ESPGHAN 2014

Abstracts from the

47th Annual Meeting of the European Society for Paediatric Gastroenterology, Hepatology and Nutrition

9 – 12 June 2014

Jerusalem, Israel
Allied Health Professional (Including Nurses & Dieticians)

AHP-0001

BEHAVIOURAL TREATMENT OF INFANTILE FEEDING DISORDERS (IFD’S) DECREASES MATERNAL ANXIETY AND DEPRESSION LEVELS

Anat Tirosh 1, Sari Alony 1, Idit Segal 2, Anat Levi 2, Lia Korenfeld 2, Tsili Zangen 2, Avi Mizrachi 2, Arie Levine 2, Tali Sinai 1*

1School of Nutritional Sciences, The Hebrew University of Jerusalem, Rehovot, Israel, 2Paediatric Gastroenterology and Nutrition Unit, Wolfson Medical Center, Holon, Israel

Objectives & Study: Mothers of IFD infants often use pathological feeding patterns (1) and suffer from a high incidence of depression and anxiety (2). It is unclear if anxiety is the underlying cause of IFD’s or a result of infants refusal to eat. In this study we examined the effects of a behavioral treatment of IFD on maternal anxiety and depression levels.

Methods: IFD infants and their mothers were treated by a multidisciplinary team (physician and dietitian) using behavioral modification without psychotherapy. Response to therapy was evaluated by measurement of maternal pathological feeding and child’s food refusal. At baseline and following 3-6 months of treatment, mothers filled out a questionnaire concerning extent of preoccupation in the child’s feeding problem and also completed the Beck's Anxiety and Depression Inventories. Total anxiety and depression scores were calculated and ranked according to severity.

Results: Thirty-two pairs of IFD infants, 23.7±16.7 months, and their mothers, participated in the study. At baseline, 90.6% of infants refused to eat, 58.1% were diagnosed as Failure to Thrive and 100% of mothers engaged in pathological feeding. Partial or full response to therapy was observed in 78% of the infant/mother dyads. Baseline maternal Anxiety Scores were mild (16.1%), moderate (9.7%) or severe (16.1%) in 41.9% of participants while 32.3% of mothers were categorized with Depression. Post-intervention levels decreased to 31.3% for anxiety and 15.6% (P < 0.05) for depression. Lowering the extent of occupation in child’s feeding problems was significantly correlated to a decrease in levels of anxiety and depression. No mothers remained in the severe category for anxiety at the end of the intervention.

Conclusion: Behavioral treatment of IFD reduced levels of occupation with the child’s feeding problem and led to an overall improvement in the severity of maternal anxiety and depression levels, suggesting that in many parents, anxiety is a result of the infant behavior.


Disclosure of Interest: A. Tirosh Conflict with: I have no COI. , S. Alony Conflict with: I have no COI. , I. Segal Conflict with: I have no COI. , A. Levi Conflict with: I have no COI. , L. Korenfeld Conflict with: I have no COI. , T. Zangen Conflict with: I have no COI. , A. Mizrachi Conflict with: I have no COI. , A. Levine Conflict with: I have no COI. , T. Sinai Conflict with: I have no COI.
CURRENT PRACTICES ACROSS THE UNITED KINGDOM REGARDING THE MONITORING AND SUPPLEMENTATION OF SODIUM IN SURGICAL INFANTS AND CHILDREN

Danielle Petersen 1,*, Vanessa Shaw 1, Anne Payne 2
1Dietetics, Great Ormond Street Hospital, London, United Kingdom, 2Peninsula Allied Health Centre, Plymouth University, Plymouth, United Kingdom

Objectives & Study: Infants and children with excessive sodium losses, for example, premature infants, those with ileostomies or cystic fibrosis are at risk of sodium depletion which may result in metabolic acidosis and poor weight gain. Experts therefore suggest that urinary sodium (UNa) should be monitored and if it is low, sodium supplements should be started. However, there are no guidelines suggesting how this is best carried out and limited evidence is available within the literature. Practices widely differ within the United Kingdom (UK) and with a lack of consensus in the literature, the development of guidelines or further research is limited. This study therefore aims to describe current practices regarding the monitoring and supplementation of sodium in paediatric surgical centres across the UK, from which guidelines or further research could be developed.

Methods: The study design was a cross-sectional descriptive survey. A questionnaire was developed and electronically sent to the Paediatric Surgical Dietitian in each of the 26 paediatric surgical centres across the UK. Total population sampling was used with one Paediatric Dietitian from each of these centres invited to partake in the survey. Completed questionnaires were returned, data analysed and the results of each of the 18 questions summarized and discussed. Where possible, the results from the survey were compared to the recommendations within the literature.

Results: 100% response rate was achieved. Results showed that all paediatric surgical centres across the UK monitored UNa and started sodium supplements if the UNa was found to be low. There was also consensus regarding the importance of sodium in relation to growth. All of these are consistent with the recommendations found in the literature. Other practices, however, varied more between centres and often between Consultants within the same centre. The two areas of practice which were found to be the most inconsistent between centres and to that suggested within the literature were: the method used to monitor UNa; and the reference values used to define a low UNa. These are two essential aspects regarding the monitoring and supplementation of sodium.

Conclusion: There is limited literature and evidence regarding the monitoring and supplementation of sodium in surgical infants and children. Furthermore, the results from this survey show that even within the areas of practice where evidence is available, current practices are not always based on these recommendations and vary significantly across the UK.

Disclosure of Interest: None Declared
REGULAR BLOOD MONITORING FOR ENTERALLY FED CHILDREN: A SYSTEMATIC REVIEW

Michelle Brooks 1,*, Catherine E Paxton 2, Tracey Cardigan 3, David C Wilson 4, Andrew R Barclay 1
1Paediatric Gastroenterology, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom,
2Paediatric Gastroenterology, NHS Lothian, Edinburgh, United Kingdom, 3Department of Nutrition and Dietetics, NHS Greater Glasgow and Clyde, Glasgow, United Kingdom, 4Child Life and Health, University of Edinburgh, Edinburgh, United Kingdom

Objectives & Study: Adult guidelines suggest 6 monthly nutrition blood test monitoring (NBTM) of patients on home enteral tube feeding (HETF)[1] but few studies evaluate NBTM of children on HETF.

Aims: To appraise evidence for the type and frequency of NBTM for children on HETF via systematic review and, if needed, to recommend how any deficit in current literature can be improved.

Methods: Systematic retrieval of all data on NBTM in patients <18yrs receiving HETF as >50% of daily requirements or as 'supplements' via a permanent feeding device. Electronic searches of Cochrane library, Medline (1946-Nov 2013) and Pubmed (to Nov 2013) were made using the key words and MeSH terms 'enteral nutrition’, ‘micronutrients’ and ‘child’. Abstract and personal collection searches were also performed. Two authors independently appraised the level of evidence and quality of the studies using the SIGN (www.sign.ac.uk) methodology. Outcomes sought were frequency of monitoring, frequency of abnormal test results and correlation with diagnosis.

Results: The search strategy yielded 3908951 hits. Combination searches of ‘enteral nutrition’ with both other terms reduced this to 5664 abstracts. 27 potential studies were read in full. 3 guidelines were relevant but not limited to our specific clinical question. 14 were excluded given they did not contain NBTM data or included paediatric data was inseperable from adult data. 10 studies were included in our review (1 EL 1-, 3 EL 2- and 6 EL 3). NBTM included Hb, ferritin, folate, B12, Fat Soluble Vitamins (FSV), Vit C, thiamine and trace elements. NBTM was at the start of HETF then ranged from 3 monthly to annually. Cumulative evidence from studies are summarised in table 1. Commonest reported deficiencies were Fe, Zn and Se. FSV deficiencies were only documented in short bowel syndrome (SBS). Multiple NBTM deficiencies were common (28-32%) in patients with neurodisabilities with low energy expenditure (EE).

<table>
<thead>
<tr>
<th>Evidence</th>
<th>No of studies (EL)</th>
<th>Total no of patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>FSV only low in SBS</td>
<td>2 (3)</td>
<td>208</td>
</tr>
<tr>
<td>Low risk pts have normal FU bloods</td>
<td>2 (3)</td>
<td>162</td>
</tr>
<tr>
<td>Low EE pts at risk of trace element deficiencies</td>
<td>3 (2-, 3)</td>
<td>200</td>
</tr>
<tr>
<td>Fibre feed reduce Fe absorption</td>
<td>2 (1-, 2-)</td>
<td>84</td>
</tr>
</tbody>
</table>

Conclusion: Paediatric data for NBTM are limited and their methodology usually ensures low evidence level. In standard patients, the data suggests that NBTM may only be necessary annually when on age appropriate feeds; FSV monitoring may not be required for this group. 'High risk' patients (including SBS and low EE patients) may require more frequent NBTM. We found no specific data for HETF children with cystic fibrosis. Future studies should examine; NBTM frequency with reference to primary diagnosis; feed type and regimen; and confounders such as RX and fibre intake.


Disclosure of Interest: None Declared
Allied Health Professional (Including Nurses & Dieticians)

AHP-0004

INADEQUATE NUTRIENT INTAKE AND SHORT STATURE IN SUBJECTS WITH DIAGNOSED MILK PROTEIN ALLERGY

Tali Sinai 1,*, Roni Amitzur-Levi 1,2, Liat Nachshon 2, Michael Goldberg 2, Efrat Monsonego-Ornan 1, Yitzhak Katz 2

1School of Nutritional Sciences, The Hebrew University of Jerusalem, Rehovot, Israel, 2The Institute of Paediatric Allergy and Immunology, Assaf Harofeh Medical Center, Zerifin, Israel

Objectives & Study: A positive association has been reported between milk consumption and growth parameters. The majority of studies examining this association have been performed in children during their growth phase. We investigated the impact of a dairy-free diet on the final stature of IgE-mediated Cow Milk Allergy (IgE-CMA) young adults. These patients, by definition, are unable to consume even minor amounts of dairy foods, since infancy.

Methods: Anthropometric data was measured in 30 IgE-CMA patients (19.5±3.1 years old) and 19 healthy subjects (control group, 21.3±3.6 years old). Age- and gender-specific SDSs were determined according to Centers for Disease Control and Prevention growth charts. Nutrient intake assessment was based on 24 hour dietary recall and presented as percent of dietary reference values (DRI's). Individuals with conditions or treatments affecting bone metabolism or growth, were excluded.

Results: Growth parameters, including height, height-SDS, Weight-SDS and BMI-SDS were significantly reduced in CMA subjects when compared to controls (p<0.05). An abnormal distribution of height-for-age was noted in the CMA group, as compared to the controls (47% versus 21% were categorized as less than the 25th percentile, respectively). In addition, height-SDS in CMA patients was significantly lower than their predicted height (mid-parental target height-SDS) (p=0.0003). The incidence of subjects consuming less than 67% of the DRI was greater in the CMA group, as compared to controls.

Conclusion: Individuals with CMA are at risk for not reaching their growth potential. Growth monitoring and appropriate dietary intervention may avoid nutritional deficiencies and growth retardation in these patients.

Disclosure of Interest: T. Sinai Conflict with: I have no COI, R. Amitzur-Levi Conflict with: I have no COI, L. Nachshon Conflict with: I have no COI, M. Goldberg Conflict with: I have no COI, E. Monsonego-Ornan Conflict with: I have no COI, Y. Katz Conflict with: I have no COI
A SURVEY OF PATIENTS, PARENTS AND ALLIED HEALTH PROFESSIONS PERCEPTIONS OF THE SERVICE LIVER DIRECT AND THE LEVEL OF SUPPORT IT OFFERS

Rachael Morton

Liver Unit, Birmingham Children's Hospital, Birmingham, United Kingdom

Objectives & Study: Liver Direct (LD) is a weekday two hour nurse led telephone and email service providing support and answers for families and Allied Health Professionals (AHPs) involved in patient care. In 2012 there were 4074 calls and emails received on LD.

Aim: To assess patients, parents and AHPs perceptions of LD and level of support offered

Methods: 10 question surveys aimed at patient, parents and AHPs perceptions of LD service. Participants were approached at clinic appointments, admissions to hospital or calls to LD for advice. These approaches ascertained an overall perspective of users’ feedback on the service.

Results: 59 surveys completed over a three week period: 51 parents; 6 patients; 2 staff. 54% sought advice in first instance from LD v 16% GP; 13% Liver Registrar; 9% local hospital and 7% consultant.

Survey demonstrated parents preferred to contact LD via telephone 77%; 21% using both telephone and email; 2% only email.

The results reflected how supported users felt using LD; time taken to respond to calls and provide advice.
24% of the respondents stated calls were answered very quickly; 49% just right; 25% too long; 1 call not answered.

Feedback from the respondents; 50% advice given was just right; 40% advice was very quick; 26% advice took too long; 56% advice very helpful and 36% advice was often useful; 2 respondents stated advice had not been helpful.

Generally respondents felt the service should be more available. Their recommendations were >33% agreed the service should be accessible in the afternoon; early evening and weekends.

To assess if we could improve our accessibility to LD, we asked if they would like contact via text messaging – 37% yes; 14% maybe: live media chat – 29% yes, 14% maybe, a booked nurse led consultation 37% yes; 27% maybe. In contrast ~50% are happy with just using email and via telephone and did not want other ways to access the service.

Words mainly used to describe how parents felt about the service-“helpful, valuable, great advice, very friendly, excellent, fantastic, informative and don’t take the service away”.

Conclusion:
LD is an excellent service and utilised vastly by patients, parents and AHPs. LD is pivotal in supporting parents if they have any questions or concerns about their child. There is a general consensus that parents would like LD opening hours extended so we are more accessible as a service. Some would like to see further developments in how they access LD service such as text messaging. However, equally half of respondents are happy with just accessing the service via the telephone and email. Our future developments will be to integrate the recommendations from parents into this service.

Acknowledgements: J.Taylor; D.Lowe; L.Pernell; C.Lloyd.

Disclosure of Interest: None Declared
PLAY PICNIC: AN EFFECTIVE TOOL FOR THE MANAGEMENT OF FOOD AVERSION IN LONG-TERM TUBE FEED DEPENDENT CHILDREN

Analou Louw 1,*, Daniella Miserotti 1, Dorin Bernadout 2, Ana-Kristina Skrapac 2, Krishna Soondrum 3
1Paediatric Speech and Language Therapy, Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom, 2Paediatric Dietetics, 3Paediatric Gastroenterology, Chelsea and Westminster Hospital NHS Foundation Trust, London, United Kingdom

Objectives & Study:
Long term tube fed children are at risk of developing oral feeding aversion (FA) and subsequent tube dependency. The cause of FA is multivariable including the underlying morbidity, interference with development of hunger/satiety cycles, lack of exposure to foods during critical periods and development of negative associations around oral feeding. The management of FA is challenging and various approaches to the reintroduction of oral feeding are known. The play picnic is a group therapy method that provides a positive environment for the child to encourage the exploration of food in the aim to develop autonomy in eating. Parents receive coaching that empowers to support and maintain these new eating skills at home.

Aim: To describe the results of a four-week play picnic pilot study.

Methods:
Tube dependent children attending a tertiary feeding clinic were assessed by speech and language therapists. If deemed safe to feed orally and suitable for the transition from tube to oral feeding a block of play picnic sessions on a weekly basis for four weeks was offered. This was modelled on a component of the Graz method of tube weaning1. Individual aims of treatment were agreed. Documented outcomes were: 1) demonstrating distress in the presence of food; 2) touching a range of foods; 3) licking food; 4) swallowing food.

Results:
8 children (5 male) attended the play picnic. The median age was 26 months (range: 10 – 81 months). All children were medically stable with a past history of gastro-oesophageal reflux and following co-morbidities: DiGeorge Syndrome with complex congenital heart disease (n= 2); extreme prematurity (n= 2); infantile myofibromatosis (n=1); Down's syndrome (n= 1). Suboptimal oral intake due to significant aversion towards food was a unifying observation with tube feed dependency (gastrostomy = 6; nasogastric tube = 2; nasojejunal tube =1).

Attendance of the sessions ranged from 25 – 100%. One participant discontinued due to illness. 7 children achieved their individual aims. None of the participants demonstrated distress in the presence of food, 7 participants touched food and subsequently licked food. 62.5% swallowed food after completion of treatment both in the clinic setting and at home. 7 parents found the play picnic useful and agreed to attend future meetings.

Conclusion:
This pilot study demonstrates that play picnics are an effective and cost efficient approach to the reintroduction of oral feeding in tube dependent children with FA. Play picnics increase the child’s autonomy with eating. Parental support allows for generalisation of the acquired oral feeding skills at home.

References:
1) www.notube.com

Disclosure of Interest: None Declared
**Gastroenterology**  
**Coeliac Disease**  
PL-G-0007  

**AGE AT GLUTEN INTRODUCTION AND RISK OF COELIAC DISEASE: FINAL RESULTS OF A PROSPECTIVE, MULTICENTRE, NUTRITIONAL INTERVENTION STUDY ON INFANTS AT FAMILY RISK**

Elena Lionetti 1,*, S Castellaneta 2, A Pulvirenti 3, E Tonutti 4, G Maggiore 5, R Francavilla 6, C Catassi 7 and Italian Working Group of Weaning and Coeliac Disease Risk  

1Department of Paediatrics, University of Catania, Catania, 2Department of Paediatrics, S.Paolo Hospital, Bari, Italy, 3Department of Clinical and Molecular Biomedical Medicine, University of Catania, Catania, Italy, 4Department of Immunopathology and Allergology, Udine Hospital, Udine, Italy, 5Biodiagene, s.r.l, Palmero, Italy, 6Department of Developmental Biomedicine, University of Bari, Italy, 7Department of Paediatrics, Universita Politecnica delle Marche, Ancona, Italy

**Objectives & Study:** The Italian Baby Study on Weaning and celiac disease (CD) risk was a prospective, multicenter, nationwide intervention trial evaluating the role of age at gluten introduction (6 versus 12 months) on CD development, in a large cohort of children at family risk of CD, that were followed from birth.  

**Methods:** Newborns at family risk of CD (at least one first-degree relative affected with CD) were recruited in 20 Italian centers from October 2003 to June 2009. Infants were randomly assigned to introduce gluten at 6 (group A) or 12 months (group B). Diet (duration of breastfeeding, adherence to the protocol, amount of gluten administered) was evaluated at 3, 6, 9, 12 and 15 months; CD serology was tested at 15 (plus HLA), 24, 36, 60 months, 8 and 10 years of age. Kaplan-Meier curves were used to describe the risk of CD in the two trial arms. Decision trees were developed by using the C.45 algorithm to investigate the presence of attributes with predictive power in the dataset.  

**Results:** Out of 707 enrolled infants, 154 (21.8 %) were in the HLA no-risk group and were discarded from further work-up. The final study-group included 553 individuals who were HLA-DQ2 and/or DQ8 positive [group A: 297 (54%), group B: 256 (46%)]. Overall, the prevalence of CD at the last follow-up (mean age = 7.9 yrs) in children at family risk of CD was 16.5 % (117/707). In the subgroup of infant at family risk with CD-predisposing HLA the prevalence of CD was 21% (117/553) [(overt and potential CD: 16.8%, and 4.3%, respectively). The risk of CD showed no significant difference between group A and B. At 2 years of age the proportion of children developing CD was significantly higher in group A as compared to group B (p=0.0001). The decision tree analysis for prediction of CD showed that the highest risk branch (leading to CD instead of not-CD) was assigned to children with a high-risk-HLA [40% of children with high-risk-HLA developed CD versus 20% of children with standard-risk-HLA (p=0.006)]. None of the other variables studied (including breastfeeding duration) was able to predict CD.  

**Conclusion:** Introducing gluten at 12 months of age did not prevent CD, but delayed the onset. Having a high-risk-HLA is an important predictor of CD. Breastfeeding duration is irrelevant for the development of CD.  

**Disclosure of Interest:** None Declared
PREVALENCE AND NATURAL HISTORY OF COELIAC DISEASE IN A COHORT OF CHILDREN HLA-DQ2+

Maria Luz Cilleruelo 1,*, Sonia Fernández 2, Juana Jimenez 3
1Paediatrics, H. U. Puerta de Hierro, Madrid, Spain, 2Paediatrics, H.U Severo Ochoa, Madrid, Spain, 3Biochemistry, H.U. Severo Ochoa, Madrid, Spain

Objectives & Study: The aim of the current study was to assess the prevalence and clinical presentation of celiac disease (CD) in a cohort of children carrying HLA-DQ2 haplotype and to evaluate environmental factors in the development of CD in this population.

Methods: Between July 2004 and July 2005 the parents of all healthy full term newborns in our hospital were invited to participate in the study. HLA-DQ2 genotyping was performed in a blood sample of the umbilical cord in order to create a cohort at risk of CD. Parents were contacted when children were 2 to 3 years old to perform a point of contact serological test (POC test). In children with positive POC test (screening group) a blood sample was collected to confirm these results by serum anti-transglutaminase 2 antibodies (anti-TG2) and endomysial antibodies (EMA). Serological testing was repeated 3-4 months later. Children with anti-TG2 \( \geq 80 \) (>10-fold the upper normal value) and/or EMA \( \geq 1:80 \) underwent an intestinal biopsy. Children with lower titers were given serological test at six month intervals. In addition to this screening group, children of the cohort with symptoms of CD prior to the start of the screening study were included (symptomatic group). Risk factors (gender, mode of delivery, breastfeeding, breastfeeding duration and age of gluten introduction) were studied in patients and referents (children with negative antibodies of the same cohort).

Results: Of the 1291 children enrolled, 362 were HLA-DQ2 + (28%, 44.5% females) and 262 (72.3%) participated in the study: 255 (screening group) and 7 (symptomatic group). In total, 9.9% (26/262, 18 females) tested positive for IgA anti-TG2 and IgA EMA. Celiac disease was diagnosed in 15/262 of the HLA-DQ2 positive children (5.7%, CI 95% 2.7%>8.7%) and 5 had a normal biopsy. 60% had gastrointestinal symptoms with or without iron-deficiency anemia, 7% weight loss or poor weight gain and 33% were asymptomatic. Five children with potential CD and six children with low-moderate levels of autoantibodies became negative (42.3%) and are still negative after 6 years of follow-up. Female gender was a risk factor OR 5.7 (95% CI 1.5-20.9) whereas breastfeeding during the gluten introduction had a protective effect OR 0.1 (95% CI 0.01-0.8).

Conclusion: Prevalence of CD in this HLA-DQ2 + cohort is about 6%. Over half of the patients had digestive symptoms. A high proportion of children between 2-3 years in the screening group showed an spontaneous and persistent disappearance of both antibodies. Breastfeeding at the time of gluten introduction could be associated with a lower risk of CD while being female presented a greater risk.

Disclosure of Interest: None Declared
**Objectives & Study:** The pathophysiology underlying pediatric chronic functional constipation (FC) is poorly understood. These children often report loss of sensation of urge to defecate. Functional magnetic resonance imaging (fMRI) studies have been used to unravel brain processing of visceral sensation in adults with functional gastrointestinal disorders. However, brain-imaging data are lacking in both adults and children with constipation. The aim is to investigate the cerebral activity in response to rectal distension in children with FC and in healthy controls (HCs).

**Methods:** 15 patients with FC (8M/7F; mean age 14.3 yrs, range 12-18 yrs) and 15 HCs (6M/9F; mean age 20.1 yrs, range 18-21 yrs) participated. Rectal barostat was performed prior to the fMRI scan. A stepwise pressure-controlled distension protocol was used to determine the pressure threshold for urge sensation. Subjects received 2 sessions of 5 stimulations consisting of repetitions of 30 sec of rectal stimulation with previous defined pressure threshold, followed by 30 sec of rest during acquisition blood oxygenation level-dependent (BOLD) fMRI. Images were acquired on a 3Tesla MRI scanner with an 8-channel SENSE head receive coil. A T2*-weighted echo planar imaging sequence was acquired with: TR/TE=3000/30 ms, slice thickness=3.0 mm, voxel size=1.72 x 1.72 x 3 mm, with 40 axial slices, in ascending mode covering the whole brain. fMRI signal differences were analyzed using SPM8 in Matlab, thresholded at p<0.001. Cerebral activation was defined as BOLD increase during rectal distension and cerebral deactivation as BOLD decrease during rectal distension.

**Results:** FC patients had higher thresholds for urgency than HCs (p<0.001). FC patients needed a mean pressure of 18.2 mmHg above MDP to provoke urge sensation, compared to a mean pressure of 8.6 mmHg above MDP in HCs. The groups were differentiated by both activated and deactivated regions in response to rectal distension. FC patients showed activation in the dorsolateral prefrontal cortex and deactivation in the median somatosensory cortex, insula and amygdala. HCs showed deactivation in the same areas, but in contrast, no regions showed significant activation in response to rectal distension.

**Conclusion:** This is the first study evaluating cerebral processing of rectal sensation in constipated patients. FC patients and HCs had a different pattern of cerebral activation and deactivation during rectal distension, suggesting different neural processing of rectal urge sensation in brain regions previously implicated in adult studies using visceral pain stimuli.

**Disclosure of Interest:** None Declared
Nervonic Acid is Important for Early Development of Premature Infants Up to 18 Months of Age

Eleni Ntoumani 1*, Cristina Lundqvist-Persson 2, Birgitta Strandvik 3, Karl-Göran Sabel 1
1 Department of Paediatrics, South Alvsborgs Hospital, Borås, Sweden, 2 Skaraborg Institute for Research and Development, Skaraborg Institute for Research and Development, Skövde, Sweden, 3 Dept of Biosciences and Nutrition, Karolinska Institutet, Stockholm, Sweden

Objectives & Study: Nervonic acid (NA, 24:1w9) is found in sphingolipids of white matter and both NA and oleic acid (OA, 18:1w9), a substrate for the synthesis of NA, are important for the biosynthesis of myelin. Incorporation in brain increases rapidly in last trimester. NA is higher in breast milk after premature compared to term birth. The objective was to examine whether NA concentrations in breast milk and plasma correlate to the developmental outcome of premature infants up to 18 months corrected age.

Methods: Data of the study population has previously been published (Lipids Health Dis 2009; 8:20). The associations between development of 51 premature infants examined at 1 and 40 weeks, and 1, 3, 6, 10, and 18 months corrected age and the NA concentrations were analyzed. Development was evaluated with Brazelton Neonatal Behavioural Assessment Scale at 1 month and from 3 months with Bayley’s Scales of Infant Development II. Fatty acid concentrations in breast milk and in infants’ plasma phospholipids at 1 week after birth, and at 40 and 44 weeks corrected age, were analyzed with gas chromatography.

Results: Plasma phospholipid NA concentrations decreased from the first week of life to week 40 (p=0.001, n=30) and further to week 44 (p=0.017, n=36). Plasma NA was significantly lower in small for gestational age (SGA) infants (p=0.003). Plasma NA at 1 week correlated to birth weight SDS and head circumference SDS (r=0.46, p=0.003, and r=0.44, p=0.006, respectively). NA in infant’s plasma at 44 weeks showed significant correlation with motor development at 6 months (r=0.35, p=0.022), both mental (r=0.36, p=0.017), orientation (r=0.37, p=0.014), emotional (r=0.35, p=0.019) and motor development (r=0.39, p=0.007) at 10 months, as well as mental development at 18 months of age (r=0.30, p=0.046). The ratio of OA/NA in plasma phospholipids at 44 weeks correlated negatively at 6, 10 and 18 months with both mental development (r= -0.35, p=0.022; r= -0.38, p=0.011; r= -0.32, p=0.034, respectively) and motor development (r= -0.40, p=0.009; r= -0.39, p=0.008; r= -0.10 p=0.518, respectively). No correlations were found to breast milk NA. Multiple regressions adjusted for background factors showed only significant associations between plasma NA at 44 weeks and mental and motor development at 10 months.

Conclusion: The results of this small study suggest that NA might be of importance for normal development in premature infants. Larger studies with longer follow up are warranted.

References: Lipids Health Dis 2009; 8:20

Disclosure of Interest: None Declared
SIXTEEN-YEAR EXPERIENCE OF MASS SCREENING FOR BILIARY ATRESIA IN TOCHIGI PREFECTURE IN JAPAN

Akira Matsui 1,*, Yan-Hong Gu 2
1Director, National Center for Child Health and Development, Tokyo, Japan 2Dpt of Hygiene and Public Health, Teikyo University School of Medicine, Tokyo, Japan

Objectives & Study: To elucidate whether mass screening (MS) for biliary atresia (BA) using stool colour card (SCC) could improve survival rate with native liver.

Methods: Bile-pigmented (No.4 to 7) and pale-pigmented (No.1 to 3) stools of one month old infants were photographed and printed on a postcard-sized SCC. Since August 1994 to March 2011, SCC was delivered to every pregnant woman by the local government together with a Maternal and Child Health Notebook. Just before one-month health check-up, a mother was asked to compare the stool colour of her infant with those of SCC and to fill in a corresponding colour number in a blank of SCC. Doctor at one-month health check-up phoned or sent a fax to a MS centre when a stool colour number was one of 1, 2 or 3. Those infants with suspected BA were referred to paediatricians or paediatric surgeons. When BA was not excluded after appropriate investigations, the diagnosis was confirmed by laparotomy or operative cholangiography. The infants with confirmed BA underwent Kasai Procedure (KP) at 8 surgical centres.

Results: During the period of 16 years and 8 months, 264,071 infants attended this MS. These were 93% of newborns who were born in the same period. 32 infants were confirmed as BA. Prevalence of BA was 1.2/10,000 (32/264,071). By one month of age, 23 of 32 patients were true-positive and the sensitivity was 71.9% . Positive predictive value was 11.4% (23/201). The percentage of BA patients within 60 days of age at KP was significantly higher than that of nationwide study 1994-2011 (63% vs. 42%). Survival rate with native liver was 70% at 5 years, 46% at 10 years and 46% at 15 years.

Conclusion: According to the introduction of MS using SCC in Tochigi Prefecture, Japan from 1994 to 2011, it was possible to improve 15-year survival rate with native liver excelling the results of best surgical centres in the world. Screening also could be repeated at 2 months of age or later for previously negative infants.

Disclosure of Interest: None Declared
LIVER VPS33B KNOCKOUT MOUSE RECAPITULATES CHOLESTATIC PHENOTYPE OF ARTHROGYROSIS RENAL DYSFUNCTION AND CHOLESTASIS SYNDROME

Holly Smith 1, Asllan Gjinovci 1, Anna Straatman-Iwanowska 1, AS Knisely 2, Paul Gissen 1, 3, 4,*

1Laboratory for Molecular Cell Biology, University College London, London, United Kingdom, 2Institute of Liver Studies/Histopathology, King’s College Hospital, London, United Kingdom, 3UCL Institute of Child Health, University College London, London, United Kingdom, 4Inherited Metabolic Diseases Unit, Great Ormond Street Hospital for Children, London, United Kingdom

Objectives & Study: The objective of the study was to develop a Vps33b mouse knockout (ko) in order to investigate the pathophysiology of the liver disease in Arthrogryposis, Renal dysfunction and Cholestasis (ARC) syndrome. ARC is a severe multisystem disorder fatal in most patients in the first year of life. Cholestasis is the predominant and often the presenting feature in ARC. Characteristic histological features of ARC liver disease include multinucleate giant cell transformation of hepatocytes, lipofuscin deposition and mislocalisation of several hepatocyte canalicular membrane proteins including Bile Salt Export Pump (BSEP) and Carcinoembryonic antigen (CEA). The in depth investigations of the phenotype in the ko included blood biochemistry, liver histology and gene and protein expression analysis.

Methods: ARC syndrome was modelled in the liver by hepatocyte specific cre-recombinase mediated Vps33b excision in the Vps33bfl/fl mouse (Taconic Artemis) using the transgenic line Alfp-cre, containing Albumin promoter elements and α-fetoprotein enhancers for expression as early as E10.5. A 0.5% cholic acid diet was fed for 2 weeks at 9-12 weeks of age to enhance the cholestatic phenotype. Hepatobiliary injury biomarker determinations were carried out on whole blood in the routine service laboratory and bile acid analysis was conducted using electrospray mass spectrometry.

Results: Vps33b levels in the liver were reduced by 70%, and the ko displayed a cholestatic phenotype with bile acids increased to an average of 12 times that of the controls. Alanine aminotransferase, Alkaline phosphatase and bilirubin levels remained unchanged. Immunostained liver exhibited an altered distribution of the apical proteins CEA and BSEP, similar to the patient phenotype. Feeding with a 0.5% cholic acid diet did not affect weight or cause jaundice, but did result in a significant increase in liver mass as well as an increase in alkaline phosphatase levels to 8 times that of control. Microscopy of liver revealed mild inflammation and bile duct proliferation. Ageing the mice to 1 year to investigate the effect of prolonged bile acid stress revealed inflammation, regions of steatosis, and development of large masses of up to 30mm in diameter histologically identified as hepatocellular carcinomas in 5/7 mice compared to 0/4 controls.

Conclusion: We were able to recapitulate the cholestatic disease that is seen in ARC patients in the Vps33b mouse knockout. Most of the Vps33b ko developed liver cancer by the age of 12 months; however, hepatobiliary malignancy has not been seen in the cases of ARC so far. Further work is required to understand the underlying mechanism of cancer development in liver specific Vps33b ko.

Disclosure of Interest: None Declared
APPLICABILITY OF 2009 NASPGHAN-ESPGHAN GUIDELINES FOR THE DIAGNOSIS AND MANAGEMENT OF GASTROESOPHAGEAL REFLUX IN CHILDREN

Paolo Quitadamo 1,*, Vaidotas Urbonas 2, Alexandra Papadopoulou 3, Enriqueta Roman 4, Danijela Jojkic Pavkov 5, Rok Orel 6, Jorge Amil Dias 7, Aco Kostovski 8, Erasmo Miele 9, Alberto Villani 10, Annamaria Staiano 11

1Department of Translational Medical Sciences, section of Paediatrics, University of Naples "Federico II", Naples, Italy, 2Vilnius University Clinic of Children’s Diseases, Vilnius University, Vilnius, Lithuania, 3First Department of Paediatrics, Athens Children’s Hospital “Agia Sophia”, University of Athens, Athens, Greece, 4Department of Paediatrics, Hospital Universitario Puerta de Hierro Majadahonda, Madrid, Spain, 5Department of Paediatrics, Institute for child and youth health care of Vojvodina, Medical Faculty, Novi Sad, Serbia, 6Department of Paediatric Gastroenterology, Hepatology, and Nutrition, Children’s Hospital, University Medical Centre, Ljubljana, Slovenia, 7Department of Paediatrics, Hospital S João, Alameda, Portugal, 8Department of paediatrics, University Children’s Hospital, Skopje, Macedonia, The Former Yugoslav Republic Of, 9Department of Translational Medical Sciences, Section of Paediatrics, University "Federico II", Naples, 10Dipartimento di Paediatria, Ospedale Pediatrico Bambino Gesù, Rome, 11Department of Translational Medical Sciences, section of Paediatrics, University "Federico II", Naples, Italy

Objectives & Study: According to a recent survey, the 2009 NASPGHAN-ESPGHAN GER guidelines are poorly adhered to by European primary care pediatricians1. The main issue raised from the survey was the prescription of unnecessary acid suppressive medications, especially in infants. No inquiry into the reasons was made. The primary objective of the present study was to assess the applicability of the guidelines in European primary care pediatricians undergoing specific trainings. The secondary objective was to evaluate the efficacy of two different training approaches.

Methods: One hundred pediatricians involved in the previous survey agreed to participate and were randomly divided into 2 groups: one group was trained in the guidelines through an online podcast and the other group through a synopsis. During the following 3 months, each involved pediatrician was asked to enroll every consecutive infant, child or adolescent with suggestive reflux symptoms. For every enrolled patient pediatricians filled-in a report concerning their diagnostic and therapeutic choices.

Results: A total of 382 patients (M/F: 186/196, infants/children/adolescents: 194/123/65) were enrolled by pediatricians. Infants with unexplained crying and/or distressed behavior who were prescribed PPIs were 3.7% compared with 45.2% of the survey data obtained before the training (p<0.05). Infants with uncomplicated recurrent regurgitation and vomiting who were prescribed PPIs were 4.5% against 37.1% of the baseline survey data (p<0.05). The overall rate of children managed in full compliance with the guidelines was 46.1% after the training compared to 1.8% before the training (p<0.05). No significant differences were seen between pediatricians from podcast and synopsis group.

Conclusion: NASPGHAN-ESPGHAN GER guidelines have a good applicability, despite they are currently poorly adhered to by European primary care pediatricians. Simple, inexpensive trainings were proven to be effective in increasing adherence by pediatricians. The increase in compliance clearly favours the role of continuous medical education through simple educational tools and subsequent assessment of practice.

Disclosure of Interest: None Declared
PREVALENCE AND NATURAL HISTORY OF INFANT DYSCHEZIA: A PROSPECTIVE COHORT STUDY

E Kramer 1, J den Hertog-Kuijl 1, L van den Broek 2, E van Leengoed 1, F Kolk 3, E Bakker 4, E Bakker-van Gijssel 5, A Bulk 6, C Kneepkens 7, Marc Benninga 8,*

1Stichting Thuiszorg Midden-Gelderland, Arnhem, Netherlands, 2GGD Kennemerland, Hoofddorp, Netherlands, 3GGD Fryslân, Leeuwarden, Netherlands, 4University of Wageningen, Wageningen, Netherlands, 5Siza Dorp Group, Arnhem, Netherlands, 6Department of youth health care VU University Medical Center, 7VU University Medical Center, 8Emma Children's Hospital / AMC, Amsterdam, Netherlands

Objectives & Study: Infant dyschezia, according to the Rome III criteria, is defined as straining and crying for at least ten minutes before successful passage of soft stools without any other health problem, in an infant younger than six months of age. Data regarding the prevalence and natural history of this functional gastrointestinal disorder is lacking. To investigate the prevalence and natural history of infant dyschezia according to the Rome III criteria.

Methods: In 2003, 124 youth health care doctors working in well-baby clinics participated in a national study focusing on the defecation pattern of infants, coined with the Dutch acronym LOOZ (Landelijk Onderzoek naar de Ontlasting bij Zuigelingen). Using a standardised questionnaire and a bowel diary, defecation patterns were recorded of infants aged 1, 2, 3 and 9 months old. In addition, feeding type and symptoms accompanying defecation were recorded.

Results: In total 1292 infants were included in this study. At 1 and 3 months of age, 51 (3.9%) and 11 (0.9%) infants fulfilled the Rome III criteria for infant dyschezia. Only 1 infant had symptoms both at 1 and at 3 months of age. Dyschezia-like symptoms were also recorded in 11 (0.9%) 9-months-old infants; 2 of them also had dyschezia at the age of 1 month. Only 3/61 (4.9%) infants with dyschezia at 1 month or 3 months had symptoms fitting the diagnosis of infant functional constipation (i.e. hard stools with a defecation frequency < 3/week) at 9 months of age.

Conclusion: This study shows that the prevalence of infant dyschezia as described by the Rome criteria is low and declines with age. Only 4.9% of infants with infant dyschezia develop constipation, close to the prevalence of infant functional constipation, suggesting that there is no causative relationship between the two conditions.

Disclosure of Interest: E. Kramer: None Declared, J. den Hertog-Kuijl: None Declared, L. van den Broek: None Declared, E. van Leengoed: None Declared, F. Kolk: None Declared, E. Bakker: None Declared, E. Bakker-van Gijssel: None Declared, A. Bulk: None Declared, C. Kneepkens: None Declared, M. Benninga Consultant for: Shire, Norgine, Sucampo
**Objectives & Study:** Acute severe ulcerative colitis (ASC) is a potentially life-threatening event. Scarce pediatric data are available about success rates of Infliximab (IFX) as a second line therapy. This study was performed in consecutively observed pediatric patients with ASC and aimed at assessing the long-term efficacy of IFX and clinical predictors of poor outcome. Patients had been recruited, after reporting of the 2011 ECCO-ESPGHAN guidelines on pediatric ASC¹.

**Methods:** Children who experienced an episode of ASC, defined as a PUCAI of at least 65 points, were evaluated. Clinical assessment through PUCAI and laboratory data (ESR, CRP, hemoglobin, albumin, hematocrit, ferritin) were recorded at admission and at day 3 and 5. All patients were treated according to above mentioned guidelines for ASC and received intravenous (iv) corticosteroids (CS). IFX was administered as second-line therapy in CS-refractory patients. In a 2-year follow up we assessed the overall colectomy rate and efficacy of IFX.

**Results:** Thirty-one patients (age: 10.6±4.88, 52% female) met the criteria for ASC: 21 (68%) responded to iv CS, while 10 (32%) received IFX for CS-refractoriness. Among the latter, 2 (20%) underwent urgent colectomy; however, at a 2-year follow up, 5 (50%) needed elective colectomy, while only 3 of the CS-responders required surgery (14%). Compared to CS-responsive patients, those CS-refractory showed a significantly shorter interval from the diagnosis of ulcerative colitis to the episode of ASC (p= 0.04) and a higher rate of colectomy at maximum follow-up (p=0.007). Patients needing colectomy differentiated from those responding to medical therapy for more frequent courses of CS prior to ASC (p=0.02), but not for laboratory values, sex, disease location, disease extension, therapy, mean PUCAI, serological markers and family history.

**Conclusion:** Although its short-term effectiveness as a rescue therapy to avoid urgent colectomy in CS-refractory children, IFX does not modify the long term colectomy rate in ASC. Frequent courses of CS are predictive of a poor long-term outcome.

**References:** ¹Am J Gastroenterol 2011;106:574-88

**Disclosure of Interest:** None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

SP-G-0016

**IBD-SPECIFIC TRANSCRIPTOME AND MICROBIOME PERTURBATIONS IN PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMC) AND MUCOSAL BIOPSIES FROM CHILDREN WITH IBD**

Towia Aron Libermann 1, Manoj Bhasin 1, Jess Kaplan 2, Kirill Korolev 3, Chris Moran 2, Leonid Mirny 4, Harland Winter 2

1Medicine, Beth Israel Deaconess Medical Center, Boston, MA, United States 2Paediatric Gastroenterology, MassGeneral Hospital for Children, Boston, MA, United States 3Biological Physics, Boston University, Boston, MA, United States, 4Physics, Massachusetts Institute of Technology, Cambridge, MA, United States

**Objectives & Study:** Although presentation of inflammatory bowel disease (IBD) in children and adults is similar, children are more likely to have changes in immune function and intestinal biome that are directly related to IBD. We initiated a systems biology approach of the transcriptome in PBMCs and the microbiome of intestinal biopsies in children with Crohn’s Disease (CD), Ulcerative Colitis (UC), non-IBD gastrointestinal (GI) inflammation (I-CTL), and no inflammation (NI-CTL), to identify IBD-specific causative pathways and biomarkers.

**Methods:** We assessed the transcriptome in PBMCs from 44 patients (14 CD, 7 UC, 11 NI-CTL and 12 I-CTL] using Affymetrix GeneChips. Differentially expressed genes were identified using unpaired univariate t-tests. Pathological mechanisms linked to pediatric IBD were assessed by systems biology analysis. A CD-specific predictor, generated using linear discriminant analysis (LDA), was validated on a published adult IBD dataset (GSE3365). 454 pyrosequencing of microbial 16S rRNA genes was performed on ileal mucosal biopsies of 94 children (23 CD, 8 UC, 63 controls [NI-CTL]). Shannon Diversity Index (SDI), Principal Component Analysis (PCA), and new algorithms were applied to compare differences in microbiota between groups.

**Results:** Supervised analysis identified 162 differentially expressed genes that separated IBD patients (CD + UC) from non-IBD patients (I-CTL + NI-CTL). Comparison of CD to I-CTL patients yielded 127 differentially expressed genes, suggesting that IBD inflammatory processes diverge from non-IBD GI inflammatory disorders. These CD-specific genes participate in neutrophils, mast cells and eosinophils (enhanced expression) and NK cells and regulatory T-cells (decreased expression). 63 transcripts distinguished CD from UC patients, including inflammasome markers and genes involved in pathogen recognition and innate immunity. The 6-gene CD predictor achieved an accuracy of 78.7% (64.4% sensitivity, 88.1% specificity) on the adult IBD dataset. Microbiome analysis of the ileal biopsy samples revealed reduced overall ileal microbial diversity in CD compared to UC and controls. The bacteria that contributed most to differences between CD and controls included a significant decrease of Roseburia (p = 0.001) and Lachnospiraceae incertae sedis (p = 0.01) in CD children.

**Conclusion:** Our findings indicate that distinct alterations in the PBMC transcriptome and ileal microbiome segregate CD from I-CTL in children. Further evaluation may reveal new physiological pathways that could result in innovative therapies and new insight into the role of specific gut microbiota and immune system shifts in pediatric IBD pathogenesis.

**Disclosure of Interest:** T. Libermann Shareholder of: anXome, company provides bioinformatics service, I am scientific founder of company, M. Bhasin: None Declared, J. Kaplan: None Declared, K. Korolev: None Declared, C. Moran: None Declared, L. Mirny: None Declared, H. Winter: None Declared
AUTOIMMUNE-MEDIATED RESPONSES DIRECTING AT BILE DUCT EPITHELIAS ARE INDUCED IN REGULATORY T CELL-DEFICIENT NEONATAL MICE EXPOSED TO LOW DOSE CMV

Jie Wen 1,*; Yongtao Xiao 1; Wei Cai 1

1Department of Paediatric Surgery, Shanghai Key Laboratory of Paediatric Gastroenterology and Nutrition, Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Objectives & Study: Recent studies indicated perinatal cytomegalovirus (CMV) infection may be an initiator of bile duct damage in biliary atresia (BA), and meanwhile deficits of Regulatory T cells (Tregs) in BA potentially allowed for exaggerated biliary injury. Although both previous CMV infection and Tregs-deficit exist in majority of BA patients, whether an initial low-dose CMV exposure in Tregs-deficient neonatal mice could induce exaggerated and progressive biliary injury is undefined.

Methods: We established a low-dose CMV (LCMV) infected Tregs-deficient neonatal mice model, mimicking the experiences of BA patients. We quantified Tregs, CD3 and CD8 lymphocytes by flow cytometry, mRNA expression for inflammatory and apoptosis associated genes by real-time PCR, and inflammatory factors by mouse inflammation antibody array. Immunofluorescence and western blot analysis were also used to detect serum autoantibodies.

Results: We found that LCMV exposure in tregs-deficient mice induced extensive inflammation directing at both intrahepatic and extrahepatic bile ducts, accompanying with injury and atresia of intrahepatic bile ducts, and partial obstruction of extrahepatic bile ducts, consistent with the elevated levels of total and direct bilirubin. Evidence for cellular and humoral autoimmunity existing in LCMV-infected Tregs-deficient mice were also obtained by detecting increased population of CD3 and CD8 lymphocytes, and serum antibodies reactive to bile duct epithelial proteins, one of which was identified as α-enolase. The decreased inhibition of aberrant activation of hepatic T-lymphocytes and autoantibodies specific to bile duct epithelia due to lack of Tregs may lead to this exaggerated intrahepatic and extrahepatic bile duct injury. Further exploring the potential mechanisms, increased hepatic expression for Th1-related genes TNF-α and IFN-γ-activated genes STAT-1, and Th1 cytokines TNF-α, Lymphotactin, IL-12p40 and MIP -1γ were identified in this model. This predominant hepatic expression for Th1-related genes and cytokines raised the possibility that Th1 response was linked to the inflammatory and autoimmunity-mediated bile duct injury in this mice model.

Conclusion: LCMV infection in Tregs-deficient mice induced autoimmune-mediated and inflammatory responses directing at bile ducts, resulting in exaggerated and progressive intrahepatic and extrahepatic bile duct injury, which may contribute to the progress of human BA.

Disclosure of Interest: None Declared
**Hepatology**

**SP-H-0018**

**SCLEROSING CHOLANGITIS AND AUTOIMMUNE HEPATITIS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE - THE WESTERN AUSTRALIAN EXPERIENCE**

Alicia Ai Wei Lim 1,*, Catherine Mews 1, David Forbes 1, Ainslie Lopez 1, Angela De Nardi 1, Madhur Ravikumara 1

1Gastroenterology, Princess Margaret Hospital for Children, Western Australia, Australia, Subiaco WA 6008, Australia

**Objectives & Study:** Primary sclerosing cholangitis (PSC), autoimmune sclerosing cholangitis (ASC) and autoimmune hepatitis (AIH) are known extra-intestinal manifestations of inflammatory bowel disease (IBD). The available data on incidence and prevalence in the paediatric population is limited. We report the data on the occurrence of PSC, ASC and AIH in our cohort of children diagnosed with IBD at the sole tertiary paediatric hospital in Western Australia.

**Methods:** A retrospective chart review was performed and all patients diagnosed with PSC, ASC and AIH between January 2004 and April 2013 were identified and cross-referenced with the department's IBD Database. All children with one of these hepatobiliary diseases in association with IBD were identified. Demographic details, age at presentation, indication for initial investigation, results of biochemical and immunological work-up, colonoscopy findings, liver histopathology and MRCP results were reviewed.

**Results:** Over the nine year period, 157 children (79 males and 78 females) were diagnosed with IBD. Of these, 12 (7.6%) were also diagnosed with either PSC (6 children), ASC (5 children) and AIH (1 child). Nine of the 12 children were males. Nine children had ulcerative colitis, 2 with IBD-Unclassified (IBDU) and one child had ileo-colonic Crohn's disease. All had pancolitis at colonoscopy. The median age at diagnosis of the hepatobiliary disease was 13.5 years (range 2-15.9 years).

In 7 children, the diagnosis of IBD and hepatobiliary disease was made concurrently. In 4 children, the diagnosis of hepatobiliary disease preceded that of IBD with median 26.5 months and in one child, hepatobiliary disease was diagnosed 8 months after diagnosis of IBD. Of the 11 children with sclerosing cholangitis, 8 had evidence of sclerosing cholangitis on MRCP while the remaining 3 children with normal MRCP had histopathological evidence on liver biopsy suggestive of small duct sclerosing cholangitis.

**Conclusion:** This study suggests that approximately 7.6% of children with IBD also have associated hepatobiliary disease (PSC, ASC or AIH). There is increasing recognition of this association, with some studies reporting up to 30% prevalence of IBD-associated hepatobiliary disease in children with colitis. We suggest that in children with IBD who have abnormal liver biochemistry, further liver specific investigations including liver biopsy and MRCP be considered since the additional diagnosis of PSC, ASC or AIH will have therapeutic and prognostic implications.

**Disclosure of Interest:** None Declared
DIFFERENTIAL EFFECT OF VITAMIN D ON NOD2- AND TLR-INDUCED CYTOKINES IN CROHNS DISEASE

Ernest Seidman 1,*, Serge Dionne 1, Mario Calderon 2, John White 2
1Gastroenterology, McGill University Health Centre, Montreal, Canada, 2Physiology, McGill Univ
Faculty of Medicine, Montreal, Canada

Objectives & Study:
Accumulating evidence implicates defective innate immunity in the pathogenesis of Crohn’s Disease (CD). More specifically, ineffectual NOD2, the most common susceptibility gene for CD, contributes to development of the disease. Vitamin D, a potent modulator of both innate and adaptive immunity, was recently shown by our group to induce NOD2 gene expression and downstream function. We thus hypothesized that supplementation with the hormonal form of vitamin D (1,25D) could beneficially modulate innate immune function in CD.

Methods: PBMC from CD (113) or controls were incubated with 40 nM 1,25-dihydroxyvitamin D (1,25D) or vehicle for 20h. The cells were then stimulated with the following PRR agonists for 20 h: LPS (100 ng/ml, from E. coli 026:B6), Pam3CSK4 (2 µg /ml), R848 (2 µg/ml) and MDP (5 µg /ml). At the end of each culture period, supernatants were collected and stored at -70C. Vehicle or 1,25D (15 nM) was added to dendritic cells (Mo-DC) in the presence of IL-4 and GM-CSF for 20h. Cells were stimulated as described above and supernatants were collected after 24h for cytokine measurements. Levels of TNFα, IL-10, IL-12/IL-23p40, IL-12p70 were measured in the supernatants by ELISA. DNA was isolated from whole blood and genotyping was carried out at the McGill University- Genome Quebec Innovation Center using the Sequenom platform.

Results:
1,25D decreased TLR-induced cytokine production and enhance cytokine levels induced by MDP, the NOD2 ligand. 1,25D increased the synergistic effect provided by NOD2 and TLR co-activation on IL-10, IL-23 and TNFα production. Whereas 1,25D inhibits TLR-induced cytokine production by Mo-DC, co-stimulation of NOD2 results in 2 fold increase in IL-10 and IL-23 production. IL-12p70 production was completely abrogated by 1,25D pretreatment. 1,25D similarly modulated cytokine production by immune cells from ulcerative colitis and healthy individuals. Importantly, Mo-DC from CD patients heterozygous for NOD2 mutations had a similar response to that from patients without NOD2 mutations. However, immune cells from patients homozygous for the 1007fs mutation were unresponsive to MDP and 1,25D.

Conclusion: Our data suggest that most CD patients might benefit from 1,25D as a potent modulator of immunity.

Disclosure of Interest: None Declared
VITAMIN D DEFICIENCY PROMOTES EPITHELIAL BARRIER DYSFUNCTION AND INTESTINAL INFLAMMATION

Amit Assa 1,*, Linda Vong 1, Naama Avitzur 1, Lee Pinnell 1, Kathene Johnson-Henry 1, Philip Sherman 1, 2

1Research Institute, The Hospital for Sick Children, Toronto, Canada 2Cell Biology Program, University of Toronto, Toronto, Canada

Objectives & Study: Vitamin D is an important modulator of the immune system and has a protective effect on mucosal barrier homeostasis. The purpose of this study was to investigate the effects of vitamin D deficiency on infection-induced changes in intestinal epithelial barrier function in-vitro, and on Citrobacter rodentium-induced colitis in mice.

Methods: Polarized epithelial Caco2-bbe cells were grown in medium with or without vitamin D and then challenged with enterohemorrhagic Escherichia coli (EHEC) serotype O157:H7. Barrier function was assessed by measuring transepithelial electrical resistance (TER), fluorescein isothiocyanate dextran (10 kilodalton) paracellular permeability, and the expression and distribution of the intercellular tight junction proteins zonula occludens (ZO)-1 and claudin-1. Weaned female C57BL/6 mice were fed either a vitamin D sufficient or deficient diet for 5 weeks and then infected with C. rodentium. Disease severity was assessed by histology to assess colonic epithelial hyperplasia, an in vivo gut permeability assay, and analysis of fecal microbiota composition.

Results: Incubation of Caco2-bbe cells with 1,25(OH)2D3 significantly blunted EHEC O157:H7-induced reductions in TER (p<0.01), decreased macromolecular permeability (p<0.05), and preserved apical junction complex structural integrity. Vitamin D deficient mice challenged with C. rodentium demonstrated increased colonic epithelial cell hyperplasia and greater epithelial barrier dysfunction (p<0.0001 and p<0.05, respectively). Vitamin D deficiency also resulted in an altered composition of the fecal microbiota both in the absence and presence of C. rodentium infection.

Conclusion: These data show that vitamin D mediates intestinal epithelial defenses against intestinal injury. Vitamin D deficiency also predisposes to more severe injury in an infectious model of colitis that could involve an altered composition and function of the gut microbiome.

Disclosure of Interest: None Declared
EXOGENOUS AND ENDOGENOUS DETERMINANTS OF VITAMIN K DEFICIENCY IN CYSTIC FIBROSIS

Patrycja Krzyzanowska 1,*, Andrzej Pogorzelski 2, Wojciech Skorupa 3, Jerzy Moczko 4, Jaroslaw Walkowiak 1

1Department of Paediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Sciences, Poznan, Poland, 2Institute of Tuberculosis and Lung Diseases, Rabka-Zdroj, Poland, 3Institute of Tuberculosis and Lung Diseases, Warsaw, Poland, 4Department of Computer Science and Statistics, Poznan University of Medical Sciences, Poznan, Poland

Objectives & Study: Vitamin K deficiency is frequently observed in patients with cystic fibrosis (CF) despite supplementation. The aim of the study was to assess frequency of vitamin K deficiency in CF patients and to identify exogenous and endogenous determinants of vitamin K body resources.

Methods: The studied group comprised of 168 CF patients aged 1-41 years. In all subjects nutritional status (standardized body weight and height, albumin concentration), genotype, clinical expression of the disease (lung function - spirometry, pancreatic exocrine function - elastase-1 in stool, biochemical markers of liver function - ALT, AST, GGT, Pseudomonas aeruginosa colonization, comorbidities), treatment (vitamin K and pancreatic enzymes supplementation, antibiotic and glucocorticoid therapy). Vitamin K status was estimated by prothrombin induced by vitamin K absence (PIVKA-II) and the percentage of undercarboxylated osteocalcin (u-OC); normal values were < 2 ng/ml and 20%, respectively.

Results: Pathological PIVKA-II concentrations (median: 3.7 ng/ml, 1st-3rd quartile: 2.4-6.0) were found in 72 (42.8%) patients. Abnormal percentages of u-OC (median: 60.9%, 1st-3rd quartile: 34.8-78.0) were observed in 60 (35.7%) subjects. Vitamin K deficiency as assessed with PIVKA-II was more frequent in patients not receiving vitamin K (p=0.002), with pancreatic insufficiency (p=0.001), with F508del/F508del genotype (p=0.048) or with two other severe mutations in both alleles of the CFTR gene (p=0.021). Vitamin K deficiency identified using u-OC was more prevalent in CF patients not receiving vitamin K (p=0.000036). Multiple regression analysis showed that PIVKA-II concentration was related to AST activity and oral antibiotic treatment in 3 preceding months (p=0.025 and p=0.003). In turn, percentage of u-OC was related to vitamin K supplementation, GGT activity and the use of inhaled glucocorticoids (p=0.005, p=0.038 and p=0.020, respectively).

Conclusion: Vitamin K deficiency is more prevalent in CF patients not receiving vitamin K, with pancreatic insufficiency, and two severe mutations in both alleles of the CFTR gene. However, there are no good predictors of vitamin K status in CF patients. Therefore, constant monitoring of its body resources should be provided.

Disclosure of Interest: None Declared
Nutrition
Clinical Trials
SP-N-0022

SERUM VITAMIN D LEVELS IN CHILDREN DEPENDED LESS ON LATITUDE THAN ON SKIN COLOUR AND DIETARY INTAKE DURING EARLY WINTER IN SWEDEN

Pia Karlsland Åkeson 1,*, Olle Hernell 2, Torbjörn Lind 2, Sven-Arne Silfverdal 2, Inger Öhlund 2
1Paediatrics, Department of Clinical Sciences, Lund University, Lund, Sweden, 2Paediatrics, Department of Clinical Sciences, Umeå University, Umeå, Sweden

Objectives & Study: In a prospective, comparative multicenter study in northern and southern Sweden, dietary intake and serum vitamin D concentrations were compared in children with fair and dark skin during the early winter season.

Methods: Five to seven year-old children with fair and dark skin in northern (latitude N 63°) (n=44/40) and southern (N 55°) (n=64/57) Sweden were studied in November and December. Dietary intake was recorded and serum concentrations of 25(OH)D determined.

Results: Serum concentrations of 25(OH)D were higher in northern than in southern Sweden in children with fair (67 vs. 59 nmol/l, p<0.05) and dark (56 vs. 42 nmol/l, p<0.001) skin, and higher in children with fair than dark skin in northern (p<0.01) and southern (p<0.001) Sweden. More than 75% of children with dark skin in southern Sweden had serum 25(OH)D levels <50 nmol/l compared with 30% in the northern part of the country. Total dietary intake of vitamin D was higher in northern than in southern Sweden in children with dark skin (p<0.01) and also tended to be higher in those with fair skin (p=0.056), but no difference was found between children with fair and dark skin within either region.

Conclusion: Despite higher latitude, serum 25(OH)D concentration was higher in children in northern than in southern Sweden during early winter season. This finding could partly have resulted from higher dietary intake of vitamin D in northern Sweden. However, dark pigmentation remains a major risk factor for vitamin D insufficiency.

Disclosure of Interest: None Declared
NOROVIRUS INFECTION IN PAEDIATRIC INTESTINAL TRANSPLANT RECIPIENTS

Esther Ramos Boluda 1*, Beatriz Fernández Caamaño 1, Teresa Herrero Diez 1, Arantxa Gil Cabañas 1, Jesús Sarría Osses 1, Manuel López Santamaría 2, Gerardo Prieto Bozano 1

1 Paediatric Gastroenterology and Nutrition, University Paediatric Hospital La Paz, Madrid, Spain
2 Paediatric Surgery, University Paediatric Hospital La Paz, Madrid, Spain

Objectives & Study: Norovirus infection causes self-limited and mild gastroenteritis in healthy people but it can be severe and/or prolonged in intestinal transplant patients. The aim was to describe clinical and development of norovirus infection in pediatric intestinal transplant receptors.

Methods: We retrospectively analyzed clinical and developmental variables of a series of norovirus infected children following intestinal transplant. Norovirus detection was performed by polymerase chain reaction (PCR) in faecal samples.

Results: A total of 51 intestinal transplantations (15 isolated intestine, 6 liver-intestine, 29 multivisceral and 1 modified multivisceral) were performed to 36 patients from January 2006 to October 2013. Norovirus infection was detected in 21 transplants (41%). These infections appeared at 477.33 ± 740.38 (21-2984) post-transplant days (134 days median). At the time of the infection, patients showed levels of tacrolimus ranging from 5 to 20 ng/ml depending of post-transplant time. All patients developed secretory diarrhea with a stool volume > 90 ml/kg/d. In 17 of 21 infected receptors an endoscopic control with ileum biopsy was performed in order to rule out acute rejection which was only seen in one of them. Eight of the patients had coinfection with other enteric viruses like rotavirus (6), adenovirus (2), coronavirus (1) and astrovirus (1). The averaged infection length was 228.8 ± 302.29 (12-944) days (58.5 days median). In 7 patients (33%) infection was prolonged, lasting more than 6 months, in 6 of them a dysfunction of the graft was associated.

Conclusion: Incidence of Norovirus infection following small bowel transplantation is very high. Infection is often prolonged and associated to other enteric viruses. Long-lasting infection is associated to graft dysfunction. Differential diagnosis with acute rejection must be done.

Disclosure of Interest: None Declared
DIOSMECTITE EFFECTS ON THE ROTAVIRUS-INDUCED OXIDATIVE STRESS, ENTEROTOXIC AND CYTOTOXIC DAMAGES IN HUMAN ENTEROCYTES

Vittoria Buccigrossi 1,*, Carla Russo 1, Basile Francesca Wanda 1, Alfredo Guarino 1
1Translational Medical Science, Section of Paediatrics, University of Naples Federico II°, Naples, Italy

Objectives & Study: Rotavirus (RV) is the most severe agent of gastroenteritis and induces a sequence of enterotoxic and cytotoxic effects in enterocytes. Diosmectite (DS) has been included in the ESPGHAN guidelines for management of gastroenteritis. We test the hypothesis that DS is effective in prevention and treatment of RV-induced ion secretion, epithelial damage and oxidative stress at the level of the enterocyte in an in-vitro experimental model.

Methods: We used a RV infection model developed in Caco-2 cell monolayers with RV strain SA11 (De Marco et al., JID 2009). RV was incubated with DS (100mg/ml) for 60 min at 37°C. The supernatant of this preparation was used to infect cells. The cytotoxic and enterotoxic effects induced by RV were evaluated by the transepithelial resistance (TER) and the short circuit current (Isc) in Ussing Chambers. NSP4 expression was evaluated by western blot. Reactive oxygen species (ROS) and reduced (GSH)/oxidated (GSSG) glutathione ratio were assessed using dichlorofluorescein (DCF) and a colorimetric assay. Phalloidin staining was used to evaluate the actin structure.

Results: DS decreased RV-induced chloride secretion as judged by Isc (0.039±0.002 vs 0.25±0.09 µA/cm²; p<0.05). This effect is associated with a reduced expression of NSP4, a viral protein involved in the enterotoxic damage. In addition, DS reduced the RV-induced ROS production (29±3.6 vs 115±33.8 RFU; p<0.05) and GSH/GSSG ratio (1.5±2.1 vs 0.1±0.3 RFU; p<0.05). The actin staining revealed that RV altered the cytoskeleton structure already after 24 hours post-infection but this damage was not detected in DS pretreated-virus. Finally, TER measurement indicated that DS reduced the cytotoxic damage induced by RV at 24 hours but not at 48-72 hours post-infection (p<0.01).

Conclusion: DS is able to significantly inhibit the chloride secretion and oxidative stress in RV-infected enterocytes. The short-term cytotoxic damage is also prevented. These data provide a new mechanism for the efficacy of DS in acute gastroenteritis.

Disclosure of Interest: None Declared
Objectives & Study: Rotavirus (RV) infection leads to watery diarrhea through multiple mechanisms. We investigated the direct role of NSP4 RV enterotoxin on: 1) the chloride secretion 2) tissue integrity and 3) cell redox state. We also investigated whether RV-induced damages were prevented by *S. boulardii* (Sb), a probiotic yeast used in the treatment of RV childhood gastroenteritis.

Methods: The enterotoxic and cytotoxic effects induced by NSP4 were evaluated by the short circuit current (Isc) and the transepithelial resistance (TEER) in Caco-2 cells mounted in Ussing chambers. RV infection was performed with SA11 strain at 10 PFU/cell. Reactive oxygen species (ROS) and glutathione reduced (GSH) and oxidated (GSSG) forms were assessed using respectively dichlorofluorescein (DCF) and a colorimetric assay. We added *S. boulardii* culture supernatant (SbS) to Caco-2 cells. In addition, intestinal biopsies were used for organ culture experiments with the aim to validate the results observed in Caco-2 cells.

