shows the complex management of this condition when occurring in young children at weaning age. In these cases, low carbohydrate milk may be preferable in preventing further episodes of D-lactic acidosis. Moreover, in contrast with other studies, our case also showed possible benefits in using D-lactate free probiotics in the management of this complication. Indeed our patient is now gradually increasing her carbohydrate intake without the need of antibiotic therapy.

NUTRITION: Nutrition in intestinal failure

N-P-138

Growth and vitamin deficiencies in children with intestinal failure receiving long-term parenteral nutrition

Esther Neelis¹, Noortje Rijnen¹, Joanne Olieman², Rene Wijnen³, Edmond Rings¹, Barbara de Koning¹, Jessie Hulst¹

¹Erasmus MC - Sophia Children's Hospital, Paediatric Gastroenterology, Rotterdam, Netherlands
²Erasmus MC - Sophia Children's Hospital, Dietetics, Rotterdam, Netherlands
³Erasmus MC - Sophia Children's Hospital, Paediatric Surgery, Rotterdam, Netherlands

Objectives and study: Children with intestinal failure (IF) receiving parenteral nutrition (PN) are at risk for growth failure and vitamin deficiencies, both during and after weaning off PN. The aim of our study was to quantify the prevalence of growth failure and vitamin deficiencies in children with IF receiving long-term PN.

Methods: A retrospective study was performed in all children with IF treated by the IF team of Erasmus Medical Centre – Sophia Children’s Hospital between 2000 and 2015. The minimum PN duration was 6 months. Height for age (HFA), weight for age (WFA) and weight for height (WFH) standard deviation scores (SDS) were calculated with the latest available Dutch reference data, taking into account gender, ethnicity and prematurity. A WFH < -2 SD was defined as underweight, whereas a height < -2 SD was indicative of growth failure. Target height (TH) SDS and TH range (TH ± 1.6 SD) were calculated. All vitamin measurements were obtained. Data were collected from the start of IF until January 1, 2015. Data are presented as frequencies and percentages or as median and interquartile range (IQR). Paired t-tests were used to compare TH SDS with HFA SDS.

Results: Fifty-nine children (27 male, 32 female) were identified. Thirty-nine (66%) were born prematurely. Twenty-two children had short bowel syndrome, 23 surgical IF but no short bowel syndrome, 13 functional IF and 1 child a combination. The most common underlying diseases were intestinal atresia (24% of the patients) and necrotizing enterocolitis (20% of the patients). Median PN duration was 15 months (IQR 9-32 months). The median follow-up duration was 3.6 years (IQR 1.8-7.5 years).

One year after start of PN, the median HFA SDS of children still on PN was -1.0 (IQR -1.8 SD - -0.1 SD). Twenty-three percent of the children still on PN had growth failure, compared to 8% of the children weaned off PN (Table 1). Differences between SD scores for TH and actual height could be calculated in 37 of 60 patients. At 12 months after start of PN, 19% of the children at PN were below their TH range compared to 0% of the children who were already weaned off PN.

Vitamin deficiencies were common, both during PN and after weaning. Vitamin A and E deficiency were prevalent during PN (35/37 (95%) and 23/27 (62%) respectively) and after weaning (21/24 (88%) and 16/25 (64%)). Fifty percent of the children had an abnormal (<50 nmol/L) vitamin D during PN (14/28) compared to 59% of the children after weaning off PN (13/22).

Table:

Table 1 Anthropometric indices below < -2 SD in children with IF 12 months after start of PN.

<table>
<thead>
<tr>
<th>Anthropometric variable</th>
<th>Children on PN N (%)</th>
<th>Children weaned off PN N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HFA SDS &lt; -2</td>
<td>7/31 (23)</td>
<td>1/12 (8)</td>
</tr>
<tr>
<td>WFA SDS &lt; -2</td>
<td>7/35 (20)</td>
<td>2/12 (17)</td>
</tr>
<tr>
<td>WFH SDS &lt; -2</td>
<td>2/31 (7)</td>
<td>1/12 (8)</td>
</tr>
<tr>
<td>Below TH range</td>
<td>5/27 (19)</td>
<td>0/10 (0)</td>
</tr>
</tbody>
</table>

Conclusion: Our study showed that one year after the start of PN, 23% of the children still dependent on PN had growth failure. Nineteen percent of the children still on PN were growing below their TH range. Vitamin deficiencies were common, both during PN and after weaning. Close nutritional monitoring and patient tailored adjustment should maximize the potential for growth and prevent vitamin deficiencies.