Results: NSP4 induced a peak of Isc at 50 min after addition on Caco-2 cell monolayers. The effect was maximal at 200ng/ml compared to controls (Isc 2.53±0.5 vs 0.8±0.6; p<0.05). NSP4 did not affect the TEER at 24-72 hours compared to RV infected cells (RV -40% vs control, p<0.01; NSP4 +5% vs control, NS). In addition, NSP4 induced ROS generation at the same levels of RV (NSP4 214±58; RV 223±76; controls 25±19 DCF fluorescence units; NSP4 vs controls and RV vs controls, p<0.05). N-acetylcysteine (NAC), a potent antioxidant, strongly inhibited ROS increase and chloride secretion induced by NSP4. Comparative experiments indicated that NSP4 results resemble effects previously observed with living RV strains on ROS increase, GSH/GSSG ratio unbalance and chloride secretion. SbS inhibited RV-induced chloride secretion by 65.3% (p<0.05), reducing ROS increase by 42.8% (p<0.05) and restoring GSH/GSSH ratio to the control level. These results were confirmed in *ex-vivo* organ culture experiments using intestinal mucosa biopsies.

Conclusion: NSP4 induced Isc increase with a dose-dependent and time-related effect. NSP4 is not involved in enterocyte damage. In addition, NSP4 enterotoxic effect is oxidative stress dependent. The comparative results between NSP4 and RV suggested that the chloride secretion induced by the virus is mainly related to NSP4 activity. *S. boulardii* counteracts RV effects acting on the oxidative stress. These data provide a new explanation for the high efficacy of *S. boulardii* against childhood diarrhea observed in clinical trials.

Disclosure of Interest: None Declared
RACECADOTRIL FOR THE TREATMENT OF ACUTE DIARRHOEA IN CHILDREN: SYSTEMATIC REVIEW AND META-ANALYSES

Morris Gordon 1*, Anthony Akobeng 2
1Blackpool Victoria Hospital, Blackpool, United Kingdom, 2Paediatric Gastroenterology, Royal Manchester Children's Hospital, Manchester, United Kingdom

Objectives & Study: Acute diarrhoea causes significant morbidity and mortality in children despite advances in oral rehydration therapy, the mainstay of treatment. Racecadotril is an antisecretory agent that selectively inhibits intestinal enkephalinase and prevent fluid/electrolyte depletion as a result of acute diarrhoea, without affecting intestinal motility. Previously published reviews of the literature were limited by a lack of consideration of adverse events and methodological issues. An up-to-date systematic review using the Cochrane Collaboration format is therefore indicated to summarise the current evidence on the use of Racecadotril for the treatment of acute diarrhoea in children.

Methods: Randomised controlled trials (RCT) comparing racecadotril to placebo or other interventions in children with acute diarrhoea, as defined by the primary studies, were included. Data sources were MEDLINE, EMBASE, Cochrane Central Register of Controlled Trials, references of retrieved articles and drug company contacts. When inadequate data was presented, authors were contacted. Data extraction and assessment of methodological quality were performed independently. Methodological quality was assessed using the Cochrane risk of bias tool. Data was analysed according to the intention to treat principle.

Results: 7 RCTs were included, 5 comparing racecadotril with placebo / no intervention, with 1 having inpatient and outpatient populations that were analysed separately. There was 1 study comparing racecadotril with pectin / caolin and 1 with loperamide. Moderate to high risk of bias was present in all studies. No significant difference in efficacy or adverse events was found in 1 study comparing racecadotril to loperamide. Meta-analysis of 4 studies with 806 participants showed significantly shorter duration of symptoms in the racecadotril group compared to placebo or no intervention (SMD -63.30 hours, 95% CI -65.23 to -61.36). Meta-analysis of 2 studies with 405 participants showed significantly less stool output in the first 48 hours of treatment in the racecadotril group (SMD -130g/kg, 95% CI -133 to -126). Meta-analysis of 3 studies with 402 participants showed significantly less stool output in the first 48 hours in the racecadotril group (SMD -2.24 stools per day, 95% CI -2.62 to -1.85). Meta-analysis of 5 studies with 949 participants showed no significant difference in adverse events between racecadotril and placebo or no intervention (OR 0.99, 95% CI 0.68 to 1.43).

Conclusion: There is some evidence from this review that racecadotril is more effective than placebo or no intervention in reducing the duration of illness and stool output in children with acute diarrhoea. However, the overall quality of the evidence and strength of this conclusion is limited due to heterogeneity and risk of bias in the studies. Racecadotril appears safe and well tolerated when compared to placebo and loperamide.

Disclosure of Interest: M. Gordon Conflict with: Travel grants and honoraria to present research at meeting and speak for companies including abbott, warner chilcott, casen fleet, ferring, norgine and danone. No company has had any involvedment in the planning, execution, write up or presentation of any work or lectures by Morris Gordon, A. Akobeng: None Declared
MODIFICATION OF SALMONELLA THYPHIMURIUM PROPAGATION IN THE INTESTINAL TRACT BY THE PROBIOTIC YEAST STRAIN SACCHAROMYCES BOULARDII: USE OF A REAL-TIME BILUMINESCENCE IMAGING TO MONITOR INFECTION

Rodolphe Pontier-Bres 1, Patrick Munro 1, Véronique Imbert 1, Emmanuel Lemichez 1, Patrick Rampal 2, Jean François Peyron 1, Dorota Czerucka 1,*
1 C3M, INSERM U1065, Nice, France, 2 Centre Scientifique de Monaco, Monaco, Monaco

Objectives & Study: Salmonella typhimurium (ST) infection is initiated when bacteria enter the host through contaminated food and move along the gastrointestinal tract (GT). The probiotic yeast Saccharomyces boulardii Biocodex (S.b-B) is prescribed for prophylaxis and treatment of diarrheal diseases caused by bacteria or antibiotics. In case of ST infection, S.b-B prevents weight loss of infected mice and decreases bacterial translocation (PLOS One 2010, e8925).

Aim: This study was designed to investigate the effect of S.b-B on ST progression in the GT of mice by using a bioluminescence approach and, evaluate the impact of the yeast on immune host response to the infection.

Methods: Bioluminescent imaging (BLI) approach was used to evaluate the effect of S.b-B on the progression of luminescent Salmonella Typhimurium (ST-lux) in mice. Photonic emission (PE) was followed in the GIT isolated after different periods post infection (PI) (15, 45, 90 min and 6 hours). RT-qPCR was used for cytokines mRNA quantification in different compartments of GIT.

Results: Kinetic of PE progression showed that during the 60 min PI, ST-lux moved slightly faster in mice treated with S.b-B than in bacteria-alone infected group. At 90 min PI all ST-lux had reached the cecum in both conditions. A strict correlation existed between light PE and, ST enumeration by CFU determination or ST 16S rRNA quantification. Adhesion of ST to S.b-B was visualized in the intestine of mice treated by the yeast and likely accounted for the elimination of the ST-lux in the feces and the lowering of ST-translocation to the spleen and liver. In the early phase of infection, S.b-B also modified the immune responses to ST by elevating IFN-γ expression and decreasing IL-4 and IL-10 expression in the intestine.

Conclusion: This study reveals that in vivo S.b-B modifies the propagation of ST along the GIT, induces a faster elimination of the bacteria in the feces, prevents bacterial translocation and finally modifies the innate immune response to the infection. Together, these findings shed light on the molecular basis of the protective effect of S.b-B during the early phase of infection by Salmonella.


Objectives & Study: Hirschsprung disease (HSCR) is the most frequent genetic cause of congenital intestinal obstruction with an incidence of 1:5000 live births. Recent studies have suggested that more genes with incomplete penetrance might be associated with the susceptibility of HSCR. The aim of the present study is to examine the contribution of genetic variants in GABRG2 gene to the susceptibility to HSCR in Han Chinese.

Methods: Accordingly, we employed a strategy combining case-control analysis with the Sequenom MassArray platform (iPLEX GOLD technology) to assess genetic variants within GABRG2 gene in 104 subjects with sporadic HSCR (84 male and 20 female, age 1.14 ± 1.83 years) and 151 normal controls (86 male and 65 female, age 1.66 ± 1.05 years) of Han Chinese origin. A total of 8 single nucleotide polymorphisms (rs209350, rs11135176, rs211037, rs169793, rs211015, rs418210, rs424740 and rs647625) were recruited from dbSNP and HapMap project database to cover ~72.0 kb region of GABRG2, with an average interval of ~9.0 kb.

Results: Genotype distributions were in Hardy-Weinberg equilibrium for all eight polymorphisms in either cases or controls (P > 0.05). We observed significant differences in both allele and genotype frequencies between 104 HSCR subjects and 151 normal controls at rs209350 and rs169793 (rs209350, allele, P = 0.002, genotype, P = 0.009; rs169793, allele, P = 0.011, genotype, P = 0.022). The C allele and CC genotype of rs209350 presented significantly higher frequencies in the HSCR subjects than in the normal controls (C allele, 75.3% versus 62.0%, OR = 1.86, 95% CI 1.25-2.78; CC genotype, 59.6% versus 39.7%). Similarly, the A allele and AA genotype of rs169793 were more common in cases compared to controls. For the eight genetic markers, haplotype analysis revealed some significant global P values, and the haplotype which combined all 8 SNPs was the most significant giving a global P = 0.0003.

Conclusion: Our results provide a first indication that common variants within GABRG2 might confer altered risk to Hirschsprung disease in Han Chinese, further supporting GABRG2 as a potential susceptibility gene for HSCR and confirming a possible role of GABRG2 in HSCR etiology.

Disclosure of Interest: None Declared
The Effect and Mechanism of Serotonin-Vagal C Fibers Pathway in Esophageal Acid Reflux-Induced Airway Hyperresponsiveness

Mizu Jiang 1,*, Xi Yang 1, Ting Zhang 1, Weizhong Gu 1, Xiaoli Shu 1
1Gastroenterology, Children's Hospital, Zhejiang University School of Medicine, Hangzhou, China

Objectives & Study: The aim of this study is to investigate the effect and mechanism of serotonin (5-hydroxytryptamine, 5-HT)-vagal C fibers in mediating esophageal acid reflux-induced airway hyperresponsiveness.

Methods: The distal esophagus of anesthetized guinea pigs was perfused with hydrochloric acid containing 1g/l pepsin for 20 min/day for 2 weeks in model group, while perfusing with ddH2O instead of hydrochloric acid in control group, and without any treatment in blank group. The changes of lung resistance and compliance to different levels of methacholine (Mch) were investigated to evaluate the airway responsiveness. The concentrations of 5-HT and its metabolic product 5-HIAA of esophageal tissue were detected by HPLC-ECD. The mRNA and protein expression of Transient receptor potential vanilloid receptor 1 (TRPV1), Serotonin Transporter (SERT), and 5HT4R of esophageal tissue were measured by RT-PCR and Western blot respectively.

Results: A significant increasing of lung resistance and decreasing of lung compliance was observed in model group which indicated airway hyperresponsiveness. An obvious ulceration and serious inflammation in the mucosa of distal esophagus was observed in model group, which also had inflammatory cell infiltrating mainly eosinophils in bronchial and lung tissues. No pathological change in the distal esophagus, bronchial and lung tissues was observed in control and blank groups. The total number of inflammatory cell, as well as the percentage of eosinophils of the bronchoalveolar lavage fluid (BALF) in model group was significantly higher than that of control and blank groups. The levels of SP and NKA in the BALF of model group were significantly increased. The concentration of 5-HT was increased and the mRNA expression of SERT was decreased in esophageal tissue of model group than that of control group and blank group, the difference had reached significant. No significant difference of mRNA expression and protein levels of TRPV1 and 5HT4R among three groups were observed. The airway responsiveness was decreased significantly after treatment either with 5HT4R antagonist GR113808 or with TRPV1 antagonist capsazepin compared to model group, which revealed the decreased airway responsiveness. In the capsazepin treatment group, the total number of inflammatory cell was also decreased significantly. The concentration of SP of BALF either in GR113808 group or in capsazepin group was decreased significantly than that in model group.

Conclusion: The 5-HT-vagal C fiber pathway might be an important factor in the pathogenesis of esophageal acid reflux-induced airway hyperresponsiveness. 5-HT4R and TRPV1 may be new attractive drug targets for GER induced cough.

Disclosure of Interest: None Declared
GENETIC DETERMINANTS OF AUTOIMMUNE GASTRITIS IN CHILDREN

Rosa Lima 1,*, Jorge Oliveira 2, Brígida Amaral 1, Emília Costa 3, Natalina Miguel 3, Francisca Costa 4, José Ramon Vizcaína 4, José Barbot 3, Rosário Santos 2, Fernando Pereira 1

1Gastroenterologia Pediátrica, Centro Hospitalar do Porto, Porto, Portugal, 2Genética Molecular, Centro Hospitalar do Porto, Porto, Portugal, 3Hematologia Pediátrica, Centro Hospitalar do Porto, Porto, Portugal, 4Anatomia Patológica, Centro Hospitalar do Porto, Porto, Portugal

Objectives & Study: The HLA DRB1 * 04 and DQB1 * 03 haplotypes are more often found in series of adults patients with autoimmune gastritis (AIG). The aim of this study was to evaluate whether variability in immunoregulator genes from the human leukocyte antigen (HLA) system (HLA-A, B, DRB1 and DQB1) and sequence variants of CTLA4 gene (c.49A>G and c.*1384G>A) predispose to AIG in children.

Methods: Eight patients with AIG, 2 males, median age 12.5 years (Group A) and a control group of 11 patients with Helicobacter pylori-related gastritis, not affected by autoimmune disease, 6 males, median age 11.5 years (Group B) were included. The patient’s sera were analyzed for gastrin, pepsinogen I and parietal cell antibodies.

DNA was extracted from peripheral blood and genotyped for HLA-A, B, DRB1 and DQB1 loci and for two single nucleotide polymorphisms (SNPs) of CTLA4 gene: c.49A>G (also known as A49G) and c.*1384G>A (CT60). Prevalence of the HLA genotypes was compared with HLA frequency in the Portuguese population based on publically available data. For statistical analysis we applied Fisher’s exact test to compare the HLA allelic frequencies of AIG patients group with the frequencies of the control group and within the Portuguese population.

Results: In Group A all patients had positive parietal cell antibodies (median: 134.5 U/mL, 97.4-215), median fasting gastrinemia of 541 pg/ml (39.7-2103) and median pepsinogen I levels of 42.2 μg/L (6.7 - 275). In Group B median gastrinemia levels was 186 pg/ml (16.2-978) and the pepsinogen I levels were 182.5 μg/L (40.1 - 210).

75% (n=6) of AIG patients carried the allele DQB1*03 which has an allelic frequency of 29% in the Portuguese population (statistically significant, P=0.01) and it was also detected in 45% of the patients in group B (P>0.05). DRB1*07, the most frequent allele in AIG patients (50%), represents only 17% of the DRB1 alleles in our population (P=0.03). However, DRB1*07 was also detected in nearly half of the patients in group B. Three alleles (A*24, A*26 and B*51) from HLA –A and B loci, had statistically different frequencies in the AIG group, when compared with the population frequencies. Their relative frequencies within group A are below 40% and were considered to be not statistically significant when compared to group B.

Regarding the CTLA4 polymorphisms, there were no statistically significant differences between the two groups (A and B).

Conclusion: Our data corroborates that HLA allele DQB1*03 appear to be associated with AIG in children. However, it should be emphasized that more patients need to be included in order to increase the statistical power of this study.

Disclosure of Interest: None Declared
**Gastroenterology**

**GI Motility and Functional GI Disorders**

PA-G-0031

THE ROLE OF INTERSTITIAL CELLS OF CAJAL IN MOTILIN RECEPTOR AGONIST ABT-229-INDUCED CONTRACTION OF INTESTINAL SMOOTH MUSCLES

Baoxi Wang 1, Chunhui Wang 1, Lingchao Wang 1, Xun Jiang 1, Li Lan 1, Yang Sun 1, Li Liu 1

1The Fourth Military Medical University, Beijing, China

**Objectives & Study:** To clarify the mechanism of motilin receptor agonists in the promotion of gastrointestinal motility, we aimed to observe the role of interstitial cells of cajal (ICC) in motilin receptor agonist-induced intestinal smooth muscle contraction.

**Methods:** ICC were damaged specifically with methylene blue and light in intestinal smooth muscle strips collected from the duodenum and colon (from rabbits and rats) and specificity was validated by electron microscope observation. The frequency and amplitude of smooth muscle contraction were recorded and compared between those with damaged ICC and those with normal ICC under the treatment of different concentrations of motilin receptor agonist ABT-229.

**Results:** Both the basal level of the contraction frequency and the amplitude were significantly reduced in tissue strips with damaged ICC, 1.06±0.24 times/min vs 17.89±1.88 times/min, (50±10)mg vs. 343±28/mg in normal tissue strips from the duodenum; 0.71±0.10 times/min vs. 5.89±1.03 times/min, and (45±10) mg vs. (724±85) mg for tissue strips from colon, respectively. In the presence of ABT-229, the construction frequency in tissue strips with damaged ICC and normal tissue strips of the duodenum were, respectively, 1.17 ±0.25 times/min vs. 8.76±1.18 times/min (P>0.05), and the amplitude was 58±11 mg vs. 597±68 mg (P < 0.001); and the construction frequency in tissue strips with damaged ICC compared to normal tissue strips from the colon was 0.78±0.11 times/min vs. 8.45±0.69 times/min (P<0.001), and the amplitude was 57±8 mg vs. 897±89 mg (P<0.05), respectively. However, in the presence of acetylcholine (10^{-6} mol/L; Ach), the ICC-damaged tissue strips generate obvious contraction.

**Conclusion:** These results indicate that the basal level of smooth muscle rhythmic contractions is mediated by ICC and the motilin receptor-mediated smooth muscle contraction requires the presence of ICC.

**Disclosure of Interest:** None Declared
Objectives & Study: To investigate the current approach of Australia and New Zealand General Paediatricians to children with gastro-oesophageal reflux symptoms, comparing practice against the NASPGHAN-ESPGHAN Guideline.

Methods: Prospective, multicentric study was carried out in Australia and New Zealand between November 2012 and June 2013. Questionnaires were distributed, consisting of multiple choice case report-like issues, concerning clinical management, the use of diagnostic tools and the treatment options for gastro-oesophageal reflux disease (GERD) in infants, children and adolescents, via email to a selected email list of paediatricians across the country.

Results: A total of 53 of 407 Paediatricians completed the study questionnaire. 71.7% generally diagnose GERD through a history of typical reflux symptoms, irrespective of the age of the child. 45.2% of Paediatricians prescribed proton pump inhibitors (PPIs) to children of all ages, whilst 39.6% prescribed mainly to infants in their practice. 39.6% of Paediatricians prescribed PPIs in infants younger than 1 year of age with uncomplicated recurrent regurgitation and vomiting in the absence of diagnostic evidence and 66% of Paediatricians prescribed PPIs in infants younger than 1 year of age with unexplained crying and/or distressed behaviour. About 50% prescribed PPIs in children older than 5 years of age with vomiting and heartburn, without specific testing. 30.7% would discontinue PPIs abruptly and only 50.9% were aware that the most frequent adverse event of PPI therapy in infants is lower respiratory tract infection. 26.4% of Paediatricians wrote >15 PPI prescriptions during the last 6 months.

Conclusion: The results of this survey, although with a poor response rate, showed that General Paediatricians in Australasia were unaware that PPIs were often not useful in children less than <1 year of age with uncomplicated regurgitation and crying in the absence of diagnostic evidence and were overprescribing in this age group. This study also confirmed that there was no general consensus on the management of gastro-oesophageal reflux disease in Australasia. This is probably due to the absence of a national guideline. Education based on the NASPGHAN-ESPGHAN guidelines should occur, following which a resurvey can be conducted to assess any changes in practice.

Disclosure of Interest: None Declared
ALTERED GUT MICROBIOTA AND ACTIVITY IN A MURINE MODEL OF AUTISM SPECTRUM DISORDERS

Caroline detheije 1, Harm Wopereis 2, Mohamed Ramadan 1, 2, Tiemen vaneejndthoven 2, Jolanda Lambert 2, Jan Knol 2, 3, Johan Garssen 1, 2, Aletta kraneveld 1, Raish Oozeer 2,*

1Utrecht University, Utrecht, Netherlands, 2Danone Nutricia Research, Utrecht, Netherlands, 3Wageningen University, Wageningen, Netherlands

Objectives & Study: Autism spectrum disorder (ASD) is a heterogeneous group of complex neurodevelopmental disorders with evidence of genetic predisposition. Gastrointestinal disturbances are reported in ASD patients and compositional changes in gut microbiota are described. However, the role of gut microbiota in brain disorders is poorly documented. Here, we used a well-characterized murine model of ASD to investigate the relation between gut microbiota and autism-like behaviour.

Methods: Using next generation sequencing technology, gut microbiota composition was investigated in a murine model of ASD induced by prenatal valproic acid (VPA) exposure. Compositional assessment of the microbiota was combined with short chain fatty acids (SCFA) and lactic acid measurements in caecum content.

Results: Our data demonstrate a transgenerational impact of in utero VPA exposure on gut microbiota in the offspring. Prenatal VPA exposure particularly affected Operational Taxonomic Units (OTUs) assigned to bacterial orders of Bacteroidales, Clostridiales and Desulfovibrionales, corroborating human ASD studies. In addition, OTUs assigned to families of Coriobacteriaceae and Erysipelotrichaceae were especially associated with male VPA-exposed offspring. The overall microbial differences of VPA in utero-exposed males deviated from those observed in females and was (i) positively associated with increased levels of caecal butyrate and (ii) inversely associated with intestinal levels of serotonin and with normal social behaviour.

Conclusion: These findings show that autistic-like behaviour is associated with altered postnatal microbial colonization and activity in a VPA-induced murine model for ASD, with preponderance in male offspring. These results open new avenues in the scientific trajectory of managing neurodevelopmental disorders by gut microbiome modulation.

**Nutrition**

**Observational and Epidemiological Studies**

PA-N-0034

**HUMAN MILK (HM): IMPACT ON GROWTH VERSUS CHRONIC LUNG DISEASE (CLD) IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS**

Aloka Patel 1,*, Harold R Bigger 1, Yimin Chen 1, Janet L Engstrom 1, Elizabeth A Dabrowski 1, Paula P Meier 1

1Rush University Medical Center, Chicago, United States

**Objectives & Study:** Previous studies have shown poor weight gain with both HM and CLD, however HM has also been associated with reduced CLD. The objective of this study was to determine the impact of HM dose on CLD and growth in VLBW infants.

**Methods:** This was a prospective cohort study of 203 symmetrically appropriate for gestational age VLBW infants born in 2008-12. Postnatal growth failure (PGF) and CLD were assessed at 36 wk postmenstrual age (PMA) (or last weekly measurement, if discharge [DC] prior to 36wk). PGF was defined as BW >10%, but 36wk weight <10% using growth standards from Olsen et al1. CLD was defined as receipt of oxygen or positive-pressure at 36 wk PMA. Daily enteral feeding volumes were used to calculate HM average proportion (%) of enteral feedings over the NICU hospitalization for each infant. The cohort was divided into HM intake quartiles (HM Quart). BW, gestational age (GA), gender, race, surfactant as a marker of intubation, caffeine, complete antenatal steroids, late onset sepsis, necrotizing enterocolitis (NEC), patent ductus arteriosus, and length of NICU hospitalization were collected. Weight growth velocity (GV) was calculated from regaining BW to discharge (DC). Data were analyzed using one-way ANOVA, Chi square and multivariable logistic and linear regressions. Two individual multivariable logistic regressions were used to model CLD using either GA or BW.

**Results:**

<table>
<thead>
<tr>
<th></th>
<th>HM Quart 1 n 51</th>
<th>HM Quart 2 n 51</th>
<th>HM Quart 3 n 51</th>
<th>HM Quart 4 n 50</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GA (wk)</td>
<td>27 ± 2</td>
<td>27 ± 2</td>
<td>28 ± 2</td>
<td>28 ± 2</td>
<td>.41</td>
</tr>
<tr>
<td>BW (g)</td>
<td>1043 ± 238</td>
<td>1034 ± 257</td>
<td>1130 ± 230</td>
<td>1070 ± 218</td>
<td>.17</td>
</tr>
<tr>
<td>Male</td>
<td>51%</td>
<td>49%</td>
<td>41%</td>
<td>50%</td>
<td>.75</td>
</tr>
<tr>
<td>Age at first feed (d)</td>
<td>5±2</td>
<td>5±3</td>
<td>5±3</td>
<td>4±3</td>
<td>.04</td>
</tr>
<tr>
<td>HM proportion (%)</td>
<td>3% ± 2%</td>
<td>17% ± 8%</td>
<td>71% ± 17%</td>
<td>100% ± 6%</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CLD</td>
<td>35%</td>
<td>31%</td>
<td>24%</td>
<td>12%</td>
<td>.039</td>
</tr>
<tr>
<td>GV (g/kg/d)</td>
<td>14.6 ± 2.0</td>
<td>15.3 ± 6.9</td>
<td>13.6 ± 2.1</td>
<td>13.8 ± 1.8</td>
<td>.11</td>
</tr>
<tr>
<td>PGF</td>
<td>29%</td>
<td>37%</td>
<td>39%</td>
<td>54%</td>
<td>.08</td>
</tr>
<tr>
<td>NICU hospitalization (d)</td>
<td>81 ± 35</td>
<td>77 ± 38</td>
<td>69 ± 32</td>
<td>64 ± 23</td>
<td>.048</td>
</tr>
</tbody>
</table>

Bivariate analyses of subject characteristics and outcomes are presented in the Table above. Multivariable logistic regression analyses demonstrated a significant dose-response protective effect of HM for CLD and a significant relationship between HM and PGF. Other significant factors in the CLD model included GA, BW, gender, NEC, PDA and GV.

**Conclusion:** Higher doses of HM feeding throughout NICU hospitalization were associated with higher rates of PGF, but a reduction in the odds of CLD with shorter length of hospitalization in VLBW infants. Follow up data from this cohort will determine the relative impact of these variables on long-term outcomes.


**Disclosure of Interest:** A. Patel Grant / Research Support for: NIH 1-NR010009; Prolacta Bioscience, H. Bigger Grant / Research Support for: NIH 1-NR010009, Y. Chen: None Declared, J. Engstrom
Nutrition

Nutrition and Metabolism, Mechanisms

PA-N-0035

DOCOSAHEXAENOIC ACID ACCRETION IN BRAIN AND OTHER ORGANS IS GREATER WHEN SUPPLIED AS PHOSPHATIDYLCHOLINE THAN AS TRIACYLGlycerol IN A PIGLET MODEL

Nana Bartke 1,*, Lei Liu 2,3, Hans van Daele 4, Peter Lawrence 3, Xia Qin 2,3, Hui Gyu Park 3, Kumar S.D. Kothapalli 3, Anthony Windust 5, Zhe Wang 2, J. Thomas Brenna 3

1Nutricia Research, Utrecht, Netherlands, 2Veterinary Medicine, Jilin University, Jilin, China, 3Division of Nutritional Sciences, Cornell University, Ithaca, NY, United States, 4BNLfood Investment sa, Wiltz, Luxembourg, 5Measurement Science and Standards Portfolio, National Research Council Canada, Ottawa, ON, Canada

Objectives & Study: Docosahexaenoic acid (DHA, 22:6n-3) is the most abundant n-3 polyunsaturated fatty acid (PUFA) in the brain. It accumulates at an accelerating rate during the pre- and postnatal phase, continuing well past the plateau of brain weight, to plateau at about 18 years of age and remain stable throughout life [1]. Preformed DHA is more efficacious for brain DHA accretion than its precursors. Dietary intake of long-chain PUFA (LCPUFA), in particular DHA, is therefore beneficial to support the optimal physical development of the brain, eyes and nerves in early life.

The aim of this study was to determine the relative efficacy of dietary DHA for accretion in brain and other organs when provided in formula to the growing piglet as a dose of 13C-DHA bound to the sn-2 positions of either phosphatidylcholine (PC) or triacylglycerol (TAG).

Methods: Piglets (n=8 per group) were fed with a fully balanced formula diet low in DHA from day 3 of life. On day 16 of life, piglets were assigned to two dosing groups and provided with a single oral dose of TAG-13C-DHA or PC-13C-DHA. On day 23, piglets were sacrificed and selected organs and red blood cells (RBC) were analyzed for 13C-DHA and other fatty acid metabolites.

Results: 13C label was detected for DHA and n3-docosapentaenoic acid (DPAn3, 22:5n-3) only among all fatty acids. 13C-DHA accretion in brain gray matter of the PC group was 1.9-fold greater than for TAG, and was similarly more efficacious in synaptosomes, retina, liver, and RBC. The 13C-DHA labeling was by far the greatest in the liver, indicating a role for that organ in the initial metabolic processing of LCPUFA, followed by export to other organs. In turn, it implies that DHA transfer from gut to bloodstream to liver in part drove the relative efficacy for tissue accretion. Apparent retro-conversion to DPAn3 was more than 2-fold greater for PC than for TAG and was much more prominent in neural tissue than in liver or RBC.

Conclusion: These data directly support greater metabolic efficacy and brain accretion for PC as a carrier for LCPUFA compared to TAG. Consistent with previous studies of arachidonic acid (ARA) and DHA measured in other species [2], the results indicate that PC is a highly efficacious source of both, DHA and ARA, the two major LCPUFA of human breast milk [3].


LONG CHAIN POLYUNSATURED FATTY ACIDS MODULATE THE IMPACT OF THE GCKR PRO446LEU POLYMORPHISM ON TRIGLYCERIDES IN ADOLESCENTS: THE HELENA STUDY

Julien Rousseaux 1,*, Alain Duhamel 2, Jean Dallongevile 3, Denes Molnar 4, Kurt Widhalm 5, Yannis Manios 6, Michael Sjöstöm 7, Anthony Kafatos 8, Christina Breidenassel 9, Marcela Gonzales-Gross 9, Magdalena Cuenca 10, Laura Censi 11, Marcos Ascensión 12, Stefaan De Henauw 13, Luis Aznar Moreno 14, Aline Meirhaeghe 3, Frédéric Gottrand 15

1Inserm U995, IFR114, University Lille-Nord-de-France, CHR de Lille, Lille, France, 2Unité de Biostatistiques, CERIM, EA2694, UDSL, Univ Lille Nord de France, CHU Lille, Lille, France, 3Inserm, U744, Institut Pasteur de Lille, Univ Lille Nord de France, UDSL, Lille, France, 4Department of paediatrics, University of Pécs, Pécs, Hungary, 5Academic Institute for Clinical Nutrition, Vienna, Austria, 6Department of Nutrition and Dietetics, Harokopio University, Athens, Greece, 7Unit for Preventive Nutrition, Department of Biosciences and Nutrition, Karolinska Institute, Huddinge, Sweden, 8Preventive Medicine & Nutrition Unit, School of Medicine, University of Crete, Heraklion, Greece, 9Facultad de la Actividad Física y del Deporte-INEF; Universidad Politécnica de Madrid, Madrid, Spain, 10Department of Medical Physiology, Faculty of Medicine, Granada University, Granada, Spain, 11National Research Institute on Food and Nutrition, Rome, Italy, 12Immunonutrition Research Group, Department of Metabolism and Nutrition, Institute of Food Science and Technology and Nutrition (ICTAN-CSIC), Madrid, Spain, 13Department of Public Health, Faculty of Medicine and Health Sciences, Ghent University, Ghent, Belgium, 14GENUD (Growth, Exercise, Nutrition and Development) Research Group, Escuela Universitaria de Ciencias de la Salud, Universidad de Zaragoza, Zaragoza, Spain, 15Inserm U995, IFR114, University Lille-Nord-de-France, CHR de Lille, Lille, France

Objectives & Study: Diet is one of the main environmental factors involved in the modulation of plasma triglycerides concentrations. The glucokinase-regulatory-protein (GCKR) is a key protein that binds to glucokinase, and regulates intracellular glucose disposal. Our aim was to investigate the influence of n-3 and n-6 polyunsaturated fatty acids (PUFAs) on the association between the GCKR rs1260326 polymorphism and triglycerides concentrations in European adolescents.

Methods: 3,528 adolescents were assessed in 10 European cities. 1/3 were randomly selected for blood collection. Anthropometric parameters were measured: height, weight, waist circumference, BMI and waist-to-height ratio were calculated. Blood dosages were performed: erythrocyte fatty acids, glucose, triglycerides, HDL and LDL-cholesterol. The GCKR rs126032 SNP was genotyped. Subjects were categorized as “high” or “low” according to the population median dosage of long-chain PUFAs (LC-PUFAs). Linear regression analyses were performed to study the association between rs1260326 and outcomes of interest. Interactions between rs1260326 and PUFAs concentrations on triglyceride concentrations were explored.

Results: After stratification on the median of total n-3 fatty acid concentrations, the association between rs1260326 and triglyceride levels was significant for the group of high n-3 LC-PUFAs values but not for the group of low n-3 LC-PUFAs values. Specific n-3 LC-PUFA analysis revealed the same pattern of results for ALA, EPA and DHA levels taken separately. After stratification on the median of total n-6 fatty acid concentrations, the association between rs1260326 and triglycerides concentrations was significant for the low n-6 LC PUFA values but not for the high n-6 LC-PUFAs values.
**Conclusion:** Our study provides for the first time evidences that long chain n-3 PUFAs interact with the *GCKR* polymorphism to increase triglycerides concentrations in healthy adolescents. This finding suggests that *GCKR* polymorphism should be taken into account for studies assessing relationships between n-3 PUFAs and lipid metabolism.

**Disclosure of Interest:** None Declared
MATERNAL LCPUFAS STATUS AND FETAL NEURODEVELOPMENT IN OBESE WOMEN

Maria Teresa Segura Moreno 1, Francisco Jose Torres-Espinola 1, Maria Carmen Lopez-Sabater 2, Luz Garcia-Valdez 1, Ricardo Rueda 3, Tania Anjos 1, Pilar Brandi-Blanco 1, Cristina Campoy 4,* and the PREOBE Group

1EURISTIKOS Excellence Centre for Paediatric Research, University of Granada, Granada, Spain, 2Department of Nutrition and Food Science, Faculty of Pharmacy, University of Barcelona, Barcelona, Spain, 3Scientific Department, Abbott Nutrition, 4Department of Paediatrics, University of Granada, Granada, Spain

Objectives & Study: Maternal pre-pregnancy obesity and excessive weight gain during pregnancy have been linked to unfavorable long-term consequences to the offspring. Since optimal fetal development depends on the maternal essential fatty acids supply and maternal obesity has been associated to a poor status of determinate nutrients, we aim to study maternal plasma long chain polyunsaturated fatty acids (LCPUFAs) and their relationship with the neurodevelopment of the offspring in obese pregnant women in comparison with normal weight pregnancies.

Methods: We conducted a case-control study nested within the PREOBE study. Mothers were classified based on their pre-pregnancy body mass index (BMI) as normal weight (18≤BMI<25 kg/m², n=48) and obese (BMI≥30 kg/m², n=14). Weight gain during pregnancy was calculated as the difference between weight at delivery and weight just before conception. Maternal blood was collected at delivery time and fatty acid composition on phospholipids fraction was measured by gas chromatography. Cognitive development of the babies was measured at 6 months of life with the Bayley III test. Differences in LCPUFA composition and weight gain were evaluated by one-way analysis of variance (ANOVA) with pre-pregnancy BMI as the main effect-factor. We used linear regression to evaluate the association between maternal LCPUFAs status and cognitive development.

Results: Maternal LCPUFAs percentage in plasma at delivery from obese women was significantly higher compared to normal weight mothers (43,58±1,72 vs 42,28±2,07, P=0,035). Weight gain during pregnancy was significantly lower in obese compared to normal weight (6,49±7,23 vs 12,49±6,25, P=0,002). Childs from obese mothers shown a significantly higher score in the Bayley scale (112,81±7,06 vs 107,44±7,94, P=0,001); a positive association between LCPUFAs in maternal plasma at delivery and babies cognitive development at 6 months of life in obese group (P=0,002) was established.

Conclusion: Babies from obese mothers seemed to have a better cognitive composite score. These results may be justified by the higher percentage of LCPUFAs observed in maternal plasma at delivery, and the positive relationship found between these two variables in the obese group. A follow-up of these children is needed in order to analyze if this effect is maintained in the long-term and how strong is this effect when other potential factors influencing brain development are considered.


Disclosure of Interest: None Declared
COMBINED LIVER KIDNEY TRANSPLANTATION: A SINGLE CENTRE EXPERIENCE

Jesus Quintero 1,*, Olalla Rodriguez 1, Leire Gondra 2, Mar Miserachs 1, Ramon Vilalta 2, Gema Ariceta 2, Ramon Charco 3

1 Paediatric Liver Transplant Unit, Hospital Universitari Vall d’Hebron, Barcelona, Spain
2 Paediatric Nephrology, Hospital Universitari Vall d’Hebron, Barcelona, Spain
3 HPB Surgery and Transplants, Hospital Universitari Vall d’Hebron, Barcelona, Spain

Objectives & Study: Combined liver–kidney transplantation (CLKT) remains a relatively infrequent procedure in children with only 10 to 30 paediatric procedures performed annually worldwide. Nevertheless, it is a recognized treatment for children with end-stage renal disease (ESRD) with accompanying liver impairment (Autosomal Recessive Polycystic Liver and Kidney Disease (ARPKLD)) or isolated enzymatic deficiencies of liver (Primary Hyperoxaluria (PH-1)). The study aims to report outcomes of CLKT in a cohort of paediatric patients.

Methods: We retrospectively analyzed all paediatric CLKT performed in our centre between September 2000 to January 2013. Patient data were obtained by reviewing inpatient and outpatient medical records and our transplant database. Donor and recipient demographic data, pre and post-operative renal and liver function, haemodialysis requirements at transplantation, complications after CLKT, survival and data of the combine transplant procedure were collected.

Results: A total of 12 CLKT were performed during the study period with a median age and weight at transplant of 9.5 years and 32.6 kilograms respectively. The indication for CLKT were ARPKLD (7/12), PH-1 (4/12) and idiopathic portal hypertension with ESRD (1/12). The median waiting time on list was 6.5 months. All but one CLKT were performed simultaneously. The normalization of renal function (defined as estimated Glomerular Filtration Rate (eGFR) > 60 mL/m²/1.73) was achieved at post-operative day 10.5 (range 4-92). Patients with PH-1 tended to present a delayed recovery of renal function compared to patients transplanted with other indications (62.5 vs 6.5 days respectively, P: 0.075). The median follow-up time was 54.0 months. Kidney graft survival rates at 6 months, 1 and 5 years were 100%, 83.3%, 75.0% respectively. We achieve a patient survival rates at 6 months, 1 and 3 years after the CLKT of 100%, 91.7% and 91%. Not other liver grafts were lost.

Conclusion: The long-term results of CLKT in children are encouraging being comparable to those obtained with isolated Liver Transplantation. The results are excellent especially if patients are evaluated and listed before they became critically ill or presented systemic manifestation of its metabolic disease. In our study, patients with PH-1 tended to present a slower recovery to eGFR than patients with ARPKLD.

Disclosure of Interest: None Declared
QUANTIFICATION OF MICROCHIMERISM AFTER MESENCHYMAL STEM CELL INFUSION FOR CHRONIC LIVER DISEASE

Alexandre Fabre 1,2,3,*, Catherine Lombard 3, Floriane Andre 3, Joachim Ravau 3, Xavier Stephenne 4, Françoise Smets 3,5, Etienne Sokal 3,5

1Service de pédiatrie Multidisciplinaire, Assistance Publique Hôpitaux de Marseille, Aix-Marseille Université, Marseille, France, 2Faculté de médecine de la Timone , Aix-Marseille Université, Marseille, France, 3Centre de Thérapie Cellulaire et Institut de Recherche Expérimentale et Clinique, Bruxelles, Belgium, 4Service de Gastroentérologie et Hépatologie Pédiatrique, Université Catholique de Louvain & Cliniques Universitaires Saint Luc, Bruxelles, Belgium, 5Service de Gastroentérologie et Hépatologie Pédiatrique, Cliniques St Luc, Bruxelles, Belgium

Objectives & Study: Cell transplantation is a promising alternative to liver transplantation. The cells can be either hepatocytes or liver derived progenitors. In both cases tracking the cell fate after infusion and monitoring the chimerism is an important point. Traditional method (sex-based FISH, HLA mismatch, Short Tandem Repeat PCR) achieve only low level of sensitivity (1%) and are seldom used. The use of quantitative Real-Time PCR based on mismatch of null allele is a promising alternative.

Methods: We selected four genes with a high level of null genotype in population (SRY, RHD, GSTM1, GSTT1). We evaluated the genotype distribution on a panel of 25 blood donor. We created an artificial chimerism based on DNA mix or liver derived progenitor to test sensitivity, accuracy and variability. We also tested the method on the biopsy of a patient which had cell progenitor infusion for G6PD deficiency. The biopsies were taken at 3.5 month and 7 month.

Results: Analysis combining the four genes had sensitivity up to 0.01% of chimerism, with a good accuracy and below 3% of coefficient of variation for intra and interassay experiment. The informativeness is 57% for the four genes. The measured chimerism of the patient was 0.045% of the total liver mass, corresponding to 5% engraftment of the transplanted cells (SD : 0.02) for the right liver biopsy and 0.025% (SD : 0.013) for the left liver biopsy at 3.5 month. At 7 month the level of chimerism was under the limit of detection but present. It should be noted that the patient presented to acute enteritis with diarrhea at five month which could be have caused to a diminished immunosuppression.

Conclusion: The chimerism determination with real-time PCR amplification of null allele is a reliable and sensitive tool. It could be easily implemented in follow up of patient with cell infusion for liver disease.

Disclosure of Interest: A. FABRE Grant / Research Support for: ADEREM, FNRS, C. LOMBARD: None Declared, F. ANDRE: None Declared, J. RAVAU: None Declared, X. STEPHENNE: None Declared, F. SMETS Conflict with: Principal investigator (clinical trial, identifier NCT01765283), E. SOKAL: None Declared
**Objectives & Study:** Wilson's disease (WD) is a rare genetic disease. Monitoring of patients is based on clinical examination, hepatic parameters and 24 hours urinary copper excretion. Recent work suggests that measuring the serum exchangeable copper (CuEXC) is a promising tool for the diagnosis of WD (1). To date, there is no data regarding CuEXC levels during follow-up of patients suffering from WD.

**Methods:** We compared mean values of CuEXC at different times of the follow-up in two groups of patients: Group 1 (n=12) patients suffering from WD newly diagnosed (n=10) or in situation of therapeutic failure (n=2); and Group 2 (n=40) patients suffering from WD on stable condition according to their therapeutic observation. Biological samples were taken for the group 1 at T0 = time of diagnosis, T1 = T+1 to 3 months, T2 = T+3 to 6 months and T3 = T > 6 months; and for the group 2 during every medical consultation between nov 2011 and oct 2013.

**Results:** In group 1: mean age was 25 +/- 14 years including 7 children, with 67% of hepatic form. CuEXC mean value at T0 was 148.1 +/- 80.8 µg/L, at T1 119.3 +/- 50.5 µg/L, at T2 87.4 +/- 56.6 µg/L, and at T3 71.5 +/- 29 µg/L (normal range 39-73 µg/L). CuEXC level was significantly higher at T0 versus T2 (p=0.005), T0 versus T3 (p=0.048) and T1 versus T3 (p=0.048). In group 2: mean age was 35 +/- 11 years including 11 children, with 72.5 % of hepatic form. CuEXC mean value in the subgroup of good observant patients was 53.2 +/- 17.6 µg/L (n=17), versus 68.7 +/- 27.6 µg/L in the subgroup of moderately good observant patients (n=19) and 77.2 +/- 10.7 µg/L in non-observant patients (n=4). We observed a nearly significant difference between good and moderately good observant patients (p=0.052) and a significant difference between good and non-observant patients (p<0.009).

**Conclusion:** Our study confirms that CuEXC is a highly valuable tool for the follow-up of WD. CuEXC decreases in a linear way under treatment and is well correlated with therapeutic observance. Further studies are needed with higher number of patients to confirm our results.


**Disclosure of Interest:** None Declared
SERUM PROINFLAMMATORY CYTOKINES AND NUTRITIONAL STATUS IN CHILDREN AND ADOLESCENTS WITH CHRONIC LIVER DISEASE

Daniele Santetti 1,*, Cristina Toscani Leal Dornelles 2, Carlos Oscar Kieling 3, Jorge Luiz Santos 3, Isabel Cristina Ribas Werlang 1, Fernanda Urruth Fontella 1, Sandra Maria Gonçalves Vieira 3, Helena Ayako Sueno Goldani 1

1Programa de Pós Graduação em Saúde da Criança e do Adolescente, Universidade Federal do Rio Grande do Sul, Porto Alegre, Brazil, 2Nutrition Service, 3Paediatric Hepatology Unit, Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

Objectives & Study: The aim of this study was to evaluate the nutritional status of children and adolescents with chronic liver disease and its association with inflammatory activity, by measurement of proinflammatory cytokines interleukin-1 beta (IL-1 β), interleukin-6 (IL-6) and tumor necrosis factor-alpha (TNF-α).

Methods: Cross-sectional study comprised of 43 children and adolescents, aged 0 to 17 years, diagnosed with chronic liver disease from a tertiary pediatric hospital in Brazil. The severity of liver disease was assessed by Child-Pugh, MELD and PELD scores. Anthropometric parameters were height/age, body mass index/age and triceps skinfold/age according to World Health Organization standards. The cutoff points for classification of nutritional status were the following: risk of malnutrition (z-score < -1.00) and malnutrition (z-score < -2.00). IL-1 β, IL-6 and TNF-α levels were assessed by commercial ELISA kits.

Results: Median (25th-75th centile) age was 60 (17-116) months, 53.5% were female. Biliary atresia accounted for 72% of cases. IL-6 values were increased in patients at nutritional risk compared to those well-nourished [7.12 (0.58-34.23) pg/mL vs 1.63 (0.53-3.43) pg/mL; P = 0.02], correlating inversely with triceps skinfold-for-age z-score (rs = -0.61; P <0.001). IL-6 levels were associated with liver disease severity assessed by Child-Pugh score (P = 0.001) and PELD score (P = 0.014). This association remained significant after adjustment for nutritional status in a linear regression model.

Conclusion: High IL-6 levels were found in children and adolescents with chronic liver disease at nutritional risk. These data could suggest that inflammatory activity may play a role in the progression of pediatric chronic liver disease and nutritional status deterioration.

Disclosure of Interest: None Declared
**Hepatology**

PA-H-0042

**LYMPHOCYTES INTRACELLULAR DEHYDROGENASES ACTIVITY IN CHILDREN WITH HEPATIC FORM OF GLYCOGEN STORAGE DISEASE**

Olga Kurbatova 1,*, Andrew Surkov 1, Svetlana Polyakova 1, Lyubov Miroshkina 1, Tatyana Izmailova 1, Galina Semenova 1, Irina Samokhina 1, Ekaterina Kapustina 1, Zoya Dukhova 1, Rustam Zakirov 1, Ekaterina Freydlin 1, Svetlana Petrichuk 1

1Scientific Centre of Children Health, RAMS, Moscow, Russian Federation

**Objectives & Study:** Glycogen storage diseases (GSD) are a group of inherited diseases, which are the results of enzymes defects catalyze reactions of glycogensynthesis or glycogenolysis. GSD are accompanied with carbohydrate metabolism disorders, which lead to others metabolic ways errors. In this connection it is interesting to investigate intracellular enzymes activities in patients with hepatic form of GSD. Activities of lymphocytes enzymes (succinate dehydrogenase (SDH), glycerol-3-phosphate-dehydrogenase(GPDH), NADH-dehydrogenase(NADH-D) end lactatdehydrogenase (LDH)) were used as the laborotory markers of energy metabolism.

**Aim.** To evaluate the diagnostic value of the lymphocytes enzymes activity in children with the hepatic form of GSD.

**Methods:** We examined 94 children with GSD at age from 13 months to 17 years. Distribution of children by disease types was: 37 children - with type-I, 24 children - type-III, 33 children - type-VI of the disease; control group consisted of 34 healthy children. Dehydrogenases activity was measured using the quantitative cytochemical method, which is based on the n-nitrotetrazolium violet ability to form insoluble formazan granules during the enzymatic reduction. The examination of received images was conducted using cytomorphodensitometry (CMD). The statistical significance was evaluated according to the Kolmogorov-Smirnov criterion (P≤0.01). All results are performed using software package STATISTICA 6.0 (StatSoft).

**Results:** We found a decrease in the SDH-activity in patients with GSD. The most significant alterations were found in type-I. Additionally, we discovered a tendency of NADH-D increase in children with GSD. This can point at the phase I compensatory activation parallel to phase II depression in the respiratory chain. Children with hepatic form GSD had a significant decrease in GPDH-activity, compared with the control group. This indicated at the disintegration of the coupling processes-glycolysis and the Krebs-cycle. LDH activity was increased in all GSD patients, but more pronounced in patients with VI and I types, which testifies to anaerobic glycolysis activation along with oxidative phosphorylation depression. Analysis of association between traditional clinical-laboratory diagnostic parameters -base excess and hepatomegaly and intracellular enzymes activity in GSD patients showed strong correlative correspondence R=0.987 and R=0.867 respectively.

**Conclusion:** Dehydrogenases activity of lymphocytes correlates with the main clinical - laboratory parameters, and can be used as an additional diagnostic criteria of energy metabolism disorders in children with GSD.

**Disclosure of Interest:** None Declared
**Objectives & Study:** Early breastfeeding reduces the risk of later obesity compared to formula-fed infants. One possible cause is the lower protein content of human milk. It was shown that protein-rich nutrition in newborns enhances the later risk of obesity. Although much evidence suggests this early protein hypothesis, the metabolic mechanism remains unknown. This study aimed to investigate the influence of different protein content on metabolic changes in formula-fed children.

**Methods:** Serum samples were drawn from children of the childhood obesity project, a European multicenter study. The concentrations of polar lipids of 6-month-old infants randomized at birth to a higher or lower protein content formula (HP=276 and LP=275, respectively) were quantified by FIA-MS/MS (Biocrates, Absolute IDQ p 150 kit). Twenty-one amino acids (AA) were quantified by LC-MS/MS combining derivatization and ion-pair chromatography. To explore metabolic changes between the groups, we used univariate mixed models adjusted for multiple testing along with multivariate analyses comprising partial least squares-discriminant analysis (PLS-DA) and random forest (RF).

**Results:** PLS and RF achieved small classification error rates of 6% and 9%, respectively. Out of 181 analyzed metabolites, 94 differed significantly between the groups. Selected variables in the RF originate from the group of the AA, acylcarnitines, and phospholipids. Branched-chain amino acids (BCAAs) were found to be the most discriminant metabolites. Isoleucine, leucine, and valine as well as their oxidation products short-chain acylcarnitines C3, C4, and C5 were significantly elevated in the HP group. Hydroxy-sphingomyeline SM (OH) C14:1 (higher in the HP) was also discriminative between the groups.

**Conclusion:** Out of the AA and acylcarnitines, the BCAA and the short-chain acylcarnitines clearly showed the strongest association with the formula group. Higher protein intake results in elevation of BCAA in HP which leads to increased insulin levels shown by previous work. Degradation products of branched-chain amino acids oxidation reveal as short-chain acylcarnitines, indicating increased use of BCAA energy sources. The higher amount of hydroxy-sphingomyelines, especially SM (OH) 14:1, in HP plasma may reflect a higher amount of this sphingomyeline in the HP formula milk. Thus, the composition of sphingomyeline in the formula may have a direct impact on membrane constitution and signal transduction in the infant.

**References:**

**Disclosure of Interest:** None Declared
Gastroenterology
Inflammatory Bowel Disease
PL-G-0044
OUTCOMES AND HEALTH SERVICE USE OF CHILDREN WITH VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE (VEO-IBD): A POPULATION-BASED STUDY FROM ONTARIO, CANADA
Eric Ian Benchimol 1, 2,*, David R Mack 1, Geoffrey C Nguyen 3, Scott B Snapper 4, Pauline Quach 2, Wenbin Li 2, Aleixo M Muise 5
1CHEO IBD Centre, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada,
2Institute for Clinical Evaluative Sciences, Ottawa, Canada, 3Gastroenterology, Mount Sinai Hospital, University of Toronto, Toronto, Canada, 4Gastroenterology, Boston Children's Hospital, Harvard University, Boston, United States, 5Gastroenterology, The Hospital for Sick Children, University of Toronto, Toronto, Canada

Objectives & Study: The Paris pediatric modification of the Montreal classification defines VEO-IBD as onset <10y. We conducted a population-based study to assess differences in outcomes in VEO-IBD patients compared to children with older onset.

Methods: The Ontario Crohn’s and Colitis Cohort is a population-based surveillance cohort of all children with IBD in Ontario, Canada. Patients <18y diagnosed with IBD between 1994-2009 were identified from health administrative data and classified as Crohn’s (CD) or ulcerative colitis (UC) using validated algorithms1. Children <10y (and predefined subgroup <6y) at diagnosis were compared to those ≥10y for outpatient and emergency department (ED) visits, hospitalizations, and surgeries. We assessed IBD-specific and IBD-related visits2. All multivariable regression models (Poisson or Cox hazard) were adjusted for income and stratified by gender due to significant interaction between gender and age.

Results: From 1994-2009, 7152 children were diagnosed with IBD (≥10y: n=6110; <10y: n=1042, <6y: n=384). Children <10y had similar number IBD-specific outpatient visits per year compared to children ≥10y (female OR 1.00, 95%CI 0.92-1.08; male OR 1.05, 95%CI 0.98-1.13). However, children <6y had fewer visits per year (female OR 0.81, 95%CI 0.71-0.92; male OR 0.88, 95%CI 0.79-0.99). This association was seen in CD, but not UC. The risk of hospitalization was lower in children <10y with CD (female HR 0.51, 95%CI 0.42-0.62; male HR 0.71, 95%CI 0.61-0.83) but higher in UC (female HR 1.36, 95%CI 1.12-1.65; male HR 1.50, 95%CI 1.25-1.81). There were fewer ED visits per year in the <10y group (female OR 0.51, 95%CI 0.39-0.68; male OR 0.61, 95%CI 0.48-0.77) and <6y group (female OR 0.11, 95%CI 0.06-0.20; male OR 0.38, 95%CI 0.25-0.56). UC ED utilization was similar amongst age groups. The hazard of intestinal resection in children with CD was lower for those <10y (female HR 0.42, 95%CI 0.30-0.58; male HR 0.59, 95%CI 0.46-0.76) and <6y (female HR 0.17, 95%CI 0.08-0.39; male HR 0.36, 95%CI 0.22-0.59). There was greater risk for colectomy in UC females <10y (HR 1.53, 95%CI 1.06-2.22), but not males (HR 0.83, 95%CI 0.54-1.27).

Conclusion: Children with VEO CD had fewer health care visits and surgeries compared with children with onset ≥10y. Children with VEO UC had similar health services use and colectomy rates compared with children ≥10y at diagnosis. These findings suggest that children with CD diagnosed <10y had more mild disease, or accessed the health system less, than those with older onset.


Disclosure of Interest: None Declared
Objectives & Study: Wheat gluten proteins are the causative agents for celiac disease (CD). *T. monococcum* is of special interest, as a candidate low-toxic wheat, although there are conflicting scientific reports about its reduced toxicity for CD patients. We used an *in vitro* system to investigate the digestibility of gliadin from *T. monococcum* cultivars (ID331 and Monlis) after a degradation with gastrointestinal proteases, as well as the impact of this process on immunogenicity in CD patients.

Methods: Gliadin digests from *T. monococcum* and *T. aestivum* were prepared using either a standard proteolysis, with only pepsin and chemotrypsin (PC), and an extended treatment that simulated gastric-digestion with pepsin (P), duodenal-digestion with trypsin, chymotrypsin, elastase and carboxypeptides (TCCE), followed by intestinal-digestion with human brush border enzymes (PTCCE-BBM). The immune stimulatory properties of the digested gliadin were investigated by assaying their ability to activate gliadin-reactive T cell lines generated from small intestinal mucosa of HLA-DQ2+ CD patients, and characterized by a large gliadin epitope recognition pathway.

Results: The results showed that the interferon (IFN)-γ response to the *T. monococcum*-gliadin was comparable to that obtained with *T. aestivum*-gliadin, after PC digestion, as previously shown (Gianfrani et al. *AJCN* 2013). By contrast, the stimulatory property of *T. monococcum*-gliadin was significantly reduced after PTCCE-BBM hydrolysis, whilst that of *T. aestivum*-gliadin remained almost unchanged. We next aimed at understanding the diversity of gastrointestinal resistant peptides in the gliadin from *T. monococcum* and *T. aestivum*. Proteins were fractionated by RP-HPLC and each fraction was hydrolyzed according to the protocol of PTCCE-BBM digestion. The hydrolysates were analyzed by LC-MS/MS. A number of peptides from *T. monococcum*-gliadin, corresponding to known immunogenic sequences were degraded during the PTCCE-BBM treatment. In contrast, many peptides from *T. aestivum*-gliadin (including the multiepitope 33-mer) remained unaffected to gastrointestinal hydrolysis.

Conclusion: Our results demonstrated that gliadin proteins in *T. monococcum* are more extensively degraded by the cocktail of gastrointestinal proteases compared to common wheat. These findings also provide new basic insights into the naturally-formed immunogenic peptides, that are released after the *in vivo* digestion of gliadin.

Disclosure of Interest: None Declared
IL-10 RECEPTOR DEFICIENT PATIENTS WITH VERY EARLY ONSET IBD EXHIBIT SEVERE ALTERATIONS IN THE GENERATION AND FUNCTION OF PRO- AND ANTI-INFLAMMATORY MACROPHAGES

Dror Shouval 1,*, Amlan Biswas 1, Katelyn McCann 1, Janneke N. Samsom 2, Johanna C. Escher 2, Raz Somech 3, Batia Weiss 3, Rita Beier 4, Laurie Conklin 5, Christen Ebens 6, Christoph Klein 7, Aleixo Muise 8, Scott Snapper 1

1Boston Children's Hospital, Boston, United States, 2Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, Netherlands, 3Edmond and Lily Safra Children's Hospital, Tel Hashomer, Israel, 4Hanover Medical School, Hanover, Germany, 5Children's National Medical Center, Washington DC, United States, 6University of Michigan, Ann Arbor, United States, 7Dr von Hauner Children’s Hospital, Munich, Germany, 8Hospital for Sick Children, Toronto, Canada

Objectives & Study: IL-10 receptor (IL-10R) mutations cause severe very early onset (VEO)IBD in humans. The specific hematopoietic cell types responsible for disease initiation in the absence of IL-10R in humans are unknown. We have recently shown that innate immune IL-10R-dependent signals are key regulators of intestinal immune homeostasis in mice, and required for differentiation of anti-inflammatory macrophages (Mφ) in the intestine and blood1. In mice and humans, Mφ can be broadly separated into pro-inflammatory M1 Mφ and anti-inflammatory M2 Mφ. The objective of the current study was to determine in humans the role of IL-10R signaling in generation and function of pro- and anti-inflammatory Mφ subsets.

Methods: We obtained PBMCs from 5 IL-10R-deficient patients, all diagnosed with severe IBD in first 3 months of life, and 5 healthy donors. Mφ were derived from sorted CD14+ monocytes that were cultured in media supplemented with M-CSF and IL-4 (for generation of M2 Mφ) or GM-CSF (for generation of M1 Mφ) for 8 days. In some experiments M2 Mφ were re-stimulated with LPS for 4 hours. Cells were analyzed by flow cytometry and qRT-PCR for different surface markers and cytokines expression. Finally, the ability of these Mφ to modulate proliferation of T naïve cells and generation of regulatory T cells was assessed in a co-culture in-vitro system.

Results: Compared to M1 Mφ taken from healthy subjects, IL-10R-deficient M1 Mφ produced significantly higher levels of IL-6, IL-12 and TNF and expressed high levels of co-stimulatory molecules. These Mφ also enhanced proliferation of T naïve cells in-vitro. Importantly, the generation and function of M2 anti-inflammatory Mφ was impaired in IL10R-deficient patients, with lower expression of several M2 Mφ markers such as MRC-1. Re-stimulation of M2 Mφ from IL-10R-deficient patients with LPS led to a significant increase in secretion of pro-inflammatory cytokines, suggesting that IL-10R-signaling regulates TLR4-dependent responses in human anti-inflammatory M2 Mφ. Finally, compared to healthy subjects, IL-10R-deficient M2 Mφ expressed lower levels of PD-L2 and promoted less generation of Tregs in vitro.

Conclusion: IL-10R-dependent signals play a critical role in generation and function of pro- and anti-inflammatory Mφ in humans. Understanding the down-stream signaling events dependent on IL-10R can aid in developing new cell specific targeted approaches for the delivery of IL-10 for treatment of VEO-IBD.

References: 1Shouval DS et al. Gastroenterology Vol. 144, Issue 5, Supplement 1, Page S-36

Disclosure of Interest: None Declared
EARLY ONSET CROHN’S DISEASE-LIKE INTESTINAL INFLAMMATION AND MDP-DEPENDENT BACTERIAL HANDLING DEFECTS IN PATIENTS WITH NIEMANN-PICK DISEASE TYPE C1

Tobias Schwerd 1,*, Huei-Ting Yang 1, Elisabeth Jameson 2, Nada Al Eisa 3, David Priestman 3, Neil Shah 4, Heiko Runz 5, Miriam Stampfer 5, Gesche Düker 6, Ed Wraith 7, Frances Platt 3, Holm Uhlig 1

1Translational Gastroenterology Unit, University of Oxford, Oxford, 2Willink Biochemical Genetics Unit, Manchester Centre for Genomic Medicine, Manchester, 3Department of Pharmacology, University of Oxford, Oxford, 4Paediatric Gastroenterology, Great Ormond Street Hospital and Institute of Child Health, London, United Kingdom, 5Institute of Human Genetics, University of Heidelberg, Heidelberg, 6Department of Paediatrics, University of Bonn, Bonn, Germany, 7Royal Manchester Children’s Hospital, Manchester, United Kingdom

Objectives & Study: Niemann-Pick type C (NPC) is an autosomal recessive neurodegenerative disorder. Mutations in the NPC1 gene cause defects in cellular lipid trafficking and lysosomal storage. Defects in genes that control autophagy, a process of degradation of cytoplasmic components within lysosomes, are associated with Crohn’s disease.

Methods: We performed a phenotypical and histological analysis of 15 patients with inflammatory bowel disease (IBD)-like immunopathology in patients with NPC. Phenotypic data were compared with a parallel cohort of IBD patients. Functional assays of bacterial handling that involved MDP response and bacterial survival were performed in monocyte-derived macrophages (MDM) pre-treated with the drug U18666A. U18666A causes lysosomal lipid accumulation and mimics the NPC1 storage phenotype.

Results: NPC1 mutations were associated with early onset intestinal inflammation compared to the Oxford IBD cohort (p<0.001). The mean age at diagnosis was 10.5 ± 7.4 years (range 3 to 33 years). Disease phenotype was classified as Crohn’s disease-like in 13/15 and as indeterminate colitis in 2/15 patients. Granulomatous colitis and perianal disease (fissures, ulcers and fistulas) were found in the majority of patients. Severe course of disease was indicated by need of therapy escalation with anti-TNFα and surgery. There was no significant association between treatment with miglustat and development of IBD-like pathology.

A functional defect in bacterial handling was observed as treatment of MDM with U18666A caused increased intracellular survival of salmonella enterica typhimurium and abrogated the MDP-mediated anti-bacterial response in macrophages with NPC phenotype.

Conclusion: Genetic defects in NPC1 increase the group of monogenic disorders that can lead to early onset Crohn’s disease-like intestinal inflammation. Defects in bacterial handling suggest that intestinal inflammation in patients with NPC might be due to interference with NOD signaling.

References: TS and HTY contributed equally to this work.

Disclosure of Interest: None Declared
AORTIC INTIMA-MEDIA THICKNESS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

Marina Aloi 1,*, Luciana Tromba 2, Valentina Rizzo 1, Anna Dilillo 1, Sara Blasi 2, Dimitra Kiltzanidi 2, Giulia D'Arcangelo 1, Giusy Romano 1, Franca Viola 1, Salvatore Cucchiara 1
1Paediatric Gastroenterology and Liver Unit, 2Department of Surgical Sciences, Sapienza University of Rome, Rome, Italy

Objectives & Study: An accelerated progression of atherosclerosis have been reported in immune-mediated disorders, such as inflammatory bowel disease (IBD). Purposes of this study were to determine the presence of early subclinical changes in the cardiovascular system in children affected with IBD and to investigate the influence of traditional and non-traditional risk factors in determining premature atherosclerosis in these patients.

Methods: We studied 34 children with IBD [25 Crohn’s disease (CD) and 9 ulcerative colitis (UC); mean age 15.12 years]; 24 subjects served as controls. Demographic data (age, sex, familiarity for diabetes, cardiovascular disease, hypertension, hypercholesterolemia), traditional risk factors for atherosclerosis (blood pressure, body mass index, active and passive smoking, dyslipidemia), UC and CD activity indexes (Pediatric Ulcerative Colitis Activity Index and Pediatric Crohn’s Disease Activity Index, respectively) were evaluated. The IMT of the abdominal aorta (aIMT) was measured by high resolution B-mode ultrasound.

Results: IBD patients were significantly more exposed to passive smoking (p=0.01), had lower cholesterol and higher inflammatory markers values than controls (p=0.04 and p=0.04, respectively). aIMT was significantly higher in patients than controls (p<0.0001). At a univariate analysis inflammatory markers of disease activity were significantly related to higher aIMT values.

Conclusion: Active inflammation in pediatric IBD is associated with arterial changes of preclinical atherosclerosis. Thus, medical care of children with IBD should include strategies preventing cardiovascular disease by maintaining the remission of the disease.

Disclosure of Interest: None Declared
INFLUENCE OF ENGINEERED LACTOCOCCUS LACTIS CAPABLE OF BINDING TUMOR NECROSIS FACTOR - ON CONCENTRATION OF TUMOR NECROSIS FACTOR-ALPHA IN CULTURE OF INFLAMED INTESTINAL TISSUE TAKEN FROM CHILDREN WITH INFLAMMATORY BOWEL DISEASE

Orel Rok 1*, Saša Simčič 2, Sanja Stopinšek 2, Borut Štrukelj 3, Aleš Berlec 4, Ajda Upelj 5, Živa Alič 5
1Children’s Hospital, University Medical Center Ljubljana, Ljubljana, Slovenia, 2Institute of Microbiology and Immunology, Faculty of Medicine, University of Ljubljana, Ljubljana, Slovenia, 3Faculty of Pharmacy, University of Ljubljana, Ljubljana, Slovenia, 4Institute Joseph Stefan, 5Faculty of Medicine, Ljubljana, Slovenia

Objectives & Study: Therapy with antibodies directed against tumor necrosis factor-α (TNF-α) has been proven to be efficient in both Crohn’s disease (CD) and ulcerative colitis (UC). In addition to antibodies, smaller molecules called affibodies showed affinity of binding TNF. Lactococcus lactis strain NZ9000 had been genetically engineered to display anti-TNF-α affibody on its surface, and its capacity of TNF binding has been proven in in vitro experiments.

Methods: Four biopsy specimen of mucosa were acquired from the same inflamed part of the colon from each of the 8 paediatric IBD patients (4 with CD, 4 with UC). After 3-hour incubation in medium with addition of vancomycin, gentamycin and colistin to exterminate indigenous microbiota, tissue samples were incubated at 37 °C,5% CO₂ for 20 hours in sterile RPMI medium, or medium with addition of non-pathogenic E. coli, “natural” strain of Lactococcus lactis without surface affibody, or engineered Lactococcus lactis strain with anti-TNF-α affibody, all in the concentration of 10⁹CFU/ml. At the end of incubation period, the concentrations of TNF-α in supernatants were measured by Human TNF-α ELISA.

Results: Mean TNF-α concentration in culture with E. coli was significantly higher than in the sterile culture (p < 0.05). Mean TNF-α concentrations in cultures with both “natural” Lactococcus lactis and with the engineered Lactococcus lactis with surface anti-TNF-α affibody were significantly lower compared with cultures in the sterile medium (p < 0.05) and in the medium with E. coli (p < 0.02). However, we found no differences between the concentration of cultures with “natural” and engineered Lactococcus lactis. Same results were obtained from separate analyses for cultures of CD and UC tissue samples.

Conclusion: In both cultures incubated with Lactococcus lactis, the TNF-α concentrations were lower compared with sterile and E.coli stimulated cultures, most probably because of the anti-inflammatory probiotic effect of the “natural” Lactococcus lactis itself. We believe that an additional TNF-α binding effect of engineered Lactococcus lactis with surface anti-TNF-α affibody might be observed by using lower concentrations of lactococci in medium, resulting in less pronounced influence on the TNF-α production. Moreover, strong anti-inflammatory effect of the “natural” strain of Lactococcus lactis, renders this strain a potential candidate for clinical studies.

Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PA-G-0050

**ADALIMUMAB AS FIRST-LINE ANTI-TNF TREATMENT IN PAEDIATRIC CROHN'S DISEASE**

Javier Martín-de-Carpi 1,*, Víctor Manuel Navas-López 2, María Navalon-Rubio 3, Enrique Llerena-Santa-Cruz 1, David Gil-Ortega 3, Vicente Varea-Calderón 1, Carlos Sierra-Salinas 2

1 Paediatric Gastroenterology and Nutrition Unit, Hospital Sant Joan De Deu, Barcelona, Spain, 2 Paediatric Gastroenterology and Nutrition Unit, Hospital Materno Infantil, Malaga, Spain, 3 Paediatric Gastroenterology and Nutrition Unit, Hospital Virgen De La Arrixaca, Murcia, Spain

**Objectives & Study:** Adalimumab (ADA), monoclonal humanized anti-TNF antibody is usually prescribed for patients who have lost response or developed intolerance to IFX. Data published thus far on the efficacy of treatment with ADA in children with CD comes from case series, retrospective studies and a clinical trial (IMAgINE 1). In the case series reported, more than 70% of patients had initially been treated with IFX. Data on short and long-term efficacy in anti-TNF naïve patients are limited.

**Methods:** Multicenter retrospective study that included CD anti-TNF naïve pediatric patients treated with ADA as first anti-TNF. PCDAI, fecal calprotectin (FC), CRP, ESR were measured at weeks 0, 12 and 52 of treatment and at the end of follow-up.

**Results:** We included 40 patients (22 females) with a mean age at diagnosis of 11.3 ± 3.7 y, a mean age at start of ADA of 12.6 ± 2.5 y, and a median of 9 months (IQR 4.3-22.3) duration from CD diagnosis to start of treatment. The time from the onset of symptoms until diagnosis of the disease was 7 months (IQR 3-12). Mean weight was 38.7±12.2 Kg. ADA induction dose was 160/80 mg in 22 (55%) patients. Standard maintenance dose was 40 mg eow in all patients. Administration of ADA was performed in combination with thiopurines in 39 patients, of whom 37 received azathioprine, and 2 6-MP due to azathioprine-intolerance. Mean duration of combo therapy was 12 m (IQR 6-14). Baseline PCDAI was 25 (IQR 15-30). Median follow up was 24 months (IQR 12-39), 35 of 40 patients at week 12, 33 of 34 patients al week 52 and 36 of 40 patients at the end of follow-up were in clinical remission (PCDAI<10). A significant decrease was also seen in FC levels, from 747 µg/g (IQR 427-854) at start of ADA treatment to 131 µg/g (IQR 50-281) at week 12 (p=0.001) and to 255 µg/g (IQR 38-532) at week 52; CRP 30 mg/L (IQR 14-52) at baseline to 1.5 mg/L (IQR 0.5-5) at week 12 (p<0.0001) and 1.3 mg/L (IQR 0.4-4) at week 52 (p<0.0001); ESR 19.5 mm (IQR 14-32) to 4.5 mm (IQR 2-12) at week 12 (p<0.0001) and to 6 mm (IQR 3-11) at week 52 (p<0.0001). 10 of 40 (25%) patients needed treatment intensification but only one patient continued on intensification schedule at the end of the follow-up. A total of 1901 doses were administered in all in the 40 patients (36 doses (IQR 20-70)) during 16 months (IQR 8-33) of treatment. Surgery was performed in 5 patients (12.5%) through the follow-up. No severe adverse reactions, infections or malignancies were reported.

**Conclusion:** ADA has shown efficacy and safety in inducing and maintaining remission in pediatric CD patients naïve to anti-TNF. Early use of ADA in our series could explain the better results compared with already published data.

**Disclosure of Interest:** J. Martín-de-Carpi Conflict with: Consultation and speaker's fees, meeting attendance support or research support from Abbvie, V. M. Navas-López Conflict with: Consultation and speaker's fees, meeting attendance support or research support from Abbvie, M. Navalon-Rubio Conflict with: Consultation and speaker's fees, meeting attendance support or research support from Abbvie, E. Llerena-Santa-Cruz: None Declared, D. Gil-Ortega: None Declared, V. Varea-Calderón: None Declared, C. Sierra-Salinas: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PA-G-0051

**ADALIMUMAB THERAPY IN CHILDREN WITH CROHN’S DISEASE PREVIOUSLY TREATED WITH INFLIXIMAB; A DUTCH NATIONWIDE STUDY**

Maarten Cozijnsen 1*, Vera Duif 2, Freddy Kokke 3, Angelika Kindermann 4, Patrick van Rheenen 5, Tim de Meij 6, Maaike Schaart 7, Gerard Damen 2, Obbe Norbruis 8, Rolf Pelleboer 9, Anita Van den Neucker 10, Herbert van Wering 11, Thalia Hummel 12, Johanna Escher 1, Lissy de Ridder 1 and on behalf of the working group: Kids with Crohn and Colitis (KiCC)

1Paediatric Gastroenterology, Erasmus Medical Center-Sophia Children's Hospital, Rotterdam, Netherlands, 2Paediatric Gastroenterology, Radboud University Nijmegen Medical Centre, Nijmegen, Netherlands, 3Paediatric Gastroenterology, Wilhelmina Children’s Hospital-University Medical Center, Utrecht, Netherlands, 4Paediatric Gastroenterology, Emma Children’s Hospital-Academic Medical Center, Amsterdam, Netherlands, 5Paediatric Gastroenterology, Beatrix Children’s Hospital-University Medical Center Groningen, Groningen, Netherlands, 6Paediatric Gastroenterology, VU University Medical Center, Amsterdam, Netherlands, 7Paediatric Gastroenterology, Willem-Alexander Kinderziekenhuis-Leiden University Medical Center, Leiden, Netherlands, 8Paediatric Gastroenterology, Princess Amalia Department of Paediatrics, Isala, Zwolle, Netherlands, 9Paediatric Gastroenterology, Catharina Hospital, Eindhoven, Netherlands, 10Paediatric Gastroenterology, Maastricht University Medical Center, Maastricht, Netherlands, 11Paediatric Gastroenterology, Amphia Hospital, Breda, Netherlands, 12Paediatric Gastroenterology, Medisch Spectrum Twente, Enschede, Netherlands

**Objectives & Study:** Adalimumab, a humanized anti-tumor necrosis factor(TNF) antibody, is an effective treatment in patients with refractory Crohn’s disease (CD). Adalimumab has received its registration for pediatric CD on the basis of a recent international multicenter study.[1] The available literature on the efficacy and safety of adalimumab in pediatric CD is limited. We aim to assess the efficacy and safety of adalimumab in clinical care.

**Methods:** In this first nationwide survey, data of all Dutch CD patients who started with adalimumab treatment before the age of 18 after failing infliximab (IFX) treatment, were collected. Demographic data, clinical response to adalimumab and adverse events were recorded.

**Results:** Fifty-two CD patients were included, treated between 2005 and 2013. Median age at diagnosis was 11 years (IQR 8-13) and 14 years (IQR 13-16) at the start of adalimumab. Median follow-up time was 11 months (IQR 4-22). In total 35 patients (67%) obtained remission(mathematically weighted pediatric Crohn’s disease activity index (wPCDAI)<12.5 or Physician Global Assessment (PGA)=0) during follow-up after a median of 2.5 months (IQR 1-7). In 18 patients (35%) adalimumab treatment failed during follow-up; either due to primary non response (n=5; 10%), a secondary loss of response (n=10; 21%) or adverse events (n=3; 6%), with a median duration until adalimumab failure of 4 months (3-17). Sub analyses show that the risk of adalimumab failure is lower when antibodies to infliximab (ATTI) were present prior to introduction of adalimumab and, second, that the reason for IFX failure, such as primary non response or secondary loss of response, influences the risk of subsequent adalimumab failure (see figure). Minor adverse effects were reported in 20 patients (38%), 1 patient (2%) developed a severe adverse effect, a severe but nonfatal infection.
Conclusion: This study demonstrates that for pediatric CD patients who previously failed infliximab therapy, adalimumab is a reasonably safe and effective drug, able to induce and maintain remission in the majority of patients. But adalimumab failure does occur in a substantial number of patients, increasingly over time.


Objectives & Study: Host’s response to mucosa-associated microbiota is considered important in the pathogenesis of ulcerative colitis (UC). Lipocalin 2 (LCN2) is an epithelial cell-derived antimicrobial peptide whose expression is mediated by Toll-like receptor 3 in colonic epithelial cells (1). CXCL16 is a bacterial scavenger receptor which has been shown to play a pivotal role in the development of experimental colitis (2). Our aim was to explore gene expression of these two host molecules related to mucosal microbiota in a cohort of children with UC.

Methods: The study cohort comprised 19 children with active UC (median (range) age 13 (7-17) years), 9 children with inactive UC (14 (4-16) years) and 14 children with non-inflamed colon (8 (3-13) years). The gene expressions of LCN2, CXCL16 and its receptor CXCR6, and IL-8, an intestinal inflammatory marker, were assessed in colonic biopsies by relative quantitative reverse transcription-PCR.

Results: The relative gene expression of IL-8 in the colonic biopsies was increased in active UC as compared to controls (p<0.001) and inactive UC (p=0.001). Again, the relative gene expression of LCN2 was increased in active UC as compared to controls (p=0.001) and inactive UC (p=0.002). The relative gene expression of CXCL16 was increased in active UC as compared to controls (p=0.006) but was comparable to inactive UC (p=0.36). The CXCL16 gene expression was also greater in active UC than in controls (p=0.033). The gene expression of IL-8 correlated with that of LCN2 and CXCL16 (r_s=0.79, p<0.001; and r_s 0.67, p=0.01, respectively). The relative gene expression of CXCR6 was comparable between the study groups.

Conclusion: The gene expression of the antimicrobial peptide LCN2 was increased in active UC and correlated well with the inflammatory marker IL-8 further supporting the role of LCN2 as a reliable marker of intestinal inflammation in patients with UC. The gene expression of the bacterial scavenger receptor CXCL16 was increased both in active UC and inactive UC as compared to control children with uninfamed colon suggesting its crucial role in the pathogenesis of UC. Both of these findings reinforce the supposed importance of mucosa-associated microbiota in UC.


Disclosure of Interest: None Declared
**Objectives & Study:** The efficacy of infliximab (IFX) in achieving clinical remission has been well established. According to the current recommendation, mucosal healing (MH) should be a major endpoint in clinical trials, apart from that increasingly used in clinical practice. However, data regarding mucosal healing in children with UC are limited. The aim of this study is to verify the impact of induction therapy with IFX on mucosal healing especially at a microscopic level.

**Methods:** Sixteen children with active UC were enrolled to this study. Colonoscopy with collected samples was performed in all patients before and after three injections of IFX. PUCAI index was used to assess clinical condition of the subjects, endoscopic features were classified according to Baron scale, disease location was classified according to Paris Classification and histological changes were precisely described according to protocol of The British Society of Gastroenterology. Patient’s condition before and after induction therapy with IFX was compared with special focus on pathological changes.

**Results:** 4 (25%) patients had left-side UC (E2); 8 (50%) had extensive UC (E3) and 4 (25%) had pancolitis (E4), respectively. Clinical improvement was observed in 14 (87.5%) patients: average PUCAI index before induction therapy with IFX was 49.0625 (max-85, min-10) and 16.25 (max-65, min-0) after IFX, respectively. Clinical remission was obtained in 75% of subjects. Endoscopic mucosal remission was achieved in 56.25% children. The average Baron scale before induction therapy with IFX was 2.5 (max-3, min-1); after IFX 1.5 (max-3, min-1) respectively. General histological improvement expressed by normal surface, crypt architecture, number of crypts and lamina propria cellularity was observed in 6 (37.5%) patients; there was no improvement in 9 (56.25%) patients; aggravation was observed in 1 patient (3.75%). Changes were not related to UC location. Reduction of inflammatory process was observed in 9 (56.25%) patients; there were no changes in 5 (31.25%) patients; in 2 (12.5%) patients inflammation was more severe.

**Conclusion:** Induction therapy with IFX has positive influence on histological changes in 37.5% of the patients. The treatment is more effective in reducing inflammatory process in the intestines (56.25% of the patients) and in improving clinical condition of children (87.5%).

**Disclosure of Interest:** J. Kierkus Speakers bureau of: MSD, abbvie, Nutricia, A. Wiernicka: None Declared, S. Szymanska: None Declared, J. Cielecka-Kuszyk: None Declared, M. Dadalski: None Declared
RISING INCIDENCE AND INCREASING SEVERITY OF VERY EARLY ONSET IBD IN IRELAND

Rebecca Wylde 1,2*, Aoife Carey 1,3, Billy Bourke 1,3,4, Anne Marie Broderick 1,3, Shona Quinn 1, Mary Hamzawi 1, Karen Gleeson 1, Seamus Hussey 1,3,4

1National Centre for Paediatric Gastroenterology (NCPG), OLCHC, Dublin, Ireland, 2Leiden University Medical Centre, Leiden, Netherlands, 3National Childrens Research Centre (NCRC), 4School of Medicine and Medical Science, University College Dublin, Dublin, Ireland

Objectives & Study: The literature describing the epidemiology and outcomes of very early onset IBD (VEO-IBD) is limited. This study examined the epidemiology, phenotype and clinical outcomes of a national cohort of Irish children with VEO-IBD from 2000 to 2012.

Methods: Irish children with IBD are cared for at a single national centre (NCPG). A retrospective review of all cases of VEO-IBD (those diagnosed <10 years of age) attending the NCPG from January 2000 to December 2012 was undertaken. Patient demographics, diagnostic work-up, initial and subsequent treatment, and long term clinical and surgical outcomes at 1, 2, 5 and/or maximum clinical follow up were recorded. Cases were phenotyped according to the Paris Classification and clinical activity was determined using Physician Global Assessment, PCDAI and PUCAI scores. Data were analysed using the Statistical Package for the Social Sciences (SPSS version 20; Chicago, Illinois, USA). All data were log transformed prior to analysis and a p value ≤0.05 was considered statistically significant. Decimal age was calculated for age of diagnosis. Linear regression analysis was used to examine incidence trends.

Results: 158 children (79 male) with VEO-IBD were identified; 78 (49%) had Crohns Disease (CD), 63 (40%) had Ulcerative Colitis (UC) and 17 (11%) had undefined IBD (IBD-U). Interestingly, 64% of children under 6 years of age were female (p=0.02). The mean incidence of VEO-IBD was 1.8/100,000. The incidence of VEO-IBD has increased from 2000-2012 (0.8-3.3/100,000/year). Median age of onset was 7.5 years (IQR; 3.42). The incidence of UC has increased from 0.6 to 1.6/100,000 (p<0.007); pancolonic UC has increased 4-fold since 2000 (p=0.005) and more severe UC disease activity at evident at presentation (p=0.05). The incidence of upper gastrointestinal CD has increased substantially (p=0.003). Males had more upper GI disease (p=0.02) and more extensive disease distribution (p=0.03). At one year follow up, 95 (64%) of the 148 patients followed, were in clinical remission with 88 (59%) in steroid-free remission. Of these, 25 (26%) children required immunomodulator treatment.. At maximum follow up (median; 60 months), 24 (15%) had commenced on biologics, 43 (27%) on immunomodulators and 20 (13%) had undergone surgery (12 UC; 8 CD).

Conclusion: The dynamics of VEO-IBD have recently changed in Ireland. Notable features include significant increases in the incidence and severity of UC, more severe VEO-IBD disease phenotypes in males and the female predominance of VEO-IBD in children under 6 years. Future prospective longitudinal studies are required to fully elucidate the factors underlying VEO-IBD.

Disclosure of Interest: None Declared
INTESTINAL ANTITRANSGLUTAMINASE ANTIBODIES TO DISCOVER GENETIC GLUTEN INTOLERANCE

Luigina De Leo 1,*, Fabiana Ziberna 1, Serena Vatta 1, Sara Quaglia 1, Vincenzo Villanacci 2, Stefano Martelossi 1, Grazia Di Leo 1, Alessandro Ventura 1, Tarcisio Not 1

1Maternal Child Health Institute, “Burlo Garofolo”, Trieste, Italy, 2Spedali Civili, Brescia, Italy

Objectives & Study: Celiac disease (CD) is characterized by the intestinal synthesis of antitransglutaminase antibodies (anti-tTG) which might represent an early stage of CD in absence of both intestinal damage and serum anti-tTG.

The aims of this study were to:
- evaluate by immunofluorescence assay (IF) the intestinal anti-tTG in patients undergoing to gastrointestinal endoscopy;
- correlate IF results with clinical, serological, histological and genetic CD markers.

Methods: This prospective study is a part of the trial: NCT00677495. The patients were analysed for HLA DQ2/8 and serum anti-tTG. Patients tested positive for intestinal anti-tTG, negative for serum anti-tTG with normal intestinal mucosa were analysed by phage display assay (PDA) for cloning specific anti-tTG derived from IGHV5-51 gene. Patients were monitored for clinical condition, serum anti-tTG concentration during gluten free diet (GFD) or gluten containing diet (GCD).

Results: 708 subjects (481F-227M, mean age 11±9 y) underwent to gastrointestinal endoscopy for gastrointestinal and extra-intestinal complaints.

494/708 tested positive for intestinal anti-tTG presented the following data:
A) 442/494 were positive for serum anti-tTG, HLA DQ2/8 and showed villous atrophy. After 1y of GFD, they were negative for serum anti-tTG and improved their clinical condition.
B) 24/494 were positive for serum anti-tTG, HLA DQ2/8 but showed normal mucosa. 18/24 symptomatic patients underwent to GFD for 1y and both serum anti-tTG and symptoms (anaemia, arthralgia, explosive diarrhea) disappeared.
C) 28/494 were negative for serum anti-tTG, positive for HLA DQ2/8 and showed normal mucosa. 25/28 were confirmed positive by PDA. 16/25 symptomatic patients underwent to GFD for 1y and improved their clinical condition (e.g. 8 patients with anaemia: Hb gr%: 9.8±0.3 in GCD vs 12.1±0.5 in GFD, p<0.001). In these 16 patients a second intestinal biopsy didn’t show intestinal anti-tTG. 9/25 asymptomatic patients after 1y of GCD were in good clinical condition and 1/18 was tested positive for serum anti-tTG. 3/28 were considered IF false positive
214/708 were negative for both intestinal and serum anti-tTG with no-CD intestinal lesions and 63/214 were positive for HLA DQ2/8.

Conclusion: Intestinal anti-tTG identified 24/708 (3%) and 25/708 (3.5%) CD patients with normal mucosa and with positive and negative serologic markers, respectively. Half of them (18/24 and 16/25) clinically improved in GFD.

The measurement of intestinal anti-tTG is a useful screening procedure to identify patients with CD-related HLA not fulfilling the CD diagnostic criteria that promptly respond to GFD.

Disclosure of Interest: None Declared
COELIAC DISEASE ANTIBODIES ARE ASSOCIATED WITH REDUCED GROWTH AND REDUCED BONE MINERAL DENSITY IN SUBCLINICAL CHILDREN: THE GENERATION R STUDY

Michelle Jansen 1,*, Jessica Kiefte - de Jong 2, Romy Gaillard 2, Vincent Jaddoe 1, 2, Albert Hofman 2, Hankje Escher 3, Herbert Hooijkaas 4, Henriette Moll 1
1Paediatrics, Erasmus Medical Center, Sophia Children’s Hospital, Rotterdam, Netherlands,
2Epidemiology, Erasmus Medical Center, Sophia Children’s Hospital, Rotterdam, Netherlands,
3Paediatric Gastroenterology and Hepatology, Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, Netherlands, 4Immunology, Erasmus Medical Center, Sophia Children's Hospital, Rotterdam, Netherlands

Objectives & Study:
‘The iceberg of celiac disease’ (CD) includes subclinical children with silent or latent CD, characterized by positive serology, but no gastrointestinal symptoms nor villous atrophy; or a later development of villous atrophy. Positive levels of antibodies against tissue transglutaminase (anti-tTG, a marker of celiac disease) have been associated with reduced weight and bone mass density at the moment of CD diagnosis. However, effects of positive levels on bone mineral density in subclinical children are not known.

Objective To assess associations between high levels of anti-tTG and height, weight, BMI and bone mass density in children from 6 months until 6 years of age.

Methods: In a population-based prospective cohort study, serum samples were analyzed for anti-tTG levels at 6 years of age. (n=4,442) Children with known celiac disease, or with a gluten free diet were excluded from analysis. Based on anti-tTG level, children were categorized into 2 groups: negative (< 7 U/ml, n=4,249), or positive anti-tTG (>7 U/ml, n=57). SDS for growth characteristics were obtained using Dutch reference growth charts. Bone mass density was measured by Dual-energy X-ray absorptiometry (DEXA). Multivariable linear regression models and linear mixed models were performed with adjustment for potential confounders.

Results: Height, weight, BMI and Bone Mass Density (SDS) at 6 years of age were lower (resp. -0.290; 95% CI -0.545;-0.036) (-0.378; 95% CI -0.635;-0.121) (-0.260 95% CI -0.492;-0.029) (-0.264; 95% CI -0.450; -0.078)) in anti-tTG positive children than in anti-tTG negative children. Second, delayed growth in height SDS/month (-0.00294; 95% CI -0.00526;-0.00062) and weight SDS/month (-0.00442; 95% CI -0.00511;-0.00373) from 6 months until 6 years was observed in anti-tTG positive children relative to anti-tTG negative children.

Conclusion: Subclinical positive anti-tTG levels in children at 6 years of age are associated with reduced bone mineral density at 6 years of age and delayed growth in height and weight from 6 months until 6 years.
Therefore, undiagnosed subclinical celiac disease has consequences for bone mineral density and normal growth development.

Disclosure of Interest: None Declared
Objectives & Study: To examine the annual incidence rate of biopsy-proven Celiac Disease (CD) among children in Sweden over a 36-year period, to assess variations by age, sex and birth cohort, and to assess the clinical impact of these changes.

Methods: The National Swedish Childhood CD Register was used to identify 9107 children aged 0-14.9 years who were diagnosed with CD during the period 1973 to 2009. Estimations for the annual incidence rate, cumulative incidence and clinical impact by age groups, calendar month and birth cohorts were made.

Results: The CD incidence is continuing to increase in the child population aged 2-14.9 years. A continued variation in CD incidence was observed in children aged 0-1.9 years, characterized by a marked decrease in most recent years. The median age at diagnosis has increased from 1.0 year in the 1970s to 6.8 years in 2009. The average number of new cases has risen from ~200 during 1973-1983 to ~600 during 2004-2009. In the birth cohorts of 2000-2002 the cumulative incidence even exceeded that of the epidemic cohorts at comparable ages. The highest cumulative incidence was observed in the birth cohorts of 1985-1995 and 2000-2002.

Conclusion: CD risk varies between birth cohorts, suggesting cyclic environmental and/or life style risk factors in CD etiology. More research on underlying risk factors is required in order to move forward with preventive strategies.

Disclosure of Interest: None Declared
MASS SCREENING FOR COELIAC DISEASE A FIVE-YEAR FOLLOW UP

Olof Sandström 1,*, Anna Myléus 2, Fredrik Norström 2, Annelie Carlsson 3, Solveig Hammarroth 4, Lotta Högberg 5, Maria van der Palz 3, Lars Stenhammar 6, Anneli Ivarsson 2

1Clinical Medicine, Epidemiology and Global Health and Clinical Sciences, Paediatrics, Umeå University, Umeå, Sweden
2Clinical Medicine, Epidemiology and Global Health, Umeå University, Umeå, Sweden
3Clinical Sciences, Paediatrics, Lund University, Lund, Sweden
4Paediatric Clinic, Norrtälje Hospital, Norrtälje, Sweden
5Clinical and Experimental Medicine, Paediatrics, 6Linköping University, Linköping, Sweden

Objectives & Study: Celiac disease (CD) often remains undetected and therefore mass screening has been suggested. Based on a CD mass screening in 2005-2006, (the ETICS study), we have conducted a five-year follow-up to assess gluten-free diet (GFD) compliance and self-reported health gain, and also to assess the proportion moving from being latent to overt CD cases.

Methods: In the school-based CD screening involving 7567 children at 12 years of age, 192 were tested positive for CD serological markers with 184 accepting small bowel biopsy, resulting in 153 new CD cases (1, 2). Five years later, we invited all 192 children, both overt CD cases and latent CD cases (those with positive CD serology but normal small bowel biopsy at initial screening) to a clinical follow-up. The CD cases were tested for anti-TG2, and responded to standardized questions about compliance to the GFD, and health changes after initiation of GFD. Latent CD cases were tested for anti-TG2 and recommended endoscopic examination if positive.

Results: Compliance to GFD (n=113): “always” or “most of the time” 86%, “sometimes” 8% and “never” 6%. Effect of GFD on experienced health (n=108): “much better” or, “better 54%, “no difference” 33%, “worse” or “much worse” 4% and “no opinion” 9%. Median anti-TG2 among the overt cases (excluding IgA deficient cases) decreased from 25.2 (range 9.1-62.9) U/mL at screening to 1.05 (range 0.10-25.2) U/mL at follow-up. Nine new CD cases were diagnosed whereof five cases presented at the clinic over the follow-up period, and additionally four at the five-year targeted screening occasion. Out of the remaining children three had an uncertain diagnosis, 14 were still non-CD cases and five declined further follow-up.

Conclusion: Self-reported compliance to the GFD was high among screening-detected CD cases, which was supported by a distinct reduction of anti-TG2. A majority reported an improved health but still, many did not experience a positive effect of the GFD. A substantial proportion (29%) of latent CD cases developed overt disease over the five-year follow-up suggesting that this group of children needs to be followed.


Disclosure of Interest: None Declared
THE CLINICAL MANIFESTATION OF COELIAC DISEASE DIAGNOSED IN PROSPECTIVE SCREENING OF CHILDREN WITH HLA RISK GENOTYPES THE TEDDY STUDY

Ola Jörnéus 1,*, Hye-Seung Lee 2, William Hagopian 3, Ville Simell 4, Kalle Kurppa 5, Carin Andrén-Aronsson 1, Michael Hummel 6, Sibylle Koletzko 6, Edwin Liu 7, Daniel Agardh 1 and the TEDDY Study Group

1Lund University, Malmö, Sweden, 2University of South Florida, Tampa, United States, 3University of Washington, Seattle, United States, 4University of Turku, Turku, Finland, 5University of Tampere, Tampere, Finland, 6Diabetes Research Institute, University Munich Medical Center, Munich, Germany, 7University of Colorado, Aurora, United States

Objectives & Study: Celiac disease is identified by the detection of tissue transglutaminase autoantibodies (tTGA) in screenings. The aim was to study if symptoms or clinical signs of celiac disease predicted tTGA levels and severity of intestinal mucosal damage detected in screening.

Methods: The Environmental Determinants of Diabetes in the Young (TEDDY) is a prospective multicentre study that investigates risk factors for type 1 diabetes and celiac disease. Children born 2004-2010 with HLA risk genotypes were followed from age 0-15 years at 6 clinical centres. Annual screening for celiac disease with tTGA was performed from 24 months of age. tTGA positive children were retested after 3 months and, if persistent tTGA positive, were referred to pediatric gastroenterologist for intestinal biopsy to confirm diagnosis when appropriate. Symptoms were reported annually in standardized questionnaires from 12 months of age.

Results: As of August 31st 2013, 795/6675 (12%) were persistent tTGA positive of whom 318/6675 (5%) were diagnosed with celiac disease. Questionnaires were available in 425/795 (53%) when the second sample for tTGA persistency was collected, including 167/318 (53%) children with celiac disease. At the time that a child met criteria for tTGA persistency (mean age 47 months, SD=18), 222 (52%) recorded no symptoms and 203 (48%) had experienced at least one symptom. When adjusted for age, HLA, and gender, tTGA persistent children with 1 symptom or more were at an increased risk of developing celiac disease (HR=1.5, 95% CI=1.1-2.1) as compared to those with no symptoms (reference) (p=0.0095). In symptomatic children, mean tTGA levels were higher (58.6 RU) compared to asymptomatic children (42.2 RU) (p=0.0185). In children with Marsh score 0 (M0), mean tTGA levels (25.3 RU) were lower than those with M2 (94.7 RU; p=0.0085), M3a (71.0 RU; p=0.004), M3b (85.1 RU; p=0.0003) and M3c (102.5 RU; p<0.0001); respectively.

Conclusion: This prospective screening demonstrates that children experiencing symptoms and present with clinical signs associated with celiac disease, tend to have higher tTGA levels and more severe intestinal mucosal findings than asymptomatic tTGA positive children. As more than half of children with tTGA and celiac disease were asymptomatic by the age of 4 years, screening for celiac disease cannot rely on standardized questionnaires in young children.

Disclosure of Interest: None Declared
OBJECTIVES & STUDY: Maternal nutrition reduction (MNR) is associated with intra-uterine growth restriction (IUGR) and increases the risk for post-natal chronic diseases such as diabetes and obesity. The mechanisms for this link remain to be established. The aim of this study was to explore effects of MNR in pregnancy on the metabolic signature of fetal baboons which reflect possible adaptation mechanisms of the fetus to MNR.

METHODS: We determined amino acid and lipid metabolites in the liver and plasma of fetuses whose mothers were either fed ad libitum (CTR) or malnourished (70% of ad libitum, MNR). Plasma and liver samples were collected at 90 d of gestation (n_MNR=8, n_CTR=6) and 165 d of gestation (n_MNR=4, n_CTR=9). Amino acids and non-esterified fatty acids were analyzed with high performance liquid chromatography/tandem mass spectrometry, while polar lipids were measured by flow-injection analysis/tandem mass spectrometry. For group comparison, Wilcoxon rank tests were performed with p<0.05 considered significant.

RESULTS: At 90 days of gestation (dG), MNR fetal plasma levels of the short-chain acylcarnitines C3.0 (p=0.02), C4.0 (p=0.01) and sum of short-chain acylcarnitines (p=0.008) were elevated. Furthermore, the ratio of the sum of short-chain acylcarnitines and the sum of branched-chain amino acids (BCAA, Leu, Ile, Val) was elevated (p=0.03). Long-chain acylcarnitine C18.0 levels were elevated in MNR fetal liver (p=0.04) at 90 dG. All of these metabolites did not differ between groups at 165 dG. Comparison of glucose levels in fetal liver between 90 dG und 165 dG showed a strong increase of glucose in the control group (p=0.004) and MNR fetuses (p=0.004).

CONCLUSION: An adaptation of fetal metabolism to maternal malnutrition occurs as early as 90 dG showing the ability of the fetus to monitor and respond to a low nutritional plane. Elevated short-chain acylcarnitine levels in fetal plasma reflect increased muscle BCAA oxidation, while higher long-chain liver acylcarnitine C18.0 levels may indicate an elevated fatty acid oxidation. Thus, fetal liver and fetal muscle adapt to the maternal under-nutrition by enhancing activity of different metabolic pathways for energy provision. These adaptations were no longer present at 165 dG. We hypothesize that compensatory mechanisms during the second half of gestation (e.g. the previously demonstrated increased PEPCK in the IUGR fetal liver) produce enough glucose to switch off the metabolic compensations in muscle and liver that occur in the first half of gestation.


Disclosure of Interest: None Declared
Nutrition

Observational and Epidemiological Studies

PA-N-0061

GEOGRAPHICAL DIFFERENCES IN COMMERCIAL INFANT FOOD CONSUMPTION IN 5 EUROPEAN COUNTRIES: RESULTS FROM THE CHOP STUDY

Melissa Theurich 1,*, Dariusz Gruszfeld 2, Katarzyna Szott 2, Annick Xhonneux 3, Veronica Luque 4, Marta Zaragoza-Jordana 5, Enrica Riva 6, Elvira Verduci 6, Berthold Koletzko 1, Veit Grote 1

1Dr. von Hauner Children's Hospital, University of Munich Medical Center, Munich, Germany, 2Department of Gastroenterology, Children's Memorial Health Institute, Warsaw, Poland, 3CHC St Vincent, Liège-Rocourt, Belgium, 4Universitat Rovira I Virgili, Taragona and Reus, Samoa, 5Universitat Rovira I Virgili, Taragona and Reus, Spain, 6University of Milan, Milan, Italy

Objectives & Study: Nutritional experiences in early life affect later food preferences and eating behaviors. In Europe, commercial infant foods (CIF) have begun to take the place of homemade foods and play a large role in the overall caloric and macronutrient intakes of young infants. Given current scientific knowledge on infant palate development, and the fundamental differences in texture and taste of CIF, questions about the role of CIF in the infant diet can be raised. The aim of this paper is to compare CIF consumption within Europe and its impact on infant energy and macronutrient intakes.

Methods: Data was drawn from the European Childhood Obesity Project, an multicenter intervention trial in Germany, Belgium, Italy, Poland and Spain that tested the effect of varying levels of protein in infant formula on the risk for childhood obesity. Complementary feeding data comes from weighted, 3-day dietary protocols at six months of age. Data from 730 formula-fed infants was used. Macronutrient and caloric intakes as well as total dietary intakes from commercial infant foods according to country of residence are compared using one-way ANOVA.

Results: Exposure to different complementary foods across Europe is varied with 708 infants (97%) reporting eating any complementary foods and 416 (57%) reporting any energy providing liquids at six months of age. Different complementary feeding practices make up for drastic differences in total macronutrient and caloric intakes. German infants reported the lowest caloric intakes among all countries (p<0.001) while Italy showed high fat (p<0.001) and protein (p<0.001) intakes compared to infants in all other countries except in Poland (p=0.069). Spanish infants had the highest average daily carbohydrate intakes and differed significantly from all other countries (p=0.001) while German infants reported the lowest carbohydrate intakes (p=0.004) of all countries. Half of all reported food intake (50% of weight) in all countries were from CIF and a large portion of the CIF were sweetened. The use of CIF varies greatly by country of residence.

Conclusion: There are varied and characteristic foods consumed by infants living in different European regions. Given the differences in caloric and macronutrient intakes partially due to high intakes of particular CIF in certain European countries, studies should be conducted to assess the nutritional adequacy of infant diets composed solely of CIF. The appropriateness of any added sugars during the complementary feeding period should be reconsidered since infants seem to be exposed to simple sugars from multiple CIF and beverages at once.

Disclosure of Interest: None Declared
Nutrition
Observational and Epidemiological Studies
PA-N-0062

NUTRITIONAL IRON STATUS IN LATE INFANCY IS ASSOCIATED WITH FEEDING TYPE AND AGE AT THE INTRODUCTION OF COMPLEMENTARY FOODS
Jeana Hong 1, 2,*, Sue Shin 3, Hyo-Jeong Jang 1, Jin Soo Moon 1, Jae Sung Ko 1, Ju Young Chang 1, 3
1 Paediatrics, Seoul National University College of Medicine, Seoul, Korea, Republic of Korea, 2 Kangwon National University Hospital, Chuncheon, Korea, Republic of Korea, 3 Seoul Metropolitan Government–Seoul National University Boramae Medical Center, Seoul, Korea, Republic of Korea

Objectives & Study: To determine the risk factors for iron deficiency (ID) in late infancy

Methods: This cross-sectional study was conducted on healthy term infants (≥ 37 weeks), aged 6–24 months, who visited a well-baby clinic for health examination and ID screenings. Information about feeding and weaning was obtained via questionnaire. ID was defined as having an abnormal value in at least 2 of 3 laboratory tests for iron status (mean corpuscular volume < 71 fL, transferrin saturation < 10%, or serum ferritin < 12 ng/mL) and iron deficiency anemia (IDA) as ID plus low hemoglobin levels (< 11 g/dL). Infants with a history of previous iron supplementation or any acute febrile illness in the previous 2 weeks were excluded.

Results: Among 600 infants, 424 infants met the inclusion criteria. ID was present in 84 infants (19.8%), and 51 infants (12.0%) had IDA. Gender, the type of feeding during the first 6 months after birth, and age at the introduction of complementary foods were significantly different between infants with ID and non-ID (p = 0.036, 0.000, and 0.004, respectively, Table). In the logistic regression analysis, exclusive or predominant breast feeding during the first 6 months after birth significantly increased the risk of ID by approximately 45-fold compared to predominant formula feeding [adjusted OR (ad-OR): 46.35; confidence interval (CI): 6.313–340.33; p = 0.000]. Introduction of complementary foods after 6 months of age also significantly increased ID risk compared to introduction of complementary foods before 6 months (ad-OR: 2.096; CI: 1.158–3.976; p = 0.015). Male gender also showed a significant positive association with ID (ad-OR: 1.908; CI: 1.134–3.210; p = 0.015).

Table.

<table>
<thead>
<tr>
<th>Characteristics</th>
<th>Total (n=424)</th>
<th>ID (n=84)</th>
<th>Non-ID (n=340)</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male/Female, n(%)</td>
<td>209 (49.3)/215 (50.7)</td>
<td>50 (59.5)/34 (40.5)</td>
<td>159 (46.8)/181 (53.2)</td>
<td>0.036</td>
</tr>
<tr>
<td>Gestational age, weeksa</td>
<td>39.3 (38.5–40.0)</td>
<td>39.0 (38.0–40.0)</td>
<td>39.6 (39.0–40.0)</td>
<td>0.117</td>
</tr>
<tr>
<td>Chronological age, monthsa</td>
<td>11.2 (10.1–12.1)</td>
<td>11.5 (10.2–12.3)</td>
<td>11.1 (10.1–12.1)</td>
<td>0.147</td>
</tr>
<tr>
<td>Birth weight, Z-scores</td>
<td>-0.17±0.81</td>
<td>-0.21±0.71</td>
<td>-0.16±0.83</td>
<td>0.593</td>
</tr>
<tr>
<td>Weight for age, Z-scores</td>
<td>0.16±1.00</td>
<td>0.19±1.12</td>
<td>0.15±0.97</td>
<td>0.719</td>
</tr>
<tr>
<td>Predominant feeding types during first 6 months, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding/Formula-feeding</td>
<td>311 (73.3)/113 (26.7)</td>
<td>83 (98.8)/1 (1.2)</td>
<td>228 (67.1)/112 (32.9)</td>
<td>0.000</td>
</tr>
<tr>
<td>Age at introduction of complementary foods, n (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 6 months/≥ 6 months</td>
<td>154 (36.3)/270 (63.7)</td>
<td>19 (22.6)/65 (77.4)</td>
<td>135 (39.7)/205 (60.3)</td>
<td>0.004</td>
</tr>
</tbody>
</table>

*aThe values are presented as the median (interquartile range).

Conclusion: ID should be suspected in breast-fed, term Korean infants in late infancy, especially in those who began complementary feeding after 6 months. Male infants also have an increased risk of ID. Introduction of complementary foods before 6 months of age in breast-fed infants may help to improve iron status in late infancy.

Disclosure of Interest: None Declared
The Value of Ret-Hb and STFR in the Diagnosis of Iron Deficiency in Healthy Children Aged 0.5 to 3 Years Living in the Southwestern Region of the Netherlands

Lieke Uijterschout 1,*, Magnus Domellöf 2, Janneke Vloemans 3, Marjolijn Akkermans 3, Rimke Vos 4, Ciska Hudig 5, Sally Babbers 6, Sascha Verbruggen 7, Margriet Veldhorst 8, Tom de Leeuw 9, Peter-Paul Teunisse 10, Johannes B van Goudoever 11, Frank Brus 3

1Paediatrics, Juliana Children's Hospital, The Hague, Netherlands, 2Department of Clinical Sciences, Paediatrics, Umeå University, Umeå, Sweden, 3Department of Paediatrics, Juliana Children's Hospital, The Hague, Netherlands, 4Haga Teaching Hospital, The Hague, Netherlands, 5Department of Clinical Chemistry, Haga Teaching Hospital, The Hague, Netherlands, 6Department of Anesthesiology, Juliana Children's Hospital, The Hague, Netherlands, 7Department of Paediatrics, Sophia Children's Hospital, Rotterdam, Netherlands, 8Paediatrics, Sophia Children's Hospital - VU Medical Center, Rotterdam - Amsterdam, Netherlands, 9Department of Anesthesiology, Sophia Children's Hospital, Rotterdam, Netherlands, 10Department of Paediatrics, Sophia Children's Hospital, Rotterdam, Netherlands, 11Department of Paediatrics, VU Medical Center - Emma Children's Hospital/Academic Medical Center, Amsterdam, Netherlands

Objectives & Study: Reticulocyte hemoglobin content (Ret-Hb) and soluble transferrin receptor (sTfR) are described as promising biomarkers in the analysis of iron status. Their measurement is recommended by the American Academy of Pediatrics in the screening of iron deficiency (ID) in infants with a hemoglobin (Hb) <110 g/L or with a high risk of nutritional ID. However, the value of Ret-Hb and sTfR in the early detection of milder forms of ID, as frequently observed in children in high-income countries is unclear.

In this study we aim to investigate the value of Ret-Hb and sTfR in the diagnosis of ID in healthy children aged 0.5 to 3 years in a high-income country.

In this prospective, cross-sectional study we analyzed Ret-Hb, sTfR, ferritin (Fer), mean cellular volume (MCV) and Hb in 400 healthy children.

Methods: In this prospective, cross-sectional study we analyzed Ret-Hb, sTfR, ferritin (Fer), mean cellular volume (MCV) and Hb in 400 healthy children.

Results: We showed that concentrations of Ret-Hb and sTfR are similar in children with and without mild ID, using the WHO cut-off of Fer <12 μg/L. A decrease in Ret-Hb concentrations was present only when Fer concentrations were <8 μg/L and no difference was observed in sTfR concentrations in children with different Fer concentrations. Fer was not associated with Ret-Hb, sTfR and MCV unless iron stores were depleted.

Conclusion: Our results showed that the discriminative value of Ret-Hb and sTfR for the detection of milder forms of depleted iron stores in young healthy children in a high-income country is limited. Our findings suggest that Fer is the most useful biomarker in the screening of ID in healthy children in high-income countries with a low prevalence of severe ID. Since our data show an effect on iron available for erythropoiesis only when Fer is <10 μg/L, this might be an appropriate cut-off value to define ID in healthy children aged 0.5 to 3 years.

Disclosure of Interest: None Declared
EXPLORE OF HUMAN MILK FORTIFICATION IN PRETERM INFANTS
Chen Wang 1*, Danhua Wang 1, Yun Cao 2, Lijuan Xie 3, Xiaomei Tong 4

1Department of Paediatrics, Peking Union Medical College Hospital, Chinese Academy of Medical Science, Beijing, China, 2Department of Neonate, Children Hospital of Fudan University, Shanghai, China, 3Department of Paediatrics, Xin Hua Hospital Affiliated to Shanghai Jiao Tong University School of Medicine, Shanghai, China, 4Department of Paediatrics, Peking University Third Hospital, Beijing, China

Objectives & Study: To explore the optimal initiative timing and advancement of human milk fortification in preterm infants to assure optimal nutritional intake and normal growth. We performed a retrospective cohort study determining the effect of initiative timing and advancement of human milk fortification on in-hospital growth and nutritional status of premature infants.

Methods: Preterm infants born at four tertiary hospitals or admitted by transport within 12 hours of birth between Nov. 2009 to Mar. 2011 with birthweights ≤1800 g who have received >50% of the milk volume as maternal breast milk that was fortified with human milk fortifier (HMF) during hospitalization were included. They were divided into early fortification group (human milk was started to be enriched with HMF before enteral intake reached 90ml/ kg·d ) and late fortification group (human milk was started to be enriched with HMF when enteral intake≥90ml/ kg·d). They also divided into rapid fortification group (time from receiving HMF to full fortification is within 3 days ) and slow fortification group (time from receiving HMF to full fortification is ≥4 days ). The comparison of morbidity, enteral nutrition, growth rate, and biochemical indices between the groups were made. Incidence of growth failure between birth and hospital discharge were made.

Results: Sixty seven subjects were included. Fortification was started when enteral intake reached 67.17±20.26ml/kg and127.00±37.03ml/kg in early and late fortification groups respectively. There were no significant differences in infant characteristics, complications or biochemical indices between the groups. In late fortification group, incidence of growth failure increased significantly (72.7% vs 42.9%, P=0.013) over time, which did not change significantly in early fortification group. In slow fortification group, incidence of growth failure increased significantly (65.4% vs 30.8%, P=0.012) over time, which did not change significantly in rapid fortification group. Rapid fortification group showed shorter length of hospitalization (34.0±15.6days vs 43.0±13.6days, P=0.02) and greater gain in weight (18.31±5.34g/ (kg·d) vs 15.66±3.65 g/ (kg·d) ,P=0.03) than slow fortification group.

Conclusion: Late or slow fortification of human milk in preterm infants appears to have been responsible for extrauterine growth restriction. Both early and rapid fortification of human milk were well tolerated and safe. It is suggested that initiation of human milk fortification be before enteral intake reaches 90ml/kg·d and that time from receiving HMF to full fortification be within 3 days.

Disclosure of Interest: None Declared
**Common ESPGHAN Topics**

**Basic Science**

PA-H-0065

**PUP RATS WITH EXPERIMENTAL BILIARY CIRRHOSIS DISPLAY NEUROMETABOLIC AND BLOOD-BRAIN-BARRIER ABNORMALITIES COMPARED TO ADULTS**

Valerie Anne McLin 1,*, Cristina Cudalbu 1, Olivier Braissant 2

1CIBM/LIFEMET, Ecole Polytechnique Fédérale Lausanne, Switzerland, 2Service de Biomédecine, CHUV/Université de Lausanne, Lausanne, Switzerland

**Objectives & Study:** Chronic liver disease (CLD) affects both adults and children and is often associated with some degree of hepatic encephalopathy (HE). In adults with CLD, the neurocognitive impairment related to covert hepatic encephalopathy is increasingly recognized. In children with CLD, there is increasing evidence of cognitive deficits early in life, but the underlying mechanism is unclear. How the developing brain responds to the metabolic changes of CLD, and how these mechanisms differ from those in adult patients are two unknowns. Thus, the aim of our study was to analyze neurometabolic profiles in a model of biliary cirrhosis in pups and adults

**Methods:** Wistar adult and pup (21 days) rats underwent bile duct ligation (BDL) and were scanned before BDL and weekly thereafter. In vivo localized spectroscopy was performed in the hippocampus on a 9.4T system. The ADC-apparent diffusion coefficient was measured in the cortex, striatum and hippocampus. Immunohistochemistry on brain tissue was performed using astrocytic and water channel markers (GFAP, AQP4).

**Results:** Table 1 Brain metabolism in pups and adults following BDL.

<table>
<thead>
<tr>
<th>Metabolite</th>
<th>Pups (8 weeks after BDL)</th>
<th>Adult (8 weeks after BDL)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glutamine (Gln)</td>
<td>← ~300%</td>
<td>← ~200%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Myo-inositol (Ins)</td>
<td>↓ ~50%</td>
<td>↓ ~30%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>ADC</td>
<td>← ~30%</td>
<td>← ~10%</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Glutamate (Glu)</td>
<td>↓ ~20%</td>
<td>↓ ~10%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Aspartate (Asp)</td>
<td>↓ ~50%</td>
<td>↓ ~30%</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Glutathione (GSH)</td>
<td>↓ ~36%</td>
<td>↓ ~9%</td>
<td>&lt;0.01 (pups)</td>
</tr>
<tr>
<td>Lactate (Lac)</td>
<td>←~30%</td>
<td>←~10%</td>
<td>&lt;0.05 (pups)</td>
</tr>
<tr>
<td>GFAP expression</td>
<td>Astrocyte swelling</td>
<td>Astrocyte swelling</td>
<td></td>
</tr>
<tr>
<td>AQP4 expression</td>
<td>←←</td>
<td>←</td>
<td></td>
</tr>
</tbody>
</table>

Following BDL, brain metabolism was more severely affected in pups than adults (Table 1). First, pups displayed a more pronounced increase of brain glutamine which was associated with marked edema in spite of ongoing osmoregulation as measured by decreased myoinositol. Second, enhanced expression of AQP4 in cerebral microcapillaries was more noticeable in pups than adults. Third, we observed a greater decrease in brain neurotransmitters and antioxidants in pups coupled with an increase in energy metabolites.

**Conclusion:** Increased AQP4 expression in the cerebral microcapillaries suggests that the underlying mechanism for higher ADC values in pups (suggestive of low grade cerebral edema) may be related to greater blood-brain barrier (BBB) permeability. We conclude that osmotic and metabolic changes are greater in pups than adults, possibly owing to differences in BBB permeability. How these two processes are linked and contribute to edema and neuro-cognitive changes remains to be determined.

**Disclosure of Interest:** None Declared
Objectives & Study: Background: Chronic infection with hepatitis B virus (HBV) induces transregulation of the host cell gene expression and may lead to malignant transformation. HBV X protein (HBx) acts as a transactivator of cellular promoters leading to upregulation of DNA methyltransferases and establishing alterations of DNA methylation and chromatin modification patterns.

Objectives of the study: To contribute to our understanding of DNA and chromatin-modifying mechanisms modulated by HBV, which are responsible for transregulation of host cells for virus particle production and malignant transformation of hepatocytes. We further studied the effect of lamivudine treatment or an antiviral vector-based RNAi strategy targeting HBx on the establishment and maintenance of DNA methylation patterns. Our research not only aimed to uncover epigenomic plasticity modulated by HBV. We also intended to contribute to the open problem, whether therapies lead to the restoration of regular epigenomic signatures, or whether hepatocytes persist in a deregulated epigenetic 'memory' state of HBV infection thus still carrying the risk for malignant transformation.

Methods: Methods: We analyzed gene expression profiles by qRT PCR arrays. DNA methylation as well as chromatin signatures of genes up- or down-regulated upon HBV infection were studied by MeDIP and ChIP, respectively, in murine cell lines transgenic for HBV. Furthermore, murine hepatocytes were transfected with GST-HBx in order to determine the role of HBx as a transactivator.

Results: Results: We identified several transregulated genes. Differential DNA methylation was shown in none of the examined examples. Chromatin signatures at selected loci within promoters were globally hypomethylated. Moreover, we observed that in our setting therapeutic strategies lead to changes in the epigenomic signature of hepatocytes. Ectopically expressed HBx led to deregulated expression patterns such as in HBV infection.

Conclusion: Conclusions: HBV infection leads to changes of the hepatocyte genome and consequently to dysregulated gene expression. Experimental therapeutic interventions efficiently suppress HBV proliferation and have an influence on epigenetic signatures that remains to be further investigated. HBx as an important transregulator influences gene expression in hepatocytes.

Disclosure of Interest: None Declared
THE COMBINATION OF LYMPHOCYTE SUBSETS AND PLASMA CYTOKINE AND CHEMOKINE LEVELS CHARACTERISES THE ADAPTATION OF THE IMMUNE SYSTEM AFTER PAEDIATRIC LIVER TRANSPLANTATION – FIRST RESULTS OF THE EUROPEAN PAEDIATRIC LIVER TRANSPLANTATION NETWORK EPLTN

I Goldschmidt 1,*, D Debray 2, L D’Antiga 3, V McLin 4, L Hierro 5, D Kelly 6, J Pawlowska 7, F Mutschler 1, E Pfister 1, C Neudörfl 8, J Keil 8, CS Falk 8, P McKiernan 6, F Lehner 1, U Baumann 1

1Hannover Medical School, Hannover, Germany, 2Hôpital Necker, Paris, France, 3Ospedali Riuniti di Bergamo, Bergamo, Italy, 4Serv. Spécialités Pédiatriques, Geneva, Switzerland, 5Hospital Infantil Universitario La Paz, Madrid, Spain, 6Birmingham Children’s Hospital, Birmingham, United Kingdom, 7Centrum Zdrowia Dziecka, Warsaw, Poland, 8Institute for Transplant Immunology, Hannover Medical School, Hannover, Germany

Objectives & Study: Individualised immunosuppressive therapy after pediatric liver transplantation (pLTX) is hampered by the lack of markers that adequately reflect the functional level of immunosuppression. Our study aims at describing immune function after pLTX in relation to clinical events, with a view to identify markers that can distinguish between under- and over-immunosuppression.

Methods: 41 children (19 m, age 2.9 (0.3-18) y) from the EPLTN network who were transplanted for endstage liver disease (biliary atresia n=13, hepatoblastoma n=6, acute liver failure n=6, other n=16) underwent immune monitoring from prior to pLTX up to 12 months after Tx. Diagnostics included quantification of immune mediators at protein level by Luminex-based Multiplex Technology in the peripheral blood and cell numbers of lymphocyte subsets (T, B, NK cells, monocytes) by Flow Cytometry. Immunosuppressive trough levels and clinical data were recorded for comparison.

Results: 14/41 children received initial immunosuppression with CsA, 27/41 received tacrolimus. Biopsy proven acute cellular rejection (BPAR) was seen in 9/41 children. In the course from pre LTx to 12 months after LTx, three major patterns could be identified among 60 cytokines, chemokines and growth factors. Th1 cytokines (IFN-g, IL-12p70) vs. Th2 cytokines (IL4, IL-5, IL-10, IL-13), CC (CCL2, CCL5) and CXC (CXCL9, CXCL10) chemokines followed the development of lymphocyte subsets (CD4+/CD8+ T, CD16+56+ NK), indicating that their plasma concentrations are influenced by the amount and activity of these cells. In some children, no significant changes in cytokine levels and cell counts were observed (group 1). In a second group, the onset of effective immunosuppression became visible by sustained reduction of cytokines in the peripheral blood despite the normal recovery of lymphocyte numbers to pre LTx levels. In children with BPAR (group 3), increased T cell numbers correlated with elevated Th1 and Th2 cytokine and chemokine levels indicating that BPAR is associated with systemic alterations of immunological markers.

Conclusion: The quantification of immune markers allows close monitoring of the onset of immunosuppression. In the future these biomarkers may provide information that might be used for tailored individualized immunosuppression, and might help to identify patients at particular risk of rejection or patients that may become tolerant.

Disclosure of Interest: I. Goldschmidt: None Declared, D. Debray: None Declared, L. D’Antiga: None Declared, V. McLin: None Declared, L. Hierro: None Declared, D. Kelly: None Declared, J. Pawlowska: None Declared, F. Mutschler: None Declared, E. Pfister: None Declared, C. Neudörfl: None Declared, J. Keil: None Declared, C. Falk: None Declared, P. McKiernan: None Declared, F. Lehner: None Declared, U. Baumann Grant / Research Support for: Supported by an unrestricted grant by Astellas Pharma¨and the German Ministry for Education and Research, IFB-Tx

JPGN, Volume 58, Supplement 1, June 2014 72
EXTRAHEPATIC ANOMALIES IN CHILDREN WITH BILIARY ATRESIA

Piotr Czubkowski 1,*; Małgorzata Rurarz 1, Irena Jankowska 1, Małgorzata Markiewicz-Kijewska 2, Joanna Pawłowska 1

1Department of Gastroenterology, Hepatology and Feeding Disorders, 2Department of Paediatric Surgery and Organ Transplantation, The Children’s Memorial Health Institute, Warsaw, Poland

Objectives & Study: Infants with biliary atresia (BA) may present with extrahepatic anomalies, mostly splenic, gastrointestinal and cardiovascular. The aim of the study was to analyze the congenital anomalies associated with BA and to determine its influence on the outcome of treatment.

Methods: We performed a retrospective review of 343 children with BA treated between 1984-2011 in our institution. The diagnosis was confirmed before Kasai hepatopancreatobilioplasty by intraoperative cholangiogram. Clinical and demographic data was collected and compared between “anomaly” and “anomaly-free” groups, with distinction of laterality defects and congenital heart defects (CHD). For the purpose of the statistics we used log-rank test, chi² and logistic regression as appropriate.

Results: In 116 (33.8%) patients we determined at least one congenital anomaly. Polysplenia was in 25 (7.2%), intestinal malrotation in 27 (7.8%), abdominal situs in 8 (2.3%). The vascular anomalies included: aberrant hepatic artery-27 (7.8%), preduodenal portal vein -13 (3.7%), and absent inferior vena cava – 1 (<1%). Congenital heart defect (CHD) was observed in 61 patients (17.8%): insignificant left-to-right interatrial shunt – PFO/ASD II (n=44), patent ductus arteriosus n=4 and complex CHD (n=13). Prematurity, bleedings during pregnancy and history of miscarriages in previous pregnancies were more common in "anomaly" group. The mean age at Kasai operation was 71 days. The 2,5 and 10-year estimated survival with native liver was 51%,37% and 26% respectively and was not worse in "anomaly" group. The risk of cholangitis and development of portal hypertension did not significantly differ between “anomaly” and “anomaly-free” group either.

Conclusion: The presence of congenital anomalies in BA does not worsen the outcome of treatment.

Disclosure of Interest: None Declared
Objectives & Study: Research has shown high-concordance between parent-proxy and child ratings of health-related quality of life (HRQOL), though parents tend to underreport more subjective domains. The current study compared HRQOL ratings of pediatric post-liver transplant patients (LT) to their parents’ on the Pediatric Liver Transplant Quality of Life Questionnaire (PeLTQL) and its related domain scores: Future Health, Coping and Adjustment, Social Emotional.

Methods: LT patients (8-18 years) completed the 26 item, and their parents completed a proxy version of the PeLTQL (higher PeLTQL scores = higher HRQOL). Similarly patients and parents completed the PedsQL Generic questionnaire. Patients completed the Children’s Depressive Inventory Short Form (CDI-S); and the Screen for Child Anxiety Related Disorders (SCARED). Parent-proxy and patient scores were compared via paired samples t-tests.

Results: 129 parent-child pairs that independently filled out the PeLTQL (Cronbach’s a = 0.85). Fifty-seven percent of patients were female (mean age 13.4±2.8 years). Patients were drawn from 4 countries (36.4% Canada, 22.5% US, 20.2% UK, 20.9% Australia). There was a significant difference between parent and patient ratings of HRQOL on the PeLTQL overall (64.2±12.6, 69.2±13.5, p < .001), the Coping and Adjustment (62.3±15.8, 67.1±16.4, p = .001) and Social Emotional Domain (66.2±14.9, 71.4±16.0, p = .000), but not on the Future Health Domain (71.2±16.6, 68.7±18.1, p = .125). For the younger age strata (n = 57), patients and parents views were more closely aligned, as there were no significant differences between QOL ratings on PeLTQL overall or domains. The SCARED and CDI-S had significant interactions with PeLTQL overall, where higher anxiety or depression was related to higher discordance between parent and patient ratings (p < .01). Patients scores on the PedsQL and the PeLTQL were highly correlated (r = .68, p < .001). There was a significant different between parents (70.5±18.5) and patients’ (74.2±19.0) scores on the PedsQL (p = .01).

Conclusion: The results show a pattern of parental underestimation of their children’s QOL on the PeLTQL and PedsQL. Concordance seems to differ as a function of child age, where higher concordance was found with younger children. Child anxiety and depression may also be related to increased discordance between parent-proxy and child ratings on PeLTQL.

Disclosure of Interest: None Declared
Objectives & Study: Along with the increase in the number of patients on TNFa antagonist therapy, more experience is gained on therapy related adverse events. In adult patients, development of skin reactions is common but there are few studies on pediatric inflammatory bowel disease (IBD); hence, this prospective study focuses on skin reactions related to infliximab therapy in pediatric patients.

Methods: All pediatric patients with IBD undergoing infliximab therapy were prospectively screened for the presence of skin manifestations at the time of infusions during a two-year study period between 1.3.2011 and 31.3.2013 at Children’s Hospital in Helsinki, Finland. Blood inflammatory markers and fecal calprotectin (FC) levels were measured at the time of infusions.

Results: During the study period, 84 children with IBD (Crohn’s disease n=64) received infliximab infusions (the median duration of therapy 12.2 months). Almost every other patient with IBD (n=40; 47.6%) presented skin reactions (Table 1) and every fifth (23.8%) with lesions considered severe. Most commonly, the patient’s ear lobes and scalp were affected with psoriasis-like manifestations, followed by their eyelids, perioral and pubic area, trunk, and the extremities. However, an HLA-Cw*0602 genotype associating with psoriasis was rare. Interestingly, most patients with skin reactions had a low degree of intestinal inflammation based on their FC levels (median level 133 mg/g versus 589 mg/g in unaffected patients; p<0.016). Seven patients (8.3% of the study group; 17% of those with skin lesions) discontinued the given therapy due to a skin reaction.

Table 1 Group differences in the 84 pediatric patients with inflammatory bowel disease (IBD) treated with the TNFa antagonist infliximab related to the presentation of drug-related skin manifestations (the values are expressed as medians (inter-quartile range) or number of patients when appropriate). *Mann Whitney U-test. **Fisher’s exact test two-sided test comparing the frequencies between patients with Crohn’s and ulcerative colitis/unclassified.

<table>
<thead>
<tr>
<th>No. of patients, total</th>
<th>No skin lesions</th>
<th>Skin lesions</th>
<th>P-value Between groups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at diagnosis of IBD</td>
<td>44</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Crohn’s disease</td>
<td>13.6 (2.9-17)</td>
<td>11.7 (9.7-13.918)</td>
<td>&lt;0.05*</td>
</tr>
<tr>
<td>Ulcerative colitis/Unclassified</td>
<td>5 (3-10)</td>
<td>9 (6-16)</td>
<td>&lt;0.05**&lt;0.05**</td>
</tr>
<tr>
<td>Induction of anti-TNFa during study</td>
<td></td>
<td></td>
<td>&lt;0.005**</td>
</tr>
<tr>
<td>Duration of infliximab (months)</td>
<td></td>
<td></td>
<td>&lt;0.0001*</td>
</tr>
<tr>
<td>Number of infliximab doses given</td>
<td></td>
<td></td>
<td>&lt;0.005*</td>
</tr>
</tbody>
</table>

Conclusion: Skin lesions are common during maintenance therapy with infliximab in pediatric patients. For most patients, skin reactions seem to coincide with a low level of intestinal inflammation. Although potentially harsh, the discontinuation of infliximab is seldom necessary.