Disclosure of interest: None Declared.
Outcome of children with short bowel syndrome (SBS)

Francesca Barbieri¹, Grazia di Leo²

¹Irccs Burlo Garofolo, Pediatrics, Trieste, Italy
²Irccs Burlo Garofolo, Trieste, Italy

Objectives and study: The successful management and prognosis of SBS in infants and children depends on length, quality, anatomy of the remaining intestine and on the clinical management. Intestinal autonomy in patients who had SBS is achieved in almost 90% of the patients and intestinal transplantation is rare. This study aims to analyse the outcome of children with short bowel syndrome (SBS) due to different causes: necrotizing enterocolitis, gastroschisis, jejunal atresia, volvulus and intestinal perforation.

Methods: Were collected demographic data, general information on disease status, and outcome of intestinal rehabilitation of patients treated for infantile onset SBS at our gastroenterology department between 1981 and 2015. Outcome measures were intestinal autonomy, intestinal and/or liver transplantation, and survival. This is a retrospective cohort study.

Results: 18 children were evaluated (11 male and 7 female), median follow-up was 10.22 years (range: 6 months-30 years). The underlying diagnoses included jejunal atresia (n=5), volvulus (n=5), gastroschisis (n=4), necrotizing enterocolitis (n=3), and intestinal perforation (n=1). Absolute small bowel length was >40 cm in 8 patients (44%), between 20 cm and 40 cm in 5 patients (28%) and <20 cm in the last 5 patients (28%). In 11 patients (61%) the ileocecal valve was still present. After a median of 1078 days (range 12 months to 18 years) on total parenteral nutrition, 15 patients (83%) reached intestinal autonomy. 7 patients (39%) developed liver disease PN and CVC sepsis correlated: in 5 patients this complications was reversible. 2 patients underwent liver-intestine transplantation for intestinal failure-associated liver failure. Another patients underwent intestinal transplantation for loss of venous access due to sepsis CVC-related. All the three patients who underwent intestinal transplantation had a small bowel length < 20 cm, were without ileocecal valve and made the transplantation before the year 2000. Three patients underwent intestinal lengthening by STEP (serial transverse enteroplasty), the median small bowel length at birth in those patients was 34.33 cm. Overall mortality was 5.8%: 1 patient died due to post-transplant lymphoma. We also describe 2 patients with short bowel syndrome (SBS) and refractory anemia who had anastomotic ulcers detected by CE.

Conclusion: Our study showed that intestinal autonomy is achieved in almost 90% also with new surgical interventions such as bowel lengthening procedures with a surgical “sparing” on the length of the bowel and today few patients require intestinal transplantation. Liver disease due to parenteral nutrition is reversible with the interruption of the parental nutrition, effectively none of our patients present this complication. Not least perianastomotic ulcers are a known cause of refractory anemia in children with a history of intestinal resection.

Disclosure of interest: “None Declared” conflict of interest
Successful Management of Infants with Intestinal Failure over Two Decades

Marcus Auth¹, Helen Garrett², Emma Jones², Joanne Minford³

¹Alder Hey Children’s NHS Foundation Trust, Paediatric Gastroenterology, Hepatology and Nutrition, Liverpool, United Kingdom
²Alder Hey Children’s NHS Foundation Trust, Dietetics, Liverpool, United Kingdom
³Alder Hey Children’s NHS Foundation Trust, Paediatric Surgery, Liverpool, United Kingdom

Objectives and study: To prevent intestinal failure-associated liver disease (IFALD) in long-term parenteral nutrition (PN)-dependent children, the protective role of early enteral nutrition and reduction of soya from intravenous lipids has been established, but practices varies. Here we present our multidisciplinary team experience in management of infants with intestinal failure two decades using enteral feeding with percutaneous gastrostomies (PG) and reduction of soya based PN.

Methods: Systematic retrospective review of infants who had a PN requirement over 27 days between 8/1996 to 11/2010. Follow-up continued until 12/2015 ranging from 5 years 1 month to 19 years 4 months. From n=113 infants 58% were male, 42% female, and gestational age was 35 (23 to 42) weeks, 107 records contained full laboratory data. 76 infants were premature; 12 were 28 weeks gestation or less. Birth weight was 2.32 kg (0.6kg to 4.5kg). When admitted to our unit, soya Intralipid® was changed to MCT/LCT Lipofundin®, and from 2007 SMOF® was introduced as rescue therapy for IFALD. Patient characteristics and results are presented as mean (range).

Results: Surgical diagnoses were predominant (87%) and comprised gastrochisis (37%), necrotising enterocolitis (28%), atresias (14%), volvulus (6%) and other. Reduced bowel length of <65cm was present in 36% and <25cm in 13%, and absence of ileocaecal valve in 21%. Medical and neurological diagnoses accounted for 13% with enteropathies (9%) and motility disorders (4.5%). A PG was inserted in 58% at an age of 107 days (14 to 431 days). Length of TPN requirement was 370 days (18-3570 days), 2 children (1.7%) underwent small bowel elongation. Enteral autonomy was achieved in 77% of children by 12 months, and 85% by 5 years.

21 children (19%) received home TPN for 33.9 months (0.7 to 113). Two children (1.7%) remain on TPN for 61.4 months (60.7 - 62) (1 NEC and 1 chronic pseudo-obstruction).

From n=107 patients on TPN, 23% demonstrated IFALD, affecting n=15 (14%) with type 3. From these 15, 9 came off TPN (60%), 2 remained on TPN and 4 died (27%).

Overall mortality was 13% (15/113), occurring at mean of 19.6, median of 8.9 (1.3 to 104) months, including sepsis (4%), and IFALD (4%).

Of 12 children referred to a quaternary transplant centre, 5 were listed for transplantation, 2 had combined liver/small bowel transplant and are off TPN, 1 had small bowel transplant and died, 1 died while on transplant list, 1 was taken off transplant list and died. From 7 children not listed for transplant, 4 children are off home TPN, 2 are still on TPN, and 1 has died.

Conclusion: Early enteral nutrition supported by PEG insertion, and MCT/LCT based or subsequently soya/MCY/olive/fish oil based PN in a multidisciplinary strategy are successful components in managing the majority of infants diagnosed with intestinal failure. In this series with long-term follow-up (5-19 years), 85% achieved enteral autonomy within 5 years of presentation. Using PG insertions and PN lipid type modifications, the proportion of severe liver disease was low (14%) and 60% of this group could be weaned off TPN.

Disclosure of interest: Emma Jones with B. Braun Melsungen (speaker fee), no other conflicts declared.

Acknowledgements to the gastroenterology, surgery and dietetic teams from our hospital.
Iron deficiency anaemia in children with short bowel syndrome

Katarzyna Olszewska¹, Elzbieta Banas¹, Malgorzata Janusz¹, Maciej Jaworski², Janusz Ksiazyk¹

¹The Children’s Memorial Health Institute, Department of Paediatrics, Nutrition and Metabolic Disorders, Warsaw, Poland
²The Children’s Memorial Health Institute, Department of Biochemistry, Radioimmunology and Experimental Medicine, Warsaw, Poland

Objectives and study: Patients with short bowel syndrome (SBS) are at high risk of nutritional deficiencies. Iron deficiency anaemia (IDA) is a consistent clinical feature of SBS. Motility disorder, nausea, anorexia, chronic fatigue have been attributed to anaemia. Anaemia has significant impact on the quality of life of affected patients. The main causes of iron deficiency (ID) in SBS is lack of iron administration with parenteral nutrition (PN), malabsorption of oral intake and inadequate enteral supplementation. They thus create negative iron balance and lead to anaemia. The prevalence of IDA in children with PN dependent SBS was the aim of the study.

Methods: 66 patients (28 females and 38 males) with SBS aged 0.45 -18.08 years (median: 5.59 years) were selected for the study. The median duration of PN was 4 years 3 months. All patients were PN dependent. 39 patients (66%) had extended small intestine resection (remnant small intestine <40 cm). 16 patients (24 %) had additionally over 50 % large intestine resection. Laboratory tests: red blood cells (RBC), hemoglobin (HB), hematocrit (HCT), vitamin B12 concentration and serum iron concentration (SIC) were assessed. Nutrient values of food intake - enteral nutrition (EN) and of parenteral nutrition (PN) were calculated. The U Mann-Whitney test was used to analyze the results.

Results: Mean concentration of HB in the research sample was 11.37 g/dl, mean concentration of HCT was 35.1 %, mean concentration of vitamin B12 was 1772.38 pg/ml and SIC was 67.6 µg/dl. In 30 patients (45 %) we recognized anaemia (decreased HB, HCT) and 46 children (70 %) had iron deficiency. No patient was vitamin B12 deficient. All patients with iron deficiency were additionally supplemented with iron parenterally or orally. Extension of resection had no evident influence on low SIC. There was statistically significant higher HB concentration in patients with greater contribution (%) of PN in mean daily energy requirements (p= 0.0004). The number of PN days per week was bigger in group of children with low HB concentration (p=0.03).

Conclusion: SBS may be related to iron deficiency anaemia. Patients with higher contribution of PN are specially exposed to IDA. The routine surveillance of anaemia indicators and consideration of modifying parenteral iron supplementation is recommended in children with SBS.

Disclosure of interest: None declared.