Disclosure of Interest: T. Mälkönen: None Declared, A. Wikström: None Declared, K. Heiskanen: None Declared, L. Merras-Salmio: None Declared, T. Sipponen: None Declared, K.-L. Kolho Grant /
Research Support for: Finnish Pediatric Research Foundation, Helsinki University Central Hospital Research Fund, Sigrid Jusélius Foundation, Consultant for: Abbvie; MSD
LONG-TERM SAFETY OF ADALIMUMAB IN PAEDIATRIC PATIENTS WITH CROHNS DISEASE

J Rosh 1, F Ruemmele 2, M Dubinsky 3, J Escher 4, J Kierkus 5, J S Hyams 6, A Lazar 7, S Eichner 8, Y Li 8, R Thakkar 8

1Goryeb Children’s Hosp/Atlantic Health, Morristown, United States, 2Univ Sorbonne Paris-Cite, Hosp Necker-Enfants Malades, Paris, France, 3Cedars-Sinai Med Ctr, Los Angeles, United States, 4Erasmuc MC-Sophia Children’s Hosp, Rotterdam, Netherlands, 5Children’s Memorial Health Inst, Warsaw, Poland, 6Connecticut Children’s Med Ctr, Hartford, CT, United States, 7AbbVie, Ludwigshafen, Germany, 8AbbVie, N Chicago, IL, United States

Objectives & Study: The safety profile of adalimumab (ADA) in children enrolled in the IMAGINE 1 clinical trial and the open-label extension (OLE) has been reported up to 3 years. A safety update, with up to 5 years of ADA exposure, is presented.

Methods: Patients (pts) completing the IMAGINE 1 trial could enroll in the OLE. Adverse events (AEs) were reported from the first dose through the June 30, 2013 cut-off or up to 70 days after the last ADA dose for any pt that received at least one dose of ADA. Rates of AEs were assessed per 100 patient-years (PY). Subgroup analysis by prior infliximab (IFX) use was performed.

Results: A total of 192 children have received at least one dose of ADA in IMAGINE 1 and the OLE, totaling 422.2 PY of exposure. As of June 30, 2013, 115/192 pts (59.9%), 82/192 (42.7%), 75/192 (39.1%), 58/192 (30.2%), and 15/192 (7.8%) have at least 1, 2, 3, 4, or 5 years of ADA exposure, respectively. An overview of the treatment-emergent AEs for all pts and by prior IFX use is shown in the table. The most common serious AE (SAE) was flare or worsening of CD and most (7/11) opportunistic infections were non-serious oral candidiasis. The exposure-adjusted rate of SAEs and AEs leading to discontinuation were significantly higher for IFX experienced pts than IFX naive pts (Table). The rate of serious infections observed between pts receiving ADA with or without concomitant immunosuppressant (IMM) and/or corticosteroid (CS) use at baseline were 3.5 E/100PY ADA monotherapy, 6.2 E/100PY ADA + IMM, 4.4 E/100PY ADA + CS, and 12.5 E/100PY ADA + IMM + CS (p=0.09). No malignancies or deaths have been reported to date.

Image:
Conclusion: No new safety risks have been identified with prolonged ADA treatment in children with Crohn’s disease. The safety profile of ADA in children with Crohn’s disease continues to be consistent with previously published reports.1,2


SUPPLEMENTATION OF INFANT FORMULA WITH BOVINE MILK FAT GLOBULE MEMBRANES IMPROVES COGNITIVE FUNCTION AND REDUCES THE INCIDENCE OF OTITIS IN FORMULA-FED TERM INFANTS

Niklas Timby,1,*, Erik Domellöf,2 Bo Lönnerdal,3 Olle Hernell,1 Magnus Domellöf1

1Clinical Sciences/Paediatrics, 2Psychology, Umeå University, Umeå, Sweden, 3Nutrition, University of California, Davis, United States

Objectives & Study: To evaluate effects of feeding an experimental formula (EF) with reduced energy (60 vs. 66 kcal/100 mL) and protein (1.20 vs. 1.27 g/100 ml) densities and supplemented with a bovine milk fat globule membrane (MFGM) concentrate vs. standard formula (SF).

Methods: In a prospective, double blinded randomized controlled trial 160 exclusively formula-fed healthy term infants were randomized to receive EF or SF from <2 months to 6 months of age. A breast-fed reference (BFR) group consisted of 80 infants. At 12 months of age, a developmental assessment with Bayley Scales of Infant and Toddler Development, Third Edition (Bayley-III) was performed. Parental reports of disease symptoms and medications were collected prospectively. Parental control of feeding was assessed with a revised Child Feeding Questionnaire (CFQ) at 4 and 12 months of age.

Results: The EF group had higher cognitive score (105.8 vs. 101.8, p=0.008) than the SF group at Bayley-III testing at 12 months of age. During the intervention, the EF group had lower incidence of otitis media (1% vs. 9%, p=0.034) and lower longitudinal prevalence of anti-pyretic medication use (p=0.012) than the SF group. There were no difference in growth or protein or energy intake between the formula-fed groups since the EF group had larger formula volume intake (864 vs. 797 ml/day, p=0.022) than the SF group. Parents of formula-fed infants had lower pressure-to-eat score (p=0.019) than parents of breast-fed infants at 12 months of age.

Conclusion: MFGM contains factors necessary for optimal cognitive and immunological development that historically have been lacking in infant formulas. Supplementation of infant formula with a bovine MFGM concentrate narrowed the gap between formula-fed and breast-fed infants with respect to cognitive development and infectious morbidity. For the formula-fed infants, a high level of self-regulation of energy intake and low parental control of feeding yielded full compensation of the differences in formula energy and protein density.

Disclosure of Interest: N. Timby: None Declared, E. Domellöf: None Declared, B. Lönnerdal Consultant for: Member of Hero scientific advisory board, O. Hernell Consultant for: Member of Hero scientific advisory board, M. Domellöf: None Declared
Nutrition
Observational and Epidemiological Studies
PD-N-0073
MALNUTRITION AND COGNITIVE FUNCTIONING IN SHWACHMAN-DIAMOND SYNDROME
Sandra Perobelli 1,*, Marianna Daldoss 1, Barouck Maurice Assael 1, Marco Cipolli 1
1CF Centre, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy

Objectives & Study: Shwachman-Diamond syndrome (SDS) is a rare autosomal recessive disorder resulting from mutations in the SBDS gene on chromosome 7q11. The SBDS gene is highly expressed in rapidly proliferating tissues, but it was found to be expressed in all embryonic stages and most adult tissues, including in the brain. Phenotypically, SDS is principally characterized by exocrine pancreatic insufficiency, bone marrow dysfunction and skeletal dysplasia. Cognitive impairment has been noted in the majority of these patients, albeit with intragroup variability: this has a serious impact on quality of life, limiting independence and socialization. This study was planned to investigate the influence of malnutrition on cognitive development.

Methods: In the last two decades 40 children with Shwachman-Diamond Syndrome (SDS) were diagnosed at the Cystic Fibrosis Center in Verona. The diagnosis was confirmed by one of the known SBDS mutations on both alleles. As part of the follow-up, regular assessment of psychomotor and cognitive development was performed using anamnestic form, parents’ report and standardized test.

Results: We show the preliminary data of the nutritional status at birth and the subsequent cognitive performance of 20 children (12 males). Pancreatic insufficiency was present in all patients at birth. The mean weight Z-score was -0.65 (SD 1.15, max 0.66/min -2.65). 13 children presented a weight Z score below 0. The cognitive assessment was performed when children were 7-14 years old. As group, SDS children showed a total Intelligence Quotient (IQ) in the low mean of normal distribution (mean 88.7, SD 9.04), while six patients showed a cognitive impairment (range: 85-66). Children with weight Z score at birth <=0 showed 87.5 mean IQ (SD 8.85); those with weight Z score at birth >0 presented 90.29 mean IQ (SD 9.88). No cognitive differences were found between the two groups.

Conclusion: These data suggest that cognitive dysfunctions are present in SDS as a primary feature and not as a consequence of the level of malnutrition observed at birth. Therefore we suggest regular assessment of psychological development of SDS children in order to offer rehabilitative interventions if problems are evidenced. This approach should be independent of malnutrition recovery.

Disclosure of Interest: None Declared
CAUSES OF "PARENTERAL NUTRITION-ASSOCIATED LIVER DISEASE "IN THE LONG-TERM NUTRITIONAL THERAPY

Przemysław Matras 1,* , Mariusz Matuszek 1, Jacek Furmaga 1, Katarzyna Wojewoda 1, Sławomir Rudzki 1
1First Chair General and Transplant Surgery and Clinical Nutrition, Medical University of Lublin, Lublin, Poland

Objectives & Study: Parenteral Nutrition is not free from numerous complications. The aim of this study is to look for the factors that induce “Parenteral Nutrition-Associated Liver Disease” (PNALD) among total parenteral nutrition (TPN) outpatients.

Methods: This is a retrospective study that includes 70 patients. In this group biochemical tests had been performed for three following months on average. The results of the biochemistry tests were divided into groups I-with and II-without complications: depending on aminotransferases level- group I: AST and ALT< 48 IU/L and group II: AST and ALT> 48IU/L, and depending on total bilirubin level- group IB:<1.2 mg/dl and IIB:>1.2 mg/dl. The supply of nutritional ingredients were compared among groups in the period preceding the laboratory tests.

Results: The differences between groups I vs.II demonstrate the daily supply of glucose that was mean 2.52 vs.3.49 g/kg (p=0.000003), glucose to lipid ratio: mean 3.76 vs.4.90 g/kg (p=0.0001), the daily number of reported non-protein energy: mean 16.73 vs.21.06 kcal/kg (p=0.0001) and the ratio of the energy from lipids to energy from amino acids: mean 2.30 vs.2.05 kcal/kg (p=0.01). The differences between groups IB vs.IIB demonstrated respectively the daily supply of glucose: mean 2.76 vs.3.46 g/kg (p=0.0007), glucose to lipid ratio: mean 3.98 vs.5.13 g/kg (p=0.01), the daily number of reported non-protein energy: mean 17.96 vs.20.36 kcal/kg (p=0.04) and the ratio of the energy from lipids to energy from amino acids: mean 2.28 vs.1.93 kcal/kg (p=0.04).

Conclusion: The parenteral nutritional treatment should to strive to reduce the absolute glucose content of the nutrient feed mixture and to reduce glucose to lipid ratio, which can decrease the incidence of PNALD. A similar effect can cause increase the ratio of energy derived from lipid originating from protein.

Disclosure of Interest: None Declared
EFFECT OF VERY EARLY PARENT TRAINING ON FEEDING INTERACTION AND INFANT EATING HABITS AT 12 MONTHS

Inbal Balog 1, Oded Pshetatzki 1, Geila Rozen 2,*, Yael Latzer 3, 4
1School of Public Health, department of Nutrition, Health and Behavior, University of Haifa, Haifa, Israel, 2Clinical Nutrition Department, Rambam Medical Center, Haifa, Israel, 3 Associate Professor, Faculty of Social Welfare and Health Sciences, University of Haifa, Haifa, Israel, 4Director, Eating Disorders Clinic, Psychiatric Division, Rambam Medical Center, Haifa, Israel

Objectives & Study: The purpose of this study was to examine whether professional training of inexperienced mothers of four month old infants will improve their feeding relationship and the infants eating habits.

Methods: First time mothers were recruited 4-6 months after delivery for a training program (intervention group). Training setting was in small workshop groups, once a week for the duration of a month. Internet based maintenance and support were continued until infants reached the age of 12 months by an experienced pediatric dietitian and social worker. The control group received no training beyond customary support given at municipal mother-child health clinics. Mealtime interaction was evaluated at the age of 12 months using the Chatoor feeding scale of videotaped feeding interaction in home setting. Viewing of tapes was blinded. Data of infants eating habits was collected using self-report questionnaires.

Results: Training program and follow-up was completed by 86 mothers. Controls of 42 mother-infant dyads were recruited. Mothers were 30 (±2.6) years old, with 16 (±2.2) years of education, all normative according to personality questionnaires, and without clinical eating disorders. When observing mealtime interaction according to Chatoor feeding scale statistically highly significant differences in favor of intervention group were found for four of the five dimensions: dyadic conflict (4.69 vs. 8.38), talk and distraction (3.75 vs. 4.9), struggle for control (2.3 vs. 4.88), maternal non-contingency (1.61 vs. 2.75). Lower results on Chatoor scale indicate a more positive mother-infant interaction during mealtime, and better response to infant’s cues. Eating habits results from self-report questionnaires indicated infants in the intervention group consumed at age 12 months less snacks, less sweets and fewer sweet-drinks. Training group mothers also reported a lower frequency of vomiting or spitting-up during mealtime. Intervention group infants were also reported as less distracted during meal time. No other differences were found between groups.

Conclusion: This research evaluated a very early maternal training program aimed at improving sensitive and consistent maternal responsiveness, as means of developing a positive feeding relationship at infancy. Results suggest that parental guidance can support the establishing of more positive feeding interaction of 12 month Old infants. This in turn may contribute to better and healthier eating habits, as well as preserving internal eating cues based on hunger and satiety. We postulate all this may prevent future eating disorders as well as obesity. Long term follow-up, and variation of groups, is necessary in order to further examine these affects and optimize training programs to better accommodate specific target populations.

Disclosure of Interest: None Declared
ZINC SUPPLEMENTATION REDUCES THE RISK OF NECROTIZING ENTEROCOLITIS IN VERY LOW BIRTH WEIGHT NEONATES: A RANDOMIZED CLINICAL TRIAL

Gianluca Terrin 1,*, Roberto Berni Canani 2, Annalisa Passariello 3, Maria Giulia Conti 4, Antonella Scipione 4, Erica Bacchio 4, Monica Malamisura 2, Ylenia Maddalena 2, Tommaso Cozzolino 2, Serena Laterza 5, Mario De Curtis 4

1Department of Gynecology-Obstetrics and Perinatal Medicine, University "La Sapienza", Rome, Italy, 2University of Naples "Federico II", Naples, Italy, 3Hospital "Dei Colli", Naples, Italy, 4University "La Sapienza", 5University "La Sapienza", Rome, Italy

Objectives & Study: Necrotizing enterocolitis (NEC) remains one of the leading causes of morbidity and mortality in premature neonates 1. Modification of immune response and alteration of epithelial barrier play a crucial role in the pathogenesis of NEC. Zinc is an ubiquitous element deeply involved in the development of immune response and essential for epithelial integrity. Preterm neonates are at high risk of zinc deficiency 2. In this study we aimed to investigate the efficacy of zinc supplementation in reducing the occurrence of NEC in preterm neonates.

Methods: A prospective, double-blind, randomized controlled study was conducted on very low birth weight neonates (birth weight < 1500 g), randomly allocated, at the 7th day of life, in zinc group (receiving 10 mg/d of zinc through a multivitamin product given by oral route) or in placebo group (receiving a similar multivitamin product without zinc). Main endpoint was the rate of neonates presenting NEC. Secondary outcome was mortality rate.

Results: We enrolled 97 neonates in the zinc group and 96 in the placebo group. Occurrence of NEC was significantly higher in placebo group (6.3%) compared to the zinc group (0%, p=0.014). Mortality risk was significantly reduced in zinc group (OR 0.275, 95%CI 0.086-0.875, p=0.021).

Conclusion: Oral supplementation with high dose of zinc reduces the risk of NEC and mortality in preterm neonates. Additional studies are advocated to investigate the mechanism by which zinc produces observed effects in this particular population.


Disclosure of Interest: None Declared
THE EFFECT OF OLIGOFRUCTOSE SUPPLEMENTATION ON BODY WEIGHT IN OVERWEIGHT AND OBESE CHILDREN: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

Anna Liber 1,*, Hania Szajewska 1
1Department of Paediatrics, The Medical University of Warsaw, Warsaw, Poland

Objectives & Study: Limited evidence suggests that the addition of oligofructose, an inulin-type fructan with known prebiotic properties, to the diets of overweight or obese adults may increase satiety, thus, reduce energy intake and body weight. Currently, there are no data on the effect of oligofructose supplementation in overweight and obese children. The aim of this study was to assess the effect of oligofructose administration for 12 weeks on the body mass index (BMI) of overweight and obese children.

Methods: Ninety-seven children aged 7 to 18 years with overweight and obesity diagnosed according to the World Health Organization criteria (BMI >85 percentile) were randomly assigned to receive oligofructose (Orafti P95, Beneo-Orafti, Belgium) or placebo (maltodextrine) for 12 weeks. Dosing of oligofructose was age dependent: 8 g/day for children aged 7-11 years and 15 g/day for children aged 12-18 years. The exclusion criteria included overweight or obesity secondary to genetic syndromes or endocrine diseases. Prior to the intervention, all children and parents received dietetic advice. Moreover, all children were encouraged to engage in physical activity. The primary outcome measure was the BMI z-score difference at the end of intervention.

Results: Data from 79 (81%) children were available for the intention-to-treat analysis. At 12 weeks, the BMI z-score difference did not differ between the experimental (n=40) and the control (n=39) groups (mean difference, MD 0.002, 95% CI -0.11 to 0.1). There was also no significant difference between groups in the mean BMI z-score (MD 0.13, 95% CI 0.44 to 0.18) and body weight reduction (MD 0.65; 95%CI -0.61 to 1.92). Adverse effects such as abdominal pain, flatulence and diarrhea were more frequently reported in the oligofructose group compared to the placebo group; however, the difference between groups was not statistically significant (relative risk 1.75, 95%CI 0.75 to 4.07).

Conclusion: Oligofructose supplementation for 12 weeks had no effect on body weight in overweight and obese children.

Disclosure of Interest: None Declared
**Objectives & Study:** In 2010, the exclusive breastfeeding rates in Indonesia was only 15%. The reasons of mother ceased breastfeeding were lack of family support and unsure about adequacy of her breastmilk. To scaling up the rates, application of the WHO’s 10 steps to successful breastfeeding and measuring macronutrient and energy content of breastmilk using human milk analyzer were studied.

**Methods:** The cohort of 100 third semester pregnant women who agreed to participate in the study were recruited consecutively from 5 community health center in Central Jakarta. The 10 steps directly applied and the breastmilk macronutrient and energy content was analyzed using MIRIS human milk analyzer. Three ml of breastmilk was expressed every 5 minutes (represented fore-transitional-hind milk) and collected at 2 weeks, 1,2,3,4,5, until 6 months old. The growth was monitored every month and documented in WHO 2006 Growth Chart by midwives and GPs.

**Results:** All infants experienced early breastfed initiation. At 4 months, 93 infants still breastfed but only 84% were exclusively. This rates was persisted until 6 months old. The level of fat tend to increased, carbohydrates tend to decreased and protein level relatively stable from foremilk to hind milk. The mean of energy content from 2 weeks to 6 months, range from 86.10 to 75.9 kcal/100 mL. Unfortunately, 57 from 84 of exclusive breastfed infants experienced weight faltering but 48 of them still in the normal range +1

**Conclusion:** The application of 10 steps to succesful breastfeeding and measuring breastmilk macronutrient and energy content could be used as strategy to scaling up exclusive breastmilk rates. The weight faltering infants should be addressed promptly since in the developed countries would decreased IQ by 4.2 (Corbett er al, 2004)

**References:** Corbett SS, Drewett RF. To what extent is failure to thrive in infancy associated with poorer cognitive development? A review and meta-analysis. J Child Psychol Psychiatry 2004;45:641–54

**Disclosure of Interest:** None Declared
Gastroenterology
GERD, Peptic Disease and Helicobacter Pylori
PD-G-0079

SIMULTANEOUS SYNCHRONISED REGISTRATION OF POLYSOMNOGRAPHY AND IMPEDANCE IN INFANTS
Johan Marchand 1, Yvan Vandenplas 1,*
1Paediatrics, UZ Brussel, Brussels, Belgium

Objectives & Study: Retrospective study analysing a time correlation between events recorded by oesophageal impedance and polysomnography in infants with a suggestive history for reflux-related respiratory events.

Methods: In 10 infants (3 boys, 7 girls) with a clinical history suggestive for GERD causing "Apparent Life Threatening Event (ALTE) - like" events, a 24-hour oesophageal pH-impedance recording and a polysomnography (respiration, heart rhythm, nasal flow, EEG, electromyography, electro-oculogram, oxygen saturation) were performed synchronised. During the polysomnographic recording (Medatec, Brussels, Belgium), the pH-impedance (MMS, Enschede, The Netherlands) data were also recorded as part of the polysomnography, allowing perfect synchronisation. Although polysomnography and impedance were synchronised, a time-frame of two minutes was allowed to consider events recorded by both techniques as "time related". Symptoms were as well recorded. Polysomnographic events that were considered relevant include: central-obstructive and mixed apnoea, desaturation, bradycardia, movement and arousal according to the "American Association of Sleep Medicine" criteria.

Results: A diagnosis of GERD according to pH-impedance criteria was made in 9/10 infants A total of 270 pH-impedance events and 45 symptoms were registered during polysomnography. In none of these (impedance events or symptoms) an obstructive apnoea within a 2-minutes time frame was observed. Ninety of the 270 impedance events and 11/45 symptoms were accompanied by arousals or movements, within the two minutes before and after the events. Only four of the impedance events could be correlated with a short central apnoea, although two of these apnoeas were accompanied by a significant desaturation. In one infant (with a diagnosis of GERD), there was a mixed apnoea prior to an impedance event (pH 1.4 up to Z4). No bradycardia was observed within the +/- 2 minute interval around impedance events.

Conclusion: We could not show a time-relation between cardio-respiratory and impedance events in a (small) group of 10 infants that were selected because of a suggestive clinical history. In individual infants, movement and/or arousal could be linked to impedance events. However, many young babies show moments of arousal and movement during normal sleep, suggesting that the time-relation may be by coincidence and not causal.

Acknowledgment. The authors thank Medatec and MMS Belgium for the technical support.

Disclosure of Interest: J. Marchand: None Declared, Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals
ACHALASIA IN CHILDREN 30 YEAR EXPERIENCE OF THE ROYAL CHILDRENS HOSPITAL, MELBOURNE

Anell Meyer 1,*, George Alex 1, Winita Hardikar 1, Donald Cameron 1, Anthony Catto-Smith 1, Di Simpson 1, Mark Oliver 1

1Gastroenterology and Clinical Nutrition, Royal Children's Hospital, Melbourne, Australia

Objectives & Study: The aim of this study was to characterise 43 paediatric patients diagnosed with achalasia and to examine the effect of early treatment strategies on the course of the disease.

Methods: A single centre cohort of patients over 30 years (1982 – 2013) was identified, and the patient data were collected by a retrospective examination of medical records. Outcomes after therapeutic interventions were evaluated.

Results: Forty three children were diagnosed with achalasia, with a male to female ratio of 1:1. Six patients (14%) had triple AAA syndrome (achalasia, alacrimia and adrenal insufficiency). The median age at presentation was 11 years (range 3 months to 17 years). The median duration of follow-up was 12 years (range 1-27 years). All patients were diagnosed based on an upper gastrointestinal contrast study with barium consistent with achalasia and an endoscopy. Forty patients had a manometry study done, two patients were too young to tolerate the procedure and in one patient the medical records were incomplete. The clinical symptoms of patients at diagnosis were regurgitation of poorly digested food (83%), dysphagia and weight loss (76%), vomiting (66%), nocturnal cough (56%); recurrent respiratory infections (39%), retrosternal chest pain (34%), choking (32%) and persistent nausea (2%). The mean duration of symptoms before diagnosis was 7 months (range 2-61 months). Surgical myotomy was the primary treatment modality in 16 patients (37%) and Botox injections to the lower oesophageal sphincter in 21 patients (49%). Three patients (7%) had pneumatic balloon dilatations, two patients (5%) opted for no treatment and one patient’s symptoms were successfully controlled for four years with a calcium channel blocker before myotomy. Of the 21 patients that initially received Botox injections, 16 (76%) subsequently underwent a surgical myotomy. In the total cohort 32 patients (74%) were treated with a surgical myotomy, 10 (31%) received an open approach and 22 (69%) a laparoscopic approach with no fundoplication. Intraoperative mucosal perforation rates were 9%, all three perforations occurred in the laparoscopic group. All three patients received Botox injections prior to myotomy, 7 (3, 9 and 13 Botox injections respectively). Eight patients (25%) had a failed response to the initial myotomy and required a repeat procedure, of these seven patients (88%) had prior Botox injections (range 1-8 injections).

Conclusion: Botox injections, pneumatic dilatation and surgical myotomy is successful immediate treatment modalities for achalasia. This study is limited by small numbers, but would suggest that there may be a higher risk of failure of myotomy and surgical complications if patients received Botox injections prior to a surgical myotomy.

Disclosure of Interest: None Declared
THE CLINICAL OVERLAP BETWEEN FUNCTIONAL GASTROINTESTINAL DISORDERS (FGIDS) ASSOCIATED WITH ABDOMINAL PAIN IN CHILDREN BASED ON ROME III CRITERIA

Anna Plocek 1,*, Ewa Toporowska-Kowalska 1

1Department of Paediatric Gastroenterology and Nutrition, University Hospital Nr 4 in Lodz, Łódź, Poland

Objectives & Study: Upper GI symptoms such as epigastric pain, burning, postprandial fullness, early satiety, heartburn and lower GI symptoms such as diarrhoea, constipation and lower abdominal pain often coexist. The aim of this study was to assess the prevalence of FGIDs in children with functional abdominal pain using the current Rome criteria and analyze the proportion of diagnoses that overlap.

Methods: Participants were 439 consecutive new pediatric patients (192 boys and 247 girls) aged 4-18 years (mean age was 11.95±3.89 years) referred to Pediatric Gastroenterology Department at Medical University of Lodz for evaluation of abdominal pain of at least 2 months’ duration. After exclusion of organic origin children suspected of functional chronic abdominal pain were categorized with the use of Rome III criteria of FGIDs associated with abdominal pain (H2a-H2d1) and Questionnaire on Pediatric Gastrointestinal Symptoms.

Results: Of the 272 children with functional etiology of abdominal pain, 238 (88%) met the criteria for at least 1 diagnosis of an FGID. 34 cases (12%) did not fulfill any diagnostic criteria. Of the 238 patients with specific diagnoses of FGIDs, 176 (74%) were given 1 diagnosis, 59 (25%) 2 and 3 (1%) 3. The most prevalent diagnoses were irritable bowel syndrome (n=104; 38%), abdominal migraine (n=51; 20%), functional abdominal pain (n=45; 17%) and functional dyspepsia (n=36; 13%). In children with 2 diagnoses of FGIDs the most common combinations were irritable bowel syndrome and aerophagia (n=15), irritable bowel syndrome and abdominal migraine (n=13) and abdominal migraine and cyclic vomiting syndrome (n=6).

Conclusion: 1. One fourth of children with FGIDs met the criteria for two or more diagnoses. 2. Irritable bowel syndrome was the most common diagnosis in children with functional abdominal pain and tended to overlap with aerophagia and abdominal migraine. 3. Overlap between functional gastrointestinal disorders may be attributed to common disease process what may determine the efficacy of therapeutic interventions.

Disclosure of Interest: None Declared
INFLAMMATORY BOWEL DISEASE IN ARMENIAN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

Gayane Gevorg Amaryan 1,*, Ruzan Juri Davtyan 2, Tamara Faddey Sarkisyan 3
1National Paediatric Centre for Familial Mediterranean Fever, Arabkir Medical Centre-Institute of Child and Adolescent Health, Yerevan, Armenia, 2National Paediatric Centre for FMF, Arabkir MC-ICAH, Yerevan, Armenia, 3Centre of Medical Genetics and Primary Health Care, Yerevan, Armenia

Objectives & Study: Familial Mediterranean Fever (FMF) is an ethnic disease for Armenian population. Frequency of carriers of MEFV mutations is 1:3, the prevalence of FMF is rather high (14-100:10000). FMF manifests mainly in childhood. Many of these cases have atypical course, which may complicate timely diagnosis. In Armenian children with FMF more often than expected, suppose to occur co-existed immune diseases: juvenile idiopathic arthritis, nonamyloid lesions of kidneys, inflammatory bowel disease (IBD). There are sufficient data on the possible link between pathogenesis of IBD and FMF. The possibility of the development of intestinal vasculities during FMF is considered. Objectives: to investigate the frequency of IBD in Armenian children with FMF.

Methods: We observed 2300 children with FMF (1408 boys and 892 girls, mean age 8.64±0.17). Diagnosis of FMF was based on Tel-Hashomer criteria and MEFV genetic analysis. The diagnosis of UC and CD was determined according to conventional endoscopic, radiologic and histologic criteria.

Results: IBD was diagnosed in 10 (0.4%) FMF patients (6 boys and 4 girls; aged from 0.6 to 16 years). Nine children were found with concomitant UC and one-with CD. The mean age of FMF manifestation was 3.5 years and the same indices for IBD onset made 7.5 years. FMF with moderate activity was diagnosed in 7 patients. High penetrance M694V mutation was determined in almost all patients (9). Severe M694V/M694V homozygous genotype had 3 FMF children with co-existed UC. They developed early and atypical onset of disease during the first year of life: the recurrent febrile abdominal colics and/or episodes of diarrhea and/or abacterial haemocolitis, and later on – myalgia, recurrent arthritis and polyserosites (peritonitis, pleurisis, pericarditis). They were resistant to conventional treatment of UC and had severe course of both diseases - UC and FMF. After determining FMF and initiation of high-dosage colchicine therapy the long-lasting remission of both diseases has been achieved and the immunosuppressive therapy was stopped. Other seven FMF children out of 10 with IBD were heterozygotes for one of MEFV mutation and most of them (4 children) had M694V mutation, others - each one for M680I, V726A, E148Q mutations.

Conclusion: MEFV mutation screening is recommended for Armenian pediatric patients with IBD, especially in case of early onset of UC, atypical courses of disease and resistancy to conventional treatment. Further study is needed to investigate the prevalence of MEFV mutations in Armenian children with UC, CD, as well as the influence of them on IBD course.

2. Gumicio D.L. et al. 2002; 845-853

Disclosure of Interest: None Declared
EXPLORING NEEDS DURING TRANSITION FROM ADOLESCENCE TO ADULTHOOD IN YOUNG ADULTS WITH INFLAMMATORY BOWEL DISEASE: A QUALITATIVE STUDY

Herbert Brill 1,, Romy Cho 1, Anne F Klassen 1, Natasha Wickert 1, Elena Tsangaris 1, John K Marshall 2

1Paediatrics, 2Medicine, McMaster University, Hamilton, Canada

Objectives & Study: The period of transition from adolescence to adulthood is a vulnerable period for individuals with IBD. Current transition strategies are based on expert opinion and limited studies on the anticipated needs of adolescents and families. The aim of this study was to identify the needs of young adults with IBD at transition by examining the views of young adults who transitioned in the past and to see if those needs differed from IBD patients diagnosed as young adults.

Methods: A qualitative interpretive description approach was utilized. Participants aged 18-30 years recruited from the McMaster University Medical Centre IBD clinic between July 2012 and May 2013. Semi-structured interviews were conducted using an interview guide with questions probing participants to discuss their needs. Interviews were audiotaped, transcribed verbatim and coded using a constant comparative method. QSR NVivo10 was used to manage the data. Sample size was established when no new additional themes were encountered.

Results: Twenty-one young adults were interviewed: 15 subjects diagnosed < 18 years of age and 6 subjects diagnosed as young adults. Among those diagnosed < 18, transition needs were identified in the key areas of psychosocial, informational, self-management, and daily living needs. Psychosocial needs were most commonly reported with subjects citing needs for support networks, removing social barriers, and coping with anger, depression, sadness, and anxiety. Subjects detailed how IBD led to intentional self-isolation from social settings. A paucity of information was reported on the impact of smoking, drugs, and alcohol use. Overcoming financial barriers and participation in decision-making were noted as the primary signs of achieving independence. Subjects diagnosed as adults more often sought peer support groups and experienced more difficulties with healthcare access, financial concerns, and social isolation. Participants with less severe disease sought more client-centered care and those with more severe disease were more likely to describe social isolation.

Conclusion: We report the first study in the transition literature of already transitioned individuals’ needs during the transition process. Individuals with IBD who have undergone transition focus most on psychosocial and financial needs rather than self-management of their chronic illness. This finding is likely generalizable to most adolescents and young adults with chronic life-long diseases. Psychosocial and financial readiness are not presently assessed in existing transition and self-management tools, and may need to incorporate these areas to more effectively measure the success of transition interventions.

BILE ACIDS IN CONGENITAL HEART DISEASE

Joerg Jahnel 1,*, Kerstin Pircher 1, Günter Fauler 2, Tatjana Stojakovic 2, Hubert Scharnagl 2, Wolfgang Erwa 2, Karl-Martin Hoffmann 1, Andrea Deutschmann 1, Gernot Grangl 1, Martin Koestenberger 1, Almuthe Christine Hauer 1

1Department of Paediatrics, Medical University Graz, Graz, Austria
2Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University Graz, Graz, Austria

Objectives & Study: Patients with congenital heart disease (CHD) may develop right ventricular load with chronic backflow of blood to the liver. We investigated whether in CHD chronic liver congestion leads to hepatic dysfunction and thus to disturbance in bile acid (BA) metabolism.

Methods: We investigated by liquid chromatography-tandem mass spectrometry (LC-MS/MS) serum total BA levels and BA profiles (5 forms of unconjugated BA, 5 of glycine- and 5 of taurine-conjugated BA) in 53 patients with CHD without known liver disease aged 0 to 53 years. Patients were grouped between "CHD with right ventricular load" (Tetralogy of Fallot [ToF], pulmonary atresia, pulmonary hypertension) and "CHD without right ventricular load" (aortic isthmus stenosis, aortic stenosis, atrial septal defect [ASD], small ventricular septal defect [VSD]). The results were correlated with clinical and laboratory data.

Results: Serum BA levels were abnormal in patients with ToF, ASD, and VSD, but not in patients with other forms of CHD. ToF patients (n=8) showed one half each elevated serum BA levels (SD: 6.9 ± 1.9 µmol/l; reference range 3.1 – 4.1 µmol/l), and diminished values (2.4 ± 0.4 µmol/l). Abnormal BA concentrations were found for glycine-conjugated cholic and chenodeoxycholic acids (CA and CDA; primary bile acids) but not for other species. Values for other "liver function test" results in the patients with hypercholaenaemia were in all patients normal. Six of 14 ASD patients had elevated BA values (10.7 ± 3.2 µmol/l; p>0.01); taurine-conjugated CA and CDA accounted for most of the increases. Four of 6 VSD patients also had elevated BA values (9.8 ± 4.1 µmol/l) accounted for by taurine conjugates of CA and CDA. No absolute or relative BA profile changes were seen in the other 8 ASD patients and 2 VSD patients.

Conclusion: Whilst some patients with CHD had altered serum BA levels, the shifts interestingly seemed independent of liver congestion. However, specific mechanisms for changes in serum BA in CHD patients are not clear at present and thus need further evaluation in future studies.

Disclosure of Interest: None Declared
**Hepatology**

PD-H-0085

**IMPACT OF DIET ON GUT MICROBIOTA AND LIVER PHENOTYPE IN CFTR KNOCKOUT MICE**

Dominique Debray 1,*, Loïc Brot 2, Haquima El Mourabit 1, Véronique Barbu 1, Dominique Rainteau 3, Harry Sokol 2, Chantal Housset 1

1UMR_S 938, UPMC & Inserm, France 2U1057/UMR 7203, UPMC & Inserm, France, 3U1057/UMR 7203, UPMC & Inserm, Paris Cedex 12, France

**Objectives & Study:** Liver disease is highly variable in patients with cystic fibrosis (CF). Likewise, liver phenotypes are diverse in CF mice. *Cftr*−/− mice in a C57BL/6J congenic background, fed a high fat liquid infant formula (Peptamen®) have been reported to develop focal biliary fibrosis. We previously showed that *Cftr*−/− mice in a C57BL/6J:129SvJ genetic background, fed a standard chow combined with polyethylene glycol (PEG), had no liver injury but impaired gallbladder emptying that disrupted bile acid enterohepatic circulation. This study was designed to assess the impact of diet on bile acid homeostasis and gut microbiota, which can promote liver injury in *Cftr*−/− mice.

**Methods:** Male *Cftr*−/− (*Cftr*tm1Unc) mice and their *Cftr*+/+ control littermates in a C57BL/6J congenic or C57BL/6J:129SvJ mixed background, were fed either Peptamen® or a standard diet combined with PEG. Investigations were performed at 3 months of age (n= 10-15 mice/group). Bile acids were analyzed by HPLC-MS/MS. Fecal microbiota composition was assessed by 16S rRNAqPCR.

**Results:** *Cftr*−/− mice were smaller than *Cftr*+/+ in all groups. A significant increase in liver/body weight ratio compared to *Cftr*+/+, and the presence of bile duct lesions, were restricted to Peptamen-fed *Cftr*−/− congenic mice. Liver steatosis was observed essentially in Peptamen-fed mice in the mixed background, irrespective of *Cftr* status. Gallbladder emptying was not impaired in *Cftr*−/− mice under Peptamen as opposed to PEG. Consistent with a higher flux of bile acids in the intestine, ileal expression of bile acid-regulated genes (SHP, IBABP, OSta/b, FGF15, ASBT) was less down-regulated in Peptamen-fed *Cftr*−/− mice, particularly in the congenic. The proportion of secondary bile acids in bile and in feces was generally higher in mice under Peptamen than PEG, but remained decreased in *Cftr*−/− mice vs controls. Compared to PEG-fed animals, Peptamen induced changes in gut microbiota, with a significant increase in the proportion of E.coli and decrease of Bifidobacterium. The increase in the proportion of E.coli under Peptamen diet was even significantly higher in *Cftr*−/− mice than in *Cftr*+/+ mice.

**Conclusion:** In *Cftr*−/− mice, Peptamen abrogates gallbladder emptying delay, and increases the intestinal flux of bile acids and the proportion of E.coli in gut microbiota. These results suggest that in addition to genetic factors, diet has a critical impact, mainly via dysbiosis, on the emergence of CF-related bile duct injury.

**Acknowledgment:** We thank Peter Durie for kindly providing us with CF congenic mice.

**Disclosure of Interest:** None Declared
LIVER STIFFNESS MEASUREMENT AND CONTROLLED ATTENUATION PARAMETER FOR ASSESSMENT OF FIBROSIS AND STEATOSIS IN CHILDREN WITH NAFLD

Wojciech Janczyk 1,*, Elzbieta Jurkiewicz 2, Aldona Wierzbicka-Rucinska 3, Anna Swiader-Lesniak 4, Jakub Kmiotek 1, Piotr Socha 1

1Gastroenterology, Hepatology and Eating Disorders, Children's Health Memorial Institute, Warsaw, Poland
2Radiology, Children's Health Memorial Institute, Warsaw, Poland
3Biochemistry and Experimental Medicine, Children's Health Memorial Institute, Warsaw, Poland
4Paediatrics, Unit of Anthropometry, Children's Health Memorial Institute, Warsaw, Poland

Objectives & Study: Liver stiffness measurement (LSM) by FibroScan® (FS) has been shown to be a valuable method in detection of liver fibrosis in adults with chronic liver diseases as HBV, HCV and non-alcoholic fatty liver disease (NAFLD). The Controlled Attenuation Parameter (CAP) available on FS allows simultaneous assessment of the degree of liver steatosis. This method seems promising especially for children with liver diseases in whom indications to perform liver biopsy are limited. We aimed at evaluating LSM and CAP in children with NAFLD compared to healthy controls and their relationship with parameters describing the degree of obesity, liver function and lipid metabolism.

Methods: We investigated 38 overweight/obese children aged 14y (11.4-15.8) [median (Q1-Q3)] with NAFLD diagnosed by presence of liver steatosis at US examination and increased ALT activity and 18 healthy controls aged 12y (6.7-15.2). NAFLD patients underwent detailed investigation including risk factors associated with metabolic syndrome. In children with NAFLD we performed MRI of the lumbar region to assess subcutaneous (SAT) and visceral adipose tissue (VAT). VAT area and SAT area at the L2-L3 and L4-L5 interspaces and total VAT and SAT volumes were determined by manual examination using image analysis software. Correlations were tested by Spearman rank test.

Results: NAFLD patients had significantly increased LSM compared to controls [5.35 (4.70-6.4) vs. 4.2 (3.6-4.4) kPa] and there was marked difference in CAP [264.5 (243-304) vs 187 (112-217) dB/m]; p<0.05. LSM correlated with all fat tissue compartments measured by MRI and HDL cholesterol (r=(-0.4)). CAP significantly correlated with waist circumference (r=0.51), extraperitoneal visceral adipose tissue (r=0.37), subcutaneous subfascial fat tissue (r=0.38) and serum levels of ALT (r=0.57), AST (r=0.42) and GGTP (r=0.5).

Conclusion: 1. LSM and CAP using Fibroscan® are easily applicable to children with NAFLD. 2. Liver stiffness and steatosis using LSM and CAP are significantly higher in NAFLD patients when compared to healthy controls. 3. Liver fat content measured by CAP correlates significantly with liver function tests and adipose visceral tissue in the extraperitoneal compartment as well as subcutaneous adipose tissue. LSM is correlated to fat tissue in all compartments but does not correlate with liver function tests.

Disclosure of Interest: None Declared
PORTAL HYPERTENSION IN CHILDREN; REVIEW OF MANAGEMENT IN THE ERA OF NON-INVASIVE PREDICTION MARKERS

Tassos Grammatikopoulos 1,*, Peter Witters 1, Dominic Hughes 1, Palaniswamy Karthikeyan 1,
Somashekar Ramakrishna 1, Mark Davenport 1, Anil Dhawan 1
1Paediatric Liver, Gl & Nutrition Centre, King's College Hospital NHS Foundation Trust, London, United Kingdom

Objectives & Study: The evidence in prediction and management of gastroesophageal(GE) varices and portal hypertension(PHT) in children remains limited. We present here the prognostic management and evolution of our PHT program

Methods: All patients presenting in our centre with suspected PHT or gastrointestinal(GI) bleeding and undergoing a first oesophagogastroduodenoscopy(OGD) between 2005-2012 were included. Clinical, biochemical and radiological data were collected and analysed.

Results: 170 patients(91M), mean age 8.8+/-5.3y, were included. 126 were diagnosed with liver disease-group A[biiliary atresia(62) AIH, CF, CHF,other] and 44(PVT)-group B. 46 patients presented with bleeding and were enrolled in an endoscopy program. In group A, 17 patients underwent liver transplantation(LT), 2 died during follow-up(sepsis) and 1(group B) had a meso-Rex shunt. In group A at first OGD there were no oesophageal varices, grade 1, 2 or 3 in 39(31%), 15(12%), 23(18%) and 49(39%) with gastric varices present in 1, 2, 4, and 20, respectively. Mean values for haemoglobin(Hb), platelet count(PLT), white cell count(WCC), INR, serum albumin, bilirubin, aspartate aminotransferase(AST), spleen size in cm and z-score, Clinical Prediction Rule(CPR), AST/platelet ratio index(APRI) were 11g/dL, 131x10^9/l, 6.2x10^9/l, 1.19, 38g/L, 44mmol/L,114 IU/L,16cm, 8.35, 103.76, 2.56, respectively. In group B there were no oesophageal varices, grade 1, 2 or 3 in 9(20%), 9(20%), 5(11%) and 21(48%) with gastric varices in 4, 2, 4, 7 and 11, respectively. Mean values for Hb, PLT, WCC, INR, serum albumin, bilirubin, AST, spleen size in cm and z-score, CPR, APRI were 10.8g/dL, 101x10^9/l, 4.3x10^9/l, 1.29, 41g/L, 15mmol/L, 55IU/L, 15.6, 7.35, 107.37, 1.54, respectively. In regards to likelihood of significant(grade ≥2) varices PLT, WCC, INR, serum bilirubin, albumin, spleen size, CPR, APRI were significant(p<0.05 for all) in group A and only Hb(p<0.05) in group B. For the presence of significant GE varices in group A and B, CPR delimited an AUROC of 0.722 and 0.662, respectively. In group A and B during secondary prophylaxis ≥2 upper GI bleeds occurred in 7 and 4 patients requiring ≥5 and ≥3 endoscopies, respectively. Overall there were 69 bleeding episodes(in 52 patients). Complications were seen in 3% of OGDs(pain/fever). Non-selective beta-blockers (NSBB) were used as adjunctive therapy in 21 group B patients. During 42mo median follow up progression of oesophageal varices was recorded in 25% and 39% in group A and B, respectively.

Conclusion: The prediction of severe GE varices from existing non-invasive markers remains challenging. 27% of our cohort presented with bleeding. PVT group showed faster variceal progression. During follow-up primary and secondary prophylaxis were successful in 95% and 74% of patients, respectively.

Disclosure of Interest: None Declared
Hepatology
PD-H-0088

PRESENTING FEATURES OF EXTRA-HEPATIC PORTAL VEIN OBSTRUCTION IN CHILDREN: A MULTICENTRE NATIONAL STUDY

Angelo Di Giorgio 1,*, Paola De Angelis 2, Mara Colusso 3, Pietro Vajro 4, Raffaele Iorio 5, Graziella Guariso 6, Silvia Riva 7, Giuseppe Maggiore 8, Giuseppe Indolfi 9, Maurizio Baldi 10, Lorenzo D’Antiga 1

and Italian Working Group on Paediatric Hepatology

1Paediatric Liver, GI and Transplantation, Hospital Papa Giovanni XXIII Bergamo, Bergamo, Italy, 2Paediatric Surgery and Endoscopy, Ospedale Pediatrico Bambino Gesù, Roma, Italy, 3Paediatric Surgery, Hospital Papa Giovanni XXIII Bergamo, Bergamo, Italy, 4Paediatric Department, University of Salerno, Salerno, Italy, 5Paediatric Liver, University Federico II, Napoli, Italy, 6Paediatric Department, University of Padova, Padova, 7Paediatric Transplantation, ISMETT, Palermo, Italy, 8Paediatric Department, University of Pisa, Pisa, Italy, 9Paediatric Liver, OSpedale Pediatrico Meyer, Firenze, Italy, 10Paediatric Department, Ospedale Infantile Regina Margherita, Torino, Italy

Objectives & Study: Non cirrhotic extrahepatic portal vein obstruction (EHPVO) is one of the main causes of portal hypertension in children. EHPVO is often underdiagnosed or misdiagnosed in the early subclinical phase and is commonly recognised after a bleeding episode that is a major cause of morbidity. We aimed to describe the presenting features of a large cohort of patients with EHPVO to determine the most common early signs of the disease and favour an early diagnosis and management in the future.

Methods: We prepared a questionnaire and sent it to the major Italian liver centres to collect data from the files of patients with EHPVO managed in the last 15 years. We collected demographic data, age and type of presentation, prevalence of premature birth, neonatal illness, associated anomalies, history of insertion of an umbilical venous catheter (UVC) after birth, blood count, liver function tests, presence of oesophageal varices and bleeding episodes at diagnosis.

Results: We collected data on 187 patients diagnosed with EHPVO in 9 centres; 46% were female, mean age at diagnosis was 4 years (SD 3.7), 102/172 (59%) were born preterm, 107/165 (65%) had a history of UVC insertion, 132/161 (82%) had associated illnesses, and namely complications of prematurity in 70 (43.5%), cardiac malformations in 12 (7.5%), non-cardiac malformations in 14 (8.5%), deep infections in 11 (7%), haematological disorders in 9 (5.5%), miscellaneous in 16 (10%). Mean white cell count at presentation was 6074/mm3 (SD 3342), mean haemoglobin 10.4 g/dl (SD 2.4), mean platelet count 141978/mm3 (SD 103583), mean INR 1.17 (SD 0.16). Patients were recruited after the following type of presentation, available in 172 patients: detection of splenomegaly in 68 (39.5%), bleeding in 63 (36.6%), hypersplenism in 9 (5.2%), by chance in the context of other investigations in 28/172 (16.3%). Of 71 patients with an available endoscopy at presentation 62 (87.3%) had already developed oesophageal varices.

Conclusion: In this large cohort of children with EHPVO it was shown that the condition is strictly associated with a neonatal disorder. History of prematurity, neonatal illness and UVC insertion should lead to rule out EHPVO. A liver doppler ultrasound performed before discharge from the neonatal unit may allow an early recognition of the disease, and avoid bleeding from oesophageal varices that are present from the early stages.

Disclosure of Interest: None Declared
GALLBLADDER ABNORMALITIES IN PAEDIATRIC AUTOIMMUNE SCLerosing Cholangitis (ASC)

Silvia Ghione 1,*, Gloria Rossi 1, Giuseppe Maggiore 1

1Department of Clinical and Experimental Medicine University of Pisa, University Hospital Santa Chiara, Pisa, Italy

Objectives & Study: To describe the gallbladder abnormalities observed on abdominal ultrasound, in a group of 31 paediatric patients affected by ASC.

Methods: Retrospective analysis of medical records of 31 paediatric patients affected by ASC (all diagnosed by cholangiography and liver biopsy) admitted to our centre from February 1998 to July 2013. During follow-up all patients performed annually abdominal ultrasound with gallbladder’s description (normal, stretched, highly stretched, hydroptic, dysmorphic, thickened/hyperechoic wall, presence of stones or masses), liver elastography, as well as regularly blood check controlling inflammatory activity (erythrocyte sedimentation rate ESR, fecal calprotectin test, bile acid concentration). Considering that abdomen ultrasound was done under fasting conditions, “normal” and “distended” gallbladder, were both considered as normal features. Statistical analysis used t-test for parametric and X² for non-parametric parameters were used.

Results: In 21 patients (77%) were found at least one gallbladder anomaly: 5 (16%) a thickened/hyperechoic wall, 4 (13%) hydrops, 4 (13%) gallstones, 3 (10%) showed a highly stretched gallbladder, 2 (6%) had a dysmorphic gallbladder and in 1 (3%) a small polyp (one patients could have more than one characteristic). The majority of the patients had ASC-related-IBD (81%). Age of diagnosis of ASC was 9.4 ± 4.8 y and the abdominal ultrasound revealing some anomalies on gallbladder was performed at mean age of 14.6 ± 6.5 yr. Comparing patients with normal gallbladder finding (19/31) and patients with anomalies (12/31) we found no differences in disease history (time between ultrasound performance and diagnosis of PSC and/or IBD) (5.7 ± 4.1 yr vs 4.5 ± 5.3 yr for ASC, p=ns and 6.22 ± 5.1 yr and 6.4 ± 7.7 yr for IBD p=ns), no differences in BMI values (0.2 ± 0.85 DS vs -0.7 ± 0.88), no difference in the liver stiffness >10 kPa (55% vs 28%, p=ns) and no particular distribution of anomalies was seen through the different diagnosis (although no patients with overlap disease showed gallbladder anomaly). Regarding inflammatory activity, patients with gallbladder anomalies showed more frequently higher level of ESR (> 25 mm/h, 26% vs 77%, p<0.05) and of fecal calprotectin (> 150 µg/g, 15% vs 70%, p<0.05), while bile acid concentration was not significantly different among the two groups (> 20 mmol/l, 62% vs 60%, p=ns).

Conclusion: Gallbladder anomalies as in adults, are a frequent finding in children with ASC and they are associated with a more active inflammatory disease. The ultrasound evidence of gallbladder abnormality during a diagnostic work-up of a chronic liver disorder should suggest the diagnosis of ASC.

Disclosure of Interest: None Declared
REFINING INDICATIONS FOR INTESTINAL RETRANSPANTATION

Francisco Hernandez 1, Ane Andres 1, Gloria Chocarro 1, Jose Encinas 1, Carlos De la Torre 1, Manuel Gamez 1, Francisco Javier Murcia 1, Nuria Leal 1, Leopoldo Martinez 1, Esther Ramos 1, Jesus Sarria 1, Eva Martinez-ojinaga 1, Manuel Molina 1, Gerardo Prieto 1, Manuel Lopez-Santamaria 1

1Paediatric Surgery, La Paz University Hospital, Madrid, 28047, Spain

Objectives & Study: Intestinal retransplantation is becoming more frequent as the number of long-term survivors of intestinal transplantation increases. We present our experience in intestinal retransplantation with special interest in the type of graft.

Methods: Patients who underwent intestinal retransplantation in our institution were included in the study. The impact of the type of primary and subsequent grafts were analyzed Long-term results were compared to the rest of the series.

Results: A total of 71 patients underwent intestinal transplantation from 1997 to 2012, among them 12 (16%) required retransplantation (2 received 3 grafts). The grafts were lost at a mean of 153 days (range 5 to 769 days). Two out of the 12 children have died (2 are on TPN) All but one of the primary grafts lost were intestine only grafts. Regarding outcome by type of graft: 6 patients with SBTx-SBTx lost their grafts, one CLSB-CLSB were also lost; and surprisingly, 5 out of the 7 cases of SBTx-MVTx, the so-called graft upgrading strategy, are alive with functioning grafts. Patients who received a MVTx as the second or third graft showed long-term outcome comparable to our main series of intestinal transplantation (5 year survival, 71 vs 58%) and this results are even better when the cause of retransplantation was rejection (acute, exfoliative or chronic). Median follow-up was 1118 (10 – 3380) days.

Conclusion: Retransplantation with multivisceral grafts showed excellent long term results, specially when the cause of previous graft failure was rejection; on the other hand, all patients who received isolated SBTx as the second graft suffered graft lost.

Disclosure of Interest: None Declared
SIGNIFICANCE OF FRUCTOSE MALABSORPTION IN CHILDREN WITH RECURRENT ABDOMINAL PAIN

David Gil Ortega 1,*, Marcos Antonio Gimenez Abadia 1, Maria Navalón Rubio 1, Inmaculada Vives Piñera 1

1Unidad de Gastroenterología, Hepatología y Nutricion Pediatría., Hospital Universitario Virgen de la Arrixaca, El Palmar (Murcia), Spain

Objectives & Study: To investigate the significance of fructose malabsorption in children with recurrent abdominal pain (RAT), through analyzing the clinical response of these patients to elimination diet and empiric treatment with metronidazol

Methods: According to our clinical protocol, from January 2005 to December 2012 in all children (0-14 years old) with RAT and hydrogen breath test after a fructose overload (H2FT) positive (n=125) we performed a 1 month elimination diet (without fructose). After that, an empiric treatment with 30 mg per kg and day during 10 days was proposed to all patients. After 30 more days an open provocation with fructose was performed. Response to both interventions was measured by a simple clinical score, including subjective perception about pain, flatulence and abdominal discomfort.

Results: After 1 month on elimination diet, 41.9% of patients referred a complete remission of symptoms (responders DR) and an additional 31.4% referred an incomplete improve (partially responders, DPR), while 27.4% did not response (non-responders, DNR). Treatment with metronidazol was applied to 65% of DR, 76.5% of DPR and 84% of DNR. After metronidazol, 20% of DR, 37.4% of DPR and a 100% of DNR normalized diet without clinical worsen. In patients who didn’t received metronidazol, 25% in DR and 14.3% of NR normalized diet without clinical worsen. After metronidazol, only 61 patient (48.8%) patients showed needing low-fructose diet to mantain clinical improvement.

Conclusion: Although fructose intolerance could not be established as cause of RAT, in clinical practice elimination with repeated challenges should be considered in those children with H2FT positive. Metronidazol empiric challenge may be useful to select children needing longer elimination diet.

Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

**PD-G-0092**

**INCIDENCE AND NATURAL HISTORY OF PAEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASE UNCLASSIFIED IN SCOTLAND**

Fiona L Cameron 1,*, Paul Henderson 2, Richard K Russell 3, David C Wilson 1, 2

1Child Life and Health, University of Edinburgh, Edinburgh, United Kingdom, 2Paediatric Gastroenterology, Royal Hospital for Sick Children, Edinburgh, United Kingdom, 3Paediatric Gastroenterology, Yorkhill Hospital, Glasgow, United Kingdom

**Objectives & Study:** Inflammatory Bowel Disease Unclassified (IBDU) accounts for approximately 10% of paediatric IBD (PIBD) and remains a common IBD subtype at diagnosis in PIBD. The natural history of IBDU includes potential evolution to Crohn’s disease (CD) or ulcerative colitis (UC) over time. Few epidemiologically robust studies of IBDU exist. We aimed to describe the incidence and the natural history of paediatric IBDU in a population-based cohort.

**Methods:** The incidence of IBDU was collected over a 10-year period (01/03-12/12) using mainly prospective data collection from the two largest Scottish paediatric gastroenterology networks, which provide care for 681,176 children <16 years (74.4% of age-relevant Scottish population). Demographics and details of diagnostic investigation and follow up data were obtained until study end (31.10.13; unless prior transition or emigration) to ascertain reclassification of IBD subtype, clinical progress and outcome at last follow up. Incidence rates and trends were calculated using publicly available population data and statistics generated using Poisson regression.

**Results:** 65 patients were initially classified as IBDU (57% male) at diagnosis with a median of 11.3yrs (range 2.6-16.9), only 5 were diagnosed under 5 years of age. The age adjusted incidence of IBDU was 0.65/100,000/yr (95%CI 0.42-0.97) in the 5-year epoch 2003-2007 and 1.14/100,000/yr (95%CI 0.81-1.56) for 2008-2012, a non-significant increase (p=0.068).

All patients had colonoscopy (74% ileal intubation), 62 (95%) had an upper GI endoscopy, the remaining 3 had small bowel imaging. 61 (94%) had radiological imaging, 44 had a barium meal and follow through with 15 (23%) having MR enterography. At diagnosis, 53 (82%) had a pancolitis, 4 (6%) had disease distal to the hepatic flexure, 5 (8%) had disease distal to the splenic flexure and 3 (4%) had proctitis. 37/65 (57%) had mild disease (defined as mild infrequent relapses) while 7/65 (11%) had severe chronically active disease with 5/65 (8%) requiring Infliximab. At a median follow up of 3.1yrs (range 0.4-6.8), 16 (25%) had their diagnosis changed (all after endoscopic re-evaluation) after a median of 1.6yrs (range 0.6-5.7), to CD in 11 and UC in 5. 10 (15%) remained IBDU despite endoscopic re-evaluation after disease relapse; 3 (4%) had colectomy and end ileostomy.

**Conclusion:** Incidence of IBDU showed a non-significant trend to rise during the 10 year study period. 25% of patients diagnosed as IBDU had their diagnosis changed following endoscopic re-evaluation, greater than previously reported by systematic review (Prenzel and Uhlig 2009) after median follow up of 1.6years. The majority of our IBDU cases have inactive or mild disease activity and so do not undergo endoscopic/radiological reassessment; a minority remain as IBDU despite re-assessment.

**Disclosure of Interest:** None Declared
**Objectives & Study:** In specialist care, faecal calprotectin is an effective screening method for paediatric inflammatory bowel disease. Faecal calprotectin may also be an easy, non-invasive screening test to guide the general practitioner as to which child needs further evaluation for suspected inflammatory bowel disease. No study has evaluated levels of faecal calprotectin in children with gastrointestinal symptoms in primary care. The objectives of this study were to evaluate faecal calprotectin levels in children presenting with abdominal pain in general practice and to investigate factors associated with test result.

**Methods:** We performed a prospective 1-year follow-up study among children aged 4-17 years presenting with abdominal pain in general practice. At inclusion and 12 months follow-up faecal calprotectin levels were measured as well as presence of parasites, bacterial infection and protozoa, and children and/or parents completed questionnaires regarding gastrointestinal symptoms. The electronic medical file of the general practitioner was reviewed to record the diagnosis.

**Results:** Of 238 children (98 boys (41.2%), median age 7.9 years) faecal calprotectin levels were measured at baseline. Twenty-eight children presented with diarrhoea. Median level at baseline was 28.0 μg/gram faeces and 62/238 (26.1%) had a faecal calprotectin level > 50 μg/g. With a cut-off value of 100 μg/g, 25 children (10.5%) had a positive test result. None of the red flag symptoms (gastrointestinal blood loss, vomiting, chronic diarrhoea, unexplained fever, and a positive family history for IBD) were associated with test results. In children with *Blastocystis hominis* a lower rate of positive tests was observed (16.3%). Of 177 children evaluated at 12 months, 28 children had calprotectin levels >50 μg/g (15.8%), of which 10 had levels >100 μg/g (5.6%). Of the 41/177 children who had a concentration > 50 μg/gram faeces at baseline, at follow up, the concentration decreased to normal for 28 children. At follow-up, thirteen children (31.7%) still had a concentration >50μg/g, of which 3 children had levels above 100μg/g. No child was diagnosed with inflammatory bowel disease. Most children were diagnosed with functional abdominal pain (n=182), 23 children had functional constipation.

**Conclusion:** Faecal calprotectin is frequently elevated in children presenting with abdominal pain in general practice, while none was diagnosed with inflammatory bowel disease. We can conclude that calprotectin levels are often above levels associated with IBD. Referral to specialist care based on calprotectin levels only will result in an increase of referrals.

**Disclosure of Interest:** None Declared
INCREASED SERUM PROTEASOME CHYMOTRYSIN-LIKE ACTIVITY IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

Justyna Branska-Januszewska 1,*, Elzbieta Jarocka-Cyrta 2, Maciej Kaczmarski 3, Anna Samocik 3, Halina Ostrowska 1

1Department of Biology, Medical University of Bialystok, Bialystok, Poland, 2Department of Paediatrics, University of Warmia and Mazury, Olsztyn, Poland, 3Department of Paediatrics, Gastroenterology and Allergology, Medical University of Bialystok, Bialystok, Poland

Objectives & Study: The proteasomes are multi-catalytic protease complexes responsible for the degradation of majority of proteins in the cytoplasm and nucleus of mammalian cells. Pro-inflammatory cytokines induce the overproduction of proteasomes containing immunosubunits with enhanced chymotrypsin-like (ChT-L) activity. There is evidence that proteasome ChT-L activity is increased in the intestinal tissue of adult patients with inflammatory bowel disease (IBD), and involved in sustained cytokine production and inflammation, both in Crohn’s disease (CD) and ulcerative colitis (UC). The objective of this study was to evaluate proteasome ChT-L activity in the serum of children with IBD, and its correlation with clinical stages of disease and laboratory markers of inflammation.

Methods: The study included 87 consecutive children with IBD: 69 UC patients (49% girls; median age 12.0 years; range 1.50-17.83), 18 children with CD (44% girls; median age 14.33 years; range 10.25-17.5). Patients treated with glucocorticosteroids were excluded. A control group consisted of 24 children (58% girls, median age 12.65 years, range 2.42-17.83) diagnosed due to constipation or functional abdominal pain. Serum proteasome ChT-L activity was measured using the fluorogenic peptide substrate, Suc-Leu-Leu-Val-Tyr-AMC. IL-6 levels were measured by enzyme-linked immunosorbent assay kit. The diagnostic potential of the proteasome ChT-L activity was analyzed using the receiver operating characteristic curve (ROC).

Results: Serum proteasome ChT-L activity was significantly higher in patients with IBD in active stage of disease (n=36; median, 35.3 pmol/min/mL) and in remission (n=51; median, 33.4 pmol/min/mL) compared to control subjects (median, 22.3 pmol/min/mL; P<0.001 in both cases). No significant difference in serum ChT-L activity was observed between patients with active and inactive IBD (P=0.645). There was also no significant difference in serum ChT-L activity between CD and UC patients (P=0.698). Neither age, gender nor disease extension affected the proteasome ChT-L activity. The ChT-L activity did not correlate with IL-6 or CRP levels, and the counts of blood cells (P>0.05 for all parameters). This serum proteasome ChT-L activity displayed a strong ability to distinguish patients with active IBD from controls, with the area under the ROC curve of 88%, which was superior to IL-6 (84%) or CRP (85%) in IBD diagnosis in our study.

Conclusion: Serum proteasome ChT-L activity is enhanced in children with IBD compared with healthy controls, independently of disease type and disease activity, and therefore, it may be a new noninvasive marker in the diagnosis of IBD in children.

Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

PD-G-0095

**ROTA VIRUS IS NOT INVOLVED IN PATHOGENESIS OF COELIAC DISEASE**

Fabiana Ziberna 1, Sara Quaglia 1, Giuditta De Lorenzo 2, Francesca Arnoldi 3, Oscar R Burrone 2,

Tarcisio Not 1,*

1Reproductive, Development and Health Sciences, IRCCS Burlo Garofolo, Trieste, Italy, 2ICGEB,

3University of Trieste, Trieste, Italy

**Objectives & Study:** Celiac disease (CD) is an autoimmune enteropathy caused by both genetic (HLA DQ2/8) and environmental factors. The participation of infectious agents in the pathogenesis of the disease was often hypothesized. Recently, new data supported the involvement of Rotavirus (RV) in the onset of CD mediated by antibodies (Abs) against the dodecapeptide (260-271 aa) of the RV outer capsid protein VP7.

Aims of our study were:
- to confirm previous results in relation to anti-RV VP7 peptide sera reactivity in untreated CD patients;
- to evaluate serum Abs concentration against specific native RV antigens in both CD and control samples.

**Methods:** We measured IgA and IgG anti-RV Abs in 3 different groups: (A) 35 serum samples of biopsy-proven CD patients (21F, 14M; aged 2-23 ys; mean 7 ys); (B) 31 serum samples of healthy, age-matched individuals (11F, 20M; aged 2-18 ys; mean 8 ys), of which 8 positive for HLA DQ2/8 and (C) 44 serum samples of healthy adults (13F, 31M; aged 19-65 ys; mean 42 ys), of which half positive for HLA DQ2/8.

Antibodies were determined by ELISA using 3 different antigens: 1) the synthetic RV VP7-derived dodecapeptide VIQVGGSNVLDI 2) the purified RV triple layered particles (TLPs), containing the native VP7 protein, and 3) the purified double layered particles (DLPs) that lack VP7 but have the highly immunogenic VP6 protein. TLPs and DLPs were purified from total extracts of MA-104 cells infected with the simian RV strain SA11.

ELISA cut-off threshold values were calculated as the mean plus 1 standard deviation of the sera control group.

**Results:** We obtained positive results as indicated in the table below:

<table>
<thead>
<tr>
<th></th>
<th>VP7 peptide</th>
<th>TLPs</th>
<th>DLPs</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>IgA</td>
<td>IgG</td>
<td>IgA</td>
</tr>
<tr>
<td>Group A</td>
<td>0/35</td>
<td>0/35</td>
<td>4/35</td>
</tr>
<tr>
<td>Group B</td>
<td>0/31</td>
<td>0/31</td>
<td>4/31</td>
</tr>
<tr>
<td>Group C</td>
<td>3/44</td>
<td>0/44</td>
<td>6/44</td>
</tr>
</tbody>
</table>

(2 HLA+) (3 HLA+) (1 HLA+)

Conclusion: Our results show that the anti-RV immune response is not restricted to CD population. In particular the synthetic RV VP7 peptide was recognized only by healthy adults sera which in turn didn’t show reactivity against the native RV TLPs antigen. This observation may be a consequence of an aspecific immune reaction against the synthetic RV VP7 peptide. Moreover we didn’t observe any significant difference about the humoral immune response against the native RV antigens among the study groups and no relationship between genetic gluten predisposition and RV immune response emerged in our study.

Our future working plan considers to search the RV viral RNA in the intestinal biopsies of RV virus-like particles positive patients by RT-PCR.

**Disclosure of Interest:** None Declared
COELIAC DISEASE DIAGNOSED BY SCREENING BECAUSE OF TYPE1 DIABETES BENEFIT FROM THE EARLY DIAGNOSIS AND HAVE A GOOD ADHERENCE TO GLUTEN FREE DIET

Alina Popp 1, 2, 3*, Katri Kaukinen 4, 5, 6, Laura Kivelä 7, Markku Maki 3, Kalle Kurppa 3
1Paediatrics, University of Medicine and Pharmacy "Carol Davila" Bucharest, Bucharest, Romania,
2Institute for Mother and Child Care, Bucharest, Romania, 3Tampere Center for Child Health Research, University of Tampere and Tampere University Hospital, Tampere, Finland,
4Gastroenterology and Alimentary Tract Surgery, Tampere University Hospital, Tampere, Finland,
5School of Medicine, University of Tampere, Tampere, Finland, 6Medicine, Seinajoki Central Hospital, Seinajoki, Finland, 7Tampere Center for Child Health Research, University of Tampere, Tampere, Finland

Objectives & Study: Current ESPGHAN guidelines advocate screening of celiac disease (CD) in children with type 1 diabetes. However, this issue is still controversial as it has been emphasized that many of these children are asymptomatic and subsequently adherence to the gluten-free diet (GFD) could be poor. It is also unclear whether such screen-detected patients have less severe histological and serological presentation at diagnosis than those with typical symptoms. We investigated the baseline characteristics and adherence to the GFD in CD children diagnosed by screening because of type 1 diabetes and compared the results with those detected by clinical suspicion.

Methods: Data were collected from 25 children with a biopsy-proven CD detected during regular type 1 diabetes surveillance (Group 1) and from 266 children diagnosed for CD in routine clinical practice (Group 2). Comparisons were made on demographic data, serology and laboratory parameters, small bowel mucosal histology and adherence to the GFD.

Results: Children in Group 1 were younger (median age 6, range 2-13 yr vs. median age 8, range 1-17 yr, p=0.035) and less symptomatic (40% vs. 86%, P <0.001) and had lower risk for growth disturbance (4% vs. 30%, p=0.005) compared with children in Group 2. In contrast, there was no significant difference between the two groups in terms of anemia and mean hemoglobin at the time of CD diagnosis, serum endomysial antibody titers, or degree of small-intestinal mucosal villous atrophy. Further, long-term (>1 yr) adherence to the GFD was excellent in both groups, as 83% of the children in Group 1 and 90% in Group 2 had adhered to a strict diet (p=0.264).

Conclusion: Despite being less symptomatic, children with CD detected due to type I diabetes surveillance did not differ from those diagnosed in routine practice in terms of serological, histological and laboratory markers of CD or in the adherence to the GFD. Furthermore, earlier diagnosis and treatment of CD in diabetic children reduced the risk of growth disturbance. Our findings further support routine screening for CD in all children with type 1 diabetes.

Disclosure of Interest: None Declared
**Objectives & Study:** Follow up of children with diagnosed Coeliac Disease (CD) on a strict gluten-free diet (GFD) involves monitoring for resolution of clinical features and normalization of serologic markers. Recent adult studies have shown that serologic markers do not necessarily correlate with dietary compliance or mucosal recovery, and recommendations for repeat intestinal biopsy after institution of a GFD have been made. The aims of this study were: 1. To determine whether anti-tissue transglutaminase IgA (tTG) and anti-deamidated gliadin peptide IgG (DGP) antibodies are sensitive and specific markers of mucosal recovery in children with CD on a GFD and 2. Whether a validated dietary questionnaire of compliance was able to identify patients with mucosal recovery.

**Methods:** 150 children with biopsy proven CD were prospectively re-evaluated with duodenal biopsies at ≥12 months on GFD, paired with repeat tTG and DGP serology. The biopsies were reviewed in a blinded fashion by 2 senior histopathologists and graded by Marsh criteria. A validated questionnaire of dietary compliance was also administered.

**Results:** Of 150 children recruited (males 65 (43%)), 27 (18%) had positive serology, and 123 (82%) had negative serology (normal or equivocal). There was strong inter-observer agreement between histopathologists. Of the 123 children with negative serology, none had Marsh type 3 enteropathy. Of the 27 patients with positive serology, only 6 had Marsh type 3 changes. Of those with positive serology and normal mucosa (17/27), none had both serologic markers positive. The sensitivity and specificity of serology as a marker of significant mucosal pathology was 75% and 85% respectively, with a positive predictive value of 22% but a negative predictive value of 98%. Of the 129 (86%) questionnaires completed, 88% reported good or excellent compliance with a GFD giving a negative predictive value of 97%.

**Conclusion:** The findings of this study suggest that using both tTG and DGP in the follow up of children with CD on a GFD may obviate the need for repeat mucosal biopsy in the majority of children. A standardized compliance questionnaire is likely to be most useful in identifying patients with reported dietary transgressions who require further evaluation.

**Disclosure of Interest:** E. Bannister: None Declared, D. Cameron Shareholder of: Nexpep company, celiac vaccine development, J. Ng: None Declared, C. Chow: None Declared, A. Catto-Smith: None Declared, M. Oliver: None Declared, G. Alex: None Declared, R. Heine: None Declared, D. Simpson: None Declared, K. McGrath: None Declared, A. Webb: None Declared, W. Hardikar: None Declared
**Clinical course of hereditary pancreatitis in children**

Grzegorz Oracz 1,*, Jaroslaw Kierkus 1, Elwira Kołodziejczyk 1, Karolina Wejnarska 1, Jozef Ryzko 1

1 Dep. of Gastroenterology, Hepatology and Feeding Disorders, The Childrens Memorial Health Institute, Warsaw, Poland

**Objectives & Study:** Hereditary pancreatitis (HP) is a rare inherited condition. The reported pediatric experience with HP is small. We reviewed our experience over the last 20 years. The aim of our study was to evaluate the clinical course of HP in children.

**Methods:** 209 children with chronic pancreatitis, hospitalized since 1988 to 2012, were enrolled into the study. The medical records of these patients were reviewed for data on the presentation, diagnostic findings and endoscopic treatment. All children were screened for the PRSS1 gene mutations.

**Results:** Hereditary pancreatitis was diagnosed in 28 patients (13.4%) (20 girls and 8 boys). PRSS1 gene mutations were found in 24 patients. We detected R122H/- in 13, R122C/- in 5, N29I/- in 5 and E79K/- in 1 patient. Family history was positive in all children with HP except one. In 4 patients without mutations diagnosis of HP was made when the patients satisfied the requirements of the family history. In one patient we found SPINK1 mutation (N34S/-). In 2 children CFTR mutation (IVS8-5T(TG)11/-) was present. There was no difference in age of the disease onset between HP group and non-HP group (7.4 vs. 9.08 years; NS). In children with PRSS1 mutation ERCP had mean 2.5° Cambridge grade, vs. 1.6°, p<0.05. 19 patients with HP had calcifications in the imagine studies (68% vs. 31%, p<0.05). Therapeutic intervention, including both surgical and endoscopic intervention, was more frequent in the HP group (75% vs. 35%; p<0.05). Pancreatic duct stenting was done in 16 children with HP (58% vs. 26%; p<0.05). ESWL was performed more frequent in HP group (20% vs. 3%; p<0.05). Endocrine pancreatic insufficiency was observed in 7 patients (25% vs. 17.6%, NS).

**Conclusion:** Hereditary pancreatitis in children has worse clinical course than CP in children without PRSS1 mutations.

**Disclosure of Interest:** None Declared
**Objectives & Study:** The esophageal intraluminal baseline impedance (BI) measurements could be a valuable indicator of esophageal mucosa integrity. Aim: To compare the esophageal BI values in children with and without esophagitis.

**Methods:** Review of MII tracings performed between May 2008 and October 2013, in children 3 to 17 yrs of age, suspected of having gastroesophageal reflux (GER). All patients underwent upper endoscopy with multiple esophageal biopsies followed by a 24 hr MII-pH study. Esophageal histology was reported by two independent pathologists in a blinded manner. Mean BI was automatically calculated in the different MII channels (ch) by the specific software without removing any episode of increased/decreased BI. T-test was used and P<0.05 was considered as statistically significant. Biopsies were classified according to a histological score. Patients with eosinophilic esophagitis were excluded.

**Results:** Tracings of 84 children, 50 male, were evaluated. Mean age was 7.4 yrs: 42 had esophagitis. Mild esophagitis (ME) was observed in 31 and 11 had moderate to severe esophagitis (SE). In distal (ch3,6) BI was significantly (P<0.05) lower in patients with esophagitis compared with those with normal mucosa. Mean baseline in SE was significantly lower than ME most in distal channels (p<0.000).

<table>
<thead>
<tr>
<th>Channel</th>
<th>Esophagitis (Omhs) (X±SD)</th>
<th>Normal mucosa (Omhs) (X±SD)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Channel 1</td>
<td>2979 ± 412</td>
<td>2494 ± 919</td>
<td>0.222</td>
</tr>
<tr>
<td>Channel 2</td>
<td>1878 ± 346</td>
<td>2102 ± 704</td>
<td>0.458</td>
</tr>
<tr>
<td>Channel 3</td>
<td>2488 ± 801</td>
<td>2148 ± 539</td>
<td>0.025</td>
</tr>
<tr>
<td>Channel 4</td>
<td>3189 ± 1542</td>
<td>2555 ± 1120</td>
<td>0.034</td>
</tr>
<tr>
<td>Channel 5</td>
<td>2405 ± 722</td>
<td>1843 ± 794</td>
<td>0.001</td>
</tr>
<tr>
<td>Channel 6</td>
<td>2243 ± 893</td>
<td>1631 ± 710</td>
<td>0.000</td>
</tr>
</tbody>
</table>

**Conclusion:** The evaluation of the BI may be a good method to predict esophageal mucosa integrity. Although time consuming, BI can be useful method to spare endoscopy in high risk patients.

**References:**

**Disclosure of Interest:** None Declared
THE COMBINED MULTIPLE INTRALUMINAL IMPEDANCE PH MONITORING IN CONSECUTIVE PROSPECTIVELY EVALUATED CHILDREN WITH FEATURES OF GASTROESOPHAGEAL REFLUX DISEASE

Paolo Rossi 1,*
Saverio Mallardo 1
Giovanni Di Nardo 1
Giuseppe Pagliaro 1
Sara Isoldi 1
Giulia Biscione 1
Salvatore Oliva 1
Salvatore Cucchiara 1
1Paediatrics, Sapienza University of Rome, Rome, Italy

OBJECTIVES & STUDY: Diagnosis of gastroesophageal reflux (GER) disease (GERD) is usually performed by combined multiple intraluminal impedance pH monitoring (MII-pH). Although guidelines of Scientific Societies are published, there is a wide variability in the approach to GER patients and often antisecretory therapy is commenced on empirical basis. We wished to analyze the diagnostic usefulness of MII-pH in a large consecutive cohort of infants and children referred by pediatricians for suspected GERD.

METHODS: 428 patients (pts) were investigated as outpatients at the GI Motility Section of our Unit; three age-range based groups were identified: A (0-12 months); B (13-96 months); C (7-16 years). Features of GERD severe enough to interfere with quality of life and were distinguished in typical (regurgitation, irritability, chest pain, pyrosis, dysphagia, vomiting) and atypical (refusal of food, pneumonia, wheezing/asthma, ALTEs, ORL signs). pH-MII and data analysis were done according to ESPGHAN EURO-PIG protocol (JPGN 2012;55:230-4). The following variables were analyzed: reflux index, symptom index, number and type of liquid reflux, number of long lasting reflux episodes, correlation symptom-reflux. The test was diagnostic of GERD if at least ≥ 2 of the previous variables were positive.

RESULTS: Of 243 pts with typical features, the MII-pH was abnormal in 109 (44,8%) while normal in 134 (55,1%) (NS); of 185 with atypical features the MII was abnormal in 94 (50,8%), but normal in 91 (49,1%) (NS). Considering the different age groups, there was no statistically significant difference in the rate of patients with +ve and -ve MII-pH both in pts with typical signs (+ve: A: 25,6%, B: 30,2%, C: 44,2%, NS) and in those with atypical signs (+ve: A: 26,8%, B: 29,3%, C: 28,7%, NS). Therapy of GERD consisted on antisecretory drugs, food thickening, positioning and was given in all pts with abnormal MII-pH, while in those with normal test, additional diagnostic work-up for disorders other than GERD was done. Response to therapy was observed in 93 and in 88 of typical and atypical pts with abnormal MII-pH, respectively. The predictive positive value of the test for response to anti-reflux therapy was 85% and 93% in typical and atypical pts, respectively. In 88% and in 95% of typical and atypical pts, respectively, with normal MII-pH a diagnosis other than GERD was performed.

CONCLUSION: The MII-pH tool is of great value in children referred for suspected GERD, both in those presenting with typical and atypical features. We suggest that MII-pH should be performed even in pts with features thought to be typical of GERD, in all the pediatric age ranges, thus avoiding an inappropriate antisecretory therapy done on empirical basis. A positive MII-pH is also predictive of a response to medical anti-GERD therapy.

DISCLOSURE OF INTEREST: None Declared
EFFECT OF MAGNESIUM ALGINATE ON GASTROESOPHAGEAL REFLUX IN INFANTS

Dario Ummarino 1,*, Elisa Sciorio 1, Felice Crocetto 1, Erasmo Miele 1, Luigi Greco 1, Annamaria Staiano 1

1Paediatric, University of Naples Federico II, Naples, Italy

Objectives & Study: Gastroesophageal reflux (GER) is a frequent benign condition of the first year of life, which can be treated with lifestyle changes and reassurance. However, some infants show distressing symptoms, which may require treatment in order to improve their quality of life. The aim of our study was to evaluate the efficacy of Mg-alginate, compared to rice starch thickened formula or to reassurance, in the treatment of GER in infants.

Methods: This prospective, comparative, randomized, controlled trial was conducted in patients younger than 1 year, affected by symptoms suggestive of GER. All patients underwent a validated questionnaire for assessment of clinical score (I-GERQ). Patients who obtained a symptom score > 7 were considered affected by GER. The patients were randomized in 3 groups according to treatment (Group A: Mg-alginate; Group B: thickened formula feeding; Group C: reassurance) and they were treated for 2 months. A clinical evaluation and score of symptoms was performed after one month (T1) and at the end (T2) of treatment.

Results: Sixty-four (85.3%) out of 75 enrolled infants (mean age±SD: 5.28±2.00 months), concluded the study. At the enrollment, the symptom scores and the demographic data in the three groups were not statistically different (P=0.14). After one month of treatment (T1), magnesium alginate showed a statistically significant improvement compared with the other two groups (OR_{Mg-Al VS TF}: 4.84; p= 0.019). This result was evident for all the GER symptoms studied, mostly on quantity and on frequency of reflux (p= 0.00). At the first control 12/25 patients (48%) treated with Mg-Alginate and 4/25 patients treated with thickened formula (16%) were healed (p 0.001), while no patient in reassurance-group was healed. At the end of the study, both patients treated with Mg-alginate and those treated with thickened formula showed a significant reduction of the symptom score (OR_{Mg-Al VS TF}: 2.66; p = 0.16). Patients randomized in group C did not show an improvement of the symptom score during the study compared with the other groups (OR_{Mg-Al VS R}: 37.5; p 0.0001; OR_{TF VS R}: 14.06; p 0.002). In particular, at the end of the study 20/24 patients (83.3%) treated with Mg-alginate and 15/23 patients treated with thickened formula (65.2%) were healed. While, in group C only 2 patients (11.7%) out of 17 showed a negative symptom score.

Conclusion: Mg-alginate seems to have an important effect on all the GER symptoms. Indeed, Mg-alginate showed an effect meaningfully higher on symptom score compared to that showed by thickened formula after one month of treatment, but not at the end of the study. Reassurance did not have any effect on symptom score.

Disclosure of Interest: None Declared
A RANDOMISED CONTROLLED TRIAL OF LACTOBACILLUS REUTERI DSM 17938 IN FUNCTIONAL ABDOMINAL PAIN OF CHILDHOOD

Zvi Weizman 1,*, Viki Blumin 1, Jaber Abu-Abed 1, Mauricio Binsztok 1

1Paediatric Gastroenterology, Soroka University Medical Center, Beer-Sheva, Israel

Objectives & Study: Abdominal-pain related functional gastrointestinal disorders are very common in childhood and are associated with significant anxiety, unnecessary testing and a major economic burden. Nevertheless, there is no documented specific treatment. Our aim was to determine the efficacy of Lactobacillus reuteri DSM 17938 in the treatment of functional abdominal pain of childhood.

Methods: A total of 101 children, aged 6-15 years, who fulfilled the Rome III criteria for functional abdominal pain were enrolled in a double-blind, randomized controlled trial, and were randomly assigned to receive either Lactobacillus reuteri DSM 17938 or placebo for 4 weeks, with further follow-up of additional 4 weeks. Response to therapy was based on a self-reported daily questionnaire monitoring frequency and severity of abdominal pain, using the 10 faces scoring system by Hicks.

Results: Lactobacillus reuteri (n=47) was significantly superior to placebo (n=46) in relieving frequency (1.9±0.8 vs. 3.6±1.7 mean episodes/week, P<0.02) and severity (4.3±2.2 vs. 7.2±3.1 mean score/week, P<0.01) of abdominal pain. There was no difference in other gastrointestinal symptoms, except for a lower incidence of perceived abdominal distention and bloating, favoring Lactobacillus reuteri (P=0.03).

Conclusion: Lactobacillus reuteri, compared to placebo, significantly reduces the frequency and severity of functional abdominal pain in children.

Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

SP-G-0103

**VIRAL INFECTIONS PROMOTE LOSS OF ORAL TOLERANCE THROUGH TYPE-1 INTERFERON INDUCTION IN COELIAC DISEASE**

Valentina Discepolo 1, Romain Bouziat 2, Jennifer Stencel 3, Mine Ikizler 3, Merlin Nanayakkara 1, Giuliana Lania 1, Alessandra Carrella 1, Marialaura Cuomo 1, Katia Ferrara 1, Renata Auricchio 1, Riccardo Troncone 1, Maria Vittoria Barone 1, Terence Dermody 3, Luis Barreiro 4, Bana Jabri 2

1Department of Translational Medical Science, University Federico II, Napoli, Italy, 2Department of Medicine, University of Chicago, Chicago (IL), United States, 3Elizabeth B. Lamb Center for Paediatric Research, Vanderbilt University School of Medicine, Nashville (TN), United States, 4Department of Paediatric, University of Montreal, Montreal, Canada

**Objectives & Study:** Environmental factors, such as viral infections, contribute to elicit autoimmune (AI) disorders in genetically susceptible individuals. Interestingly, rotavirus (a dsRNA virus) infections have been associated to CD. Type-1 Interferon (IFN), a group of innate cytokines induced upon viral infections, are upregulated in some AI diseases. Interestingly chronic treatment with either IFN-α or IFN-β (both members of the type-1 IFN family) may elicit AI disorders, including CD. In this study we aimed to investigate whether viral infections (in particular reovirus, a dsRNA viruses) may contribute to CD induction through type-1 IFNs up-regulation.

**Methods:** To detect anti-reovirus antibodies, serum samples from at least 50 controls (CTR) and 50 CD patients were tested in a plaque-reduction neutralization assay, performed using a wild-type reovirus strain (T1L) and L929 cells. RNA from duodenal biopsies of 20 CTR and 20 CD patients was tested for IFN-α, IFN-β, Mx1 (IFN inducible gene) expression by qPCR. MxA protein expression was evaluated by immunohistochemistry (IHC) in duodenal paraffin-embedded sections.

**Results:** A higher number of CD patients showed elevated anti-reovirus serum titers compared to CTR (p=0.06), suggesting either a more recent infection or an increased frequency of infections overtime. A significant up-regulation of Mx-1, IFN-α and IFN-β was found in small intestinal biopsies of CD patients (p<0.01 vs CTR). Increased MxA protein levels (WB and IHC) were shown in the epithelium and in the lamina propria of CD patients. Interestingly, among CD patients, individuals showing the highest anti-viral serum titers were found to over-express MxA in the gut.

To test whether reovirus could promote the breakdown of oral tolerance in vivo, we administered orally either T1L or IFN-β to wild type mice, showing in both cases a loss of tolerance towards an oral antigen (compared to sham-fed mice). Furthermore T1L induced high levels of type-1 IFN in the intestinal lamina propria of infected mice.

**Conclusion:** This study describes for the first time an association between reoviral infections and CD, depending on type-1 IFN up-regulation in the gut. Our data suggest that viral infections, even without inducing immunopathology, may trigger a pro-inflammatory response in the small intestinal mucosa that ultimately leads to the breakdown of tolerance towards oral antigens. Moreover, identifying specific viruses related to CD may help designing future preventive strategies for at risk subjects.

**Disclosure of Interest:** None Declared
OBJECTIVES & STUDY: Although acute pancreatitis (AP) is usually self-limiting in children, a subset develops acute recurrent pancreatitis (ARP) or progresses to chronic pancreatitis (CP). The lives of these patients are altered by multiple hospital admissions, physical, emotional and social stress. The epidemiology, etiologies, pathogenesis, natural history and outcome of these disorders in childhood are not well-understood.

METHODS: We created a multi-center consortium, INSPPIRE (International Study group of Pediatric Pancreatitis: In search for a cure) to investigate the epidemiology, etiologies, pathogenesis, natural history and outcome of pediatric ARP and CP. Information was collected on Patient and Physician questionnaires and transferred into REDCap™ (Research Electronic Data Capture); entries were tabulated and analyzed.

RESULTS: From September 1, 2012 to August 31, 2013, we enrolled 194 patients with ARP or CP, <19 years of age, (55% F). Most were Caucasian (82%). Approximately 65% of patients reported episodic pain (20% mild-moderate, 45% severe) and ~35% constant pain (30% mild-moderate, 5% severe). Clinical evaluation led to a diagnosis of CP in 88 patients. Gene mutations were found in 98 of 138 tested (PRSS1 (52/131); CFTR (35/134, either allele), SPINK1 (27/117); CTRC (4/80)). Obstructive factors were found in 64 children; pancreas divisum was most common. Toxic/metabolic diagnoses were sporadic (10 medication-related, 5 hyperlipidemia, 3 kidney disease, 1 cigarette smoking, 7 other). Five children had autoimmune pancreatitis. A cause was not identified in 24 patients. Average number of attacks was 16.6 ± 9 per patient; average number of hospitalizations 6 ± 0.8 per patient. 112 children with ARP or CP missed an average of 5.7 ± 0.2 school-days per month.

CONCLUSION: We have successfully engaged in a unique collaborative effort to conduct studies in children with ARP and CP. Early data reveal that genetic and obstructive factors are the main causes of pediatric ARP and CP. ARP and CP significantly impact the lives of affected children. Our future goals are to define the natural history of these diseases in children, determine responses to therapy, and investigate the role of genetic modifiers on disease onset and outcome.

REFERENCES: Supported by NIH R21 DK096327, CTSA 2UL1 TR000442-06 and REDCap

Disclosure of Interest: None Declared
**Gastroenterology**

**Cystic Fibrosis and Pancreatic Disorders**

SP-G-0105

**ETIOLOGY OF CHRONIC PANCREATITIS IN PAEDIATRIC AGE: A STUDY OF 66 GENES BY NEXT GENERATION SEQUENCING**

Valentina Sofia ¹, Fabio Majo ², Letizia Dasacco ³, Cecilia Surace ⁴, Federico Alghisi ² ⁷, Anna Cristina Tomaiuolo ⁴, Vincenza Lucidi ², Adriano Angioni ⁴

¹Cytogenetics and Molecular Genetics Unit, ²Cystic Fibrosis Unit, Bambino Gesù Children's Hospital, Rome, Italy ³Cytogenetics and Molecular Genetics Unit, ⁴Cytogenetics and Molecular Genetics Unit, Bambino Gesù Children's Hospital, Rome, Italy

**Objectives & Study:** Chronic pancreatitis (CP) is usually investigated by the analysis of 8 genes (SPINK1, PRSS1, PRSS2, CTRC, CASR, CFTR, CTSB e KRT8). However in the majority of patients it is not possible to identify a causing mutation in such genes. Objective of our study is to investigate a large panel of genes involved in several pancreatic pathways.

**Methods:** We enrolled pediatric patients with CP diagnosed according to Mannheim criteria followed at the Cystic Fibrosis Unit of Bambino Gesù Children’s Hospital. Molecular analysis was performed using Next Generation Sequencing (NGS). The panel of searched mutation was customized to include 66 genes. Missense mutations found were analyzed with two bioinformatic softwares (PolyPhen-2 and Align – GVGD) that use multiple alignments with “conservate” gene sequences to evaluate the impact of the change in aminoacidic structure on protein functionality.

**Results:** We analyzed samples from 44 patients (39 had Idiopathic CP and 5 patients had cystic fibrosis) and 15 healthy controls. Median age of the patients was 9 years (3-17 years). One causing mutation was found in 21 patients. CFTR gene mutations were found in 10 patients (5 of them with cystic fibrosis), whereas 38 causing mutations were found studying the other genes.

**Conclusion:** NGS promises to be a new, economic efficient and cheap technique. The large panel analysis allowed to identify 9 patients that would have not been found with standard criteria. Those data need to be confirmed by further functional analysis and familial studies.

**Disclosure of Interest:** None Declared
**Nutrition**

**Nutrition and Metabolism, Mechanisms**

SP-N-0106

**VITAMIN E ADDED TO INTRALIPID AND ENRICHED IN OMEGAVEN PROTECTS AGAINST PNALD IN TPN-FED PRETERM PIGS**

Kenneth Ng 1, Barbara Stoll 2, Miguel Saenz de Pipaon 3, Oluyinka Olutoye 4, Douglas Burrin 2,*

1Section Paediatric Gastroenterology, Hepatology, and Nutrition, 2USDA Children's Nutrition Research Center, Baylor College of Medicine, Houston, TX, United States, 3Neonatology, La Paz University Hospital, Madrid, Spain, 4Paediatric Surgery, Baylor College of Medicine, Houston, TX, United States

**Objectives & Study:** Prolonged parenteral nutrition (PN) may lead to cholestasis and parenteral nutrition associated liver disease (PNALD). The etiology of PNALD is unknown, but plant phytosterols in soybean oil emulsions (e.g. Intralipid) have been suggested to negatively impact bile acid homeostasis (BAH) by antagonizing the bile acid sensing farnesoid X receptor (FXR). The fish oil emulsion Omegaven, abundant in vitamin E and docosahexaenoic acid (DHA) yet devoid of phytosterols, may positively impact the nuclear receptors pregnane X (PXR) and peroxisome proliferator-activated receptor-alpha (PPARα) receptors. We investigated the serum and hepatic tissue bile acid, serum biomarkers of liver injury, as well as target genes involved in BAH and fatty acid metabolism in TPN-fed preterm pigs given 4 different lipid emulsions.

**Methods:** Preterm pigs were assigned to receive 14 days of either, 1) TPN + Intralipid (100% soybean oil)(IL); 2) TPN + Intralipid + Vitamin E (ILE); 3) TPN + Omegaven (100% fish oil)(OV); or 4) TPN + Omegaven + Phytosterols (PS). The final vitamin E concentration in the ILE group equaled the concentration in Omegaven. The three principal phytosterols found in Intralipid (campesterol, β-sitosterol, & stigmasterol) were added to Omegaven in the PS group.

**Results:** Serum levels of direct bilirubin, ALT, GGT, triglyceride, LDL and hepatic triglyceride content were significantly lower (P<0.05) in the ILE, OV, and PS compared to IL pigs. CYP7A1 expression was lower (P<0.05) in the ILE, OV, and PS groups vs. IL. CYP3A29 and MRP2 expression were higher in ILE, OV, and PS groups vs. IL. OSTα (bile acid efflux transporter) expression was lower (P<0.05) in the ILE, OV, and PS groups vs. IL. BSEP (canalicular bile acid export) was slightly lower in the ILE, OV, and PS pigs vs. IL. CPT1A and CYP2E1 were higher in ILE, OV, and PS vs. IL pigs. Addition of phytosterols to Omegaven did not induce evidence of liver injury. The findings suggest that increased vitamin E and DHA are associated with up-regulated expression of PXR and PPARα downstream targets genes involved in bile acid and fatty acid metabolism and oxidation. These changes result in decreased bile acid synthesis and increased bile acid breakdown and canalicular bilirubin export; this triggered a compensatory down-regulation of the alternative bile acid export pathway (OSTα). Increased mitochondrial and microsomal fatty acid oxidation protects against hepatic triglyceride accumulation and steatosis.

**Conclusion:** Vitamin E and DHA enriched in fish-oil emulsions protects hepatocytes via activation of bile acid and fatty acid metabolism. The beneficial effects of vitamin E in ILE group occurred despite the presence of abundant phytosterols.

**Disclosure of Interest:** K. Ng Grant / Research Support for: ASPEN, B. Stoll: None Declared, M. Saenz de Pipaon: None Declared, O. Olutoye: None Declared, D. Burrin Grant / Research Support for: Fresenius Kabi
BOVINE LACTOFERRIN REDUCES INTESTINAL DAMAGE IN A RAT MODEL OF NECROTIZING ENTEROCOLITIS

Anja Wittke 1, Jennifer Arriola 2, Zeina Jouni 1, Bohuslav Dvorak 2, 3, *

1Mead Johnson Paediatric Nutrition Institute, Evansville, United States, 2Paediatrics, The University of Arizona, Tucson, United States, 3Paediatrics, NorthShore University HealthSystem, Evanston, United States

Objectives & Study: Necrotizing enterocolitis (NEC) is a major cause of morbidity and mortality in premature infants. Although effective treatments for NEC are still not available, clinical and experimental studies show that maternal milk reduces the incidence of NEC. Lactoferrin, a glycoprotein with established anti-inflammatory and anti-microbial properties, is plentifully presented in human milk, but absent in infant formulas. A clinical study suggested that oral administration of bovine lactoferrin (bLF) to preterm neonates protects against sepsis and partially reduces NEC. However, the mechanism responsible for this protection has not been investigated.

Objective: To evaluate the effects of orally administered bLF on the development of NEC injury and intestinal inflammation in the rat NEC model

Methods: Premature rat pups were assigned to one of three dietary groups: formula-fed rats (FF), rats fed with formula supplemented with bLF, 120 mg/kg BW/day (low-bLF) and 743 mg/kg BW/day (high-bLF). All groups were exposed to asphyxia/cold stress to induce NEC. After 96 hours, all animals were sacrificed and ileal tissue was collected. Intestinal injury, ileal morphology, expression of cytokines and mucins, and antimicrobial products were evaluated.

Results: The incidence of NEC was reduced from 67% in the FF group to 36% in the high-bLF group (p<0.05) and to 38% in the low-bLF group (p=0.06). Ileal villi length was significantly increased in both bLF-fed groups compared to the FF group (p<0.05). Cytokine expression in the ileum and Paneth cell products were not different between groups. Although, ileal mRNA expression of mucins was not significantly different among the groups, immunohistochemistry revealed a significant increase of Muc2 positive goblet cells in the low-LF (p<0.05) and high-LF (p<0.01) groups compared to the FF group.

Conclusion: Oral administration of bovine lactoferrin significantly reduced NEC incidence in a neonatal rat model. The protective effect of bLF was associated with increased mucin-producing goblet cells in the terminal ileum and changed ileal morphology.

Supported by a grant from Mead Johnson Nutrition.

Disclosure of Interest: None Declared
EFFECT OF HEPATIC FUNCTION IN PRETERM INFANTS RECEIVING PARENTERAL LIPIDS EMULSIONS BASED ON OLIVE OIL COMPARED WITH SOYBEAN OIL

Ying Wang 1,*, Kejun Zhou 2, Wei Cai 2, Qingya Tang 1, Li Hong 3, Yi Feng 3, Li-na Lu 1

1Clinical nutrition, Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China, 2Shanghai Institute of Paediatric Research, 3Clinical nutrition, Shanghai Children’s Medical Center, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

Objectives & Study: The development of parenteral nutrition (PN) has altered the outcome for extremely premature neonates and infants. Hepatobiliary dysfunction remains a significant life-threatening complication. The aim of this study was to assess the effect of hepatic in preterm infants receiving parenteral lipids emulsions based on olive oil compared with soybean oil in a prospective randomized blinded study.

Methods: 100 preterm infants from two children’s centers were randomly assigned to either Intralipid (Frensenius kabi) group or ClinOleic(Baxter) group. PN support was done according to guidelines for the use of nutritional support in critically ill neonates. The primary endpoint was liver function, The secondary endpoints were primary bile acids( cholic acid: CA, glycocholate : GC, taurocholate : TC, chenodeoxycholate : CDC, glycochenodeoxycholate : GCDC, taurochenodeoxycholate: TCDC). Liver function tests and primary bile acids were recorded just before commencement of PN then once weekly.

Results: No statistically significant difference was seen between groups in TBA, ALT, AST, AKP, GGT and Tbi. In the Intralipid group, the serum level of Dbi was significantly higher after PN for 7 days (p<0.05); but there was no difference in ClinOleic group (see table 1). In the ClinOleic group, the level of CA/CDC increased with the time of PN (p<0.05). In the Intralipid group, the TC/CA, TG/CA, TC+TG/CA, TCDC/CDC and TCDC+GCDC/CDC level increased significantly with the time of PN (p<0.05), but there were no significant changes in ClinOleic group.

Table 1 Results of the liver function tests between CLinOleic group and Intralipid group

<table>
<thead>
<tr>
<th></th>
<th>PN-0(ClinOleic)</th>
<th>PN-7(ClinOleic)</th>
<th>PN-14(ClinOleic)</th>
<th>p§</th>
<th>PN-0(Intralipid)</th>
<th>PN-7(Intralipid)</th>
<th>PN-14(Intralipid)</th>
<th>p§</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>TBA(μmol/L)</td>
<td>11.52±7.86</td>
<td>14.11±10.40</td>
<td>20.26±12.16</td>
<td>0.001</td>
<td>14.21±19.61</td>
<td>18.35±20.42</td>
<td>25.84±14.69</td>
<td>0.009</td>
<td>0.159</td>
</tr>
<tr>
<td>ALT(IU/L)</td>
<td>7.80±3.27</td>
<td>7.81±2.40</td>
<td>8.39±4.09</td>
<td>0.625</td>
<td>7.86±5.41</td>
<td>7.57±2.82</td>
<td>8.85±6.17</td>
<td>0.424</td>
<td>0.502</td>
</tr>
<tr>
<td>AST(IU/L)</td>
<td>52.44±33.48</td>
<td>32.93±32.78</td>
<td>29.15±14.27</td>
<td>0.000</td>
<td>50.42±23.28</td>
<td>29.58±15.05</td>
<td>25.57±12.40</td>
<td>0.000</td>
<td>0.100</td>
</tr>
<tr>
<td>AKP(IU/L)</td>
<td>202.36±70.03</td>
<td>268.90±87.79</td>
<td>292.59±114.27</td>
<td>0.000</td>
<td>211.84±67.30</td>
<td>252.48±94.02</td>
<td>295.48±113.85</td>
<td>0.000</td>
<td>0.780</td>
</tr>
<tr>
<td>GGT(IU/L)</td>
<td>206.16±193.40</td>
<td>127.69±105.07</td>
<td>138.78±104.80</td>
<td>0.018</td>
<td>214.60±105.35</td>
<td>111.80±59.97</td>
<td>134.96±110.98</td>
<td>0.000</td>
<td>0.356</td>
</tr>
<tr>
<td>Tbi(μmol/L)</td>
<td>61.37±40.74</td>
<td>142.81±49.22</td>
<td>70.68±45.13</td>
<td>0.000</td>
<td>44.88±39.46</td>
<td>153.89±62.50</td>
<td>65.52±51.89</td>
<td>0.000</td>
<td>0.614</td>
</tr>
<tr>
<td>Dbi(μmol/L)</td>
<td>9.40±4.01</td>
<td>15.96±21.28</td>
<td>12.45±6.15</td>
<td>0.056</td>
<td>10.10±3.11</td>
<td>17.21±19.54*</td>
<td>11.35±5.08</td>
<td>0.008</td>
<td>0.039</td>
</tr>
</tbody>
</table>

Conclusion: Olive oil lipid emulsion can improve hepatic tolerance in preterm infants, suggesting a hepatoprotective effect. But it is still unknown of the long-term effects. And the level of bile acids might help the treatment of PNAC.

Disclosure of Interest: None Declared
OUTCOME OF CHILDREN WITH INTESTINAL FAILURE ASSOCIATED LIVER DISEASE - REPORT FROM A SINGLE CENTRE

Jeremy Rajanayagam 1 *, Susan V Beath 1, Henry Gowen 2, Jane Hartley 1, Sharif Khalid 1, Paulo Muiesan 3, Carla Lloyd 1, Darius Mirza 4, Girish Gupte 1

1 Hepatology, Birmingham Children's Hospital, Birmingham, United Kingdom, 2 British Intestinal Failure Registry, Institute of Child Health, Birmingham, United Kingdom, 3 Hepatology, 4 Transplant and Hepatobiliary, Queen Elizabeth, Birmingham, United Kingdom

Objectives & Study: Background: Intestinal failure associated liver disease (IFALD) is a significant life-threatening complication in children on long-term parenteral nutrition [1]. Onset of IFALD is an indication for referral for intestinal transplantation (ITx), however decisions pertaining to the suitability, graft type and timing of intestinal transplant remains a significant clinical challenge.

Objective: To evaluate the severity of disease and outcome of children with IFALD referred to Birmingham Children’s Hospital for the consideration of intestinal transplantation (ITx).

Methods: Retrospective analysis of 247 children with IFALD assessed for ITx. IFALD was classified according to total serum Bilirubin (SBr) at assessment: (i) none/mild: SBr <50 (ii) moderate: SBr 50-100 (iii) severe: SBr 100-200 and (iv) end-stage: SBr >200 [2].

Results: In our cohort, 247 children underwent assessment for ITx (124F:123M, median age 10months (range 1-190 months)).

Figure 1. Outcome of children according to severity of IFALD

<table>
<thead>
<tr>
<th>IFALD</th>
<th>Tx</th>
<th>No Tx</th>
<th>NoTx off-PN</th>
<th>NoTx on-PN</th>
<th>No Tx died</th>
<th>Lost to FU (No Tx)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No/Mild n=77</td>
<td>20</td>
<td>57</td>
<td>16</td>
<td>6</td>
<td>8</td>
<td>27</td>
</tr>
<tr>
<td>Moderate n=10</td>
<td>4</td>
<td>6</td>
<td>0</td>
<td>1</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Severe n=44</td>
<td>27</td>
<td>17</td>
<td>8</td>
<td>1</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>End-stage n=116</td>
<td>34</td>
<td>82</td>
<td>7</td>
<td>5</td>
<td>61</td>
<td>9</td>
</tr>
</tbody>
</table>

After assessment, 84 were considered stable on parenteral nutrition; 3 recommended for non-transplant surgery; 129 recommended for transplantation; and 31 children considered unsuitable for transplant. Proportion of children successfully weaned off PN according to severity was (i) 20% (ii) 0% (iii) 16% and (iv) 7%. PN dependent patient survival in the absence of transplantation and according to IFALD severity was (i) 78% (ii) 50% (iii) 57% and (iv) 21%. Hundred and twenty six patients were waitlisted for transplant, mean duration 265 days (range 8-1166days). Waitlist mortality was highest in patients with severe and end-stage IFALD at 26% and 38%, respectively. Sixty one children with end stage liver disease died waiting for ITx. Post-transplant survival according to disease severity was (i) 55% (ii) 75% (iii) 63% and (iv) 47%.

Conclusion: Severity of IFALD is associated with PN dependence and waitlist mortality. Early referral and transplantation prior to onset of severe disease is ideal.

**Hepatology**

PL-H-0110

**INTESTINAL PERMEABILITY IS INCREASED IN PAEDIATRIC NON ALCOHOLIC FATTY LIVER DISEASE, AND CORRELATES WITH LIVER DISEASE SEVERITY**

Valentina Giorgio 1,*, Daniela Liccardo 2, Claudia Della Corte 2, Francesca Ferretti 2, Aldo Mico 3, Silvana Pescosolido 4, Riccardo Congia 5, Luca Miele 6, Valerio Nobili 2

1Hepatometabolic Unit, Bambino Gesù Children Hospital and University of Sacred Heart of Rome, Rome, Italy · 2Hepatometabolic Unit, Bambino Gesù Children Hospital, Rome, Italy · 3General Paediatrician, ASL RM/C, 4General Paediatrician, ASL RM/D, 5Paediatrics, University of Cagliari, Cagliari, Italy · 6Internal Medicine, Catholic University of Sacred Heart, Rome, Italy

**Objectives & Study:** Alterations of the gut microbiota and increased intestinal permeability (IP) seem to play a major role in non alcoholic liver disease (NAFLD) development and progression to non alcoholic steatohepatitis (NASH). We aimed to investigate the prevalence of altered IP in children with NAFLD, and to study its potential association with the stage of liver disease and the development of systemic endotoxemia.

**Methods:** We performed a case control study in the setting of 2 tertiary care centres. We studied IP in children with biopsy proven NAFLD/NASH, compared to controls, using the lactulose (L) and mannitol (M) bowel permeability test, and evaluated the correlations between this phenomenon and i) the stage of the disease, ii) lipopolysaccharides (LPS) blood levels.

**Results:** 39 consecutive patients (30 males, mean age 12 years) and 21 controls (14 males, mean age 11.8 years) were studied. The L/M ratio resulted impaired in 12/39 patients (31%) versus none of the controls. IP was significantly higher in children with NAFLD (L/M ratios: 0.038±0.037 vs 0.008±0.007, p < 0.05). Within the NAFLD group, IP was significantly increased in children with NASH compared to those with steatosis only (0.05±0.04 vs 0.03 vs 0.03, p < 0.05). The pathologic L/M ratio was significantly correlated with portal inflammation (p = 0.02), fibrosis (p = 0.0002) and ballooning (p = 0.003). Blood LPS levels were significantly higher in children with NASH compared to those with steatosis only (2.27 ± 0.68 vs 2.80 ± 0.35, p < 0.05).

**Conclusion:** IP is increased in children with NAFLD, and correlates with the severity of liver disease, suggesting that the impaired IP may act as a major factor in NAFLD progression.

**Disclosure of Interest:** None Declared
SEVERE AND RAPID DISEASE COURSE OF INFANTS PRESENTING WITH LYSOSOMAL ACID LIPASE DEFICIENCY

S A Jones 1,*, M Banikazemi 2, M Bialer 3, A Chan 4, S Cederbaum 5, A Dhawan 6, M Di Rocco 7, J Domm 8, S Eckert 9, G Enns 10, D Finegold 11, J Gargus 12, O Guardamagna 13, C Hendriksz 14, J Raiman 15, L Selim 16, R Tripuraneni 9, C B Whitley 17, O Zaki 18, A G Quinn 9, V Valayannopoulos 19

1University of Manchester, Manchester, United Kingdom, 2New York Presbyterian Hospital, New York, United States, 3North Shore Long Island Jewish Hospital, Manhasset, United States, 4University of Alberta Health Services, Edmonton, Canada, 5Univ of California - Los Angeles, Los Angeles, United States, 6Kings College Hospital NHS Foundation Trust, London, United Kingdom, 7Gaslini Institute, Genoa, Italy, 8Vanderbilt Children's Hospital, Nashville, United States, 9Synageva BioPharma Corp., Lexington, Massachusetts, United States, 10Stanford University, Stanford, 11Children's Hospital of Pittsburgh, Pittsburgh, United States, 12University of California, Irvine, Irvine, United States, 13Regina Margherita Hospital, Turin, Italy, 14Birmingham Children's Hospital, Birmingham, United Kingdom, 15Hospital for Sick Children, Toronto, Canada, 16Cairo University Children's Hospital, Cairo, Egypt, 17Univ of Minnesota, Minneapolis, United States, 18Ain Shams Hospital, Cairo, Egypt, 19Hôpital Necker-Enfants Malades, Paris, France

Objectives & Study: Lysosomal Acid Lipase Deficiency (LAL D) presenting in infants, historically called Wolman disease, is usually fatal within the 1st year of life. Malabsorption, growth failure, and severe hepatic disease (fibrosis/cirrhosis) are prominent clinical abnormalities that appear to be important contributors to the early mortality. Most of the published case series are small.

Methods: This is the first natural history study of a large group of LAL D patients (pts) diagnosed prior to age 2. Information was summarized from clinical chart abstractions.

Results: 40 pts with a clinical diagnosis of LAL D between 1985 and 2012 were enrolled and 36 eligible pts were analyzed. Median age (range) for all pts at symptom onset, at diagnosis, and at death were 1.0 month (0 - 6.0), 2.6 months (mos) (1.0 - 17.7), and 3.7 mos (1.4 - 46.3) respectively. 9 pts underwent hematopoietic stem cell transplant (HSCT) with 7 deaths before 9 mos of age, one at 26.9 mos and one at 46.3 mos. A 10th patient, a HSCT & liver transplant recipient, died at 37.3 mos. The median ALT and/or AST were abnormal at diagnosis and markedly increased with disease progression. This increase occurred over a relatively short time frame as the median and mean duration from diagnosis to death (n=31 with available data) were 0.7 and 2.8 mos respectively. 26 pts had confirmed growth failure within the first 6 mos of life. The median age of death for these 26 pts was 3.5 mos with no untransplanted patient (n=21) surviving more than 7.1 mos.

Conclusion: Without effective interventions LAL D infants with growth failure have a rapidly progressive clinical course resulting in significant morbidity and universal mortality during the first year of life.

EVALUATION OF THE IN VITRO ANTI-FIBROTIC PROPERTIES OF ADULT-DERIVED HUMAN LIVER STEM/PROGENITOR CELLS

Silvia Berardis 1*, Françoise Smets 1, Jonathan Evraerts 1, Pascale Lemoine 2, Adil El Taghdouini 3, Leo Van Grunsven 3, Patrick Henriet 2, Mustapha Najimi 1, Etienne Sokal 1

1Laboratory of Paediatric Hepatology and Cell Therapy, 2Cell Biology Unit, de Duve Institute, Université Catholique de Louvain, Brussels, Belgium, 3Liver Cell Biology Lab (LIVR), Vrije Universiteit Brussels, Brussels, Belgium

Objectives & Study: Liver fibrosis, a worldwide health problem, is the consequence of a wound healing process and is characterized by the excessive accumulation of extracellular matrix into the liver parenchyma, in response to chronic injury. Nowadays, the most effective treatment remains liver transplantation even significant hurdles are hampering its wide clinical accessibility. Emerging cell therapy approaches are currently under investigation since mesenchymal stem cells display immuno-modulatory properties and the capacity to differentiate into hepatocyte-like cells. The aim of the present work is to evaluate the ability of Adult derived human liver mesenchymal stem/progenitor cells (ADHLSC) to inhibit the activation of human hepatic stellate cells (HSC), a major process of liver fibrosis.

Methods: We studied the influence of ADHLSC on activated HSC in vitro using indirect co-culture systems (Transwell). HSC were seeded in the lower chamber while ADHLSC (at different ratios) were placed on the membrane insert. Recovered HSC number and viability were evaluated by microscopy and biochemical assays whereas proliferation was analyzed using flow cytometry and immunocytochemistry. HSC secretion profile was evaluated by Elisa and Luminex.

Results: A significant decrease in HSC number was noted after 24 hours co-culture with ADHLSC and maintained up to 7 days. This decrease of HSC number was inversely proportional to the number of ADHLSC used. The effect of ADHLSC on recovered HSC number was also obtained when only using conditioned culture medium of ADHLSC. This was confirmed using both manual counting and the CCK-8 biochemical assay. Further investigations revealed that the decrease of HSC number was correlated to both delayed plating and inhibition of proliferation. An increase of HSC blocked in G0/G1 phase and a decrease of the number of cells in the G2/M phase was noticed. Ki-67 nuclei immunostaining analysis confirmed the flow cytometry results. These data were correlated to a significant decrease of pro-collagen I and a concomitant increase of HGF, IL-6 as well as metalloproteinases MMP1 & MMP2 in the culture supernatants of HSC.

Conclusion: ADHLSC efficiently inhibited in vitro HSC proliferation and secretion profile mainly via paracrine mechanisms. This suggests that ADHLSC secretome may account for the promising anti-fibrotic potential of these cells.

Disclosure of Interest: None Declared
**Hepatology**

PL-H-0113

**PHASE I/II PROSPECTIVE, OPEN LABEL, MULTICENTER, PARTIALLY RANDOMIZED, SAFETY STUDY OF ONE CYCLE OF PROMETHERA HEPASTEM® IN UREA CYCLE DEFECTS AND CRIGLER-NAJJAR SYNDROME**

Françoise Smets, Dries Dobbelaere, Patrick McKiernan, Giuliano Torre, Carlo Dionisi-Vici, Pierre Broué, Emmanuel Jacquemin, Ana Isabel Lopes, Isabel Gonçalves, Hanna Mandel, Joanna Pawłowska, Eyal Shteyer, Riki Shapiro, François Eyskens, Els Van De Vijver, Philippe Clapuyt, Paul Gissen, Joelle Thonnard, Eric Halioua, Béatrice De Vos, Etienne MS Sokal, and The Hepastem Investigator Working Group

1Cliniques Universitaires St Luc, Brussels, Belgium, 2Pediatrie, CHU Lille, Lille, France, 3Birmingham Children's Hospital, Birmingham, United Kingdom, 4Bambino Jesu, Rome, Italy, 5CHU Toulouse, Toulouse, 6CHU Bicêtre, Le Kremlin Bicêtre, France, 7Hospital Santa Maria, Lisbon, 8Univ Coimbra, Coimbra, Portugal, 9Rambam Med center, Haifa, Israel, 10Children's Memorial Health Institute, Warsaw, Poland, 11Hadassah Med Center, Jerusalem, 12Schneider Med Center, Tel Aviv, Israel, 13UZA, Antwerp, Belgium, 14Great Ormond Street Hospital, London, United Kingdom, 15Promethera, Mont St Guibert, 16Ped Gi & Hepatology, Cliniques Universitaires St Luc, Brussels, Belgium

**Objectives & Study:** Children suffering from urea cycle disorders or Crigler-Najjar syndrome, experience life threatening events, neurological damage, and poor quality of life. Cell based liver regenerative medicine aims to restore a missing enzyme function by liver stem cells classified as Advanced Therapy Medicinal Products (ATMP).

**Methods:** Promethera is conducting a Phase I/II prospective, open label, multicenter, partially randomized, safety study of one cycle of Promethera HepaStem® in urea cycle defects and Crigler-Najjar Syndrome. The study design includes 3 different weight cohorts and 3 different dosages (0.25% to 4% of liver mass) infused over 1 to 4 days. A dose escalation approach was implemented. The primary objective of this study is to document the safety of infusing progenitor cells. Twenty patients were infused at 6 different European centers, 14 patients with urea cycle diseases and 6 patients with Crigler-Najjar syndrome.

**Results:** Six adolescents, 11 children, 2 toddlers and one infant received various dosages of HepaStem. During the infusion cycle, controlling the following parameters was essential to ensure the safety of the patients: (1) coagulation parameters, (2) liver haemodynamics, (3) catheter stability and (4) metabolic status for UCD patients. Adverse events related to the infusion procedure were more frequently reported in the high dosage groups and were manageable. No infections related to viral safety of the cells were reported. In the follow-up period, adverse events including infections were in line with events expected for this population of young adolescent and children.

**Conclusion:** This phase I/II clinical trial shows that stem cell technology can be successfully transferred from early hospital research to pharmaceutical development and that hepatic progenitor cells can be safely infused in children with inborn errors of liver metabolism. Safety data collected thus far support the good tolerability of HepaStem® when compared to other cell therapy fields. Long term follow-up of the patients is ongoing.

**Disclosure of Interest:** F. Smets Conflict with: PI, D. Dobbelaere: None Declared, P. McKiernan: None Declared, G. Torre: None Declared, C. Dionisi-Vici: None Declared, P. Broué: None Declared, E. Jacquemin: None Declared, A. I. Lopes: None Declared, I. Gonçalves: None Declared, H. Mandel: None Declared, J. Pawłowska: None Declared, E. Shteyer: None Declared, R. Shapiro: None
AAV8 MEDIATED GENE DELIVERY IN TYROSINEMIA MOUSE MODEL

Norman Junge 1, 2, *, Qinggong Yuan 2, 3, 4, Asha Balakrishnan 2, 3, Thu Huong Vu 2, Sabine Brandes 2, 3, Ulrich Baumann 1, Toni Cathomen 5, Michael Ott 2, 3, 4, Amar Deep Sharma 3, 4

1Pediatric Gastroenterology and Hepatology, Hannover Medical School, Hannover, Germany, 2TWINCORE, Centre for Experimental and Clinical Infection Research, 3Gastroenterology, Hepatology and Endocrinology, 4Cluster of Excellence REBIRTH, Hannover Medical School, Hannover, Hannover, Germany, 5Institute for Cell and Gene Therapy, University Medical Center Freiburg, Freiburg, Germany

Objectives & Study: Recombinant adeno-associated virus [rAAV] vectors are promising vehicles for gene therapy. Serotype 8 of rAAV vectors efficiently target the liver and have so far shown to be safe in clinical applications and in animal models. Long term transgene expression from episomal vector genomes was observed in the adult normal liver with only rare genomic integration events. In the growing or diseased liver with hepatocyte proliferation, however, transgene expression from the viral epigenomes is assumed to be lost. In the present study we analysed therapeutic rAAV 8 mediated gene transfer (Fah cDNA) in the Fah-/- mouse model, which resembles human hereditary tyrosinemia. Liver physiology and function in these animals can be maintained with the drug Nitisinone [NTBC]. In the absence of NTBC gene corrected hepatocytes proliferate and repopulate the liver.

Methods: rAAV8 vector genomes expressing the Fah cDNA under transcriptional control of transthyretin promoter and a second construct with the same transgene cassette, but flanked by homologous sequences (620 bp left and 749 bp right) of the ROSA26 locus were generated. Virus was produced according to published methods (293 cells, cesium chloride density-gradient centrifugation) and was injected at low dose (2.1x10^8 VP) into the tail vein of 5 Fah-/- (C57BL/6 Fah δ-exon 5) mice for each vector. NTBC was withdrawn after injection. Tissues were harvested after 45 days by partial hepatectomy [PH] and analyzed by immunohistochemistry as well as qPCR. After recovery of the liver (~ 90 days after rAAV injection) hepatocytes were isolated by collagenase perfusion and transplanted into secondary recipients (1x10^6 hepatocytes/mouse, intrasplenic injection).

Results: Injection of low dose rAAV8 resulted in survival of non NTBC treated mice. At PH, 45 days after injection, we observed multiple large clusters of hepatocytes expressing FAH protein as determined by immunohistochemistry with no obvious difference for the two vector types. Mice survived after PH up to know (150 days) without NTBC. From secondary recipients for each vector only 1 out of 5 mice showed repopulation of the liver indicating only rare integration events of rAAV8.

Conclusion: Even in an extensive state of hepatocyte proliferation Fah transgene expression from rAAV vectors can rescue the phenotype of FAH deficient hepatocytes in vivo. This result can most likely not be explained by frequent random integrations, since hepatocytes from primary rAAV injected animals could repopulate only 1 out 5 secondary recipients. Homologous recombination did not affect the repopulation capacity in secondary transplanted animals.

Disclosure of Interest: None Declared
Early Intervention with Long-Chain Polyunsaturated Fatty Acids Can Prevent Inflammatory Processes in the Brain That Are Associated with an Obesogenic Diet Later in Life

Ilse A.C. Arnoldussen, Peter Y. Wielinga, Marieke H. Schoemaker, Robert Kleemann, Gabriele Gross, Eric A.F. van Tol, Teake Kooistra, Amanda J. Kiliaan

Department of Anatomy, Radboud University Medical Center, Donders Institute for Brain, Cognition and Behavior, Nijmegen, Netherlands, TNO Metabolic Health Research, Leiden, Netherlands, Global Discovery, Mead Johnson Nutrition, Nijmegen, Netherlands

Objectives & Study: Obesity represents a major global health problem that is associated with cognitive dysfunction and changes in the central nervous system. We previously reported that early life supplementation with long-chain polyunsaturated fatty acids Arachidonic acid (ARA) and Docosahexaenoic acid (DHA) can attenuate body weight gain and improve adipose tissue quality later in life in a humanized mouse model for hyperlipidemia and mild obesity. The aim of the present study was to investigate in the same experimental model whether potential detrimental effects of an obesogenic diet on brain structure and function could be prevented by early intervention with ARA/DHA.

Methods: Four-week old male ApoE*3Leiden mice were fed regular lab chow with or without a mixture of ARA (0.129 wt%) and DHA (0.088 wt%). From 12 until 20 weeks of age, the mice were provided with a mildly obesogenic “Western-type” high-fat/high-carbohydrate (HFHC) diet. Control mice received regular chow throughout the entire study. RNA was isolated from snap frozen brain tissues at 20 weeks of age and subjected to gene expression analyses using Illumina mouse microarrays and quantitative Real-Time PCR.

Results: Microarray analysis revealed that pretreatment of animals with ARA/DHA can influence the changes in brain gene expression evoked by HFHC feeding. Both gene expression analysis methods consistently demonstrated that brain TNFα gene expression was increased after HFHC diet feeding as compared to the regular chow fed group. Strikingly, this detrimental effect could be prevented by ARA/DHA intervention early in life. Similar results were obtained for other genes of interest (e.g. BDNF, Caspase-3, Leptin) that were included in our microarray dataset.

Conclusion: This study suggests that inflammatory processes in the brain caused by an obesogenic diet later in life can be reduced by early ARA/DHA supplementation. As this central inflammatory process may also affect cognitive functioning associated with obesity, functional brain read outs and potential mechanisms involved will be further explored.

**Gastroenterology**

**GERD, Peptic Disease and Helicobacter Pylori**

PL-G-0116

**GASTRIC JUICE COMPOSITION AND ACID SUPPRESSION IN PAEDIATRIC GASTROESOPHAGEAL REFLUX DISEASE**

Rachel Van Der Pol 1,*, Marije Smits 1, Tamara Dekker 2, Rudi de Waart 3, Lara Ravanetti 2, Rene Lutter 2, Marc Benninga 1, Michiel van Wijk 1

1Department Of Paediatric Gastroenterology and Nutrition, Emma Children’s Hospital, Academic Medical Center, 2Departments of Respiratory Medicine and Experimental Immunology, 3Tytgat Institute for Liver and Intestinal Research, Academic Medical Center, Amsterdam, Netherlands

**Objectives & Study:** Gastric acid suppression is justified to prevent severe gastro esophageal reflux (GER) disease related complications. However, it does not reduce the total amount and proximal extent of GER in the esophagus and non-acid components are able to induce (extra-esophageal) GER symptoms as well. No data on the composition of gastric juice (GJ) in children using gastric acid suppression exists. We therefore aimed to assess whether the composition of gastric juice in children using proton pump inhibitors (PPIs) differs, compared to that of their controls.

**Methods:** Infants and children (0-18 years) on proton pump inhibitors (PPIs) for at least six weeks and a control group not using anti reflux medication, were included. GJ was obtained through an existing nasogastric or a percutaneous endoscopic gastrostomy tube/ Mic-key gastrostomy. In the collected GJ (5 ml), pH, pepsin activity, bile salts and endotoxin (LPS) levels were determined. Pepsin was measured using a fluorometric assay using 4-Methyl-Coumaryl-7-Amide (MCA) substrate with/without pepstatin. Concentrations of deconjugated and taurine/glycine-conjugated bile salts were assessed by reverse-phase HPLC. Levels of LPS were determined using the spectrophotometric Limulus Amebocyte Lysate assay.

**Results:** GJ was analyzed from 16 children with (median: 3.8 yrs, range: 17.6 years) and 16 children (4.0 yrs, range: 16.0) without PPI therapy. Median duration of PPI treatment was 24 weeks (range: 514 weeks). Gastric pH was 5.0 (range: 5.0) and 1.0 (range: 4.5) in the PPI and control group respectively (p <0.001). Pepsin, unconjugated bile salts, and endotoxin were not significantly different in the two groups. Total taurine conjugated bile salts, and specifically taurocholate, was significantly higher in the PPI group (p=0.01 and p=0.005). pH and concentration of deconjugated bile and conjugated bile salts were significantly associated (p=0.006 and p=0.02). Endotoxin and bile salts were not significantly associated

**Conclusion:** Taurine conjugated bile acids are significantly higher in children chronically using PPIs compared to controls. Moreover acidity of gastric pH correlated negatively with deconjugated and conjugated bile salts. These findings imply that GJ under chronic proton pump inhibition contains non-acid components potentially harmful to esophageal mucosa and bronchial tissue.

**Disclosure of Interest**: None Declared
Gastroenterology
GI Motility and Functional GI Disorders
PL-G-0117

PRE- AND PERINATAL STRESS AND IRRITABLE BOWEL SYNDROME IN YOUNG ADULTS A NATIONAL REGISTER-BASED COHORT STUDY

Ola Olén 1,*, Olof Stephansson 1, Ann-Sofie Backman 1, Hans Törnblom 2, Magnus Simrén 2, Maria Altman 1
1Department of Internal Medicine, Karolinska Institutet, Stockholm, Sweden, 2Department of Internal Medicine and Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Objectives & Study: Functional gastrointestinal disorders (FGID), including irritable bowel syndrome (IBS) are common in both childhood and adulthood and are associated with impaired quality of life and substantial health care costs. The etiology of IBS is multifactorial, but poorly understood. Animal and human data suggest that adverse early life events such as pain or stress may induce long-term changes in the nociceptive circuitry but the few studies have conflicting results and studies regarding prematurity are lacking.

Methods: We identified all Swedish children born between 1973-1992 in the national medical birth register. We had access to all diagnostic codes for hospital based outpatient visits 2001-2009 (The Swedish patient register) and identified all individuals who were diagnosed with IBS (K58) after they had turned 18 years. Individuals with diagnoses that could have been mistaken for IBS were excluded (e.g. celiac disease, inflammatory bowel disease). We compared occurrence of pre- and perinatal stress in individuals with and without IBS using multiple logistic regression.

Results: 2,080,098 children were born in Sweden between 1973-1992. After turning 18 years, 22,557 of them were diagnosed with IBS in hospital based outpatient care. Girls had an increased risk of IBS as young adults (Odds Ratio 3.24 (95% CI 3.15-3.34)). Compared to individuals in the highest education category, individuals in the median and lowest education category were at a decreased risk of IBS (0.73(0.63-0.85) and 0.81(0.70-0.95) respectively). Neither high, nor low birth weight was a risk factor for IBS in young adults. Preterm birth, postterm birth and Apgar score <7 at 5 min were all protective factors for IBS in young adults (0.80(0.75-0.85); 0.94(0.90-0.99); 0.74(0.64-0.85)). Other protective factors were neonatal distress (fetal distress before, during and/or after delivery including neonatal signs of anoxia/hypoxia), respiratory distress, transient tachypnoea, hypoglycaemia and neonatal infections (0.81(0.75-0.89); 0.58(0.45-0.75); 0.73(0.63-0.84); 0.70(0.55-0.88); 0.73(0.61-0.87)).

Conclusion: In this large population-based study, variables representing pre- and perinatal stress were protective factors for IBS in young adults. Except for female sex, we found no strong pre- and perinatal risk factors for IBS in young adults.

Disclosure of Interest: None Declared
PREVALENCE OF SENSITIZATION AND ALLERGY TO SOY IN CHILDREN

Yitzhak Katz 1,*, Pedro Gutierrez-Castrellon 2, Rudolfo Rivas 3, Bee Wah Lee 4, Pedro Alarcon 5
1Allergy Asthma and Immunology, Assaf Hrofeh Medical Center, Beer-Yaakov, Israel, 2National Institute of Perinatology, Hospital General, Mexico City, Mexico, 3Instituto Mexicano del Seguro Social, Mexico City, Mexico, 4Paediatrics, National University of Singapore, Singapore, 5National Institute of Child Health, Lima, Peru

Objectives & Study: Since 1943 cases of sensitization or allergy to soy-based products has been described. However there is no reliable evidenced based data to estimate the true prevalence of IgE-mediated sensitization and allergy to soy. Consequently, there is no consensus on clinical and epidemiological importance of the problem. We conducted a systematic review of the published information on soy sensitization and allergy in an attempt to establish the adjusted prevalence of IgE mediated soy sensitization and allergies in infants and children. A secondary analysis was done to evaluate impact of age (under and over six months) on the reported prevalence.

Methods: Systematic review with meta-analysis of the studies published from 1909 to 2013 on the reported prevalence of IgE sensitization or allergy to soy in infants and children, with secondary analysis of the risk in those infants under 6 months was carried out. A sensitive search of the evidence was performed in ARTEMISA, PubMed, Embase, LILACS, Cochrane controlled trials register, Bandolier and DARE, using the GRADE system to classify the quality of articles.

Results: We identified 40 studies that allowed us to establish a weighted prevalence of challenge proven soy allergies 0.27% (0.0%>0.5%) for general population, between 0.4% and 3.1% (average 1.9%) for referred population and 0-12.9% (2.7%) for atopic children. The prevalence of positive SPT in high risk children after the use of soy-based formulas was 8.7% (0-37.9%) and presence of sIgE to soy was 8.8% (5.4-31.4%). The prevalence of self reported (by parents) soy allergy in infants younger than 6 months of age was 0.1% compared to 0.2% in the general population of children up to 19 years old.

Conclusion: Opposing to what some authors have described, evidence shows that the prevalence of allergies to soy and of IgE sensitization to the use of soy-based infant formulas are less than we have been reported and communicating. There is no evidence to indicate that there is a higher risk of developing soy allergy those infants under 6 months. We recommend studies be carried out with more robust methodology that reduces the diverse biases and identified heterogeneity in order to establish conclusive recommendations.

Disclosure of Interest: None Declared
Objectives & Study: Paediatric Crohn’s disease (CD) is associated with alterations in body composition. Intra-abdominal adipose tissue (IAAT) is the adipose compartment most strongly associated with chronic inflammation; intestinal adipose tissue expansion observed in surgical specimens is a recognised hallmark of CD. Adipocytes can function as macrophage-like cells in the inflammatory cascade, releasing adipokines such as IL-6, TNF-α. For the first time we use magnetic resonance imaging (MRI) as a method of measuring body composition in paediatric CD, specifically for quantifying intra-abdominal adipose tissue (IAAT).

Methods: Children (7-18 years) with CD were recruited from a tertiary Paediatric Gastroenterology department; healthy children were recruited to act as controls from general paediatric outpatients, Chelsea and Westminster hospital. Ethical approval was obtained. Volumes of the following abdominal compartments; Total abdominal adipose tissue (TAAT), IAAT, subcutaneous adipose tissue (SCA) and abdominal muscle (MU) were quantified from MRI images for all subjects; volumes were expressed in litres. Analysis: Compartment volumes were adjusted for body size by derivation of a height (Ht) index for each compartment (Compartment/(Ht)^2). They were also expressed as a ratio of TAAT:MU, and IAAT:SCA. Measures were analysed according to disease activity; remission/mild (Paediatric Crohn's Disease Activity Index (PCDAI) 0≤29), moderate/severe (PCDAI≥30). We have not yet fulfilled our recruitment target thus we present the descriptive statistics.

Results: 29 children were recruited; Mean age (±SD) (Controls (C): 14.4 ± 1.9yrs, n=6 (♀2); remission/mild (R/M): 14.2 ± 2.2yrs, n=12 (♀6); moderate/severe (M/S): 13.5 ± 1.4yrs, n=11 (♀5); Mean BMI (C): 19.3 ± 2.7kg/m^2; R/M: 19.6 ± 4.3kg/m^2; M/S: 16.6 ± 2.9 kg/m^2. The median [IQR] of TAAT:MU for each group; C: 0.61 [0.52-0.83]; R/M: 0.90 [0.60-1.50]; M/S: 1.26 [0.87-1.76]. For IAAT:SCA; C: 0.42 [0.27-0.54]; R/M: 0.37 [0.23-0.71]; M/S: 0.68 [0.36-1.20]. At the time of MRI scan no child was on systemic steroids. The plots the Figure, below represent the median Compartment/(Ht)^2 (bar); IQR (box) and range (error bars).
**Conclusion:** Using MRI methodology we show that IAAT and related compartments can be quantified in children with CD. Our preliminary results indicate that moderate/severe disease is associated with lower muscle mass and higher IAAT. In severe disease despite lower BMI, there is evidence of higher IAAT; this implies that IAAT is mediated by local gastrointestinal inflammation

**Disclosure of Interest:** None Declared
EFFECTS OF CESAREAN SECTION AND INFANT FEEDING CHOICES ON EARLY WEIGHT GAIN AND LATER OBESITY RISK

Martina Weber 1,*, Veit Grote 1, Annick Xhonneux 2, Elena Dain 3, Veronica Luque 4, Natalia Ferre 5, Elvira Verduci 6, Dariusz Gruszfeld 7, Berthold Koletzko 1 on behalf of The Childhood Obesity Trial Study Group

1Department of Metabolic and Nutritional Medicine, Dr. von Hauner Children's Hospital, Munich, Germany, 2CHC St. Vincent, Liège-Rocourt, 3Université Libre de Bruxelles, Brussels, Belgium, 4Universita Rovira i Virgili, Reus, 5Universita Rovira i Virgili, Tarragona, Spain, 6University of Milan, Milan, Italy, 7Children's Memorial Health Institute, Warsaw, Poland

Objectives & Study: Associations between Cesarean section and obesity risk later in life are recently discussed. Differences in the gut microbiota with effects on the infant’s metabolism might be causal for the increased risk of rapid early weight gain and later obesity. One of the key drivers for early weight gain is the choice of infant feeding. Based on a randomized clinical trial set-up with different protein content infant formula and breastfeeding, we studied associations of feeding choices and Cesarean delivery with weight gain during the first 12 months of life and the risk for obesity at six years.

Methods: Children of the Childhood Obesity Project, a multicenter randomized European intervention trial on two different protein content infant formulas (higher HP; lower LP) and breastfeeding (BF), were anthropometrically examined at inclusion in the study (n=1676), at 12 months (n=1046) and at six years of age (n=657). Weight gain in the first year was assessed as difference in weight z-scores based on the WHO growth reference study. Obesity at six years of age was defined by the Obesity Task force cut-off values for BMI. We used linear and logistic regression models to analyze the associations of Cesarean section and infant feeding on early weight gain and obesity risk, respectively.

Results: Weight gain during the first year of life was significantly higher in infants born by Cesarean section (weight gain difference 0.26 SD, P<0.001). Feeding choice did not interact with the effect of Cesarean section but showed significant effects on weight gain (HP vs. LP 0.25, HP vs. BF 0.62, LP vs. BF 0.37; P<0.001 respectively). Prevalence of obesity was 4.2% in children delivered by vaginal birth vs. 11.0% in those born by Cesarean section. Including infant feeding choice in the model, the risk to become obese was 2.97 (95% CI 1.50 to 5.87, P=0.002) times increased by a Cesarean section while the risk increase of HP compared to BF was 3.97 (1.55 to 10.16; P=0.004) and no significant effect of LP vs. BF was estimated. Interaction terms did not reach statistical significance.

Conclusion: The presented study reveals Cesarean section as a high risk factor for increased early weight gain and later obesity. This relation is independent of the feeding choice. Underlying mechanisms have to be revealed in further studies on microbiom and metabolom to understand and diminish the observed negative effects of Cesarean section.

Disclosure of Interest: None Declared
Nutrition

Observational and Epidemiological Studies

PL-N-0121

CORD BLOOD N-3 LC-PUFA CONCENTRATION AFFECTS ADIPONECTIN LEVELS AT 10 YEARS OF AGE. RESULTS FROM THE LISAPLUS STUDY

Marie Standl 1,*, Hans Demmelmaier 2, Berthold Koletzko 2, Joachim Heinrich 1

1Institute of Epidemiology I, Helmholtz Zentrum München – German Research Center for Environmental Health, Neuherberg, Germany, 2University of Munich Medical Centre, Dr. von Hauner Children’s Hospital, Munich, Germany

Objectives & Study: An elevated ratio of n-6 to n-3 long-chain (LC-) PUFAs may be a potential risk factor for development of obesity. N-3 LC-PUFAs are thought to alter adiponectin levels, and thus may have a beneficial effect on weight development. We analysed the association between n-3 LC-PUFA concentrations in cord blood and adiponectin levels at the age of 10 years.

Methods: Fatty acid composition was measured in cord blood and at 10 years of age and adiponectin was measured only at 10 years of age in 249 children from the Munich LISAplus birth cohort study. All fatty acids with 14 to 24 carbon atoms were measured by gas chromatography. N-3 LC-PUFA and n-6 LC-PUFA was calculated by summing up all n-3 fatty acids and n-6 fatty acids, respectively, with 20 or more carbon atoms. Linear regression models were used to assess associations between n-3 LC-PUFA, n-6 LC-PUFA and the n-6/n-3 ratio in cord blood with adiponectin levels at 10 years of age. Concentrations of LC-PUFAs were grouped into tertiles because of their apparent non-linear relationship with adiponectin. Regression models were adjusted for sex, total sum of fatty acids in cord blood and at 10 years of age, fasting status, BMI at 10 years, exact age at 10 years, maternal age at birth, maternal BMI before pregnancy, maternal education level, birth weight, gestational age, breastfeeding, onset of puberty and LC-PUFA concentration at 10 years of age.

Results: The cord blood concentration of n-3 LC-PUFA was significantly associated with adiponectin levels at 10 years of age (2nd tertile versus 1st tertile: \( \beta = 1.84, 95\% \text{CI} = (0.53, 3.15) \) and 3rd tertile versus 1st tertile: \( 0.86 (-0.50, 2.22) \), \( p \)-value = 0.003 (ANOVA) after adjustment for potential confounding factors. The cord blood concentration of n-6 LC-PUFA and the ratio of n-6 to n-3 LC-PUFAs were not associated with adiponectin levels.

Conclusion: Our results suggest that a higher n-3 LC-PUFA concentration in cord blood is associated with a higher concentration of adiponectin at 10 years of age.

Disclosure of Interest: None Declared
HEREDITARY FRUCTOSE INTOLERANCE IN CHILDREN: CORRELATION BETWEEN DIETARY INTAKE OF FRUCTOSE AND LIVER DISEASE

Maria Giovanna Puoti 1,*, Fabiola Di Dato 1, Marinella Acconciagioco 1, Fabrizia Chiatto 1, Maria Immacolata Spagnuolo 1, Giancarlo Parenti 1, Raffaele Iorio 1

1Department of Translational Medical Science, Section of Paediatrics, University Federico II, Naples, Italy

Objectives & Study: Hereditary Fructose Intolerance (HFI) is a genetic inborn error of fructose metabolism, responsible for severe liver disease, if untreated. Currently, treatment only relies on strict fructose-free diet. The fructose exact amount allowed each day to maintain metabolic control is unknown. Recommendations for the amount of fructose allowed each day, vary in the literature from 20 to 40 mg/kg/day to as little as 1500 mg/day. It is also not clear if continued intake of small amounts of fructose is associated with chronic liver damage. The aim of this study was to analyze the correspondence between compliance to dietary therapy and liver disease in HFI patients.

Methods: Nineteen patients (10 males) with diagnosis of HFI, confirmed by molecular analysis (mean age at diagnosis 8.7±6.4 months), were enrolled. In all patients (mean age at the time of evaluation 15.8±7.11 years) the daily intake of fructose was calculated using a food diary compiled for 7 days. The patients that assumed a daily intake of fructose up to 40 mg/day were considered to have a good compliance to diet. In all patients liver function was evaluated through transaminases serum levels at the time of diagnosis and every year until the end of follow-up (mean duration 12.9 years; range 4.5-20.2). Values of AST and ALT less than 40 U/l suggest a good liver function.

Results: Nine (47.4%) patients assumed a fructose amount less than 40 mg/day (mean daily intake of fructose 14.7±12.5 mg/day). Ten (52.6%) patients had poor compliance to therapy (mean daily intake of fructose 91±38.7 mg/day). The patients with good compliance to diet did not differ from those with poor compliance respect to the age at diagnosis (7.7± 4.3 months versus 9.8± 8.7 months, p=NS), age at the time of evaluation (18.5±9 years versus 18.6±6.8 years, p=NS) and follow-up (12.3±5.1 years versus 13±6.7 years, p=NS). The degree of compliance to diet did not correlate with liver function because 4 (44.4%) of 9 patients with good compliance showed hypertransaminasemia and 5 (55.6%) did not show it. Four (40%) of 10 patients with poor compliance to diet showed hypertransaminasemia and 6 (60%) did not show it (AST 40±20 UI/L versus 40±17 UI/L, ALT 53±39 UI/L versus 40±17 UI/L, p=NS).

Conclusion: HFI patients have different tolerance to the amount of fructose taken with diet. The degree of compliance to diet did not correlate with control of liver disease. It is likely that other factors, in addition to compliance to therapy, probably the type of mutation, affect hepatic involvement. Further studies are required to confirm these preliminary results.


Disclosure of Interest: None Declared
SERUM BILE ACIDS IN CHILDREN AND ADOLESCENTS EXPECTED (NORMAL) RANGES
Joerg Jahnel 1,*, Barbara Stering 1, Günter Fauler 2, Tatjana Stojakovic 2, Hubert Scharnagl 2, Wolfgang Erwa 2, Karl-Martin Hoffmann 1, Andrea Deutschmann 1, Almuthe Christine Hauer 1
1Department of Paediatrics, 2Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University Graz, Graz, Austria

Objectives & Study: Serum bile acid (BA) determination is conducted during evaluation of hepatobiliary disease. Well-defined reference ranges for serum BA concentrations in children and adolescents are lacking so far. Therefore, we aimed to establish such ranges in our patients.

Methods: Using liquid chromatography-tandem mass spectrometry (LC-MS/MS), we determined total serum BA levels and BA profiles (5 unconjugated BA species with 5 glycine- and 5 taurine-conjugated BA species) in 194 healthy persons aged between 1 week and 18 years. Physical examination found no abnormalities. All individuals were undergoing routine evaluation for hepatic disease; as part of screening, values for biomarkers of hepatobiliary injury were assessed. None had abnormal values for any such biomarker. The patients had no other concomitant disease.

Results: Babies aged 5 months or less (n=17) had serum BA levels lower (SD 3.9 – 6.3 µmol/l) than did children aged between 6 and 24 months (n=13; 6.6 – 9.4 µmol/l). After this age, serum BA levels decreased. Serum BA concentrations in children between 2 and 5 years (n=22) were significantly (p<0.01) higher (4.3 – 6.4 µmol/l) than in children between 5 and 11 years (n=44; 3.6 – 5.1 µmol/l). Children 11 years old or more (n=98) had serum BA concentrations comparable with adult levels (3.1 – 4.1 µmol/l). In no age-cohort did serum BA values differ between genders. Proportional distributions of BA species did not differ among age cohorts.

Conclusion: This study of serum BA value ranges by LS-MS/MS in children and adolescents shows that serum BA values vary substantially in the first years of life. Values physiologic at one age may be suspect for hypercholanaemia at another age. Thus, clinical laboratories should establish age-differentiated expected-value ranges for serum BA concentrations and present results of serum BA determinations in age-specific contexts. In addition, the causes of the variation in serum BA levels need further clarification.

Disclosure of Interest: None Declared
**Hepatology**

PD-H-0124

MIR-200A PROTECTS LIVER CELLS FROM OXIDATIVE STRESS-INDUCED DEATH THROUGH REPRESSING THE P38 MITOGEN-ACTIVATED PROTEIN KINASE-HEAT SHOCK PROTEIN 27 PATHWAY

Yongtao Xiao 1, 2,*, Wei Cai 1, 2, 3

1Gastroenterology and Nutrition, Shanghai Institute of Paediatric Research, Shanghai, China,
2Shanghai Key Laboratory of Paediatric Gastroenterology and Nutrition, Shanghai, China,
3Department of Paediatric Surgery, Xin Hua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

**Objectives & Study:** Our team recently reported that peroxides contaminating total parenteral nutrition (TPN) contribute to liver cells oxidative stress, which was cited as a possible cause of TPN associated hepatic injury. The aim of this study was to investigate the mechanisms of oxidative stress-induced hepatic injury and to prevent TPN-associated liver injury.

**Methods:** We examined the effect of hydrogen peroxide (H2O2) on miR-200s expression in an immortal liver cell (L02) with quantitative polymerase chain reaction (qPCR) analysis. Apoptosis, Cell Cycle, and Cell Proliferation analysis were performed to determine the growth of L02 cells with different treatments. The membrane-permeant JC-1 dye was used to monitor mitochondrial membrane potential. Dual-Luciferase Reporter (DLR) Assay was to analyse whether miR-200s bind to MAPK14 3' untranslated region. The alteration of p38 Mitogen-Activated Protein Kinase (MAPK)-Heat Shock Protein (HSP) 27 Pathway was analysed by Western-bLOTS.

**Results:** The expression of the miR-200s (miR-200a, b, c and 141) was induced within 1 h of treatment, reached its maximum between 2 and 3 h after treatment with 400 mM H2O2. The death of L02 cells was significantly enhanced by H2O2 treatment at the indicated time (0, 1, 2 and 3 h). Meanwhile, the p38 MAPK-HSP27 pathway was significantly enlarged in response to H2O2. With using bioinformatics tool, miR-200s were predicted to target MAPK14 3' untranslated region. The dual luciferase reporter and western-blot assay showed miR-200a but not miR-200b,c or miR-141 repressed the expression of MAPK14 significantly, which provided evidence of a direct link between miR-200a and MAPK14 (encoding p38α protein). Overexpressing miR-200a in L02 cells altered MAPK response to H2O2 by down-regulation of p38α. This reduction prevented the expected accumulation of the phosphorylated form of p38α and led to the subsequent decreased phosphorylation of HSP27, one of the major downstream effectors of p38α, thereby, protected L02 cells against H2O2-induced death, suggesting that miR-200a was involved in the regulation of the MAPK pathway. MAPK14 knockdown by siRNAs repressing the p38α-HSP27 signalling and inhibiting cell death that mimicking effects of miR-200a under H2O2 treatment. Conversely, MAPK14 gene overexpressing in L02 cells blocked protective effects of miR-200a in response to H2O2. Presently, we are investigating whether miR-200a can prevent oxidative stress-induced liver injury in TPN animal model.

**Conclusion:** Our works showed that miR-200a target p38α-HSP27 pathway and modulate the oxidative stress response. Enhanced expression of these miR-200a mimics p38α deficiency and protects liver cells from H2O2-induced death, suggesting miR-200a may be a potential reagent to prevent TPN-induced liver injury.

**Disclosure of Interest:** None Declared
**Hepatology**

PD-H-0125

**BLINDED ASSESSMENT OF LIVER-HISTOLOGY IN AUTOIMMUNE LIVER DISEASE**

Norman Junge 1,*, Miriam Tiedau 1, Jerome Schlue 2, Alexander Quaas 3, Ulrich Baumann 1

1 Paediatric Gastroenterology and Hepatology, 2 Institute for Pathology, Hannover Medical School, Hannover, Germany, 3 Institute of Pathology, University Medical Center Hamburg-Eppendorf, Hamburg, Germany

**Objectives & Study:** Assessment of liver histology is essential for the diagnosis, grading, staging and phenotyping of autoimmune liver disease [AILD]. The aim of this study was to evaluate the reproducibility of liver-histology results and the correlation of a suspected diagnosis based on histology to the clinical diagnosis based on standard criteria.

**Methods:** We identified 61 patients (37 female; mean age 11.4; median 12.5; min 1.7; max 17.6 years at initial liver biopsy), who have been diagnosed by Autoimmune Hepatitis Score [AIHS] (IAHG 1999), initial liver biopsy and if indicated cholangiopraphy as autoimmune hepatitis (AIH) n=30, primary sclerosing cholangitis (PSC) n=15 or overlap-syndrome/AISC n=16. Liver biopsies in these patients were performed in average 6.3 (1.6-17.2) years ago and were re-evaluated for this study by two blinded senior liver pathologists. Re-evaluation followed a self designed questionnaire asking for presence of interface hepatitis, lymphoplasmacytic infiltration, rosetting, signs of bile duct involvement, periductal concentric fibrosis, signs typical for other liver disease and for features of the ISHAK score. Final diagnosis was summarised into 4 subgroups: AIH, PSC, Overlap, non classifiable. Statistical analysis was done by Wilcoxon signed rank test.

**Results:** Both pathologist reached consensus in classifying all biopsies as AILD. Each pathologist stated 21% of cases (partly overlapping) as “none classifiable”. The diagnosis from histological re-evaluation was consistent with the primary diagnosis in 89% in one pathologist and in 79% in the other. 6 patients with an initial AIHS>16 were labelled as PSC from at least one pathologist, 3 of them have had cholangiography with inconclusive result in two. High consistency (86%) for present periductal concentric fibrosis could be observed. The evaluation of Ishak Score differed for all aspects (interface hepatitis median 1.9 to 0.75; focal apoptosis and inflammation 1.3 to 1.6; portal inflammation 2 to 1.6; fibrosis/cirrhoses 3.3 to 3.7), except confluent necrosis (0.44 to 0.47), between both pathologists significantly (p<0.05). When applying the re-evaluated histology to the AIHS final AIHS between both re-evaluations differed significantly (mean 14.3 and 15.5; p=0.027) with shift in AIHS between probable and definite or rather probable and none AIH in 19 and between none and definite AIH in 3 cases.

**Conclusion:** Liver histology remains a powerful tool but inter-observer variability can be significant and is perhaps in our study increased, due to missing clinical informations and limited evaluable stainings in at least some cases. Especially the assessment of early bile duct lesions and the interpretation of inflammation vary considerably and impact on therapeutic considerations. Our findings also reiterate the need for routine bile duct imaging for a timely identification of bile lesions.

**Disclosure of Interest:** None Declared
INFLUENCE OF PARTIAL EXTERNAL BILIARY DIVERSION ON THE LIPID PROFILE OF CHILDREN WITH PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS

Irena Jankowska 1*, Aldona Wierzbicka 2, Dorota Gliwicz 1, Joanna Pawlowska 1, Piotr Kaliciński 3, Piotr Socha 1

1Gastroenterology, Hepatology and Nutritional Disturbances, 2Biochemistry and Experimental Medicine, 3Paediatric Surgery and Organ Transplantation, CMHI, Warsaw, Poland

Objectives & Study: There are only a few studies which estimated the effects of partial external biliary diversion (PEBD) on lipid profile in children with progressive familial intrahepatic cholestasis (PFIC). The aim of our study was to compare the average concentrations of several lipid parameters: cholesterol, triglycerides, phospholipids and apolipoprotein A1, B and E before and 6 months after PEBD.

Methods: Lipid parameters were evaluated in children with PFIC before and 6 months after PEBD: cholesterol was measured in 26 patients, triglycerides and phospholipids were estimated in 21 patients, and apolipoprotein A1, B and E were measured in 16 patients.

Results: In all children plasma cholesterol, triglycerides, and phospholipid concentrations decreased significantly after PEBD (p < 0.001) (table 1). We observed a significant increase in the average concentration of Apo-A1 and the significant decrease in the average concentration of Apo-B. No effect of treatment on the mean concentration of Apo-E was noticed (table 1).

Table 1. Lipid parameters before and after PEBD

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before PEBD (mean±SD)</th>
<th>After PEBD (mean±SD)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholesterol (mg/dl) (n=26)</td>
<td>195.3±51.6</td>
<td>142.6±50.8</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Triglycerides (mg/dl) (n=21)</td>
<td>200.3±133.8</td>
<td>121.9±89.9</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Phospholipids (mg/dl) (n=21)</td>
<td>210.8±93.2</td>
<td>177.6±75.3</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Apo-A1 (g/l) (n=16)</td>
<td>0.62±0.3</td>
<td>1.08±0.53</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Apo-B (g/l) (n=16)</td>
<td>1.21±0.52</td>
<td>0.93±0.47</td>
<td>p &lt;0.001</td>
</tr>
<tr>
<td>Apo-E (mg/l) (n=16)</td>
<td>6.64±1.13</td>
<td>6.36±0.84</td>
<td>Ns</td>
</tr>
</tbody>
</table>

Conclusion: The beneficial effect of surgical treatment (relief of cholestasis) was associated with a significant decrease of cholesterol, triglycerides and phospholipids which was associated with normalization of apolipoprotein A1 concentration. These findings confirm the direct relationship of cholestasis with disturbed lipid metabolism in PFIC and allow to speculate on the possible mechanism of PEBD in treatment of PFIC.

Disclosure of Interest: None Declared
GROWING UP WITH BILIARY ATRESIA WITHOUT LIVER TRANSPLANTATION; A SINGLE CENTRE EXPERIENCE.

Vandana Jain 1,*, Vinod Kolimarala 1, Mark Davenport 1, Nigel Heaton 2, Marianne Samyn 1

1Paediatric Gastroenterology, Hepatology and Nutrition Centre, KCH, London, United Kingdom
2Institute of Liver Studies, KCH, London, United Kingdom

Objectives & Study: To evaluate outcomes in adulthood of biliary atresia not requiring liver transplantation in the paediatric age group.

Methods: A single centre retrospective analysis, comprising 268 patients who underwent KP between 1980-96.

Results: After KP, 107/268 (40%) survived with their native liver for at least 16 years. Ninety-seven (43M:54F) are followed up in our centre, and provide our study group; 10 were referred to other adult liver centres. Out of the remaining (n=161); 123 (76%) underwent liver transplantation (LT) <16yrs, 18 (11%) died and 20 (13%) were lost to follow up. At a median age of 20.6 yrs (range 16-32) at last follow-up, 81 (84%) remain with their native liver (Group 1) whilst 16 had LT or are currently listed (Group 2). 2 patients died, one post LT. Characteristics of Group 1 are listed in Table 1. 7% of patients had at least 1 episode of cholangitis, and in 9%, varices were seen at endoscopy. Heterogeneity of liver parenchyma on US was seen in 78% and present in all with SBR > 20 umol/l. In this group one patient died during pregnancy. In Group 2, 14/16 patients underwent LT and 2 are listed for LT. Documentation for 15 patients was available. Median age at LT was 18.8 yrs (range 16.5-27.1) after median waiting time for LT of 11.5 mths (range 2-63). Median SBR and albumin at time of listing were 137 umol/l and 32 mg/dl respectively. Indications for LT were recurrent cholangitis with synthetic failure (n=7), synthetic failure (n=4), cholangitis (n=2), hepatocellular carcinoma (n=1) and portal hypertension (n=1). The listed patients have been on the waiting list for 27 and 35 mths respectively. Model for End Stage liver disease (MELD) median score at listing was 17 (range: 11-31) and worsened in 5 patients whilst on the waiting list. Two patients required re-transplantation for chronic rejection, of which one died following CMV infection. Overall, four patients had 6 successful pregnancies of whom 1 is currently listed for LT and 1 is pregnant. One patient, with SBR 29 umol/l and portal hypertension died during pregnancy from a variceal bleed.

<table>
<thead>
<tr>
<th>Native liver (n=81)</th>
<th>SBR &lt;20 umol/l (n=55)</th>
<th>SBR &gt;20 umol/l (n=26)</th>
</tr>
</thead>
<tbody>
<tr>
<td>AST (&lt;50 IU/l)</td>
<td>46</td>
<td>14</td>
</tr>
<tr>
<td>Platelet count (&gt;100)</td>
<td>46</td>
<td>8</td>
</tr>
<tr>
<td>Albumin (&gt;35 mg/dl) and INR &lt;1.2</td>
<td>53</td>
<td>19</td>
</tr>
<tr>
<td>No splenomegaly on US</td>
<td>24</td>
<td>2</td>
</tr>
<tr>
<td>All of the above</td>
<td>21</td>
<td>1</td>
</tr>
</tbody>
</table>

Conclusion: In our patient cohort, 84% are alive with their native liver, with 69% of patients demonstrating normal SBR levels and 26% showing no evidence of progressive liver disease. The most common indications for LT in adulthood, are recurrent cholangitis and/or synthetic dysfunction

Disclosure of Interest: None Declared
PROSPECTIVE STUDY ON HEPATITIS COMPlicated WITH MYCOPLASMA PNEUMONIAE INFECTION IN KOREAN CHILDREN

Kyu Won Kim 1,*, Jae Jin Sung 1, Eell Ryoo 1, Hann Tchah 1

1Department of Paediatrics, Graduate School of Medicine, Gachon University, Incheon, Korea, Republic Of Korea

Objectives & Study: Mycoplasma pneumoniae (MP) infection is a major cause of respiratory infections in school-aged children. Extrapulmonary manifestations of MP infection are common, but liver involvement of MP infection has been rarely reported, and none of these reports were done prospectively. Here, we present clinical characteristics of MP hepatitis to provide a basis for diagnosis and treatment.

Methods: Prospective study was performed on 1,044 patients of MP infection diagnosed serologically with MP IgM at Gil Medical Center, Incheon, Korea from January 2006 to December 2012. We reviewed 80 cases among these patients, who had elevated level of serum AST and ALT greater than 50 IU/L respectively without any other specific liver disorders.

Results: Hepatitis occurred in 7.7% of MP infection, especially in fall and winter times. Male to female ratio was 1.7 : 1 and the mean age was 5 years and 5 months. The common symptoms were cough (95.0%), fever (86.3%) and sputum (76.3%). Among gastrointestinal manifestations, anorexia (55.0%) was the most common symptom, followed by nausea/vomiting, diarrhea, and abdominal pain. In addition to hepatomegaly (5%) and splenomegaly (3.8%), coarse breathing sound (70.0%) was the most common physical manifestation, followed by rale, pharyngeal injection, and decreased breathing sound.

Mean level of AST and ALT was 100.65 IU/L and 118.73 IU/L, respectively. Hyperbilirubinemia was noted in only one case. Lobar or lobular pneumonia (78.5%) was the most common finding in chest X-ray and left lower lobe (39.2%) was most commonly affected. Pleural effusion was noted in 13.7%. Serum AST/ALT level was normalized within 7.5 days on average without any complications and mean duration of hospitalization was 11.3 days.

Conclusion: MP associated hepatitis is not uncommon and has relatively good prognosis. Therefore, clinicians should be concerned about liver involvement of MP infection and avoid further unnecessary evaluation in hepatitis associated with MP.

Disclosure of Interest: None Declared
THE EFFECT OF MILK PROTEINS ON CATCH-UP GROWTH IN YOUNG RATS

Majdi Masarwi, Moshe Philip, Raanan Shamir, Galia Gat-Yablonski
1Felsentein Medical Research Center, Petah-Tikva, Israel, 2Sackler School of Medicine, Tel Aviv University, Tel-Aviv, Israel, 3The Jesse Z and Sara Lea Shafer Institute for Endocrinology and Diabetes, National Center for Childhood Diabetes, Schneider Children's Medical Center of Israel, Petah-Tikva, Israel

Objectives & Study: Malnutrition-induced growth stunting is common mainly in underdeveloped countries. When proper food is administered, it is usually associated with spontaneous catch-up growth (CU). Although in most children the growth pattern is corrected with no effect on final height, in many cases a permanent growth deficit occurs. Furthermore, recent studies have also shown that CU growth may be associated with late metabolic effects. Milk is an important source of nutrients supporting growth, such as high-quality proteins, lactose and minerals. The ratio between the most prevalent milk proteins (casein and lactalbumin) is different in human milk compared to the cow's milk used for baby formula. The objective of this study was to examine the effect of milk proteins on the efficiency of CU growth.

Methods: Young (24 days old) Sprague Dawley rats were housed individually. The control group (AL) was allowed free access to food throughout the entire study. All other rats were subjected to 40% of food restriction for 36 days. Following this period, one group was kept restricted until the end of the study (RES). The other five groups were re-fed with no restriction for additional 24 days. The source of protein in their food was: 1) grains (regular chow) (CU); 2) Casein; 3) Lactalbumin (Lact); 4) A combination of 80% lactalbumin and 20% casein; 5) A combination of 80% casein and 20% lactalbumin.

Results: The average body weight of all re-fed animals was significantly lower compared to the AL group and higher than RES. In spite of similar food consumption, animals in the Lact group had the lowest body weight (p= 0.008). However, there was no significant difference in humeral bone length between all the re-fed groups.

Conclusion: These results may suggest that feeding with a higher ratio of lactalbumin in the diet may be beneficial as it increases bone length similar to all other food compositions, while keeping a lower body weight. These results may have significant clinical value as CU growth is sometimes associated with late onset metabolic diseases and obesity.

Disclosure of Interest: None Declared
**Errors in Introducing Solid Food in Constanta County, Romania**

Cristina Maria Mihai¹*, Adriana Balasa¹, Larisia Mihai¹, Viviana Cuzic¹, Pinzaru Anca Daniela¹, Georgiana Raluca Jalba¹

¹Paediatric Department for Diabetes, Nutrition, and Metabolic Disorders, Clinical County Emergency Hospital of Constanta, Romania, Constanta, Romania

**Objectives & Study:** The aim of this study is to highlight common mistakes encountered in introducing solid foods in infants diet.

**Methods:** The study consisted in evaluation of 2000 children between 6 months and 2 years, hospitalized in the Pediatric Clinic of the Clinical County Emergency Hospital of Constanta during November 2011–May 2012. All patients were evaluated based on several parameters, included in a questionnaire designed to collect information directly from the parents, containing questions for both parents (age, background environment, studies, type organization of the family, addictions, chronic diseases), and children (age, sex, breastfeeding, age of introducing complementary food, type of complementary food used).

**Results:** According to the information gathered in the study the mean age of introducing complementary food is 5 months (69%). From the total number of 2000 case in about 25% the children were introduced solid food before 3 months, and in 10% after 8 months. In 850 cases of children were given solid foods inappropriate for their age when introducing complementary foods. For example, they were given biscuits in combination with fruits since 3 months and half in 47 cases, soft banana cereal after the age of 9 months in 120 cases, a whole egg before 5 months in 302 cases, yogurt with fruit: 381 cases).

The study has revealed an early introduction of solid foods (before 3 months and half) in 286 cases, and also a delayed introduction (after 9 months) in about 221 cases. Other common mistakes:
- the introduction time of meat in infant’s diet was between 4 months in 17.08%, 6 months in 45.38%, 14 months in 2.47%.
- age of children to whom it was offered soda were 2 months in 1.99%, 7 months in 14.95%, 9 month in 15.94%.
- children to whom it was offered salt before the first year were male in 43.28% and female in 49, 89%.

**Conclusion:** In more than 850 cases have been reported errors in regard to the introduction of solid foods. The lower income and the lower level of education for both mother and father are the primary reason for an early introduction of solid food (in about 25% the children were introduced solide food before 3 months). Children will be followed in the coming years in order to observe the impact of diet errors made in the first 2 years on the future development.

**References:**

**Disclosure of Interest:** None Declared
THE EARLYBIRD DIABETES STUDY: FUTURE PERSPECTIVES FROM SERUM LIPIDOME AND METABONOME IN CHILDHOOD

Ivan Montoliu 1, Ornella Cominetti 2, Joanne Hosking 3, Alison Jeffery 3, Laetitia Da Silva 2, Sebastiano Collino 2, Fiona Beguelin 2, Max Scherer 2, Jonathan Pinkney 4, Linda Voss 4, Terrence Wilkin 5, Francois-Pierre Martin 2.*

1Analytical Science, Nestle Research Center, Lausanne, Switzerland, 2Molecular Biomarkers Core, Nestlé Institute of Health Sciences SA, Lausanne, Switzerland, 3Plymouth University and Peninsula Schools of Medicine and Dentistry, Plymouth, United Kingdom, 4Plymouth University and Peninsula Schools of Medicine and Dentistry Plymouth, United Kingdom, 5University of Exeter, Plymouth, United Kingdom

Objectives & Study: Increasing evidence highlights that the origin of childhood overweight and diabetes are rooted very early in life. Furthermore, additional risk factors seem likely to operate at different ages, and are under the influence of the staging into puberty. A better understanding of diabetes susceptibility, the age at which it is acquired, and the causal biological processes are fundamental to enable better prevention and management. The EarlyBird study is an observational study initiated in 2000 in order to investigate the childhood origins of diabetes. The study is based on a cohort of 347 children monitored from age 5 to 16.

Methods: The cohort was recruited from Plymouth primary schools, and children have been followed at 6- and 12-month intervals for various parameters, including anthropometric measures, health updates, body composition and clinical measures. Shotgun lipidomic and 1H nuclear magnetic resonance based metabonomic analyses were conducted on sera collected from 40 subjects from age 5 to 14. The 40 subjects were selected based on the evolution of HOMA-IR levels during childhood to span a wide range of levels of insulin resistance.

Results: The age was reflected via temporal changes in serum lipidome and metabonome, including lipids (lipoproteins, triacylglycerols, diacylglycerols, phospholipids), and organic acids (amino acids, lactate, acetate, etc…). For instance, branched chain amino acid showed peculiar oscillatory patterns overtime, with compound specific variations in the pubertal period. Integration of omics data with HOMA-IR and age revealed a significant interaction with branched chain amino acids and lipid composition (VLDL and triglycerides). In future, biological interpretation of these metabolite and lipid patterns will help in generating novel insights into how the maturation of biological processes may influence the systemic metabolic phenotype. For instance, age and pubertal changes are known to have a profound impact on substrate preference and utilisation, a complex process that can be reflected in the compensatory gluconeogenetic pathways.

Conclusion: Application of metabonomics to serum profiling enables the study of metabolism in a longitudinal fashion and may in the future allow the forecasting of metabolic events associated to changes in metabolic and nutritional requirements of infants during childhood.

Disclosure of Interest: I. Montoliu Employee of: Work for Nestec Ltd. part of the Nestlé Food and Beverage Company., O. Cominetti Employee of: Work for nestle institute of health sciences, part of the Nestlé Food and Beverage Company., J. Hosking: None Declared, A. Jeffery: None Declared, L. Da Silva Employee of: Work for nestle institute of health sciences, part of the Nestlé Food and Beverage Company., S. Collino Employee of: Work for nestle institute of health sciences, part of the Nestlé Food and Beverage Company., F. Beguelin Employee of: Work for nestle institute of health sciences, part of the Nestlé Food and Beverage Company., M. Scherer Employee of: ABF GmbH, Germany, J. Pinkney: None Declared, L. Voss: None Declared, T. Wilkin: None Declared, F.-P. Martin
Employee of: Work for nestle institute of health sciences, part of the Nestlé Food and Beverage Company.
**Objective & Study:** Human milk contains all the nutrients necessary to support infant growth and development, including a rich repertoire of human milk oligosaccharides (HMOs). In contrast, only trace amounts of oligosaccharides are present in mature bovine milk and in milk-based infant formula. Several potential health benefits of HMOs have been studied and postulated over the years including prebiotic properties and prevention of certain infections. On the other hand some studies show an association of breast feeding with higher cognitive development than infant formula feeding. Since 2’FL is the most abundant oligosaccharide in breast milk, we decided to explore its effect in an animal model of learning and memory processes. **Objective:** To study the potential effect of dietary supplementation with 2’FL in learning and memory skills in mice using the Intellicages® system for behavioral assessment. **Methods:** 2.5 month-old male C57BL/6 mice were used. Animals were divided in 2 experimental groups (n=28), fed on control AIN-93M rodent diet with or without 2’FL (350mg 2’FL/day/kg B.W.). After a period of 7 days on the diets the mice were evaluated for spatial and working memory, and operant conditioning paradigms using the Intellicage® system. **Results:** Mice fed on 2’FL showed faster spatial learning skills with respect to the control group (61 vs. 51.2 percent of correct visits, p=0.0024). There was also a modest but significant improvement of working memory in the 2’FL group compared to control (32.5 vs. 30.3 percent of correct visits, p=0.0143). For operant conditioning, a higher proportion of mice fed on the 2’FL diet reached the criterion 8X during early learning sessions on the first day compared to control animals (60.71% vs. 28.57%, p=0.0156). The operant conditioning paradigm was repeated after a washout period. Interestingly, the difference in the performance between 2’FL and control groups was dramatically improved with regard to the first test (85.71% of animals reached the criteria vs 14.3%, p<0.0001). **Conclusion:** Our results demonstrate dietary supplementation with 2’FL for one week enhances learning and memory abilities in mice and thus, its consumption may confer cognitive advantages. **Disclosure of Interest:** None Declared
**Nutrition**

**Observational and Epidemiological Studies**

PD-N-0133

**BELGIAN SPORTING ADOLESCENTS DRINK MORE ALCOHOL THAN NON-SPORTING.**

Thierry Devreker 1,*, Tine Decraene 2, Yvan Vandenplas 1

1Paediatric Gastro-enterology, 2Universitair Kinderziekenhuis Brussel, Brussel, Belgium

**Objectives & Study:** Intuitively we associate sport with health and performance and expect a healthy lifestyle. Sport participation can improve motor skills, physical and mental health, and psychosocial development. Since binge drinking in adolescents is a recent phenomenon, we looked at alcohol consumption in non-sporting and sporting adolescents.

**Methods:** 650 questionnaires asking for information on drinking habits and lifestyle were sent to schools, sport clubs and youth organizations. 476/513 received questionnaires could be included: 269 (56.5%) girls and 207 (43.5%) boys. Age distribution was 146 (30.7%) 12-14 years, 199 (41.8%) 14-16 years and 131 (27.5%) 16-18 years. Our population included 123 (25.8%) non sporters and 353 (74.2%) sporters of which 172 recreational, 158 competition and 23 topsporters. In order to allow comparison, every alcohol use was expressed as a mean standard glass alcohol per day (sga/d).

**Results:** 158 (76.3%) boys and 201 (74.7%) girls consumed once alcohol. Alcohol use between 12 and 14 years is 0.09 sga/d for sporters and 0.08 sga/d for non sporters (NS); between 14 and 16 years we found 0.36 sga/d for sporters and 0.2 sga/d for non sporters (p<0.05) and between 16 and 18 years 0.93 sga/d for sporters and 0.34 sga/d for non sporters (p<0.05). There was no gender difference. The purpose and intensity of sport influences the drinking habits. Topsporters drink less alcohol than the others. 12-14 and 14-16 year old competition sporters drink more than recreational sporters: 12-14 y: 0.31 sga/d competition and 0.21 sga/d recreation (p<0.05) and for the age group 14 -16 years: 1.73 competition and 1.14 sga/d recreation (p<0.05). Inversely, between 16 and 18 years we found a huge increase in alcohol use in recreational sporters (3.99 sga/d) compared to competition sporter (0.99 sga/d) (p<0.01).

**Conclusion:** Organized sport participation is associated with a higher alcohol use of adolescents. This finding was identical in boys and girls. In the 12-16 year old group, the intensity of sport performance is positively related to the alcohol consumption. Alcohol abuse in the 16-18 year group participating in recreational sport becomes a real health hazard. These findings suggest that preventive measurements are warranted.

**Disclosure of Interest:** None Declared
THE REASON FOR PREMATURE BIRTH MAY INFLUENCE HUMAN MILK FEEDING IN VERY LOW BIRTH WEIGHT (VLBW) INFANTS

Harold R Bigger 1,* , Aloka Patel 1, 1 , Janet L Engstrom 1 , Paula P Meier 1

1Rush University Medical Center, Chicago, United States

Objectives & Study: Human milk (HM) feeding is influenced by social and environmental factors in the Neonatal Intensive Care Unit (NICU) but little has been studied about the influence of the medical reason for prematurity on HM feedings in VLBW infants. The study examined the cumulative proportion of HM received by VLBW infants during the NICU hospitalization, and at days 1-14 and 1-28 relative to the reason for prematurity.

Methods: Two hundred eighty-five VLBW infants who ever received HM out of 291 infants enrolled in an ongoing larger study of HM feeding during 2008-2012 were examined. Daily volumes (mLs) of HM and non-HM feeding were measured. Donor human milk was not used in this cohort. The cumulative proportion of HM to enteral feedings were calculated as mL HM/total mL enteral intake x 100 for the NICU hospitalization, days 1-14, and days 1-28. Because multiple reasons may be associated with each premature birth, infants were assigned to a single hierarchical category based on maternal data from the medical record. This hierarchy is maintained in the order of reasons for prematurity presented in the table.

Results: The median cumulative proportions of HM to enteral feedings for each reason for prematurity category are summarized in the table for the three time periods. Only during days 1-14 were there differences in HM intake based on reason for prematurity (Kruskal-Wallis test, p=0.003). In this time period only pre-eclampsia/eclampsia showed a lower proportion of HM intake (Mann-Whitney test, p=0.000).

<table>
<thead>
<tr>
<th>Reason for prematurity</th>
<th>n (%)</th>
<th>Cumulative Proportion of HM median (IQR)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>days 1-14</td>
</tr>
<tr>
<td>chorioamnionitis</td>
<td>52 (18.2%)</td>
<td>1.00 (1.00-1.00)</td>
</tr>
<tr>
<td>preterm labor</td>
<td>78 (27.4%)</td>
<td>1.00 (0.93-1.00)</td>
</tr>
<tr>
<td>premature rupture of membranes</td>
<td>32 (11.2%)</td>
<td>1.00 (0.77-1.00)</td>
</tr>
<tr>
<td>pre-eclampsia/eclampsia</td>
<td>72 (25.3%)</td>
<td>0.95 (0.40-1.00)</td>
</tr>
<tr>
<td>placental/cord problems</td>
<td>21 (7.4%)</td>
<td>1.00 (0.84-1.00)</td>
</tr>
<tr>
<td>fetal factors</td>
<td>18 (6.3%)</td>
<td>1.00 (0.99-1.00)</td>
</tr>
<tr>
<td>maternal factors</td>
<td>12 (4.2%)</td>
<td>1.00 (0.15-1.00)</td>
</tr>
<tr>
<td>total</td>
<td>285 (100%)</td>
<td>1.00 (0.84-1.00)</td>
</tr>
</tbody>
</table>

* 15 infants were discharged prior to 28 days, 7 of whom were in the pre-eclampsia/eclampsia group.

Conclusion: VLBW infants who were delivered because of pre-eclampsia/eclampsia received a lower proportion of HM than other VLBW infants during the critical first 14 days of life. This difference was no longer present by the time of discharge. The reasons underlying this disparity require further investigation to develop interventions for these mothers who comprise a significant proportion of women who deliver preterm.

Role and Mechanism of Action of 5-Hydroxytryptamine and Its Effects on Esophageal Smooth Muscle Motility in Rats

Mizu Jiang, Ting Zhang, Xiaoli Shu, Weizhong Gu, Xi Yang, Xia Yang

Gastroenterology, Children’s Hospital, Zhejiang University School of Medicine, Hangzhou, China

Objectives & Study: Gastroesophageal reflux diseases (GERD) are believed to be motility disorders, but their pathogenesis has not been clarified. The aim of this study was to explore the role and mechanism of action of 5-hydroxytryptamine (serotonin, 5-HT) in terms of esophageal smooth muscle motility in rats.

Methods: The effects of 5-HT, a 5-HT reuptake inhibitor (citalopram), and a 5-HT4 receptor (5-HT4R) antagonist (GR113808) on the tunica muscularis of the esophageal mucosa and the lower esophageal sphincter (LES) were studied in a standard organ chamber. The esophageal smooth muscle cells (ESMC) were cultured, loaded with a specific Ca2+ fluorescence indicator, Fluo-3/AM, and examined using laser confocal microscopy. The effect of 5-HT on the intracellular free Ca2+ concentration was measured by fluorescent intensity (FI), and the changes were observed after incubation with GR13808, the PKA inhibitor H-89, and the L-type calcium channel blocker verapamil hydrochloride after the removal of extracellular Ca2+.

Results: The cumulative addition of 5-HT produced a concentration-dependent relaxant role for the pre-contraction of the tunica muscularis of esophageal mucosa, but the relaxant role was significantly decreased when GR113808 was added (P<0.05). The cumulative addition of 5-HT stimulated concentration-dependent contractions of LES, and the effects were significantly decreased when GR113808 was added (P<0.05). Citalopram caused contraction of the tunica muscularis of esophageal mucosa and the LES at a concentration of 0.1 mM. 5-HT was observed to increase the ESMC intracellular free Ca2+ concentration. The effect was effectively inhibited by incubation with GR113808, H-89, and verapamil hydrochloride after removal of the extracellular Ca2+.

Conclusion: 5-HT had a relaxant effect on the tunica muscularis of the esophageal mucosa and caused contraction of the LES strips in vitro by acting on the 5-HT4R. 5-HT can increase the intracellular free Ca2+ concentration of esophageal smooth muscle cells by acting on the 5-HT4R.

Disclosure of Interest: None Declared
FURTHER PROGRESS IN THE UNDERSTANDING OF CONGENITAL TUFTING ENTEROPATHY

Julie Salomon 1,2,* , Danielle Canioni 3, Julie Lemaire 4, Florence Campeotto 1, Jerome Viala 5, Marc Bellaiche 5, Jeremy Magescas 2, Nicole Brousse 3, Francoise Poirier 2, Benoit Ladoux 2, Olivier Goulet 1, Delphine Delacour 2

1Gastropediatry, Necker, Sorbonne Paris Cité, Paris, France, 2CNRS, IJM, 3Pathology, Necker, Sorbonne Paris Cité, Paris, France, 4Gastropediatry, Trousseau, 5Gastropediatry, Robert Debré, Paris, France

Objectives & Study: EPCAM and SPINT2 mutations results in Congenital Tufting Enteropathy (CTE), which pathophysiology remains unknown. We aimed at understanding the respective roles of the proteins encoded by EPCAM and SPINT2 in enterocytes, and at characterizing the impact of their loss of function on intestinal morphogenesis and homeostasis.

Methods: We have initiated a study on intestinal biopsies of patients (n=22) and on cellular models. CTE duodenal biopsies have been analyzed according to the patient’s genotype (n=7 EPCAM and n=7 SPINT2) and compared to control biopsies (n=8). We performed ultrastructural analyses using transmission electron microscopy, as well as analyses of cell differentiation and polarization protein markers, using confocal microscopy. Stable depletions of EpCAM and SPINT2 have been conducted following a lentiviral shRNA strategy on Caco2 cells, and knockdown clones have been analyzed in classical 2D cultures. In parallel, we developed 3D enterocyte cultures on synthetic villi using soft lithography techniques. The geometry of this support recapitulates the villous topology and constrains.

Results: In both tissue and cultured cells, EpCAM and SPINT2 differently interact with adhesive structures and cytoskeletal networks. Confocal analyses of CTE biopsies showed specific mislocalization of brush border, terminal web hallmarks, and components of cell adhesion complexes; no effect on extracellular matrix was noticed. Ultrastructural study revealed microvillus “tufting” and atrophy, absence of a terminal web area, aberrant desmosomes and cell-cell contacts. Both EPCAM and SPINT2 depleted cells display striking mistargeting of tight junctions, brush border components and polarity organizers along basolateral membranes. Such loss of enterocyte organization lead to aberrant monolayer homeostasis on 2D cultures as well as on synthetic villi, mimicking tissue defects observed in CTE biopsies. Cell-cell contacts were more affected in EPCAM mutated enterocytes, whereas cell-extracellular matrix contacts, unusual intracellular vacuoles and supranumerous centrioles were specifically observed in SPINT2 mutated enterocytes.

Conclusion: The parallel characterization of CTE patients and of cultured enterocytes demonstrate that EpCAM and SPINT2 are new key players in enterocyte’s organization. The different but overlapping panels of cellular abnormalities suggest that EpCAM and SPINT2 belong to distinct pathways both regulating cell adhesion and cytoskeleton dynamics. Their inactivation deeply disrupts establishment and maintenance of intestinal epithelium morphology leading to CTE phenotype.

Disclosure of Interest: None Declared
HEALTH-RELATED QUALITY OF LIFE ASSESSMENTS IN ADOLESCENTS WITH SCREENING-DETECTED COELIAC DISEASE: BEFORE DIAGNOSIS AND AFTER ONE YEAR WITH GLUTEN-FREE DIET

Anna Myléus 1,*, Solveig Petersen 1,2, Annelie Carlsson 3, Solveig Hammaroth 4, Lotta Högberg 5, Katrina Nordyke 1, Hans Stenlund 1, Anneli Ivarsson 1

1Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå, Sweden 2Clinical Sciences, Child and Adolescent Psychiatry, Umeå, Sweden, 3Paediatrics, Clinical Sciences, Lund, Sweden, 4Paediatric Clinic, Norrtälje Hospital, Norrtälje, Sweden, 5Clinical and Experimental Medicine, Division of Paediatrics, Linköping, Sweden

Objectives & Study: To investigate if adolescents diagnosed with celiac disease (CD) through screening are affected by the diagnosis and treatment (gluten-free diet, GFD), we assessed their health-related quality of life (HRQoL) before diagnosis and after one year, as compared to the HRQoL development in their peers without CD.

Methods: A prospective nested case-referent study emanating from a school-based multicenter screening study (ETICS- Exploring the Iceberg of Celiacs in Sweden) conducted among Swedish 12-year-olds. The screening study has previously been described in detail (Myléus et al, 2009). Participants provided blood samples for analyses of CD serological markers and alongside completed a questionnaire. One year later, the questionnaire was repeated by the adolescents with screening-detected biopsy-verified CD (n=111; 58 girls) and referents without CD (n=507; 298 girls). HRQoL was measured using Kidscreen, a validated generic self-report instrument with 52 items. Scores were linearly transformed into a 0-100 scale with higher values indicating better HRQoL. Mean values with standard deviations (mean±SD) were compared before and after (Wilcoxon signed rank test), as well as between cases and referents at each time point (Mann-Whitney U test).

Results: Before diagnosis, the adolescents with screening-detected CD had similar HRQoL as their peers without CD (84.2±9.1 vs. 82.0±10.9; P=0.11). One year later, HRQoL had decreased in all adolescents, but the decrease was more pronounced among those without CD. At follow-up, adolescents with screening-detected CD treated with GFD reported better HRQoL than their peers (82.5±11.7 vs. 79.6±12.2; P=0.024). Stratification by sex showed similar results.

Conclusion: Our findings suggest that adolescents with screening-detected CD can benefit from diagnosis and treatment with GDF although they did not report worse HRQoL than their peers prior to knowledge of their disease. When moving into adolescence the HRQoL declines, as previously shown by others.


Disclosure of Interest: None Declared
CLINICAL PRESENTATION OF COELIAC DISEASE IS NO LONGER CHANGING IN FINLAND

Laura Kivelä 1,*, Katri Kaukinen 2, Markku Mäki 1, Kalle Kurppa 1
1Centre for Child Health Research, 2 Department of Gastroenterology and Alimentary Tract Surgery, Tampere University and University Hospital, Tampere, Finland

Objectives & Study: Recent decades have witnessed major changes in the presentation of celiac disease, as the incidence and age at diagnosis have increased and different atypical symptoms have become more common. Interestingly, similar changes have been recognized also in some other autoimmune diseases. However, latest evidence suggests that in certain Western countries changes in for example incidences of type 1 diabetes and Crohn’s disease may have reached a plateau. Accordingly, we hypothesized that in a developed country with high prevalence the presentation of celiac disease is no more changing.

Methods: Altogether 353 children with celiac disease from the early 1960s to the present were collected from our patient series and extensive demographic, clinical, serologic and histological data and the prevalence of associated diseases were analyzed.

Results: The median age at diagnosis was approximately 4 yr before the 1980s but has remained steadily higher (8-10 yr) since. Before the 21st century the main clinical presentation was predominantly (56-67%) gastrointestinal; thereafter this proportion decreased rapidly and has remained stable (44-49%) since. At the same time the percentage of screening-detected patients increased from <5% to 28-36%. Diarrhea and vomiting became rarer after the 1990s (from 50-62% to 26-29%; from 18-21% to <5%, respectively); simultaneously the prevalence of stomach pains and constipation increased from 30-33% to 49-57% and from <5% to 10-14%, respectively. Poor growth was common (69%) before the 1980s; subsequently it has remained less frequent (23-36%). Previously common (43-62%) total villous atrophy in biopsy was present only in a minority (22-27%) of children after the 1980s. There has been no systematic change in the gender distribution, the prevalence of anemia or mean hemoglobin values after the 1960s. Previously rare (2%) concomitant type 1 diabetes has become more common (6-10%) since the 1980s, while the prevalence of concomitant thyroid disease has gradually declined from 6% to 1%.

Conclusion: Most of the clinical, serological and histological variables in celiac disease changed considerably during the 1980s-1990s. In contrast, and in accord with some other autoimmune diseases, there have been no marked changes during the last decade. The results are not explained solely by changes in the diagnostics, suggesting that environmental factors contribute to this phenomenon.

Disclosure of Interest: None Declared
IS THERE AN INCREASED INCIDENCE OF COELIAC DISEASE IN CYSTIC FIBROSIS?
Ilse Julia Broekaert 1*, Silke van Koningsbruggen-Rietschel 1, Stela Radojska 2, Birgit Gathof 2, Ernst Rietschel 1
1 CF Center, University Children’s Hospital, 2 Transfusion Medicine, University Hospital of Cologne, Cologne, Germany

Objectives & Study: Both celiac disease (CD) and cystic fibrosis (CF) show symptoms of intestinal malabsorption and clinical symptoms may be masked by CF. The coexistence of CD and CF has been reported and an increased incidence of CD in CF has been suggested. The objective was to determine whether there is an increased incidence of celiac disease and propose possible risk factors for the predisposition of CD in CF.

Methods: In 129 CF patients at the Cystic Fibrosis Center Cologne, Germany, celiac serology and HLA-DQ2 and –DQ8 screening was performed. Tissue transglutaminase (tTG), antiendomysial antibodies (EMA) and deaminated gliadine peptide (DGP) were analyzed using ELISA (tTG, DGP) and indirect immunofluorescence (EMA). HLA typing was performed by PCR using sequence specific primers. Informed consent was obtained by all patients or care-givers respectively. 6 patients below the age of 2 years were excluded for further analysis because of lack of sensitivity of celiac serology.

Results: In 123 CF patients 9 showed elevated celiac serology, 2 were diagnosed with celiac disease (cf. table). Both patients were heterozygous for HLA-DQ2 and pancreatic insufficient, as 92% of our tested CF patients. 44 (36%) carried HLA-DQ2, 24 (20%) HLA-DQ8. 58 (47%) carried neither HLA-DQ2 nor –DQ8. In the German population the prevalence of HLA-DQ2 is approximately 32% and HLA-DQ8 17% (www.allelefrequencies.net).

<table>
<thead>
<tr>
<th>Patient</th>
<th>CF-genotype</th>
<th>pancreatic status</th>
<th>tTG-IgA (&lt;20 RU/ml)</th>
<th>EMA-IgA (&lt;1:10)</th>
<th>DGP-IgA (&lt;25 RU/ml)</th>
<th>DGP-IgG (&lt;25 RU/ml)</th>
<th>Marsh classification</th>
<th>HLA-DQ2</th>
<th>HLA-DQ8</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F508del/W1282X</td>
<td>PI</td>
<td>&gt;200</td>
<td>&gt;200</td>
<td>&gt;200</td>
<td>IIIa</td>
<td>positive</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>F508del/F508del</td>
<td>PI</td>
<td>&gt;20000</td>
<td>1:10240</td>
<td>58</td>
<td>54</td>
<td>-</td>
<td>positive</td>
<td>negative</td>
</tr>
<tr>
<td>3</td>
<td>F508del/F508del</td>
<td>PI</td>
<td>44</td>
<td>1:10</td>
<td>41</td>
<td>57</td>
<td>0</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>F508del/IVS12+1G&gt;C</td>
<td>PI</td>
<td>44</td>
<td>1:10</td>
<td>negative</td>
<td>negative</td>
<td>0</td>
<td>negative</td>
<td>positive</td>
</tr>
<tr>
<td>5</td>
<td>F508del/3849+10kBC&gt;T</td>
<td>PS</td>
<td>80</td>
<td>negative</td>
<td>negative</td>
<td>negative</td>
<td>-</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>F508del/F508del</td>
<td>PI</td>
<td>negative</td>
<td>negative</td>
<td>33</td>
<td>negative</td>
<td>-</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F508del/F508del</td>
<td>PI</td>
<td>negative</td>
<td>negative</td>
<td>55</td>
<td>negative</td>
<td>-</td>
<td>positive</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>N1303K/Q220X</td>
<td>PI</td>
<td>negative</td>
<td>negative</td>
<td>33</td>
<td>negative</td>
<td>-</td>
<td>negative</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>PI</td>
<td>118</td>
<td>1:20</td>
<td>30</td>
<td>44</td>
<td>-</td>
<td>negative</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: We could show a high prevalence of elevated celiac serology in CF patients. 2 patients (1.5%) had CD (both HLA-DQ2 and high tTG-IgA or positive histology) whereas the general prevalence of CD in Germany is about 0.7%. HLA-DQ2–DQ8-typing was very useful to discriminate CD patients from only elevated celiac serology. Mechanisms for elevated celiac serology could be intestinal inflammation which may enhance the development of CD. Pancreatic insufficiency may be a risk factor for celiac disease increasing intestinal antigenic load. All CF-patients who carry either HLA-DQ2 or –DQ8 will be followed up with celiac serology testing on a regular basis.

Disclosure of Interest: None Declared
EVALUATION OF PRO/ANTIINFLAMMATORY MARKERS IN PATIENTS WITH FOOD ALLERGY BEFORE AND AFTER TREATMENT

Manolya Kara Acar 1, Omer Faruk Beser 2*, Dildar Konukoglu 3, Haluk Cokugras 4, Tulay Erkan 2, Tufan Kutlu 2, Fügenc Cullu Cokugras 2

1Department of Paediatrics, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey
2Paediatric Gastroenterology, Hepatology and Nutrition, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey
3Department of Medical Biochemistry, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey
4Paediatric Allergy, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey

Objectives & Study: Inflammation has an important role in the pathogenesis of food allergy (FA). In order to show the relationship between inflammation and FA and whether these markers can be used in the diagnosis and clinical follow up, we evaluated serum TNF-α, IL-6 and fecal calprotectin (FC) levels before and after treatment.

Methods: Sixty new patients between the age of 0-36 months were included in study. Thirty-seven of them were either f1 (egg white specific IgE) or f2 (milk specific IgE) positive and were diagnosed as IgE mediated FA. Specific IgE levels were found to be negative in 23 of patients, whom had clinical symptoms such as urticaria, vomiting, diarrhea or bloody stool after having suspected food and symptoms had disappeared after cessation. They were diagnosed as non IgE mediated FA. Twenty-four healthy children between the age of 0-36 months with no known allergic or gastrointestinal disorders were included in control group. Blood and fecal samples were taken within the infection free period. Complete blood count, total IgE, serum TNF-α, IL-6 and FC levels were evaluated in both patient and control group. Serum TNF-α, IL-6 and FC levels were reassessed four weeks after treatment in the patient group.

Results: Fecal calprotectin levels were found to be significantly higher in the patients group before treatment (602.10±538.07μg/g) when compared to control subjects (399.21±267.08 μg/g), (p=0.024). In IgE mediated FA group serum IL-6 levels before treatment (21.81±25.35 pg/mL) was higher than IL-6 levels of non IgE mediated FA. Specific IgE levels were found to be negative in 23 of patients, whom had clinical symptoms such as urticaria, vomiting, diarrhea or bloody stool after having suspected food and symptoms had disappeared after cessation. They were diagnosed as non IgE mediated FA. Twenty-four healthy children between the age of 0-36 months with no known allergic or gastrointestinal disorders were included in control group. Blood and fecal samples were taken within the infection free period. Complete blood count, total IgE, serum TNF-α, IL-6 and FC levels were evaluated in both patient and control group. Serum TNF-α, IL-6 and FC levels were reassessed four weeks after treatment in the patient group.

Conclusion: Serum TNF-α, IL-6 and FC levels decreased significantly in patients after treatment. It shows us the role of inflammation in the pathogenesis of FA. Especially FC can be used as a non invasive marker in the follow up of patients with FA.

Disclosure of Interest: None Declared
TRANSGLUTAMINASE EXPRESSION AND COELIAC ANTIBODIES IN THE PANCREAS IN DIABETES MELLITUS

Ilma Rita Korponay-Szabo 1,2,*, Maarit Oikarinen 3, Jutta E Laiho 3, Kaija Laurila 4, Markku Mäki 4, Heikki Hyöty 3 and The nPOD Study Group

1Paediatrics, University of Debrecen, Debrecen, Hungary, 2Tampere Center for Child Health Research, Tampere, Finland, 3Virology, University of Tampere, Tampere, Finland, 4Tampere Center for Child Health Research, University of Tampere Medical School, Tampere, Finland

Objectives & Study: Coeliac disease and type-1 diabetes (T1DM) are often co-existing and share common genetic background. However, it is still a question whether coeliac disease can directly induce damage of the pancreas leading to endocrine insufficiency. The aim of this study was to investigate if pancreas tissue is an autoantigenic target for coeliac anti-transglutaminase (TG2) antibodies in vivo and whether the development of T1DM has temporal relationship with anti-TG2 antibody production in clinical cohorts.

Methods: Frozen pancreas and full thickness duodenum tissue specimens from cadaveric organ donors with T1DM (n=22), diabetes antibody positive subjects (n=11) and non-diabetic controls (n=21) were obtained through the Network of Pancreatic Organ Donors with Diabetes. The tissues were investigated for transglutaminase and glucagon expression, in vivo-bound celiac disease-related IgA antibodies, CD3 and gamma-delta T cell counts by immunohistochemistry in a blinded fashion without knowledge of the clinical details. In an independent cohort of 1354 childhood T1DM cases anti-TG2 and endomysial antibody (EMA) screening was performed to detect undiagnosed coeliac disease. Clinical T1DM diagnoses following the diagnosis and treatment of coeliac disease were evaluated in a prospective cohort of 5040 coeliac disease cases followed up serologically for 1-32 years after the prescription of a gluten-free diet.

Results: IgA class coeliac antibodies bound to TG2 were detected around the islets and the acinar structures in 5 of the diabetic pancreas specimens and in the corresponding duodenum samples within the mucosa and in the gut wall muscular layer endomysium. All control pancreas samples were negative for IgA deposition. One non-diabetic donor had slight endomysial positivity in the gut wall but no IgA in the pancreas. The frequency of serum anti-TG2 and EMA positivity was 227/1354 (16.8%) in patients first diagnosed with T1DM. Subsequent T1DM developed in 10/5040 (0.19%, p<0.001) coeliac cases, but only 4 of these were properly treated for >6 months and had lasting seronegativity on a gluten-free diet.

Conclusion: Pancreas tissues express the transglutaminase 2 autoantigen important for coeliac disease pathology. Celiac antibodies bound to the pancreas may initiate inflammation and tissue damage leading to diabetes. Clinical data indicate that diabetes is developing during the time when coeliac anti-TG2 antibodies are actively produced, and thus a fraction of T1DM cases may be preventable by screening and treatment for coeliac disease at an early age.

The authors thank the paediatric gastroenterology and diabetes outpatient departments in Hungarian county hospitals for participating in the coeliac disease registry and diabetes screening.

Disclosure of Interest: None Declared
Objectives & Study: Etiologies of recurrent pancreatitis in children include anatomical anomalies, hereditary, metabolic and autoimmune disorders. A significant number of patients remain with a diagnosis of idiopathic pancreatitis. The advent of genetic analysis and electrophysiologic testing may further assist in the diagnostic process. Evidence has shown that specific genetic mutations in the cationic trypsinogen gene PRSS1, SPINK1, CTRC and CFTR genes cause pancreatitis. The aim was to present the work-up of children with recurrent pancreatitis (at least 2 episodes) referred for genetic analysis and electrophysiologic testing.

Methods: Children with recurrent, acute pancreatitis with no known etiology were referred to the Electrophysiology Laboratory, Division of Pediatric GI at Hadassah University Hospital for genetic testing as well as evaluation of CFTR function by Nasal Potential Difference (NPD) testing.

Results: 39 children with recurrent pancreatitis who had normal imaging studies, fasting lipids and IgG4 were evaluated. The mean age was 11±5 years (range 1.5-18 yrs), 82% were Jewish, 18% Arab. 8 (20%) patients carried PRSS1 gene mutation (K23R(5), R112H(2) and D21A(1)). 1 patient had K172E/-(CTRC) mutation, 1 had I42M(SPINK1)/V235I(CTRC) together with ∆F508/5T, 1 patient had R67H(SPINK1)/V235I(CTRC) and 1 patient was homozygote for R67H (SPINK1). 4 patients out of 39 submitted for CFTR gene testing showed mutations (∆F508/L997F, ∆F508/5T, W1282/5T(12TG) and L997F/-). 33 (85%) patients underwent sweat testing; 1 patient had >60 mmol/L with no CFTR mutation found. 31 (79%) patients had NPD testing, 2 (5%) with abnormal results.

Conclusion: This is the first study on recurrent pancreatitis in Israeli children examining both the presence of susceptibility gene mutations for pancreatitis and CFTR dysfunction. 28% of children with recurrent pancreatitis carry mutations for Hereditary Pancreatitis including rare mutations (K23R) and 5% with evidence of CFTR dysfunction showing the importance of genetic and functional work up of these children.

Disclosure of Interest: None Declared
International Prospective Study of Distal Intestinal Obstruction Syndrome (DIOS)

Michael Wilschanski, Vincenzina Lucidi, Natalia Kashirskaya, Helmut Ellemunter, Maria Fotoulaki, Roderick Houwen, Eddy Robberecht, Anne Munck and DIOS Research Group

Objectives & Study: DIOS is a unique intestinal complication of CF characterized by complete or incomplete intestinal obstruction by viscid faecal material in the terminal ileum and proximal colon. An increase in incidence has been noted and this is the first multinational prospective study on the natural history of DIOS.

Methods: 28 Centers in 10 countries reported new cases of DIOS in children from 2009-2012 in a study organized by the CF ESPGHAN Working Group. DIOS classification was based on the ESPGHAN CF Working Group Criteria. Each new case was reported and sent to the coordinating center in Paris (Ethical approval was obtained in each country)

Results: 102 cases were reported, 60% were males; age was 14.4 [6.5-23.5] years. The patients were divided into 2 groups: complete obstruction (A) and incomplete obstruction (B). There was no difference in age, genotype, CF liver disease, or chronic Pseudomonas infection. 54% had a previous episode of DIOS.

<table>
<thead>
<tr>
<th>DIOS</th>
<th>Complete obstruction (A)</th>
<th>Incomplete obstruction (B)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients %</td>
<td>45</td>
<td>55</td>
</tr>
<tr>
<td>Meconium ileus %</td>
<td>48</td>
<td>33</td>
</tr>
<tr>
<td>Pancreatic insufficient %</td>
<td>96</td>
<td>89</td>
</tr>
<tr>
<td>Constipation%</td>
<td>26</td>
<td>51</td>
</tr>
<tr>
<td>Hospitalisation duration, days</td>
<td>5 [3-7]</td>
<td>3[1-4]</td>
</tr>
</tbody>
</table>

BMI mean (SD) was 20.1 (2.2), half the patients had mild wt loss, anorexia in 63%, only A had vomiting. Outdoor temperature was >20° in 52%. Only 2% and 9% patients respectively were on a high fiber or high fat diet. Poor compliance with enzymes was uncommon and over half the patients were on PPI. All A required IV hydration, non-opioid (85%) or opioid (17%) relief, 87% Gastrografin enema or polyethylene glycol (PEG) lavage, 4% required a colonoscopy and 9% surgery in 2 centers only; and B mostly received IV hydration (97%) and non opioid pain relief (55%) and 58% Gastrografin enema or PEG lavage. Overall 84 % were prescribed maintenance therapy.

Conclusion: DIOS in children has a multifactorial cause; it may be related to climate but not to compliance.

Disclosure of Interest: None Declared
**Objectives & Study:** Inflammation and angiogenesis play a prominent role in inflammatory bowel disease. Thalidomide, as an inhibitor of inflammation and angiogenesis, is a new potent therapy option for refractory Crohn’s disease (CD).

**Methods:** To evaluate the long-term clinical efficacy and safety of thalidomide therapy in pediatric CD patients who failed to conventional medications or with tuberculosis. We also aim to investigate the effect of oral thalidomide therapy on angiogenesis in pediatric CD patients.

**Results:** A total of 17 patients (9 boys and 8 girls) aged 11.8±5.2 years with refractory CD diagnosed at the mean age of 10.2±4.3 years were included in this study. Patients administered thalidomide (2mg/kg/d) orally at baseline. The clinical activity of disease was assessed by Pediatric Crohn’s Disease Activity Index (PCDAI) at baseline and at 1, 3, 6, 12 months. Weight gain, laboratory evaluations and corticosteroids reduction were also used to assess clinical response. Adverse effects were recorded at each visit. In addition, colonoscopy examination after treatment was performed in 10 patients during this study. Vascular endothelial growth factor (VEGF) and CD31 for microvessel density were measured by immunohistochemistry in the pre-treatment, post-treatment and control groups. The intestinal mucosa of VEGF protein level was also evaluated by western blot.

**Conclusion:** All 15 patients completed 12 months follow-up. Mean PCDAI was 41.0±11.9 at baseline, the values at 1, 3, 6 and 12 months decreased to 15.2±9.6, 5.3±5.0, 3±3.4 and 2.3±2.6, respectively. Eleven of 12 patients who were received corticosteroids discontinued them at 12 months. The mean period was 3.1±1.5months. ESR and CRP, PLT levels decreased after thalidomide treatment, and there was an increment in hemoglobin level. All patients had significant weight gain and the mean increment was 11.6±6.4kg. Three patients occurred in fatigue and 2 in drowsiness. One patient presented transient liver function abnormality. Immunohistochemical expression of VEGF and CD31 in refractory CD patients was higher than those in the control group, while they were significantly reduced after thalidomide therapy. The VEGF levels in intestinal mucosa were down-regulated in post-treatment group compared with pre-treatment group.

**References:** Thalidomide long-term treatment appears to be clinically effective and well tolerated. It is a relatively safe drug to refractory Crohn’s disease patients and those with tuberculosis in children. Mechanisms of thalidomide success in CD might be associated with inhibition of angiogenesis, and mediated by suppression of VEGF expression in mucosa.

**Disclosure of Interest:** None Declared
COMPARATIVE EFFICACY OF PROBIOTICS FOR TREATMENT OF IRRITABLE BOWEL SYNDROME IN CHILDREN AND ADULTS: A SYSTEMATIC REVIEW AND META-ANALYSIS

Andrea Lo Vecchio 1,*, Eugenia Bruzzese 1, Antonietta Giannattasio 2, Ilaria Liguoro 1, Riccardo Scotto 1, Maria Cristina Fedele 1, Serena Orlando 1, Alfredo Guarino 1

1Department of Translational Medical Science, University of Naples "Federico II", Naples, Italy,
2Medical and Health Sciences Department, University of Molise, Campobasso, Italy

Objectives & Study: Probiotics may have a role in reducing the severity of symptoms in IBS. The objective of the study was to systematically review the evidence on treatment with probiotics in children and adults with IBS, and to perform a meta-analysis of the major clinical outcomes used to compare the effects of probiotic administration in different age ranges.

Methods: Medline and CENTRAL databases were searched for randomized controlled trials on the use of probiotics in children and adults with IBS (defined according to age-specific Rome I, II, III criteria). Trials scoring ≥3 according to the Linde Internal Validity Scale (LIVS) were included in meta-analysis.

Results: Thirty-one trials published from 2005 to 2012 (4 on children and 27 on adults) were included in the qualitative analysis and 23 in the meta-analysis. The major common outcome to both age categories were: presence and frequency of abdominal pain, and abdominal distention. Differently from adults, children treated with probiotics had a significant improvement in severity (SMD -0.25, 95% CI -0.45 to -0.05, p<0.001) and frequency (SMD -1.05, 95% CI -1.44 to -0.66, p<0.001) of abdominal pain. A significant reduction of abdominal distention was observed in adults (SMD -0.21, 95% CI -0.35 to -0.08, p=0.002) and even more in children (SMD -2.15, 95% CI -2.80 to -1.50). Standardized IBS symptoms scores (SMD -0.15, 95% CI -0.92 to 0.62, p=0.70) and quality of life scores (SMD -0.10, 95% CI -0.28 to 0.08, p=0.26) were not significantly affected by probiotic in adult population and data were not available in children.

Conclusion: There is a high heterogeneity among studies largely due to changes in Rome I to III criteria. However, probiotics may reduce IBS-related symptoms, mainly abdominal pain and distention. This effect is stronger in children than in adults.

Disclosure of Interest: None Declared
**Objectives & Study:** New methods for cystic fibrosis (CF) diagnosis and screening are needed to maximize the number of patients receiving early treatment, and to monitor the efficacy of new drugs in clinical trials. Although the labial minor salivary glands (LMSGs) secrete mucus, little is known about LMSGs involvement in CF. The research hypothesis was that the morphology of LMSGs and the mucosa of the lower lip differ in patients with cystic fibrosis (CF) compared to healthy subjects (HS). The aim of the study was to perform comprehensive morphometry of LMSGs and the mucosa of the lower lip in CF patients and HS using optical coherence tomography (OCT), a non-invasive technique enabling micrometer-resolution tissue imaging in vivo.

**Methods:** Eighteen patients with CF (mean age ± SD: 27.1 ± 7.8 years; 14 female, 4 male) and 18 healthy subjects (26.4 ± 2.7 years; 14 female, 4 male) were recruited for the study. Clinical data were gathered through a questionnaire. OCT imaging of the lower lip mucosa and LMSGs was performed. Volumetric datasets covering ~230 mm² field and ~2 mm depth were acquired in all volunteers using a prototype OCT system (~3 seconds per dataset). Twenty morphometric parameters were defined to describe the volume, the surface density, and the reflectivity of LMSGs, as well as the thickness, and the reflectivity of the layers of the mucosa of the lower lip. The data were analyzed manually using Fiji imaging processing package. The Mann-Whitney U test was employed to compare the two groups. The study was approved by the Institutional Review Board at Poznan University of Medical Sciences.

**Results:** The median LMSGs’ surface density in patients with CF was 2.85 glands/cm² (1st-3rd quartile: 2.38-4.11) and 4.63 glands/cm² (3.22-6.04) in HS (p = 0.04). The distribution of values of the remaining 19 morphometric parameters did not differ between CF patients and HS. No relationships between clinical expression of the disease and the morphometric parameters was found.

**Conclusion:** OCT allows for non-invasive in vivo imaging and morphometry of LMSGs and the mucosa of the lower lip. LMSGs’ surface density was lower in patients with CF compared to HS. This observation may point to a previously unknown characteristic of CF and requires further research.

**Disclosure of Interest:** None Declared
TIMP-1 INHIBITS OCCLUDIN DEGRADATION IN CACO-2 CELLS

Amir Bein 1,*, Dror Mandel 2,3, Betty Schwartz 1, Ronit Lubetzky 3,4

1School of Nutritional Sciences, Institute of Biochemistry, Food Science and Nutrition, The Hebrew University of Jerusalem, Rehovot, Israel, 2Neonatology, Tel Aviv Medical Center, Tel Aviv, Israel, 3Sackler School of Medicine, Tel Aviv University, 4Paediatrics, Tel Aviv Medical Center, Tel Aviv, Israel

Objectives & Study: Matrix metalloproteinases (MMPs) are a group of endopeptidases that play a key role in the degradation of the extracellular matrix. The natural inhibitors of MMPs are the tissue inhibitors of metalloproteinases (TIMPs). Changes in the balance between MMPs and TIMPs levels are crucial determinants to pathological processes outcome. We have recently demonstrated that there are differences in the expression of TIMP-1 between preterm and term milk (Lubetzky et al, JPGN, 2010). Occludin is a major tight junction protein that plays a role in maintaining the gut barrier impermeable. One of the pathological manifestations of gastrointestinal inflammatory processes (e.g Necrotizing EnteroColitis (NEC)) is the disarray of tight and adherent junctions. The prevention of Occludin degradation may provide a potential intervention approach to avoid gastrointestinal inflammatory processes in which the gut wall becomes permeable. Thus, we aimed to investigate the potential role of TIMP-1 in the prevention of Occludin degradation in confluent cultures of Caco-2 intestinal human cells (mimicking intestinal epithelium model).

Methods: Cell Culture - Human colon cell line Caco-2 (American Type Culture Collection- ATCC), was cultured in growth medium (DMEM-Sigma Aldrich) supplemented with 20% (v/v) Fetal Bovine Serum (SAFC Biosciences) and Penicillin Streptomycin Nystatin – solution (Biolab-chemicals) 0.2% (v/v). Cells were grown in 37°C humidified atmosphere 95% air and 5% CO2.

TIMP1 experiments - Confluent Caco-2 cells were trypsinized, counted and seeded (3x10^5) in 12 well plates (Nunc A/S). After 48 hrs. cells were washed, the medium was replaced to complete growth medium supplemented with 0.5% (v/v) Fetal Bovine Serum, and cells were treated for 12 hrs. with recombinant TIMP1 (Aviva Systems Biology), at 10, 100 and 200 ng/ml. At the end of the 12 hours treatment, cells were lysed with RIPA lysis buffer or Tri reagent (Sigma) and kept in -80°C until further analysis.

Results: TIMP-1 inhibits MMP-2 activity by up to 43% (at a concentration of 200 ng/ml). This inhibition of activity is associated with the prevention of Occludin degradation in Caco-2 cells. These changes at the protein level were not observed at the mRNA Occludin levels. In addition, TIMP-1 did not affect differentiation of Caco-2 cells and did not trigger apoptosis in these cells.

Conclusion: Our study showed that TIMP-1 retained tight junction integrity by inhibiting MMP-2 activity. Preventing the degradation of structural tight junction proteins such as Occludin by natural components of HM like TIMP-1 might slow or change the course of inflammatory processes, and can provide a possible mechanisms that may explain the protective effect of HM on NEC development.

Disclosure of Interest: A. Bein: None Declared, D. Mandel: None Declared, B. Schwartz: None Declared, R. Lubetzky Grant / Research Support for: ESPGHAN 2011 Paediatric Nutrition Research Award for Young Investigators
ENDOPLASMIC RETICULUM STRESS IS INVOLVED IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE

Enrica Prete 1,*, Anna Negroni 1, Vincenzo Cesi 1, Laura Stronati 1, Salvatore Oliva 2, Marina Aloi 2, Giovanni Di Nardo 2, Salvatore Cucchiara 2

1 Department of Radiobiology and Human Health, ENEA, 2 Paediatric Gastroenterology and Liver Unit, Sapienza University of Rome, Rome, Italy

Objectives & Study: Inflammatory bowel disease (IBD) is a group of chronic inflammatory disorders, including Crohn’s disease (CD) and ulcerative colitis (UC). Although the precise cause of these diseases is still unknown, recent studies link the endoplasmic reticulum (ER) stress to IBD pathogenesis. ER stress is due to the accumulation of misfolded or unfolded proteins in the ER and invokes a biological response called the unfolded protein response (UPR), which is orchestrated by three main proximal effectors: PERK-ATF4, ATF6p90-ATF6p50 and IRE1-XBP1. The aim of the present study is to investigate the activation of UPR in pediatric IBD.

Methods: Inflamed and uninflamed biotic specimens were taken during ileo-colonoscopy from the ileum and/or the colon of 10 patients with CD, 10 with UC and 10 age-matched controls, referred to our Pediatric Gastroenterology Unit. RNA and proteins were extracted and expression levels of the most representative molecules of the three UPR pathways (spliced and unspliced XBP1, IRE, ATF4, PERK, ATF6, PDIA4, EIF2A, HSPA5) were analyzed by real-time PCR and western blot. IL-8 mRNA expression was used as an indicator of tissue inflammation.

Results: HSPA5, PDIA4, spliced and unspliced XBP1 mRNA was significantly increased in inflamed colonic specimens of all patients. The same result was obtained for HSPA5, PDIA4 and pIRE protein expression. No difference between uninflamed mucosal specimens of the patients and control tissues was observed.

Conclusion: We show for the first time that UPR is activated in the inflamed colonic mucosa of a cohort of children with CD and UC, suggesting a role of ER stress in the mechanisms of pediatric IBD.

Disclosure of Interest: None Declared
ROLE OF WNT/β-CATENIN SIGNALING CASCADE DURING INTESTINAL ADAPTATION IN A RAT MODEL OF SHORT BOWEL SYNDROME

Igor Sukhotnik 1, Alex Roitburt 2, Yulia Pollak 2, Drora Berkowitz 3
1Dept Paediatric Surgery B, Bnai Zion Medical Center, 2Laboratory of Intestinal Adaptation and Recovery, 3Dept of Paediatric Surgery and Paediatric Gastroenterology and Nutrition, Bnai Zion Medical Center, Haifa, Israel, Technion-Israel Institute of Technology, The Ruth & Bruce Rappaport Faculty of Medicine, Haifa, Israel

Objectives & Study: Growing evidence suggests that the Wnt/β-catenin signaling cascade is implicated in the control of stem cell activity, cell proliferation, lineage commitment, and cell survival during normal development and tissue regeneration of the gastrointestinal epithelium. The roles of this signaling cascade in stimulation of cell proliferation after massive small bowel resection are unknown. The purpose of this study was to evaluate the role of Wnt/β-catenin signaling during 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. Parameters of intestinal adaptation, enterocyte proliferation and apoptosis, were determined two weeks after operation. Illumina's Digital Gene Expression (DGE) analysis was used to determine Wnt/β-catenin signaling gene expression profiling. Twelve Wnt/β-catenin-related genes and β-catenin protein expression were determined using Real Time PCR, Western blotting and immunohistochemistry.

Results: From the total amount of 20000 probes, 20 genes related to Wnt/β-catenin signaling were investigated. From these genes, 7 genes were found to be up-regulated and 8 genes to be down-regulated in SBS vs sham animals with a relative change in gene expression level of 20% or more. From twelve genes determined by Real Time PCR, nine genes were down regulated in SBS rats compared to control animals including target gene c-MYC. SBS-rats also showed a significant decrease in β-catenin protein compared to control animals.

Conclusion: Two weeks following massive bowel resection in rats, Wnt/β-catenin signaling pathway is inhibited. In addition, it appears that cell differentiation rather than proliferation is important in the late stages of intestinal adaptation.

Disclosure of Interest: None Declared
SUCCESSFUL LIVER TRANSPLANTATION FOR BUDD CHIARI SYNDROME DUE TO ADAMTS 13 DEFICIENCY

Yael Mozer Glassberg 1,2,*, Baruch Yerushalmi 3, Joanne Yacobovich 2,4, Eitan Mor 2,5, Michael Gurevich 5, Riki Shapiro 1,2, Ari Silbermintz 1, Rachel Bergerin 1, Hannah Tamary 2,4, Raanan Shamir 1,2

1Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Medical Center of Israel, Petach Tikva, Israel, 2Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel, 3Paediatric Gastroenterology Unit, Soroka Medical Center, Ben-Gurion University of the Negev, Beer Sheva, Israel, 4Hematology Unit, Schneider Children's Medical Center of Israel, Petach Tikva, Israel, 5Department of Transplantation, Rabin Medical Center Beilinson Hospital, Petach Tikva, Israel

Objectives & Study: ADAMTS13 is a plasma metalloproteinase that regulates platelet adhesion and aggregation through cleavage of von Willebrand factor multimers. In humans, congenital or acquired deficiency in ADAMTS13 causes thrombotic thrombocytopenic purpura (TTP), a condition characterized by thrombocytopenia and hemolytic anemia with microvascular platelet thrombi. We report on a case of ADAMTS13 deficiency and Budd Chiari syndrome (BCS) that was referred for liver transplantation (LT).

Methods: Since ADAMTS13 is produced by endothelial cells and hepatocytes, post transplantation thrombotic complications and ADAMTS13 status post transplantation could not be predicted. We describe the first reported LT for BCS in a patient with congenital ADAMTS 13 deficiency, emphasizing the pre and post-transplant evaluation and follow-up.

Results: This 12 years old boy, of Bedouin ancestry, first presented 18 months prior to LT with BCS and a TTP like picture. Diagnosis of ADAMTS 13 deficiency was confirmed by plasma levels below 3%, absence of anti-ADAMTS 13 autoantibodies and molecular diagnosis. Due to failure of conservative treatments (medications and invasive radiology), LT was offered to the family as a lifesaving procedure. LT was performed with continuous administration of fresh frozen plasma maintaining enzymatic activity above 20%. Post transplantation and off plasma administration, ADAMTS 13 blood levels increased to 47% with complete cure of the patient primary and secondary disease.

Conclusion: This first report in the literature of LT for ADAMTS 13 deficiency suggests that LT can offer a complete cure of the disease.

Disclosure of Interest: None Declared
USE OF WIRELESS CAPSULE ENDOSCOPY (WCE) IN CHILDREN FOLLOWING ISOLATED/COMBINED TRANSPLANTATION.
Clare James ¹, Ronald Bremner ¹, Girish Gupte ²
¹Gastroenterology, ²Hepatology, Birmingham Children's Hospital, Birmingham, United Kingdom

Objectives & Study: The small bowel (SB) is difficult to access with upper and lower Endoscopy (UGE/LGE), even in those intestinal transplant recipients with ileostomies access is still limited. WCE is a non invasive technology provides a unique opportunity to visualise the entire bowel in a minimally invasive manner. This retrospective study reviews clinical cases of children undergoing WCE following intestinal transplantation (Tx). WCE was used in addition to conventional investigations to see if it further pathology (site and severity) could be found.

Methods: We performed 4 WCE examinations in 4 patients aged between (4-16 years) between 2011 and 2012. Two patients swallowed the capsule and two patients had capsules placed endoscopically into the duodenum, under general anaesthetic.

Results: WCE revealed pathological changes in all 4 patients (Table 1).

Table 1

<table>
<thead>
<tr>
<th>Patient</th>
<th>M/F</th>
<th>Age</th>
<th>Type of Tx</th>
<th>Time after of Tx</th>
<th>Indication for WCE</th>
<th>SB investigations done</th>
<th>SB WCE Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F</td>
<td>4years</td>
<td>Combined Intestinal Tx</td>
<td>16/12</td>
<td>Bleeding</td>
<td>UGE/Ileoscopy Radiology: CT Abdo, Baft</td>
<td>Small ulcers and deep ulceration, patchy redness and bleeding.</td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>8years</td>
<td>Isolated Intestinal Tx</td>
<td>19/12</td>
<td>Ongoing symptoms of diarrhoea and bleeding following treatment for acute rejection.</td>
<td>UGE/LGE Radiology: CT abdo, Baft, Loopgram</td>
<td>Ulcerative and inflammatory changes suggestive of rejection and segment mucosal loss.</td>
</tr>
<tr>
<td>3</td>
<td>F</td>
<td>15years</td>
<td>Combined Intestinal TX</td>
<td>73/12</td>
<td>Bleeding</td>
<td>UGE/Ileoscopy Radiology: CT abdo, Baft.</td>
<td>Gastric erosions, mild small bowel erythema no ulcers seen.</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>16years</td>
<td>Isolated Intestinal TX</td>
<td>39/12</td>
<td>Bleeding</td>
<td>UGE/LGE Radiology: CT abdo, Baft.</td>
<td>Deep ulceration and mucosal loss, bleeding throughout small bowel, suggestive of severe rejection.</td>
</tr>
</tbody>
</table>

Baft: Barium follow through, CT abdo: Computerised Tomography Scan of Abdomen.

Conclusion: WCE revealed lesions of greater severity than those seen by UGE/LGE and Ileoscopy. WCE permitted a minimally invasive approach to identifying site and severity of mucosal lesions in children post intestinal transplantation when conventional investigations had been unhelpful. The results from the Wireless Capsule Endoscopies evaluated and directed treatment options.

Disclosure of Interest: None Declared
Common ESPGHAN Topics
Transplantation
PD-H-0152

PAEDIATRIC INTESTINAL FAILURE: IS IT POSSIBLE TO RESCUE PATIENTS FROM THE TRANSPLANT LIST?
Veronica Busoni 1,*, Marina Orsi 1, Pablo Lobos 2, Rodrigo Sanchez Claria 3, Fernando Frangi 4, Laura Ungar 5, Daniel D'Agostino 1
1Paediatric Gastroenterology Hepatology and Liver Intestinal Transplantation, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
2Paediatric Surgery, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
3Transplant Surgery, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina
4Paediatrics, 5Paediatric Nutrition, Hospital Italiano de Buenos Aires, Buenos Aires, Argentina

Objectives & Study: Intestinal Rehabilitation should be the primary goal in the treatment of patients with intestinal failure (IF). Parenteral Nutrition (PN) complications are the main indications for small bowel transplantation, but its morbidity and mortality still remains high. Intestinal rehabilitation in transplant candidates is under debate. Our aim was to describe the outcomes of intestinal rehabilitation program (IRP) in children listed for intestinal transplantation.

Methods: Pre-transplant evaluation was performed in IF patients with signs or symptoms of PN complications. Patients with confirmed PN complications were listed for either intestinal, liver-intestinal or multivisceral transplantation. While on transplant list, patients were included in IRP. Nutritional (PN lipid emulsions, escalating enteral feeds), pharmacological (antimotility agents, ursodeoxicolic acid, rotatory antibiotics) and surgical interventions (lengthening procedures, ostomy closures) were applied in every case. Serial Transverse Enteroplasty (STEP) procedure was performed in patients with dilated residual small bowel.

Results: Between December 2008-November 2013, 53 children with IF were referred to our center. Median age was 0.5 years (0-14 y). A pre-transplant evaluation was performed in 26/53, the remaining 27 initiated IRP. 20/26 patients were listed for transplantation (7 liver-intestinal, 1 multivisceral and 12 isolated small bowel) and 6/26 were considered not suitable for transplant. 5/20 listed candidates were transplanted and 4 are still waiting. 3/20 died on waiting list (2 hepatointestinal and 1 multivisceral). 40% of listed candidates (8/20) were finally discharged from the list because they were weaned from PN (mean increase in weight for length z-score: +2.48). In 6/8, STEP procedure was performed; 2 of these 6 children had an advanced liver fibrosis (Metavir F3 and F4) with normal liver synthesis, and they were off PN at 7 and 1 months post STEP respectively, with a mean follow-up of 18 months post STEP.

Conclusion: Even in children who have formal indications for intestinal transplantation and while on waiting list, maximal efforts should be made to achieve intestinal autonomy, avoiding the need for transplantation and improving survival. Intestinal lengthening procedures should not be contraindicated in listed patients unless they have advanced irreversible liver disease with significant portal hypertension.

Disclosure of Interest: None Declared
Objectives & Study: Prucalopride (PRU) is a selective, high-affinity, 5-HT₄ receptor agonist, with gastrointestinal prokinetic properties that is approved in the EU for the symptomatic treatment of chronic constipation in women in whom laxatives fail to provide adequate relief. This study aimed to evaluate the efficacy and safety of PRU in children aged ≥6 months to <18 years with functional constipation.

Methods: This multicenter, randomized, placebo-controlled, double-blind phase 3 trial (NCT01330381) enrolled children diagnosed using ROME III criteria. Patients received PRU (≤50kg: 0.04 mg/kg oral solution; >50kg 2 mg tablet) or placebo (PLA) once daily for 8 weeks. The primary efficacy endpoint was the proportion of patients with an average of ≥3 spontaneous bowel movements (SBM) per week, and ≤1 fecal incontinence episode per 2 weeks in children who had acquired toileting skills, calculated over weeks 5–8 (responders). Endpoints were derived from daily e-diaries and questionnaires completed by children and parents. Adverse events, clinical laboratory values, and electrocardiograms (ECGs) were monitored.

Results: Efficacy and safety were assessed in 213 (107 PLA, 106 PRU) patients. Their age distribution was: 25% <4y, 50% 4–<12y and 25% 12–<18y; their mean age was 8.3 years (SD: 4.6 years); 55.4% were female. At screening, 62.3% of those in the PRU group and 55.1% of those in the PLA group had a history of fecal incontinence, and 60.4% and 55.1% of those in the PRU and PLA groups, respectively, had a history of ≤1 SBM/week on average. The proportion of responders was similar in both treatment groups (PRU 17.0%; PLA 17.8%). No statistically significant difference in the primary efficacy endpoint was seen when stratified by sex, age group or country. No meaningful differences were observed between PRU and PLA in the secondary efficacy endpoints, including patients’ satisfaction with treatment and their perception of disease severity. Overall, the incidence of treatment-emergent adverse events (TEAEs) was similar in the PRU (69.8%) and PLA groups (60.7%). The most common (>10%) TEAEs in the PRU group were headache, pyrexia, abdominal pain and vomiting. There were no meaningful shifts in clinical chemistry, hematology, urinalysis or ECG parameters.

Conclusion: In this study PRU (≤50kg: 0.04 mg/kg oral solution; >50kg 2 mg tablet) was not more effective than PLA in children with functional constipation. PRU was generally well tolerated.

A DOUBLE-BLIND RANDOMIZED CONTROLLED TRIAL OF A THICKENED AMINO-ACID-BASED FORMULA IN CHILDREN ALLERGIC TO COW'S MILK AND TO PROTEIN HYDROLYSATES

Christophe Dupont 1, Nicolas Kalach 2, Elena Bradatan 3, Alain Lachaux 4, Francois Payot 4, Lydie Guénard-Bilbault 5, Frederic De blay 5, Riad Hatahet 6, Sandra Mullier 7

1Hospital Necker, Paris, 2Saint Vincent de Paul Hospital, Lille, France, 3Regional Hospital, Namur, Belgium, 4University and Paediatric Hospital of Lyon, Lyon, 5Regional University Hospital, Strasbourg, 6Paediatrician Allergologist, Forbach, France, 7Queen Fabiola Children's University Hospital, Brussels, Belgium

Objectives & Study: Children with cow milk protein allergy (CMPA) may also be allergic to extensively hydrolyzed protein formulas (eHF) designed to help overcome CMPA. Amino-acid-based formulas (AAFs) are recommended in such cases, though up to now, no AAF has been clinically tested in infants allergic to eHF.

Methods: 86 infants were randomized in a double-blind controlled trial comparing a “thickened” AAF (United Pharmaceuticals) and a commercially available “reference” AAF. Only patients whose symptoms did not improve with an eHF were included. CMPA was confirmed through a double blind placebo controlled food challenge. Digestive, cutaneous and respiratory symptoms as well as growth parameters were assessed at 1 month in a 6-months long trial.

Results: At 1 month, both formulas were tolerated (100% of children for “thickened” AAF and 95% for “reference” AAF). CMA and eHF allergy were confirmed in 75 children: all tolerated the tested formulas. The main allergic symptom disappeared completely within 1 month in 26/42 (61.9%) and 17/33 (51.5%) respectively with the “thickened” and the “reference” AAF (ns). All parameters related to the quality of life improved significantly with the thickened AAF. Among others, crying time decreased by $98\pm185.4$ minutes (p<0.001) and sleeping time increased by $64.6\pm146.9$ min (p=0.009) (versus respectively $28\pm62.3$ minutes (p=0.014) and $29.0\pm143.6$ (ns) with the “reference AAF”). Infants had significantly more normal stools with the “thickened AAF” (90.5% vs 66.7%, p=0.011). Regurgitations disappeared completely in 65.4% with the “thickened AAF” vs. 42.3% with the reference one (ns). Weight-for-age z-score increased by $0.1\pm0.3$ (mean±SD) for the “thickened” AAF and $0.2\pm0.4$ for the “reference” AAF (ns). BMI z-scores increased respectively by $0.2\pm0.5$and $0\pm0.7$ (ns) during the first month follow-up.

Conclusion: This is the first randomized controlled trial of AAF efficacy in CMPA associated with eHF allergy. The “thickened” AAF was tolerated by all infants; symptoms improved significantly as of the 1st month and growth parameters were appropriate.

Disclosure of Interest: C. Dupont Grant / Research Support for: Coordinator fees, N. Kalach: None Declared, E. Bradatan: None Declared, A. Lachaux: None Declared, F. Payot: None Declared, L. Guénard-Bilbault : None Declared, F. De blay: None Declared, R. Hatahet: None Declared, S. Mullier: None Declared
META-ANALYSIS ON: EFFECT OF LACTOSE-FREE FORMULA ON MANAGEMENT OF ACUTE_DIARRHEA IN CHILDREN

Lin Wang 1,*, Ying Huang 1, Cui Fang Zheng 1
1Children’s Hospital of Fudan University, Shanghai, China

Objectives & Study: Acute diarrhea is a common ailment in children especially in the developing world. Prolonged diarrhea results in villous atrophy and disaccharidase deficiency, especially lactase deficiency. Whether in cute diarrhea of less than two weeks’ duration a similar situation exists is still debatable, and withholding lactose containing breast-milk and formula is common practice in many places. The aim of this meta-analysis is to evaluate the clinical outcomes of lactose-free formula for treatment of children suffering from acute diarrhea.

Methods: We searched PubMed, EMBASE, the Cochrane Library and Chinese databases of CNKI, Wanfang Database. Reference lists of relevant trials were also scanned. Randomized controlled trials involving lactose-free formula for the treatment of acute diarrhea for children younger than 3 years old were enrolled into this review. Treatment failure rates and duration of diarrhea were extracted as primary outcomes, and weight gain as secondary outcome. Data were synthesized and analyzed by using the Review Manager 5.2 software. The risks of bias of the included trials were assessed by using the standard Cochrane criteria. Risk ratios were presented for dichotomous outcomes with 95% confidence intervals (95%CI). For continuous outcomes, mean difference was calculated with 95% CI.

Results: 14 studies (n=1275) that met the inclusion criteria were identified. Three trials didn’t report explicitly the methods of random-sequence generation, one had high risk of other bias. Five were at high risk of bias of incomplete data, and two were at high risk of bias for selective bias. Funnel plot showed no significant publication bias. Treatment failure rates were lower for lactose-free formula compared with lactose containing formula (RR:0.46, 95%CI [0.35,0.60], P<0.00001), especially for those including severe dehydration. Those who received lactose-free formulas, in comparison with those on lactose-containing formulas, had shorter duration of diarrhea (MD: -0.95, 95%CI [-1.15,-0.74], P<0.00001). No significant increase in weight was found during dietary treatment of lactose-free or lactose containing formula according to six included trials.

Conclusion: There is evidence that lactose-free formulas has lower treatment failure rates and can shorten the duration of diarrhea. More high quality clinical trials are needed to clarify the effect.

Disclosure of Interest: None Declared
**Disclosure of Interest:** None Declared

**Hepatology**

SP-H-0156

**METAL-RESPONSIVE ELEMENTS AS NEW PLAYERS IN THE PATHOGENESIS OF WILSON’S DISEASE**

Amelie Stalke 1,2,* , Eva-Doreen Pfister 1, Ulrich Baumann 1, Brigitte Schlegelberger 2, Nils von Neuhoff 2

1Paediatric Gastroenterology and Hepatology, Hannover Medical School, Hannover, Germany

2Institute of Cell and Molecular Pathology, Hannover Medical School, Hannover, Germany

**Objectives & Study:** Establishing the diagnosis of Wilson’s disease (WD) may be difficult, especially in patients who exhibit clinical WD symptoms but lack a detectable ATP7B mutation. In addition, a clear correlation between genotype and phenotype is lacking. Previous studies revealed decreased liver ATP7B mRNA expression in genetically proven WD patients compared to controls. This decrease was also observed in patients with typical WD symptoms but without an ATP7B mutation. Metal-responsive elements (MREs) are likely to be linked to this downregulation. MREs (a, c, d and e) can be found in the ATP7B promoter region and modulate the promoter activity by binding transcription factors (TF) in a metal ion concentration-dependent mechanism. An interaction partner in the ATP7B gene is already known for MREa. The aim of our study is to unveil and characterize further MRE-interacting TF that might orchestrate ATP7B mRNA expression in patients with or without genetically detectable WD.

**Methods:** Nuclear proteins were extracted from human immortalized liver cell line cells (THLE2). To screen for protein-DNA interactions, an electrophoretic mobility shift assay (EMSA) was performed by incubating the nuclear extract with biotin-labeled double-stranded 31 bp probe corresponding to the ATP7B MREc sequence. To confirm the specificity of protein-DNA binding and to narrow down the protein binding site, excessive amounts of wild-type and mutated unlabeled MREc oligonucleotides were used as competitors.

**Results:** A highly specific protein binding on the MREc probe was revealed by EMSA experiments. By using mutated MREc competitor oligonucleotides it could be shown that two nucleotides of the consensus sequence and a further three nucleotides adjacent to the downstream part of the consensus sequence are responsible for TF binding.

**Conclusion:** Our findings demonstrate that the regulatory MREc sequence of the ATP7B gene is specifically bound by at least one protein. A downregulation of this TF or disturbed interaction between TF and MREc may explain the decreased ATP7B mRNA expression in WD and could provide new insights into the pathogenesis of WD.

**Disclosure of Interest:** None Declared
**Hepatology**

SP-H-0157

**NEONATAL TREATMENT USING A NOVEL, HYBRID RECOMBINANT AAVPIGGYBAC TRANSPOSON VECTOR RESULTS IN ROBUST, LONG-TERM PHENOTYPE CORRECTION OF THE PROGRESSIVE FAMILIAL INTRAHEPATIC CHOLESTASIS TYPE 3 MOUSE MODEL IN VIVO**

Susan M Siew 1,2,*, Sharon C Cunningham 1, Ian E Alexander 1

1Gene Therapy Research Unit, Children's Medical Research Institute, Sydney, Australia
2Department of Gastroenterology, The Children's Hospital at Westmead, Sydney, Australia

**Objectives & Study:** Efficient liver-targeted gene transfer using recombinant adeno-associated viral (rAAV) vectors has led to promising therapeutic efficacy in pre-clinical models and clinical trials. We have previously demonstrated that chronic liver pathology impedes vector delivery and hepatocyte transduction, necessitating intervention prior to disease onset, such as in neonates. However, delivery of conventional, predominantly non-integrating rAAV vectors to juvenile mice results in loss of persistent transgene expression in the liver due to rapid liver growth and hepatocyte proliferation. The piggyBac transposon system permits stable genomic modification of mammalian cells, but targeted delivery is relatively inefficient in vivo. We aimed to develop a hybrid vector, utilising high transduction efficiency of rAAV together with piggyBac transposase-mediated somatic integration to stably express human ABCB4 under a hepatocyte-specific promoter/enhancer in vivo, and to correct chronic liver disease in a murine model of Progressive Familial Intrahepatic Cholestasis type 3, lacking canalicular phosphatidylcholine translocation.

**Methods:** Neonatal Abcb4-/- mice were injected intraperitoneally with 5x10^{11} vector genomes of the hybrid vector, encoding hABCB4, co-administered with a rAAV expressing piggyBac transposase (pBase+). A comparison of biochemistry, bile composition, hepatosplenomegaly and liver histopathology was made with untreated homozygotes and those that received the same dose of hybrid vector, but without co-administered transposase vector (pBase-) at 4, 8, 12 and 16 weeks of age.

**Results:** The pBase+ cohort had stable, persistent expression of hABCB4, resulting in phenotype correction, extending into adulthood. A single therapeutic injection at birth led to >10-fold increased mean biliary phosphatidylcholine (PC) concentration, with comparable levels in juvenile and adult animals: treated (pBase+) mean PC concentration 55.0% of wild-type mice, compared with untreated and pBase- cohorts, 4.5% and 3.8% wildtype level, respectively (p<0.0001). pBase+ homozygotes exhibited no hepatosplenomegaly with dramatically reduced periportal inflammation and liver fibrosis, in contrast to age-matched untreated and pBase- cohorts. Reduced liver fibrosis on histopathology was confirmed by lower hydroxyproline concentrations in pBase+ livers.

**Conclusion:** This novel and powerful hybrid rAAV-piggyBac transposon vector strategy has potential for treating a wide array of inherited liver diseases with early onset. With further development and safety assessments, this may translate into future therapeutic benefit for paediatric patients.

**Disclosure of Interest:** None Declared
THE GASTROINTESTINAL MANIFESTATION OF CONSTITUTIONAL MISMATCH REPAIR DEFICIENCY SYNDROME

Shlomi Cohen 1,*, Revital Kariv 2, Inbal Barnes-Kedar 3, Yael Goldberg 4, Elizabeth E Half 5, Marissa Halperin 6, Sara Morgentern 6, Eli Pikarski 7, Nurit Magal 8, Gidon Soroka 9, Hagit N Baris 8, Zohar Levi 10

1Paediatric Gastroenterology Unit, "Dana-Dwek" Children's Hospital, Tel Aviv Souraski Medical Center, Tel Aviv, Israel, 2Gastroenterology Dep, Tel Aviv medical Center, Tel Aviv, Israel, 3Genetics Institute, Rabin Medical Center, Petach Tikva, Israel, 4Oncology Dep, Hadassah, Jerusalem, 5Gastroenterology, Rambam, Haifa, Israel, 6Pathology, Rabin Medical Center, Petach Tikva, Israel, 7Pathology, Hadassah, Jerusalem, 8Genetic Institute, Rabin Medical Center, Petach Tikva, Israel, 9Surgery , Bney Zion Medical Center, Haifa, Israel, 10Gi Cancer Service, Gastroenterology Division, Rabin Medical Center, Petach Tikva, Israel

Objectives & Study: Biallelic mismatch repair deficiency mutation is a new cancer syndrome characterized by childhood hematological malignancies, brain tumors, early age colonic adenomatous polyps, colonic and small bowel cancer. We aim to share our insights in a series of subjects that underwent comprehensive gastrointestinal work-up.

Methods: Included subjects with verified biallelic carriage that underwent complete gastrointestinal evaluation.

Results: Ten patients from 6 families were observed in this cohort. These 10 patients were at a mean age of 13.3 years (range 6-20), 60% are male and their origin is Jewish and Arab equally. Consanguinity was noticed in 4 out of the six families. Two of our patients died at the age of 14 and 19 yr due to brain cancer. Of the 10 cases, 5 (50%) had PMS2 mutations, 3 (30%) had MSH6 mutations, 1 (10%) had MSH2 mutations and 1(10%) had MSH2/MSH6 mutations. Eight patients had colonic involvement with adenomatous polyps in varying degree of dysplasia or cancer. Two of our youngest patients did not have colonic or gastric involvement at all. Regarding extraintestinal malignancies; 5 had high grade brain glioma and 1 had T-cell lymphoma. All of our patients have Neurofibromatosis like features – as Café au lait spots.

Conclusion: Biallelic mismatch repair deficiency syndrome is an unrecognized syndrome that combine gastrointestinal, hematological and brain tumors at the pediatric age. Their gastrointestinal manifestation includes multiple adenomatous polyps with varying degree of dysplasia including early cases of colonic cancer. Increasing awareness and knowledge of this syndrome can improve survival of these patients.

Disclosure of Interest: None Declared
ELEVATED FAECAL CALPROTECTIN DOES NOT DIFFERENTIATE BETWEEN IBD AND A JUVENILE POLYP

Vincent Pluimakers 1,*, Freddy Kokke 1, Michiel Houben 2, Peter Nikkels 3, Roderick Houwen 1, Victorien Wolters 1
1Paediatric Gastroenterology, UMC Utrecht, Utrecht 2Paediatrics, UMC Utrecht, Utrecht 3Pathology, UMC Utrecht, Utrecht, Netherlands

Objectives & Study: Faecal calprotectin is commonly used as an initial screening test in patients with suspected IBD. Generally a cut off value above 50 µg/gr faeces is used, resulting in a 98% sensitivity for detecting IBD and a 44% specificity. Using a higher cut off value increases specificity, but reduces sensitivity, with a suggested optimal cut-off value of 300 µg/gr faeces. Only a small proportion of non-IBD patients are reported to have a faecal calprotectin above this value (Henderson et al, Am J Gastroenterol 2012). Our clinical impression was that patients with a juvenile polyp (JP) also frequently present with levels exceeding 300 µg/gr faeces. Therefore our aim was to investigate faecal calprotectin levels in patients with JP and compare these levels with patients with newly diagnosed IBD.

Methods: Files of all patients who had a diagnostic endoscopy between January 2009 and August 2013 were studied. A diagnosis of JP or IBD was made based on histology. Faecal calprotectin for all patients with either JP or IBD was retrieved, if available.

Results: Amongst the 2169 diagnostic endoscopies done in the study period a total of 37 patients with a juvenile polyp (histological proven) were identified, and 77 patients with newly diagnosed IBD. Faecal calprotectin was determined in 19 of the patients with JP (mean level 1329 µg/gr, range <30-5250) and in 76 patients with IBD (mean level 3105 µg/gr; range <30-24013, P<0.001). All patients with IBD had a faecal calprotectin above 50 µg/gr faeces, and 18/19 patients with JP. A calprotectin above 300 µg/gr was found in 13/20 patients with JP and in 74/76 patients with IBD.

Conclusion: Elevated faecal calprotectin levels are frequently found in patients with a juvenile polyp as well as in pediatric IBD. Levels of calprotectine do not help in differentiating these conditions.


Disclosure of Interest: None Declared
THE USE OF VIDEOFLUOROSCOPIC SWALLOWING STUDY FOR THE DIAGNOSTIC AND DETERMINING THERAPY OF SWALLOWING DISORDERS IN CHILDREN WITH NEUROLOGICAL DISABILITIES

Ewa Winnicka 1,*, Dorota Majak 2, Anna Rybak 1

1Department of Gastroenterology, Hepatology and Feeding Disorders, 2Department of Radiology, The Children’s Memorial Health Institute, Warsaw, Poland

Objectives & Study: Swallowing disorders are a relevant but often unrecognized and underestimated problem in patients suffering from neurological diseases. Sometimes they lead to aspiration pneumonia. The aim of this study is to show the therapeutic methods and videofluoroscopic swallowing studies’ (VFSS) findings in children with neurological diseases and symptoms of swallowing disorders treated in Department of Gastroenterology, Hepatology and Feeding Disorders

Methods: A total of 23 children were enrolled in this retrospective study. All patients presented with neurological symptoms and swallowing disorders, therefore they were referred to VFSS. 35% of patients, despite of neurological disorder, suffered from cardio-respiratory problems or anatomic-functional problems. Indications for VFSS were defined by a physician and speech-language pathologist. Outcomes were reviewed by a radiologist and speech-language pathologist. A type of feeding, compensation or rehabilitation was recommended by speech-language pathologist. The swallowing problems, VFSS findings and recommendation after examination were analyzed.

Results: The most common reason for VFSS referral was 'the safety of swallowing' (SS) 65 %. For the rest of patients the reason for VFSS was to access the function of swallowing (FS, 17 %) or both: SS and FS (17 %). 17 children (74 %) presented with respiratory symptoms as a cause of swallowing disorders and the necessity for VFSS. Aspiration was observed in 60 % of patients, oropharyngeal residue in 13 %, residue and penetration in 22% of all patients. 13 out of 14 children, who showed aspiration presented with silent aspiration during VFSS (93 %). The VFSS outcomes indicated the necessity to modify oral feeding in 15 children (65 %). In 9 patients (40 %) oral feeding was discontinued. Rehabilitation without oral feeding was ordered in 11 patient (48 %), general swallowing rehabilitation with the oral use of foods in 9 children (40 %). Compensation using different food consistency was used in 10 patient (43 %), compensation by proper positioning and modified feeding technique was adopted in 8 children (35 %).

Conclusion: The VFSS is helpful for diagnosis and determining the treatment in neurological children suffering from swallowing disorders. The most of our patients mainly presented swallowing disorders with silent aspirations. Not in all of this situations patients had preceding respiratory symptoms. VFSS allowed to choose a proper therapy and to determine the way of feeding in neurological patients.

Disclosure of Interest: None Declared
OVERVIEW OF COMBINED LIVER AND KIDNEY TRANSPLANTATION IN CHILDREN IN THE UK

Jackie Logan¹ *, Khalid Sharif ¹, Larissa Kerecuk ², Carla Lloyd ¹, Patrick McKiernan ¹
¹Liver Unit, ²Nephrology, Birmingham Children's Hospital, Birmingham, United Kingdom

Objectives & Study: Aim
To describe a single UK centres experience of Combined Liver and Kidney Transplantation in Children (CLKT).

Introduction
The 1st Combined Liver and Kidney Transplant (CLKT) worldwide took place in 1984 (Margreiter et al 1984). Since then CLKT has been carried out as a recognised treatment for End Stage Renal Disease (ESRD) with associated liver disease. There is little published data on CLKT in children.

Methods: A retrospective study was carried out on all patients who underwent CLKT at our centre.

Results: Children were usually referred from local renal units and were assessed for transplant jointly by the paediatric hepatology and renal teams.

The first CLKT was undertaken in March 1994. Since then a total of 38 children have received a CLKT. The most common indications for CLKT were ESRD due to Fibropolycystic Disease (n=24) and Primary Hyperoxaluria type 1 (n=11).

Median age (range) and weight at transplant was 5.5 years (1.5-15 years) and 20.5 kg (9.1-57.25 kg). Median survival since transplant is 5 years (1 month- 14 years). Actuarial 14 year patient and renal graft survival is 80%.

Of the 5 deaths, 2 were in the peri-operative period and the other 3 late deaths due respectively to vascular thrombosis, sepsis and seizures.

10% had an episode of histologically proven acute liver rejection and 5% acute kidney rejection. All rejection episodes were successfully treated with pulsed corticosteroids.

Currently all patients are well although one is receiving dialysis whilst waiting for a renal retransplant. 7 patients have been successfully transferred to adult services.

Conclusion: In our experience CLKT is a highly successful long term treatment for ESRD with associated liver disease. Subsequent quality of life is excellent and there is a low incidence of renal rejection.

Disclosure of Interest: None Declared
ALLIED HEALTH PROFESSIONAL (INCLUDING NURSES & DIETICIANS)

PO-AHP-0003

IS NUTRITIONAL STATUS IMPORTANT FOR CLINICAL OUTCOMES OF CHILDREN AFTER CARDIAC SURGERY?

Maria Carolina Witkowski 1,*, Maria Antonieta Moraes 2, Cora Maria Firpo 3, Helena Ayako Sueno Goldani 4

1Paediatric Nursing, Clinical's Hospital, Porto Alegre, Brazil, 2Clinical Research, Clinical's Hospital, Porto Alegre, Brazil, 3Paediatric Cardiology, Cardiology Hospital, Porto Alegre, Brazil, 4Paediatric Gastroenterology, Clinical's Hospital, Porto Alegre, Brazil

OBJECTIVES & STUDY: The success of the pediatric postoperative cardiac surgery depends on several factors. The maintenance of adequate nutritional status in these patients is a challenge for the multidisciplinary team. The aim of this study was to assess the nutritional status and clinical outcome of children with congenital heart disease postoperatively.

METHODS: Clinical and anthropometric data of 140 children (77 girls) who were in the first 72 hours of postoperative pediatric cardiac surgery were reviewed and data were recorded. Anthropometric parameters employed were body mass index-for-age (BMI/A), weight-for-age (W/A), height-for-age (H/A), according to World Health Organization (WHO) references (1). Measurements were presented as z-scores (SDS) and the type of cardiac surgery. Risk of malnutrition was defined based on SDS < -1.00 and malnutrition as SDS < -2.00. The outcomes analyzed were discharge from the intensive care unit and death. SPSS v18.0 was used for statistical analysis. Student’s t test and X² for categorical variables were used.

RESULTS: The mean age of presentation in the group was 13.7 ± 10.3 months, whereas the average weight of the children was 7.2 ± 2.9 kg. The mean SDS was -2.0 for BMI/A, -2.1 for W/A, and -1.1 for H/A. Surgical procedures were as follows: total correction of tetralogy of Fallot in 26 (18.6%), ventricular septal defect closure in 13 (9.3%), atrioventricular septal defect closure in 12 (8.6%) and coarctation of aorta in 11 (7.9%). Analyzing the 72 hours after surgery as the clinical outcome of all patients, 27 (19.3%) of children were discharged from intensive care unit (ICU) and 10 (7.1%) of the children died. Regarding nutritional status of children who had been discharged from ICU and who died, it was found no significant difference in the anthropometric parameters (P = 0.462). In the group of children with cyanotic congenital heart disease the mean SDS for BMI/A was -1.4, for W/A was -2.6 and for H/A was -2.7. In patients with restricted physical activity such as coarctation of aorta, mean SDS of -1.5 for BMI/A, -1.8 for W/A, and -1.1 for H/A were found.

CONCLUSION: The clinical outcome is not directly related to the nutritional status of patients after cardiac surgery. Early identification of nutritional status in specific groups of patients can provide a better approach focusing the better management of these patients.


DISCLOSURE OF INTEREST: None Declared
AN EVALUATION OF A TWO MEMBER TEAM APPROACH TO ASSESSING CHILDREN WITH WEIGHT AND EATING PROBLEMS

Emma Gotthardsson 1, Lotta Söderberg 1.*

1Barn- och Ungdomsmedicinska kliniken, Skanes Universitssjukhus, 20502 Malmö, Sweden

Objectives & Study: Historically children at our clinic with eating and/or weight problems has been treated and followed in many different ways. A few years ago in an attempt to assure the quality of the work an eating outpatient clinic was initiated. The individual visits take one hour and are lead by a dietician and a speech and language pathologist. At the outpatient clinic eating, feeding, nutrition and communication during the meal are assessed. A medical assessment should have been initiated before the first visit. In this study we wanted to evaluate the outcome of this new team approach.

Methods: All children that attended the eating outpatient clinic from August 2012 to the end of August 2013 were included. Referring medical speciality, reasons of consultation and diagnose of interest was noted. Ages of the children, numbers of meetings and need of psychosocial professional was included. The dietician and speech and language pathologists’ opinion of the eating outpatient clinic was taken in to account.

Results: During one year 80 children were at the eating outpatient clinic, at totally 134 visits. 41 children visited the clinic once, the rest 2-6 times. 50 of the children had an age between 0-3 years, 15 children 3-6 years and 15 children 6-16 years. The group consisted of 28 (35 %) girls and 52 (65 %) boys. 36 of the children came from paediatric gastroenterologists, 20 from paediatricians, 9 from the medical children ward, 5 from paediatric endocrinologists and 4 from other medical fields. Reasons for consulting the eating outpatient clinic was food refusal in 79 % of the patients, weight loss in 69 % of the children, 26 % had parental stress regarding the feeding situation, swallowing problems were reported in 14 % of the children, 11 % had problems with vomiting and 7 % had oral motor problems. We found that 10 % of the children had gastrostomi, 21 % of the children were born premature, 20 % had a diagnosis that otherwise affects their eating, 11 % had contact with a rehabilitation unit and 28 % of the children was or had previously been referred to a psychosocial specialist. The dietician and the speech and language pathologist both thought that the new way of organizing their work lead to higher efficiency and quality of work when assessing nutrition and eating/feeding. They both felt that they needed fewer meetings with the patient and that they quicker could recommend the right interventions.

Conclusion: With small recourses a combined eating outpatient clinic with assessments by speech and language pathologist and dietician can be time effective. The joint assessment can give an increased understanding and better treatment for children with eating and/or weight problems under the condition that there is an active cooperation with other medical professionals and professionals specializing in the psychosocial problems in the eating situation.

Disclosure of Interest: None Declared
**Allied Health Professional (Including Nurses & Dieticians)**

PO-AHP-0005

**COMPARISON BETWEEN PAPER - VERSUS WEB-BASED DIETARY RECORDS**

Evgen Benedik 1,*, Barbara Koroušić Seljak 2, Marjan Simčič 3, Irena Rogelj 3, Borut Bratanič 1, Eric L. Ding 4, Rok Orel 1, Nataša Fidler Mis 1

1University Medical Centre Ljubljana, University Children’s Hospital, Slovenia, 2Jožef Stefan Institute, 3University of Ljubljana, Biotechnical Faculty, Ljubljana, Slovenia, 4Harvard School of Public Health, Boston, United States

**Objectives & Study:** Paper-based dietary records (Paper-DR) can potentially be replaced by Web-based dietary records (Web-DR) in epidemiological studies and in clinical practice to reduce the time, logistic burden, and costs of data processing. The purpose of the study was to compare a four-day Paper-DR with a four-day Web-DR for the same individuals, matched for the same four days, across a range of nutritional parameters.

**Methods:** We compared matching of different food items (n=1103) from 32 Paper-DR and Web-DR for 49 parameters (energy, 18 macronutrients, major fat categories, alcohol and 24 micronutrients: 12 vitamins, 6 minerals and 6 trace elements) conducted among 16 pregnant Slovenian volunteers (age-range: 24–36 years; pregnancy gestation range: 13–36 weeks) in four days. Paper-DRs completed by volunteers were then coded into the Web-based version (referred to as Paper-Web-DR) independently by an experienced research dietitian. Volunteers were also assessed to complete evaluations of the user-acceptability of Paper-DR and Web-DR. The study was approved by the Slovenian Ethics Committee and is part of the project entitled “My-Milk” (http://www.moje-mleko.si/en/; registered at ClinicalTrials.gov as NCT01548313).

**Results:** The Wilcoxon signed-rank test comparing mean rank differences among 49 parameters, recorded with Paper-Web-DR versus Web-DR, resulted in insignificant differences among all nutrient items, except for free sugars ($P<0.001$), α-linolenic acid ($P=0.041$), folate ($P=0.036$) and pantothenic acid ($P=0.023$). Volunteers found Paper-DR equally time-consuming as Web-DR (average: 18±16 min versus 19±8 min), though the majority of the volunteers (75%) preferred Web-DR.

**Conclusion:** Paper-DR and Web-DR compared favorably across a range of nutritional parameters, with few exceptions. Web-DR is more convenient for the majority with computer literacy and access to computers or mobile devices which have substantial logistic and cost advantages for researchers and clinical dietitians.

**Disclosure of Interest:** None Declared
Objectives & Study: There is little information on the bioavailability of vitamins, minerals, and trace elements in pediatric feeds in children who are fed enterally for a long period of time. The effects of gastrointestinal dysmotility, which is often present in children on long term gastrostomy feeding, has not been studied regarding micronutrient absorption. In addition, there is a lack of agreed protocols for monitoring micronutrient intake and status in children on long term enteral nutrition.

Aim: We conducted an audit on micronutrient intake in children who received at least 50% of their daily intake by formula via gastrostomy.

Methods: Dietitians records for 75 children with gastrostomy were reviewed. 45 children were fed at least 50% of their daily intake by gastrostomy feeding. Data from 41 (4 missing) children were analysed. The daily intake of micronutrients was calculated by a computer program (DietistNet) based on Nordic Nutrition Recommendation, NNR (for healthy children) and licensed from Kostdata, Sweden.

Results: There were 22 girls and 19 boys, median age 7.5 (range 0.8-18.5 years). A feeding gastrostomy button was placed at median age 3.5 (0.1-11.9) years. Intake of at least one micronutrient higher than 150% of NNR was found in 40/41 children. Excess intake of the following micronutrients were found: Vitamins: Fat soluble; vit A 10/41, vit D 19/41, vit E 39/41. Water soluble: vit C 32/41, thiamin 27/41, riboflavin 22/41, B6 22/41, B12 30/41, niacin 5/41, folic acid 21/41. Minerals: zink 26/41, phosphate 7/41, selenium 14/41, calcium 8/41, iron 13/41. The overall excess intake was median 5 (1-14) of various micronutrients.

Conclusion: This audit reports excessive micronutrient intake in children fed by gastrostomy. We can not conclude that this results in nutritional or medical side-effects. However, further studies are warranted to clarify if micronutrient content recommendations of commercially available formulas are adequate.

Disclosure of Interest: None Declared
AUDIT OF A PROTOCOL FOR BIOCHEMICAL MONITORING OF LONG-TERM ENTERAL NUTRITION

Charlotte Blank 1, Ellen Alge 1, Yigael Finkel 2

1 Sachs’ Children and Youth Hospital, Stockholm, Sweden, 2 Dept of Clinical Science and Education, Karolinska Institutet, Stockholm, Sweden

Objectives & Study: Background: There is no agreed protocol for monitoring micronutrient status in children on long term enteral nutrition. Based on results of a questionnaire to 42 pediatric gastroenterologist we set up a protocol with 25 biochemical analyses to monitor clinically stable children on long-term enteral nutrition yearly. Aim: To audit results of nutrition monitoring protocol in children who received at least 50% of their daily intake by formula via gastrostomy.

Methods: Children: 45/75 children managed by the nutrition team fulfilled the inclusion criteria, but 4 were excluded due to incomplete data. All had neuro/muscular functional impairment, many were on anti-epileptic medications. All gastrostomies had been inserted by laparoscopic method by pediatric surgeons. Results of biochemistry test from the last 18 months were included. Results obtained during intercurrent disease were excluded.

Results: We studied 41 children (22 girls) their median age 7.5 (0.8-18.5) years, with a feeding gastrostomy inserted at median age 2.6 (0.1-11.5) years. From our 25 items list we selected micronutrient status and renal function. The results outside reference values were: Low hemoglobin 1/41, 25-OH vitamin D 21/41, albumin 14/41, iron 6/41, calcium 2/41, High ASAT 11/41, urea 11/41, transferrin-receptor 7/41

Conclusion: Low vitamin D levels were commonly found. The results of biochemical monitoring are probably influenced by both underlying disease(s)/syndromes and concurrent medical therapy.

Disclosure of Interest: None Declared
INCREASED IL15 EXPRESSION ON MONOCYTES AND DENDRITIC CELLS OF COELIAC PATIENTS

Katia Ferrara 1,*, Valentina Discepolo 1,2, Sara Santagata 1, Marialaura Cuomo 1, Marco Sarno 1, Alessandra Carrella 1, Giuliana Lania 1, Renata Auricchio 1, Salvatore Auricchio 1, Delia Zanzi 1, Maria Vittoria Barone 1, Riccardo Troncone 1
1Translational Medical Science, ELFID, University Federico II, Naples, Italy, 2The University of Chicago Coeliac Disease Center, University of Chicago (IL), Chicago, United States

Objectives & Study: IL15 is a pro-inflammatory cytokine known to play a pivotal role in the pathogenesis of celiac disease (CD). While intestinal dendritic Cells (DCs) are known to orchestrate the interplay between innate and adaptive immune responses, few is known about peripheral DCs in CD patients. Moreover, the role of IL15 outside the gut has not been explored yet. This study aims to investigate the expression of IL-15 in peripheral Monocytes and monocyte-derived DCs of CD patients and its functional implications.

Methods: Monocytes and CD8+ T-cells were purified from Peripheral Blood Mononuclear Cells from healthy donors (CTR), untreated and gluten free diet (GFD) celiac patients. DCs were generated from monocytes after 6-day-culture with IL-4 and GM-CSF. IL15 expression was evaluated by flow cytometry and RT-PCR. In vitro proliferation assay was performed co-colturing monocytes/DCs with CD8+ T cells in presence or absence of a neutralizing anti-IL15 antibody.

Results: Cytofluorimetric analysis showed an increased expression of IL15 on peripheral cells from CD patients. Compared to monocytes and DCs from healthy subjects (MFI±SD, 38±14 and 42.7±22.6 respectively) IL15 MFI was significantly higher in active CD (140±86.5 and 77.2±49.3, p<0.01) and GFD patients (120±79 and 83.3±27.7, p<0.001). We observed also a greater percentage of monocytes and DCs expressing IL15 from active CD (mean±sd 34.4±18.5 and 13.7±14.4, p<0.05) and GFD patients (22.2±7.25 and 14.1±13, p<0.05) compared to CTR (15.5±9.1 and 5.9±5.4). Preliminary RT-PCR data confirmed the increased IL15 expression in both cell types. To test whether IL15 overexpression had any functional consequence we investigated proliferation of CD8+ T cells in response to IL15. As expected, co-colturing CD8+ T cells with allogenic monocytes and DCs from CD patients induced a strong proliferative response, that was prevented by anti-IL15 blocking antibodies.

Conclusion: Higher IL15 levels have been shown in peripheral monocytes and monocyte-derived DCs of both treated and untreated CD patients, suggesting a constitutive alteration beyond this observation. Interestingly monocytes and DCs from CD patients but not from controls can induce allogenic CD8+ T cells proliferation in an IL15-depended fashion. These findings support the hypothesis that in CD an overexpression of IL15 is present also outside the initial site of inflammation and may contribute to the promotion of systemic autoimmune processes.

Disclosure of Interest: None Declared
Gastroenterology
Coeliac Disease
PO-G-0009

REPEATED ANTIBIOTIC EXPOSURE IS ASSOCIATED WITH INCREASED RISK OF COELIAC DISEASE IN A PROSPECTIVE BIRTH COHORT

Ketil Stordal 1,* Lars Christian Stene 1
1Epidemiology, Norwegian Institute of Public Health, Oslo, Norway

Objectives & Study: The early gut microflora is thought to be involved in the development of tolerance to food antigens, and is modified by breastfeeding and mode of delivery. Antibiotics may alter the developing gut microflora. We aimed to study the association between exposure to antibiotics from intrauterine life and up to 18 months and later celiac disease in childhood.

Methods: In a prospective birth cohort study with children born from 1999-2009, children with celiac disease were identified through reporting by parental questionnaires at 7 and 8 years and by linkage to the Norwegian Patient Register. The ESPGHAN diagnostic criteria were required for diagnosis. A total of 650 cases of celiac disease (399 females, 61%) were identified from 107 806 live births (6.0/1000) with the diagnosis recorded at a minimum of two occasions in NPR or indicated from parental questionnaire. Detailed questionnaires regarding diet, infections and any use of antibiotics were completed by the parents when the child was 6 and 18 months old, and information about perinatal antibiotic treatment was obtained from the medical birth registry.

Results: The mean age of the cohort at analysis was 7.4 years (median 7.5, range 3.5-13.5 years). 559 children with celiac disease had complete data up to 6 months and 489 up to 18 months, and 89010 and 75824 remained of the non-celiac controls in the analysis, respectively.

2.5 % received antibiotics during the first hospital stay, 7.4% reported use of oral antibiotics between 0 and 6 months and 26.2% from 6-18 months of age. 7.5% had two or more antibiotic courses before 18 months of age. Any antibiotics versus none to the infant as a newborn (adjusted OR 1.02, 95% CI 0.56-1.87), from 0-6 months (adjusted OR 1.09, 95% CI 0.85-1.40) or from 6-18 (adjusted OR 1.21, 95% CI 0.99-1.49) was not significantly associated with the risk of later celiac disease after adjustment for maternal celiac disease, sex, age of child, gluten introduction after 6 months, breastfeeding, mode of delivery and number of infections during the time period of antibiotic exposure. Two or more courses of antibiotics versus none from birth up to 18 months age were associated with an increased risk of celiac disease (adjusted OR 1.65, 95% CI 1.19-2.29). The total number of reported infections before age 18 months was 9.6 in children with later celiac disease compared to 8.8 in non-celiac (p=0.006), and remained significantly associated with later celiac disease after adjustment for infection and other covariates (aOR 1.018 per episode, 95% CI 1.001-1.034, p=0.035). Antibiotics given to the mother during pregnancy or lactation was not associated with later risk of celiac disease in the offspring.

Conclusion: Repeated antibiotic therapy from 0-18 months of life was associated with an increased risk for celiac disease, and the association was independent of the number of infections in the child.

Disclosure of Interest: None Declared
Objectives & Study: Upper GI endoscopies are still required to diagnose the majority of celiac children, notwithstanding the recently updated ESPGHAN criteria. The “multiple-biopsy” approach both in the duodenum and in the bulb has been suggested by several guidelines as the best strategy to confirm the diagnosis of celiac disease (CD); however, this approach increases the invasiveness of the endoscopic procedure itself and is fairly time-consuming. Our aim was to evaluate the diagnostic yield of a single biopsy guided by narrow-band imaging (NBI) combined to water immersion technique (WIT), in the assessment of CD in a prospective, single center, pediatric study.

Methods: We enrolled 43 children (12 males; mean age: 7.2 years; age range: 1.25-15.25 years) with suspected CD (positive anti-transglutaminase and antiendomisial antibodies) undergoing upper GI endoscopy to compare single “NBI plus WIT”-guided biopsy versus the standard, duodenal and bulbar, “multiple-biopsy” approach (2 random biopsies in the bulb, 4 random biopsies in the 2nd-3rd duodenal portion). “NBI-plus-WIT” endoscopic severity was classified on a Likert scale as normal, altered with mild modifications (nodular mucosa, scalloping) or clearly altered (reduction and flattening of “plicae”); inter-observer variability between two different physicians was also assessed with regards to endoscopic judgments. Histology was graded according to the Marsh-Oberhuber classification.

Results: Diagnosis of CD was confirmed in 40 out of 43 children (the remaining 3 were diagnosed as potential CD). “NBI plus WIT” approach correctly diagnosed 35 out of 40 celiac children, with a diagnostic sensitivity of 87.5% (C.I.: 77.3-97.7); none among the studied patients showed an exclusive, “NBI plus WIT”-detected histological damage. Clearly altered pattern at “NBI plus WIT” endoscopic visualization was significantly associated to villous atrophy both at “NBI plus WIT”-guided biopsy and at multiple biopsy sampling (Spearman Rho 0.637 and 0.496). High anti-transglutaminase antibody titer (≥10 times upper limit normal) was also associated to clearly altered pattern at “NBI plus WIT” endoscopic visualization. Concordance of “NBI plus WIT” endoscopic assessments was fairly high between two different operators (K: 0.884). After the passage through the pylorus of the endoscope, mean NBI plus WIT procedure time was 53.6 sec (SD: 12.7 sec), whereas mean time for multiple biopsy sampling was 218.2 sec (SD: 38.3 sec) (p<0.0001).

Conclusion: Albeit time- and resource-saving, single “NBI plus WIT”-guided biopsy is not as effective as the well established “multiple-biopsy” approach in confirming the diagnosis of CD.

Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0011

ALTERED LPP SUB-CELLULAR DISTRIBUTION IDENTIFIES A COELIAC CELLULAR PHENOTYPE INDUCIBLE IN CONTROLS BY THE GLIADIN PEPTIDE P31-43

Merlin Nanayakkara 1, Giuliana Lania 1, Roberta Kosova 1, Marco Sarno 1, Marialaura Cuomo 1, Martina Galatola 1, Katia Ferrara 1, Stefania Gagliardi 1, Marzia Spagnardi 1, Alessandra Gaito 1, Pio Stellato 1, Luigi Greco 1, Riccardo Troncone 1, Salvatore Auricchio 1, Maria Vittoria Barone 1

1Department of Translational Medical Science, ELFID University of Naples "Federico II", Naples, Italy

**Objectives & Study:** Celiac disease (CD) is a frequent inflammatory intestinal disease, with a genetic background, caused by gliadin-containing food. Alterations in the cell shape and actin cytoskeleton are present in celiac enterocytes, and gliadin peptides induce actin rearrangements in both the CD mucosa and cell lines. The locus of the human Lipoma Preferred Partner (LPP) gene was identified as strongly associated with CD using both genome-wide association (GWAS) and expression studies. In an effort to link genomic alterations and CD phenotype we analyzed focal adhesion number, their proteins and LPP sub-cellular distribution in CD patients on a Gluten-Free Diet (GFD) and controls, without and with treatment with A-gliadin peptide P31-43.

**Methods:** Immunofluorescence (IF) and Western blot (WB) analysis were used to study focal adhesions and LPP sub-cellular localization in CD fibroblasts. LPP mRNA levels were studied by PCR.

**Results:** Focal adhesions were significantly increased in CD fibroblasts in comparison to controls. Paxillin- and FAK-positive focal adhesions were 36.7+/- 11.59 and 37.7+/-5.18 in controls and 75+/-9.41 and 70+/-7.39 in CD fibroblasts. WB analysis revealed an increase of both non- and phosphorylated paxillin and FAK protein in fibroblasts from CD patients in comparison to controls. Treatment with P31-43 increased both paxillin and FAK positive focal adhesions in CD fibroblasts and in controls. LPP mRNA and protein levels were similar in CD and control fibroblasts. The IF analysis using an antibody against paxillin and LPP revealed that LPP co-localized with paxillin in focal adhesions. Separating the nuclear and cytosolic protein fractions, a different sub-cellular localization of LPP in CD fibroblasts in comparison to controls was shown, independent from LPP genotype. P31-43 treatment reproduced the CD phenotype in controls, with increased LPP localization in focal adhesions.

**Conclusion:** In fibroblasts from all CD patients constitutive alterations of cell shape and adhesion are present, involving LPP. This “CD cellular phenotype” is reproduced in control cells following treatment with P31-43, implying a close association between these alterations and CD pathogenesis.

**Disclosure of Interest:** None Declared
INTESTINAL ANTI-TISSUE TRANSGLUTAMINASE ANTIBODIES POSITIVELY CORRELATE WITH THE DEGREE OF MUCOSAL DAMAGE AND INVERSELY WITH THE DURATION OF GLUTEN-FREE DIET

Renata Auricchio 1,*, Antonella Tosco 1, Rosita Aitoro 1, Erasmo Miele 1, Domenico Ponticelli 1, Maria Primario 1, Vera Rotondi Aufiero 1, Marianna Paccone 1, Riccardo Troncone 1, Mariantonia Maglio 1

1 European Laboratory for the Investigation of Food Induced Diseases (ELFID), University Federico II, Naples, Italy

Objectives & Study: Serum anti-tissue transglutaminase2 (TG2) antibodies level correlate with the degree of mucosal damage and decrease on a gluten-free diet (GFD). Anti-TG2 antibodies are produced in the small intestinal mucosa, deposited below the epithelium, and secreted in biopsy culture supernatants. Our aim was to correlate the levels of intestinal anti-TG2 antibodies with the degree of mucosal damage as well as with the duration of GFD.

Methods: We enrolled 34 active and 71 potential CD patients with grade Marsh 3 (3a=13, 3b=11, 3c=10) and Marsh 0/1 (0=34, 1=37) lesion, respectively, and 24 patients on GFD from at least 2 years. Mucosal deposits in intestinal biopsies were detected by double immunofluorescence. Intestinal fragments were cultured for 24h with medium, and in some experiments with PTG/P3143 (1mg/ml, 100γ/ml, respectively). Anti-TG2 antibodies secreted into supernatants were measured by ELISA.

Results: All active CD patients secreted into culture medium high titers of anti-TG2 antibodies (range 15.26-2000U/ml), that increased with the worsening of mucosal injury, from grade Marsh 3a to Marsh 3c lesion (Spearman r=0.71; p<0.0001). 70/71 potential CD patients produced anti-TG2 antibodies into supernatants with significantly lower titers, ranging from 4.2 to 1247.0 U/ml. When CD patients on a GFD were considered, 15/24 secreted low titers of anti-TG2 antibodies (range 3.3-27.2U/ml). 8/9 negative patients were on a GFD from more than 10 years, and an inverse correlation between antibody titers and duration of GFD was found (Spearman r = -0.52, p<0.01). In all active CD, 53/71 potential CD and 6/24 CD patients on GFD anti-TG2 deposits were detected. However, among the 18 potential CD patients without mucosal deposits, only one was also negative for anti-TG2 secreted into supernatants. Among the 6 CD patients on GFD positive, 5 were on GFD from less than 6 years and secreted anti-TG2 into culture medium with titers ranging from 22 to 27 U/ml. The intensity of staining of mucosal deposits of anti-TG2 was directly correlated with titers of secreted anti-TG2 (Spearman r= 0.63, p<0.001). Finally, in vitro challenge with PTG/P31-43 was not able to induce secretion of anti-TG2 antibodies into culture medium from all, but one, CD patients on GFD.

Conclusion: Measurement of intestinal antibodies in biopsy supernatants proves to be quantitative and more sensitive than detection by immunofluorescence. Intestinal anti-TG2 antibodies titers, as in the serum, positively correlate with the degree of mucosal damage and inversely with the duration of gluten-free diet.

Disclosure of Interest: None Declared
ARE ESPGHAN 2011 GUIDELINES FOR COELIAC DISEASE ALSO SUITABLE FOR ASYMPTOMATIC PATIENTS?

Chiara Maria Trovato 1,*, Francesco Valitutti 1, Ilaria Celletti 1, Stefania Leoni 1, Silvia Gatti 1, Donatella Iorfida 1, Monica Montuori 1, Caterina Anania 1, Annarita Vestri 2, Maria Barbato 1, Salvatore Cucchiara 1

1Dept. of Paediatrics, 2Dept. of Public Health and Infectious Diseases, Sapienza University, Rome, Italy

Objectives & Study: In 2011, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) has released its updated guidelines on celiac disease (CD) diagnosis. According to these new guidelines, symptomatic children with anti-transglutaminase (anti-tTG2) antibody levels ≥ 10 times upper limit normal (ULN) could avoid duodenal biopsies if the HLA test and serum anti-endomysial antibodies (EMA) are positive. So far, both symptomatic patients with anti-tTG2 titer <10 times ULN and those asymptomatic should undergo upper endoscopy with multiple duodenal biopsies to confirm a suspected CD. The aim of this study was to assess the accuracy of serological tests in asymptomatic patients to diagnose CD.

Methods: We retrospectively assessed 286 children and adolescents (mean age: 8.3 years; age range: 10 months-17 years) who had received a CD diagnosis based on elevated titer of anti-tTG2, EMA positivity, histology and HLA typing. All patients (95 boys, 191 girls) were positive for anti-tTG2 and EMA. Patients were distinguished between symptomatic and asymptomatic while histological lesions were graded according to the Marsh-Oberhuber (MO) criteria. Statistical evaluation was made with the Fisher exact test.

Results: Among the 286 EMA positive biopsied children, 196 (68.53%) had anti-tTG2 titers ≥ 10 times ULN. Among them, a group of 156 (54.54 %) children also had symptoms suggestive of CD (namely “high-titer” symptomatic children); of these, 142 (91.02%) showed severe lesion degree (3a, 3b, 3c MO). On the contrary, 40 out of 196 (13.98%) children were asymptomatic (namely “high-titer” asymptomatic children); 37 (92.5%) of them showed severe lesion degree (3a,3b, 3c MO). No difference was found between “high-titer” symptomatic children and “high-titer” asymptomatic children with regards to histological damage (Fisher exact test p=1,000).

Conclusion: Our results indicate that the absence of symptoms in children with anti-tTG2 titers >10 times ULN and positive EMA antibodies does not undermine a possible “biopsy-sparing” CD diagnosis. The “biopsy-sparing” protocol seems to be applicable to both symptomatic and asymptomatic patients with anti-tTG2 titer >10 times ULN, EMA positivity and HLA-DQ2/DQ8.

Disclosure of Interest: None Declared
A CONSTITUTIVE ALTERATION OF EGF/EGFR ACTIVATION AND TRAFFICKING DEFINE A CD CELLULAR PHENOTYPE INDUCIBLE BY GLIADIN PEPTIDE P31-43

Giuliana Lania 1,*, Merlin Nanayakkara 1, Roberta Kosova 1, Marco Sarno 1, Alessandra Carrella 1, Katia Ferrara 1, Stefania Gagliardi 1, Ivan Nista 1, Elio Fabio Esilio 1, Alessandra Gaito 1, Riccardo Troncone 1, Salvatore Auricchio 1, Maria Vittoria Barone 1
1Department of Translational Medical Sciences, ELFID University of Naples "Federico II", Naples, Italy

Objectives & Study: Celiac disease (CD) occurs frequently, and is caused by ingestion of cereal prolams in genetically predisposed. The small intestinal damage depends on an intestinal stress/innate immune response to certain gliadin peptides (e.g., A-gliadin P31-43) in association with an adaptive immune response to other gliadin peptides (e.g., A-gliadin P57-68). Gliadin and peptide P31-43 affect epithelial growth factor receptor (EGFR) signaling and CD enterocyte proliferation. The reason why the stress/innate immune and proliferative responses to certain gliadin peptides are present in CD and not in control intestine is so far unknown. The aim of this work is to investigate if, in CD, a constitutive alteration of enterocyte proliferation and signaling exists that may represent a predisposing condition to the damaging effects of gliadin.

Methods: Immunofluorescence and immunohistochemistry were used to study signaling and proliferation in CD fibroblasts and intestinal biopsies in the presence or absence of gliadin peptides. Western blot (WB) analysis and quantitative PCR were also used.

Results: In CD enterocytes proliferation is increased and enhancement of Epidermal Growth Factor Receptor (EGFR)/ligand system is present, in comparison to controls. EGFR and EGF trafficking in both CD enterocytes and fibroblasts is constitutively delayed with respect to controls. Moreover, in CD enterocytes and fibroblasts we found increase of the phosphorylated downstream signaling molecule Extracellular Signal Regulated Kinase (ERK); block of the ERK activation normalizes enterocytes proliferation in CD mucosa. P31–43 gliadin peptide alters EGFR and EGF signalling and trafficking in CD cells, as well as in controls, but in the latter only transiently.

Conclusion: The same pathway, which gliadin and gliadin peptide P31-43 can interfere with, is constitutively altered in CD cells. This observation potentially explains the specificity of the damaging effects of certain gliadin peptides on CD intestine.

Disclosure of Interest: None Declared
Gastroenterology

Coeliac Disease

PO-G-0015

DIAGNOSIS OF COELIAC DISEASE: IS STILL THERE A CORRELATION BETWEEN SEROLOGICAL MARKERS AND HISTOLOGICAL DAMAGE IN THE NEW CRITERIA AGE?

Matilde Rossi 1,* , Roberta Annibali 1, Simona Gatti 1, Claudio Marabini 1, Lisa Tonelli 1, Alessandra Palpacelli 1, Veronica Albano 1, Carlo Catassi 1

1Department of Paediatrics, Università Politecnica delle Marche, Ancona, Italy

Objectives & Study: According to the new European guidelines, biopsy can be avoided in the diagnosis of celiac disease (CD) in symptomatic children, with high antibody titer and HLA-DQ2/DQ8 genotypes. Application of the new criteria has an important impact on the health care system. To analyze the temporal trend of upper endoscopy performed for diagnosis of CD in children referred to our centre and to compare features of children diagnosed with and without biopsy.

Methods: Data from 141 children with CD (diagnosed between Jan 2011 and Jun 2013) were retrospectively reviewed. Earlier than 2011 we used to confirm diagnosis of CD with biopsy in all patients, while in Jan 2011 the new diagnostic criteria were pioneeringly applied in our centre. Clinical presentation, levels of serum IgA-anti-transglutaminase (tTG), IgG-deamidated-gliadin-peptides (DGP) and anti-endomisial antibodies (EMA), histological findings (Marsh classification) and HLA DQ2-DQ8 were collected for each patient. The temporal trend of biopsy/diagnosis ratio was analyzed. Clinical and serological findings were compared between 2 groups (children with a biopsy-proven diagnosis and without biopsy). Correlation between levels of antibodies and Marsh grade was identified.

Results: One hundred forty-one patients (mean age 7.32 years, SD 4.26, F/M: 2.47) were diagnosed with CD. The majority (47.2%) presented with typical symptoms, 28.8% had atypical presentation and 24% were asymptomatic. Diagnosis of CD was confirmed in 132 (92.8%). HLA DQ2-cis was found to be the most prevalent haplotype (31%). Overall 85 patients (60%) underwent biopsy and the remaining 56 (40%) did not require histological confirmation. The biopsy/diagnosis ratio was: 35/65 (53%), 28/47 (59%) and 22/29 (75%) in 2011, 2012 and in the first semester of 2013, respectively. Patients requiring biopsy were found to be 4-years older (p = 0.001) and to have lower values of tTG (p = 0.05) and DGP (p = 0.001) compared to those in which biopsy has been avoided. In the biopsy group 76 had major intestinal changes (Marsh 2–3). The remaining 9 patients (Marsh 0–1) were considered as having potential-CD. Increasing Marsh score was positively correlated with mean values of tTG (p = 0.040) and DGP (p = 0.057).

Conclusion: The new guidelines have dramatically reduced the number of children requiring biopsy for CD in our centre. Interestingly, our data show that in the group of children that did required biopsy, a positive correlation between levels of tTG and DGP antibodies and severity of the histological lesions can still be found. This finding further supports the validity of the new guidelines.

Disclosure of Interest: None Declared
**LACTOBACILLUS PARACASEI CBA L74 PREVENTS ENTRANCE OFUNDIGESTED GLIADIN PEPTIDES AND ROTAVIRUS IN CACO-2 CELLS**

Marco Sarno 1,*  Vittoria Buccigrossi 1, Merlin Nanayakkara 1, Giuliana Lania 1, Roberta Kosova 1, Marialaura Cuomo 1, Stefania Gagliardi 1, Francesca Passannanti 1, Carla Russo 1, Riccardo Troncone 1, Alfredo Guarino 1, Maria Vittoria Barone 1

1Department of Translational Medical Science, ELFID University of Naples "Federico II", Naples, Italy

**Objectives & Study:** Recent reports describe a role of probiotics as therapeutic approach for Celiac Disease (CD). Besides, rotavirus (RV) infections are described as a potential risk factor for CD development. Undigested A-gliadin peptides P31-43 and P57-68 are central to CD pathogenesis, entering in enterocytes in vesicular compartments by endocytosis and inducing an innate and an adaptive immune response respectively. Our aim is to test the effect of probiotic Lactobacillus Paracasei (LP) CBA L74 and its supernatant on P31-43, P57-68 and RV entrance in Caco-2 cells to verify its protective effect. The effect of supernatant on ROS production in RV infected Caco-2 was also tested.

**Methods:** We cultivated LP CBA L74, obtaining $10^8$ CFU/ml, and its supernatant was obtained by centrifugation and filtration. Caco-2 cells were treated with LP CBA L74 or with its filtered supernatant at 37°, CO₂ 5%, for 30 minutes, and then labeled P31-43/P57-68 or RV were added to cells cultures. We studied entrance of labeled peptides by fluorescence assay. RV entrance was assessed by direct immunofluorescence and the reactive oxygen species (ROS) production by dichlorofluorescein fluorimetric assay in Caco-2 cells infected with RV with or without bacterial supernatant.

**Results:** LP CBA L74 inhibited both P31-43 (FI reduction: 67.28%, P < 0.001) and P57-68 (FI reduction: 37.05%, P < 0.001) entrance respect to control. LP CBA L74 supernatant was also able to induce decrease of both gliadin peptides entrance in Caco-2 cells (FI reduction: 49.38% and 29.67% respectively, P < 0.001), indicating that this biological effect was due to some product included in LP CBA L74 supernatant. Supernatant significantly prevented RV entrance and ROS production (reduction of 56%, P < 0.001) in RV infected Caco-2 cells, showing a potential protective effect in RV infections.

**Conclusion:** LP CBA L74 and its supernatant, reduce P31-43, P57-68 and RV entrance in Caco-2 cells probably acting on the endocytic trafficking. Moreover supernatant can protect Caco2 cells from RV mediated increase of ROS.

This study is the first attempt to explain the molecular mechanisms of probiotic effects in the prevention of both RV infections and undigested gliadin peptides toxic effects.

**Disclosure of Interest:** None Declared
Gastroenterology
Coeliac Disease
PO-G-0017

INVolvEMENT OF THYMIC STROMAL LYMPHopoietIN AND PEROxisOME PROLIFERATOR-ACTIVATED RECEPTOR? IN COELIAC DISEASE

Erna Sziksz 1,2,* , Kriszta Molnár 1 , Rita Lippai 1 , Domonkos Pap 1 , Anna Önody 1 , Apor Veres-Székely 1 , Beáta Szébeni 1,2 , Péter Vörös 1 , Hajnalka Győrffy 3 , Gábor Veres 1 , Tivadar Tulassay 1,2 , Ádám Vannay 1,2 , Andráss Arató 1

1st Department of Paediatrics, Semmelweis University, Budapest, Hungary, 2Research Group for Paediatrics and Nephrology, Hungarian Academy of Sciences and Semmelweis University, Budapest, Hungary, 32nd Department of Pathology, Semmelweis University, Budapest, Hungary

Objectives & Study: Coeliac disease (CD) is an autoimmune disorder characterized by an abnormal immune response and villous atrophy in susceptible individuals to dietary gluten. Better understanding of the inflammatory processes in CD may contribute to the development of novel alternative therapies. Peroxisome proliferator-activated receptor (PPARγ) was shown to have anti-inflammatory and cytoprotective effects in several diseases. Furthermore PPARγ agonist inhibited the thymic stromal lymphopoietin (TSLP)-induced maturation of dendritic cells suggesting the suppressive effect of PPARγ on TSLP-stimulated processes. Since our knowledge about the role of PPARγ and TSLP in gastrointestinal diseases is incomplete, our aim was to clarify their involvement in CD.

Methods: Duodenal biopsy specimens were collected from 19 children with untreated CD, 5 children with treated CD (maintained on gluten free diet, GFD) and 10 controls. PPARγ, TSLP and TSLPR mRNA expression and protein levels were determined by real-time PCR and Western blot, respectively. Localization was detected by immunofluorescence staining.

Results: In the duodenal mucosa of children with CD the mRNA expression and also the protein levels of PPARγ decreased and at the same time expression of TSLP significantly increased compared to controls (p<0.05). In accordance with the immunofluorescence staining following GFD treatment the mRNA expression and protein amount of PPARγ were significantly elevated while that of TSLP markedly decreased (p<0.05).

Conclusion: Decreased amount of PPARγ and the simultaneously increased levels of TSLP in the duodenal mucosa of children with newly diagnosed CD suggest their involvement in the pathomechanism of CD. We hypothesize that PPARγ may be an inhibitory regulator of the TSLP-stimulated inflammatory processes.

Disclosure of Interest: None Declared
COMPLEMENTARY BLOOD INVESTIGATIONS IN THE DIAGNOSIS AND FOLLOW-UP OF COELIAC CHILDREN: ARE THEY NECESSARY?

Margreet MS Wessels 1,*, Sabine L Vriezinga 1, Iris I van Veen 1, Bibi Funke-Kupper 1, Hein Putter 2, MLuisa Mearin 1

1Paediatric Gastroenterology, 2Statistics, LUMC, Leiden, Netherlands

Objectives & Study: Laboratory investigations regarding iron, calcium and vitamin deficiency together with thyroid disease are advised for children with coeliac disease (CD) both at diagnosis and during follow-up. Primary aim was to determine the frequency of iron, folate and vitamin B12 deficiency, hypocalcaemia and thyroid dysfunction in children with CD at diagnosis and during follow-up. Secondary aim was to assess if these investigations should be part of the clinical control of the children.

Methods: The laboratory results on Hemoglobin (Hb), Ferritin (Fe), Folate (Fo), vitamin B12 (vB12), Calcium (Ca), Free Thyroxine (FT4) and Thyroid Stimulating Hormone (TSH), done as part of the clinical work-up for the diagnosis and follow-up of children with CD attending the LUMC between 2009 and 2013 were investigated. Abnormal results were defined according to the LUMC laboratory references: Hb < 6.9 mmol/L (<7 yrs), < 6.5 mmol/L (7-15 yrs), < 6.0 mmol/L (>15 yrs); Fe < 12 ug/L (<5 yrs), < 15 ug/L (> 5 yrs); Fo < 10 nmol/L; vB12 < 150 pmol/L; Ca < 2.15 mmol/L; FT4 < 10 pmol/L; TSH > 4.8 mU/L. The frequency of abnormal results was analyzed with a generalized linear mixed model (GLMM), providing model based percentages accounting for missing values. Where appropriate, Pearson’s Chi-square test for trend, unpaired t-test and one-way ANOVA were used.

Results: Complementary blood investigations were done 236 times in 102 CD children: 27 times at time of diagnosis and 48, 55, 38, 38 and 30 times during the 1st, 2nd, 3rd, 4th and 5th year after diagnosis respectively. The patients had a mean age at diagnosis of 6.2 yrs(1.0-17.7), 71% were female, with a mean duration of follow-up of 3.6 years(0-8.8). 83% Of blood investigations were complete for all parameters. At diagnosis, 34% and 10% of the children had low levels of both Fe and Fo and of B12 respectively. Iron deficiency anemia was present in 8% of the patients. There were no children with hypocalcaemia or thyroid disease. During follow-up, low Fe levels were present in 4% of the children. None of the patients had iron deficiency anemia. Elevated TSH levels were seen in 7% of the children, in all cases with normal FT4 levels, therefore ruling out thyroid disease.

Conclusion: Fe, Fo and vB12 measurements are relevant at the time of diagnosis of CD. However, in absence of specific symptoms, thyroid function and Fe, Fo, vB12 and Ca measurements should not be performed during the follow-up clinical controls of children with CD.

Disclosure of Interest: None Declared
ADOLESCENTS EXPERIENCE LIVING WITH SCREENING-DETECTED COELIAC DISEASE 5 YEARS AFTER DIAGNOSIS

Katrina Nordyke 1, Anna Rosén 1, Maria Emmelin 2, Anneli Ivarsson 1
1Public Health and Clinical Medicine, Epidemiology and Global Health Unit, Umeå University, Umeå, Sweden, 2Clinical Sciences, Social Medicine and Global Health, Lund University, Lund, Sweden

Objectives & Study: Mass screening could identify those with unrecognized celiac disease (CD), but the experience of being detected through screening and living with screening-detected CD should be explored before considering this intervention. In this study, the perceptions, practices, and beliefs of adolescents with screening-detected CD are explored five years after their diagnosis.

Methods: A CD screening study involving 12-year-olds, known as “ETICS” (Exploring The Iceberg of Celiacs in Sweden), provided a platform to explore benefits and harms of CD screening. Screening-detected adolescents were invited to write narratives one and five years after diagnosis. They described: how it felt to be diagnosed, how life changed, how it works with food, and how they feel about screening all children. From the 151 screening-detected adolescents, 91 wrote one year after and 72 wrote five years after. A qualitative content analysis resulted in the overall theme and four categories describing issues related to the experience of living with screening-detected CD for five years.

Results: The overall theme, “Internalizing the threat of risk”, illustrates that for these adolescents being detected through screening and the threat of future health complications impacted how they felt about the diagnosis, coped with the gluten-free diet (GFD), and thought about CD screening. This theme is supported by four categories: "Maintaining an imposed disease identity", "Moving from forced food changes to adapted diet routines", "Enduring beliefs of being spared negative consequences", and "Continuing to fear it is "all in vain". Even after five years of living with CD, these adolescents have maintained an imposed disease identity continuing to describe how they were diagnosed because of the screening. Specific foods and environments were the focus after one year, but after five years they also described routines, coping strategies, and the financial burden associated with the GFD, moving from forced food changes to adapted diet routines. They still believed that by being diagnosed and following the GFD they are being spared negative consequences, also why they believed all kids should be screened. Some still doubt they really have CD and worry being detected and eating a GFD may not be beneficial, continuing to fear it is “all in vain”.

Conclusion: Being screening-detected and the length of time the adolescents have lived with CD has impacted how they have integrated the disease into their lives. Some have adjusted to the disease and feel grateful they were detected, while others still doubt they have it or that being detected was beneficial. These finding illustrate the lasting impact disease screening may have, the importance of providing a high standard of care when approaching and diagnosing individuals, and the need to provide those with screening-detected CD continued support as they learn about CD and adapt to the GFD.

Disclosure of Interest: None Declared
COELIAC DISEASE DIAGNOSIS: A NEW ERA


1Gastroenterology Unit, Hospital La Fe, Valencia, Spain, 2Gastroenterology Unit, H. Puerta de Hierro, Madrid, Spain, 3Gastroenterology Unit, H. Puerta de Hierro, Madrid, Spain, 4Gastroenterology Unit, H La Paz, Madrid, Spain, 5Gastroenterology Unit, H.Virgen de la Candelaria, Tenerife, Spain, 6Gastroenterology Unit, H. Virgen Camino, Pamplona, Spain, 7Gastroenterology Unit, H de Vigo, Vigo, Spain, 8Gastroenterology Unit, H. Virgen Rocio, Sevilla, Tenerife, Spain, 9Gastroenterology Unit, H. Virgen Salud, Toledo, Spain, 10Gastroenterology Unit, H. Donostia, San Sebastian, Spain, 11Gastroenterology Unit, H. San Pedro, Caceres, Spain, 12Gastroenterology Unit, H. de Santiago, Santiago Compostela, Spain, 13Gastroenterology Unit, H. Valdecilla, Santander, Spain, 14Gastroenterology Unit, H. Maternoinfantil Las Palmas, Canarias, Spain, 15Gastroenterology Unit, H. Txagorribu, Vitoria, 16Gastroenterology Unit, H SAS Jerez de la Frontera, Cadiz, Spain, 17Gastroenterology Unit, H U de Fuenlabrada, Madrid, Spain, 18Gastroenterology Unit, H Doce de Octubre, Madrid, Spain, 19Gastroenterology Unit, H U Guadalajara, Guadalajara, Spain, 20Gastroenterology Unit, H.U Canarias, Canarias, Spain

Objectives & Study: To assess the application of the new 2012 ESPGHAN recommendations for Celiac Disease (CD) diagnosis.

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

Results: From 1/01/2012 till 31/10/2013 a total of 1801 new CD cases were reported by the 53 investigation centers participating in the national survey. In 576 cases (32 %) no small bowel biopsy (SBB) was performed. Of these, 22 were asymptomatic, 60 more had tissue transglutaminase antibodies (TTG) lower than 10 times the upper level of normal (ULN), and in 494 TTG was > 10xULN. In this last subset of patients 33 endomisial antibodies (EMA) were not available and 5 more were negative; in 28 HLA was not determined and 3 were DQ2.2. Overall 425 out of 576 truly complied with the new criteria for CD diagnosis without a SBB, i.e. 74%. It is noteworthy that in 151 cases (26 %) with no SBB of them a diagnosis of CD was confirmed although not complying with the recommendations, herein being included asymptomatic children (3,8%) and patients with TTG < 10x ULN (10.8%).

Conclusion: Nowadays in the Spanish paediatric population still a minority of cases were diagnosed without a SBB, although in comparison with previous data the percentage has increased significantly from 8% in the year 2011 till 32% in the present 2012-2013 survey. Although the majority of them truly fulfilled the 2012 ESPGHAN criteria which permit to avoid a SBB in selected cases, however it is a source of concern that about ¼ of cases did not complied. A note of caution has to be uttered at this early stage of implementation of the new criteria so as to avoid CD overdiagnosis in the near future.

Disclosure of Interest: None Declared
A BAYESIAN APPROACH TO IMPROVE THE IDENTIFICATION OF SUBJECT WITH AN HIGH RISK OF COELIAC DISEASE

Pio Stellato 1,*, Giuseppina Gambino 1, Camilla Panico 1, Martina Galatola 1,2, Donatella Cielo 1,3, Sara Baselice 1, Andrea Smarrazzo 1, Francesca Tucci 1, Renata Auricchio 3,4, Luigi Greco 1
1Department of Translational Medical Sciences, 2Department of Molecular Medicine and Medical Biotechnology, 3European Laboratory for the Investigation of Food Induced Diseases (ELFID), 4Translational Medical Sciences, University of Naples "Federico II", Napoli, Italy

Objectives & Study: Coeliac Disease (CD) is an immune-mediated disorder caused by ingestion of gluten in genetically susceptible individuals. HLA can explain about 40% of hereditability and in the last years were identified about 60 others candidates genes. In a previous study, using a Bayesian approach, we improve the estimate of CD risk in siblings by three non HLA genes (LPP, RGS1 and cREL). We decided to analyze a new independent cohort of CD family using the same approach to validate our predictive model that can improve the identification of high-risk subjects among first-degree relatives.

Methods: The validation cohort is made up by of 293 subjects from “at risk” families with a case, they include: 71 probands, 191 healthy relatives and 31 other celiac patients. All individuals were typed for HLA and 3 single nucleotide polymorphisms (SNPs) in non-HLA genes: RGS1 (rs2816316), LPP (rs1464510), REL (rs842647) identified in our previous study. A Bayesian approach was used to assign a score (BS) to each detected HLA+SNPs genotype combination. We then classified CD sibs as at low or at high risk if their BS was respectively < or ≥ median BS value within each HLA risk group.

Results: 84% of our cohort is DQ2 and/or DQ8 positive and only 16% is DQ2 and DQ8 negative. 21% of healthy relatives belong to higher HLA risk class and is exposed to an high risk of developing CD. The probability to get CD (estimated by the Bayes score) rises with the number of “A risk alleles” in non-HLA SNPs and improve the estimation of risk in the moderate HLA-risk class. Considering the distribution of all the sibs under or above median BS, a larger number of affected sibs showed a BS greater than or equal to median value than non affected sibs.

Conclusion: In order to validate a new diagnostic tool, it is crucial to confirm our results in a new independent cohort. In our previous work we demonstrated that the Bayesian approach brought us a significant enhancement of diagnostic sensitivity compared with HLA only (79% Vs 51%) and an improvement in negative predicting value (NPV) (95% Vs 90%). Here, with a validation cohort we have not only confirmed our previous data, but also enhanced the NPV that raised from 95% to 96% and the diagnostic sensitivity increasing from 79% to 84%. Now we are still extending the validation cohort to definitively confirm our model, but we think these results, although not definitive, should be considered a significant and robust improvement in the estimation of risk with only 3 genotypes.

Disclosure of Interest: None Declared
PLACENTAL IMMUNE RESPONSE TO GLIADIN IN DIET COMPLIANT COELIAC PATIENTS

Burcu Volkan 1,*, Aysin Tulunay 2, Deniz Ertem 1

1Paediatric Gastroenterology, 2Department of Immunology, Marmara University School of Medicine, Istanbul, Turkey

Objectives & Study: Celiac disease is associated with reproductive disorders such as delayed menarche, amenorrhea, early menopause, recurrent abortions, infertility and adverse pregnancy outcome in patients who are not compliant to gluten free diet (GFD). The current knowledge regarding the pathogenesis of reproductive problems is still obscure. Nutrient and vitamin deficiency secondary to malabsorption may impair fetal growth as well as gliadin induced inflammation and apoptosis of the placenta. The aim this study was to evaluate immune response of the decidual mononuclear cells, isolated from GFD compliant celiac patients to gliadin.

Methods: Decidual leucocyte population (CD3+ T lymphocytes, CD4+ lymphocytes, CD8+ lymphocytes, CD16+ NK cells, CD56+ NK cells) isolated from placenta of compliant celiac patients, was assessed by flow cytometry. Decidual mononuclear cells were cultured with pt-gliadin (digested gliadin), phytohemaglutinine (PHA) or pt-gliadin+PHA for 72 hours, and expression of CD69, which shows the activation of lymphocyte, was assessed by flow cytometry. Subsequently, secretion of Th1 (IFN-γ IL-15, IL-17), Th2 (IL-4, IL-10) cytokines and, sHLA-G were measured by ELISA. Control placentas were obtained from healthy pregnant women who were matched for age and parity.

Results: Sixteen pregnant women (8 celiac patients, 8 healthy controls) have participated in this study. There was no difference between the patients and controls regarding gestational age and birth weight of the newborns. Flow cytometric analysis of CD3+, CD4+, CD8+ lymphocytes and CD3+CD16+CD56+ (NKT) cell, CD16+CD56+ (NK) cells did not vary significantly between celiac patients and controls. In control placenta, the percentage of CD3+ T cells expressing CD69 activation molecule was significantly increased after exposure to pt-gliadin+PHA (p=0.038), however expression of CD69 activation molecule on NK and NKT cells did not vary between two groups. In celiac placenta, NK cells were activated more than NKT cells after exposure to gliadin (p=0.03). pt-gliadin stimulated IL-10, IFN-γ and IL-15 secretion from cultured decidual mononuclear cells of celiac women were significantly higher than control group (p=0.028, p=0.01, p=0.01 respectively).

Conclusion: There was no difference in leucocyte population, isolated from the decidua of celiac and control groups. The CD3+ T lymphocytes, NK cells and NKT cells, isolated from the decidua were activated after antigenic stimulation in both patients and controls, however decidual NK cells were activated more than NKT and CD3+ cells after gliadin stimulation in celiac patients. The profile of secreted cytokines shift in favor of Th1 activity in celiac patients.

Disclosure of Interest: None Declared
COELIAC DISEASE AND IMMUNOGLOBULIN IGA NEPHROPATHY: THE MISSING LINK

Cristina Antonella Nadalutti 1,*, Katri Kaukinen 1, Kaija Laurila 1, Katri Lindfors 1, Jukka Mustonen 1,
Markku Mäki 1, Ilma R Korponay-Szabó 2, 3

1School of Medicine, University of Tampere, Tampere, Finland, 2Paediatrics, Univ. of Debrecen,
Debrecen, Hungary, 3Coeliac Disease Centre, Heim Pál Children's Hospital, Budapest, Hungary

Objectives & Study: Subjects with celiac disease (CD) have increased risk of renal disease. Even though it has been suggested an association between CD and IgA nephropathy (IgAN), the results so far reported are controversial. This is the first work that has considered that celiac IgA autoantibodies against transglutaminase 2 (TG2) could target the kidney, and their release in the urine through tissue damage may be a potential marker for IgAN. The aim of this study was to investigate the presence of celiac IgA and TG2 in the urine of untreated CD patients with undiagnosed renal dysfunction and in the kidney biopsy samples of patients with established nephropathy.

Methods: We performed a prospective cohort study which included 37 consecutive individuals with newly diagnosed CD (Marsh stage III, median age: 7 years) and no previously known renal disease or pathologic proteinuria. All these patients were positive for IgA anti-TG2 in the serum. Urine samples were investigated by ELISA, rapid test and immunoblotting for anti-TG2 antibodies and diverse transglutaminase antigens (TG2 and TG4) and compared with a control group of 10 healthy subjects. Potential individuals with CD-related IgAN were identified by serologic screening and by the presence of IgA deposits in the kidney and the corresponding co-localization of IgA autoantibodies with TG2 in a group of 12 adult patients with IgAN.

Results: We found 17 of 37 subjects with newly diagnosed CD (46%) to be positive both for the presence of IgA anti-TG2 and TG2 antigen in the urine samples, in contrast to reference individuals which were all negative. None of the urine samples contained TG4 or antibodies against TG4. Five of out the 12 kidney biopsy samples contained IgA deposits co-localizing with tissue TG2, predominantly around renal tubules. IgA was also present in the glomeruli which, however, corresponded only partially with TG2.

Conclusion: We conclude that the presence of IgA anti-TG2 deposits around renal tubules may give rise to the IgA and TG2 leakage into the urine observed in untreated CD patients deserving awareness of renal function in these subjects. Rapid test-based detection of urinary anti-TG2 antibodies is very simple and painless, and despite its low sensitivity, positive results strongly suggest the presence of CD.

Disclosure of Interest: None Declared
**Objectives & Study:** Celiac disease (CD) is an immune response in the duodenum triggered by gluten in genetically predisposed subjects. Eosinophilic esophagitis (EE) is an esophageal immune response to various ingested antigens, that are often difficult to identify. Co-existence in the same patient had been reported in children. Our aim is to estimate the prevalence of EE among children with CD in our institution.

**Methods:** Children who had esophago-gastro-duodenoscopy (EGD) for histological confirmation of CD between January 2008 and October 2013 were evaluated. Esophageal biopsies were obtained when there were abnormal endoscopic findings. We identified the patients who had both EE and CD and reviewed their medical records for demographic, clinical, and endoscopic findings.

**Results:** We identified 160 CD patients and 31 EE patients from 1230 endoscopies performed during the study period. The prevalence of EE in all children diagnosed with CD was 2.5% (4 of 160). Four children with CD all had positive celiac serologies, and also met the histological findings consistent with EE, three of them had typical endoscopic findings of furrows and exudates suggestive of EE, and the fourth had a reportedly normal Esophagus. Median eosinophil count was 65 per high power field (range 30-100). Only one 18 months old infant presented with dysphagia to solid food. In 3 patients EE was an endoscopic and pathologic incidental finding. The EE did not resolve with gluten free diet in all 4 patients, but improved with elimination diet.

**Conclusion:** The reported frequency of EE among CD patients is 2.5%, and in most cases EE was asymptomatic and an incidental finding. EE did not respond to a gluten/wheat free diet but did respond to an elimination diet.

**Disclosure of Interest:** None Declared
ELECTIVE CAESAREAN DELIVERY IS ASSOCIATED WITH INCREASED COELIAC DISEASE RISK IN BOYS, BUT NOT IN GIRLS

Fredinah Namatovu 1,*, Anneli Ivarsson 2, Marie Lindkvist 2, Cecilia Olsson 3, Ulf Högberg 4, Anna Myleus 1, Olof Sandstrom 5

1Public Health and Clinical Medicine, 2Umeå University, Umeå, Sweden, 3Food and Nutrition, Umeå University, Umeå, Sweden, 4Women's and Children's Health, Obstetrics and Gynaecology, Uppsala University, Uppsala, Sweden, 5Clinical Medicine and Paediatric, Umeå University, Umeå, Sweden

Objectives & Study: There is conflicting evidence concerning caesarean section (CS) as a risk factor for celiac disease (CD) in offsprings. Our aim was to investigate whether CS posed a risk for CD, and whether or not the risk differed with sex.

Methods: We used the Swedish Initiative for Research on Microdata in the Medical and Social Sciences to access linked data from the Swedish Medical Birth Register on births in Sweden from 1991 to 2009, and the National Swedish Childhood CD Register to access data on CD cases diagnosed before the age of 15 years during this period. The study population consisted of 1 912 204 live births from which 6 596 offsprings later developed CD. We included information on maternal smoking, mode of delivery, gestational age, sex of the child, small intestinal biopsy evaluation, and month and age for CD diagnosis.

Results: A positive association was found between elective CS and CD in offsprings [adjusted odds ratio (OR) 1.26; 95% confidence interval (CI) 1.09-1.46]. After stratifying for sex it was revealed that only boys had an increased CD risk, with an adjusted OR of 1.64 (95% CI 1.25-2.17), the risk became none significant in girls (OR 1.12; 95% CI 0.94-1.33). No association with CD risk was found for any CS, assisted delivery, maternal smoking, or gestational age.

Conclusion: Our study confirms that elective CS is a risk factor for CD, but clarifies that this is true only for boys. We hypothesize that this might be due to boys being more susceptible to environmental and lifestyle factors associated with intestinal dysbiosis, i.e. microbial imbalances.

Disclosure of Interest: None Declared
CHARACTERISTICS OF PAEDIATRIC COELIAC DISEASE PATIENTS WHO ARE LOST TO FOLLOW UP AT A TERTIARY REFERRAL CENTER

Liron Barnea 1,2,*, Yael Mozer Glassberg 1,2, Iva Hojsak 3, Raanan Shamir 1,2
1Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Medical Center of Israel, Petach Tikva, Israel, 2Sackler Faculty of Medicine, Tel-Aviv University, Tel Aviv, Israel, 3Referral Center for Paediatric Gastroenterology and Nutrition, Children’s Hospital Zagreb, University Hospital Center “Sestre Milosrdnice”, Zagreb, Croatia

Objectives & Study: Celiac Disease (CD) requires lifelong adherence to a gluten free diet (GFD). Regular follow-up is recommended for monitoring adherence to GFD and detection of complications. Using the electronic database of our health maintenance organization, enabling a review of patients’ medical history, we recently showed that 35% of children with CD were lost to celiac-related follow-up. Our Aim was to explore the characteristics of patients who were lost to follow-up (LTFU), in an attempt to identify barriers for compliance with medical care and follow-up.

Methods: A cross-sectional telephone-based questionnaire study was performed on 50 pediatric CD patients who were LTFU between the years 1999-2009 at our institute. The same questionnaire was administered to a matched control population of 52 patients who attend follow-up visits regularly. The questionnaire included demographic data, frequency of follow-up, celiac serology and assessment of adherence to GFD using the validated Biagi score. Assessment of risk factors included family history for CD, clinical presentation, membership in a celiac association and distance from our institute.

Results: There was no difference in the age at diagnosis and in gender between the groups. LTFU patients were more likely not to adhere to a GFD (average Biagi score of 2.0±1.4) compared to controls (3.0±1.0, p<0.001). Only 22% of LTFU patients performed periodic celiac serology compared to 82% of controls (p<0.001). Moreover, electronic data showed that although blood was drawn for other reasons, celiac serology was not done. Last celiac serology tests were positive in 50% of LTFU compared to only 25% of controls (p=0.009). A significant factor associated with being LTFU was non-membership in the National Celiac Association (24% LTFU vs 44% in controls p=0.031). Of note, although statistical significance was not reached, single case of CD in the family and greater distance from our medical center were more common in the LTFU group.

Conclusion: LTFU is commonly associated with non-adherence to GFD and to positive serology. Thus, risk factors for LFTU should be identified and addressed.

Disclosure of Interest: None Declared
EPCAM IMMUNOSTAINING IN THE PATHOPHYSIOLOGY OF PAEDIATRIC COELIAC DISEASE

Thomas Attard 1, 2,*, Seth Septer 3, James Degaetano 4

1Paediatrics, Mater Dei Hospital, Msida, Malta, 2Paediatrics Gastroenterology, Children's Mercy Hospital, Kansas City, United States, 3Paediatrics Gastroenterology, Children's Mercy Hospital, Kansas City, United States, 4Pathology, Mater Dei Hospital, Msida, Malta

Objectives & Study: Epithelial Cell Adhesion/Activating Molecule (EpCAM) is a pleotropic molecule expressed in most healthy epithelial tissues and in many carcinomas. It is integral to desmosome function through its interaction with Claudin and Actin and thus modulates cell adhesion and migration. Tight junction integrity has been implicated in both animal model and human studies of celiac disease. Furthermore, defects of EpCAM expression have been implicated in the pathophysiology of Tufting Enteropathy, a malabsorptive disorder that shares several commonalities with celiac disease. The role of EpCAM in celiac disease is unknown; herein we studied the expression of EpCAM in epithelial biopsies of pediatric patients newly diagnosed with celiac disease.

Methods: Twenty-six consecutive patients diagnosed with celiac disease at our institution (MDH) from 2009 were included in the study; three patients were excluded because of incomplete clinical information. Demographic, clinical, serologic, endoscopic and histologic findings were accessed from the clinical chart and accrued in a dedicated study database. Immunohistochemistry on paraffin-embedded tissue from the initial diagnostic endoscopy was performed as previously described (1) using EPCAM antibody (1:300, Cell Signaling Technology). Statistical analysis was performed using SigmaStat®.

Results: Our cohort included 13 female subjects, the mean age (SD) was 8.1(3.7) years; celiacs with negative EpCAM staining of duodenal biopsies (n=13) tended to be older (9.1 years SD 4.4) than normal (n=10; 6.9 years SD 2.5) although the difference did not achieve statistical significance. EpCAM staining of duodenal biopsies did not correlate with the severity of histological findings (Marsh classification) at the time of diagnosis. Negative EPCAM staining in diabetic children diagnosed with celiac was as common as in non-diabetic children. Negative EPCAM staining did not correlate with pre-endoscopy anti-tTG IgA levels (defined as < / > 200 IU/L). However, negative EPCAM staining was predictive of persistent elevation of anti tTG IgA approximately 6 months after institution of gluten free diet in patients diagnosed with celiac (4:1 cf 5:6 - PPV 0.8; albeit this did not achieve statistical significance).

Conclusion: In this study we have shown heterogeneity in duodenal EpCAM expression in celiacs. Differences in EpCAM staining do not reflect the histologic severity of the disease but may be related to different pathophysiological mechanisms involving desmosome integrity. The observed association between absent EpCAM expression and persistent serologic abnormalities deserves further study.


Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0028

GA ANTI- TISSUE TRANSGLUTAMINASE AND IGG ANTI-DEAMIDATED GLIADIN PEPTIDES.

**BEST COMBINATION ANTIBODIES FOR PREDICTING COELIAC DISEASE (CD)**

Messere Gabriela 1,*, Gonzalo Ortiz 1, Patricia Caglio 1, Reynoso Ricardo 1, Vidal Jorge 1, Sosa Patricia 1, Toca M del Carmen 1

1Hospital Nacional A. Posadas, Buenos Aires, Argentina

**Objectives & Study:** Serum assays for immunoglobulin (Ig) A antibodies against tissue transglutaminase (anti-tTG) and endomysium (EmA) have improved the diagnosis of CD, because of their high specificity and sensitivity. However they have shown less sensitivity in children younger than 3 years old. IgA and IgG antibodies against deamidated gliadin peptides (AGA DGP) have been used with better results in this age group. To evaluate the predictive value of IgA anti-tTG, IgA EmA, and IgA and IgG AGA DGP and their effectiveness in different combinations for diagnosing CD.

**Methods:** Prospective, descriptive study. Serum of 136 children with CD and 58 controls (non CD patients) all diagnosis confirmed or excluded by intestinal biopsy. 61% females, mean age 78,4m, were tested at the time of the biopsy.

**Results:** One hundred five of 133 with CD had abnormal IgA AGA DGP and one hundred twenty two of 134 with CD had abnormal IgG AGA DGP. Two of 58 non CD had abnormal IgA and IgG AGA DGP. One hundred twenty eight were positive for EmA and 130 for anti-tTG. All the children without CD had EmA and anti-tTG normal. Four of 6 negative anti-tTG were CD patients younger than 3 years old, four of them had abnormal IgG AGA DGP. The combination of IgG AGA DGP + anti-tTG had a positive correlation with duodenal atrophy in 134 of 136 CD patients and 133 of 136 with the combination of IgG AGA DGP + EmA. Patients with normal tests did not show oligosymptomatic or silent clinical disease or mild histological changes (Marsh 2).

<table>
<thead>
<tr>
<th></th>
<th>IgA AGA DGP</th>
<th>IgG AGA DGP</th>
<th>EmA</th>
<th>tTG</th>
<th>EmA+ IgG AGA DGP</th>
<th>tTG+ IgG AGA DGP</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>105+/28 -</td>
<td>122+/12-</td>
<td>128+/8-</td>
<td>130+/6-</td>
<td>136+/3-</td>
<td>134+/2-</td>
</tr>
<tr>
<td></td>
<td>2+/56 -</td>
<td>2+/56 -</td>
<td>0+/58-</td>
<td>0+/58-</td>
<td>0+/58-</td>
<td>0+/58-</td>
</tr>
<tr>
<td>Sensitivity</td>
<td>79%</td>
<td>91%</td>
<td>94%</td>
<td>96%</td>
<td>98%</td>
<td>99%</td>
</tr>
<tr>
<td>Specificity</td>
<td>97%</td>
<td>97%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
<td>100%</td>
</tr>
<tr>
<td>PPV</td>
<td>98</td>
<td>98</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>NPV</td>
<td>67</td>
<td>82</td>
<td>87</td>
<td>90</td>
<td>95</td>
<td>97</td>
</tr>
</tbody>
</table>

PPV: positive predictive value  
NPV: negative predictive value

**Conclusion:** In this study the association of IgA anti-tTG with IgG anti-DGP proved to be the best combination for diagnosing CD, especially in younger than 3 years old.

**Disclosure of Interest:** None Declared
**Atherosclerotic Risk Factors in Children with Coeliac Disease**

Anna Rybak 1,*, Aldona Wierzbicka 2, Piotr Socha 3, Anna Stolarczyk 3, Bożena Cukrowska 4, Łukasz Obyrcki 3, Zbigniew Wawer 2, Beata Oralewska 1, Anna Szafarska-Opolawska 5, Barbara Iwańczak 6, Elżbieta Cyra-Jarocka 7, Urszula Grzybowska-Chlebowczyk 8, Wojciech Cichy 9, Grażyna Czaja-Bulsa 10, Jerzy Socha 1

1 Department of Gastroenterology, Hepatology and Feeding Disorders, Children's Memorial Health Institute, 2 Department of Biochemistry and Experimental Medicine, 3 Department of Gastroenterology, Hepatology and Feeding Disorders, 4 Department of Pathology, Children’s Memorial Health Institute, Warsaw, Poland, 5 Department of Paediatrics, Allergology and Gastroenterology, Collegium Medicum Nicolaus Copernicus University, Bydgoszcz, 6 Department of Paediatrics, Gastroenterology and Nutrition, Medical University of Wroclaw, Wroclaw, Poland, 7 Department of Paediatrics, Gastroenterology and Allergology, Medical University, Białystok, Poland, 8 Department of Paediatrics, Medical University of Silesia, Katowice, Poland, 9 Department of Paediatrics, Gastroenterology and Metabolic Diseases, University of Medical Sciences, Poznań, Poland, 10 Department of Paediatrics, Gastroenterology and Rheumatology, Independent Specialist Public Health Care, Szczecin, Poland

**Objectives & Study:** Coeliac disease (CD) is complex autoimmune disorder occurring in genetically susceptible individuals. Some studies show that dietary interventions in childhood may impact physical condition later in life. There is limited data on the impact of gluten-free diet (GFD) on the risk of developing cardiovascular diseases. Taking reports concerning increased cardiovascular episodes among patients with CD into consideration, we present hereby our study concerning the impact of gluten-free diet on the biochemical risk factors of atherosclerosis.

**Methods:** We enrolled 277 patients with CD from 7 Polish clinics into the study (210 children treated for at least 5 years and 67 children included in the study on the day of CD diagnosis and observed for 1 year on GFD). We obtained selected clinical data and we assessed lipid profile, apolipoproteins (A1, B, E), lipoprotein (a), homocysteine, as well as antioxidants (folic and uric acid) and high sensitivity CRP (hCRP) for all patients. The compliance to GFD was verified using anti-transglutaminase and deamidated-gliadin-peptide antibodies. As a reference group, we used the data of 95 healthy children recruited for another project, for which we had the results of selected parameters.

**Results:** We found significantly lower concentrations of total cholesterol, lipoprotein LDL-C, apolipoprotein A1, B as well as hCRP in all children with CD. We showed decreased level (< 5 ng/ml) of folic acid among 46% of children treated for >5 years, moreover we showed significant decrease of folic acid level already after 1 year of GFD (12 vs 5.6 ng/ml; p<0.001). We also found significant negative correlation of z-score BMI with HDL and APO A1 level (r=-0.33;p=0.015 and r=-0.28;p=0.038, respectively) and modest positive correlation of z-score BMI with atherogenic factor of total cholesterol–HDL ratio and LDL–HDL ratio (r=0.40;p=0.002 and r=0.36;p=0.006, respectively). Analysis of physical activity showed increase in the insulin levels with the inactivity (r=0.36;p=0.0025). We also found positive correlation of the sleep duration with the adiponectin level (r=0.41; p=0.011).

**Conclusion:** In children with CD treated with GFD, decreased level of folic acid together with increased BMI, sedentary behavior and improper lipid profile may predispose to atherosclerosis on the long run. Our data suggest the need of screening for metabolic cardiovascular risk in children with CD.

**Disclosure of Interest:** None Declared
ETHNICITY AND HIGH SOCIO ECONOMIC STATUS PLAYS A SIGNIFICANT ROLE IN PAEDIATRIC COELIAC DISEASE. A CROSS SECTIONAL STUDY OF 1.2 MILLION CHILDREN

Zohar Levi 1, 2*, Raanan Shamir 2, 3, Becca Feldman 4, Moshe Hoshen 4, Ran Balicer 4, Rachel Gingold 5

1Gastroenterology, Rabin Medical Center, Petach Tikva, Israel, 2Tel Aviv University, Tel Aviv, Israel, 3Institute of Gastroenterology, Nutrition and Liver Diseases, Petach Tikva, Israel, 4Clalit Research Institute, Tel Aviv, Israel, 5Gastroenterology, RMC, Petach Tikva, Israel

Objectives & Study: We sought to estimate the prevalence of pediatric Celiac Disease (CD) in Israel as well its associated socio-demographic factors.

Methods: We studied 1,220,156 subjects aged 2-18 years who belonged to the Clalit Health Services (CHS) at the end of 2013. Data were extracted from the CHS database. CD was defined as having both positive tissue transglutaminase antibodies (TTG) and positive endomysial antibodies (EMA). Logistic regression analysis for the association of gender, ethnicity and socioeconomic state (high, medium, low according to clinic classification) with CD was performed.

Results: A total of 9.7% (118,728 subjects) had TTG testing, 5% (60,847 subjects) had EMA testing. CD was found in 0.14% of the total population (1,753 subjects): 0.16% (1269 subjects) were Jewish children, 0.03% (124 subjects) Arab children and 0.34% (360 subjects) were Bedouin Arabs; p<0.001. Factors found significant in the multivariable analysis associated with CD diagnosis were: ethnicity [Bedouin Arabs OR = 9.6; 95% CI: 7.8-11.9; Jews OR = 3.87; 95% CI: 3.10-4.70 compared to Arabs; p<0.001], socio economic status [High OR: 1.81, 95% CI: 1.58-2.0; medium OR: 1.01, 95% CI: 0.95-1.23 compared to low; p<0.001] and gender [females OR = 1.75, 95% CI: 1.25-1.92; p<0.001].

Conclusion: About 9.7% of the pediatric population covered by CHS is tested for CD. The prevalence of serology positive CD in the pediatric population in Israel is 0.14%. Ethnicity, particularly being Bedouin and SES play a significant role in pediatric CD pointing to the importance of the interplay between genes and environment in the pathogenesis of CD.

Disclosure of Interest: None Declared
SATISFACTION OF PARENTS WITH COELIAC RELATED HEALTH CARE OF THEIR CHILDREN

Margreet MS Wessels ¹,*, M Elske van den Akker-van Marle ², Sabine L Vriezinga ¹, M Luisa Mearin ¹

¹Paediatric Gastroenterology, ²Health Economics, LUMC, Leiden, Netherlands

Objectives & Study: Diagnosis and follow-up of patients with coeliac disease (CD) is done according to (inter)national guidelines. There is a tendency in the current health care services to concentration of care, for example by care pathways and expertise centers. Little is known about satisfaction of CD patients with their CD related health care. Aims were to assess in the Netherlands: 1. the satisfaction of parents with the CD related health care of their children, and 2. whether satisfaction is increased in patients who attend a CD Expertise Center (CDEC).

Methods: CDEC was defined as a medical center with a dedicated CD outpatient department, standardized CD care according to (inter)national guidelines and CD specific research. Patient satisfaction was assessed using the Dutch version of Ware’s Patient Satisfaction Questionnaire III (PSQ3). The PSQ3 measures specific aspects of care, that is (with number of items per domain), general satisfaction (6), technical competence (7), interpersonal aspects (7), communication (5), time spent with the doctor (2) and access to care (12), each scored on a 0-100 scale. Parents of CD children attending a CDEC were asked by letter to complete the PSQ3 on paper or online. Parents of patients attending no CDEC were invited to participate through the Journal and online facilities of the Dutch Coeliac Society. Age, sex and age at CD diagnosis of the participating individuals were recorded. The Mann-Whitney U test was used for statistical analysis with a p-value of <0.05 considered significant.

Results:

Regarding CDEC patients, 265 parents of CD children were invited to participate. Questionnaires were completed by 45% of parents of CDEC attending children. 81 Questionnaires were filled in by parents of no CDEC attending children. Of all questionnaires, 9% could not be used in the analysis due to incomplete or inconsistent data. The results (mean scores of satisfaction) are shown in the table.

<table>
<thead>
<tr>
<th>Satisfaction domains</th>
<th>Children non-CDEC (n=81)</th>
<th>Children CDEC (n=119)</th>
</tr>
</thead>
<tbody>
<tr>
<td>General</td>
<td>66</td>
<td>78*</td>
</tr>
<tr>
<td>Technical competence</td>
<td>70</td>
<td>79*</td>
</tr>
<tr>
<td>Interpersonal aspects</td>
<td>79</td>
<td>85*</td>
</tr>
<tr>
<td>Communication</td>
<td>78</td>
<td>83</td>
</tr>
<tr>
<td>Time spent with doctor</td>
<td>73</td>
<td>77</td>
</tr>
<tr>
<td>Access to care</td>
<td>66</td>
<td>70</td>
</tr>
<tr>
<td>Overall</td>
<td>72</td>
<td>79*</td>
</tr>
</tbody>
</table>

* p<0.05, children non-CDEC versus children CDEC

Conclusion: The overall satisfaction of Dutch parents with the CD related health care of their children is high. Expertise care for children with CD leads to a significantly higher general satisfaction and appreciation of technical competence and interpersonal aspects as reported by their parents.

Disclosure of Interest: None Declared
PILOT STUDY: ANTIGLIADIN ANTIBODIES LEVELS IN BREAST MILK OF COELIAC AND NON-COELIAC MOTHERS

Maria Roca Llorens 1,*, Miguel Bolonio 1, David Hervas 2, Ester Donat 3, Begoña Polo 3, Etna Masip 3, Gemma Castillejo 4, Eva Martinez-Ojinaga 5, M Carmen Mena 6, Isabel Polanco 6, Carmen Ribes-Koninckx 3

1Paediatric Gastrohepatology Investigation laboratorium, Hospital Universitario y Politecnico La Fe, Valencia, Spain
2Biostatistics Unit, Instituto de Investigación Sanitaria La Fe, Valencia, Spain
3Paediatric Gastrohepatology Unit, Hospital Universitario y Politecnico La Fe, Valencia, Spain
4Hospital Universitari San Joan Reus, Spain
5Hospital Universitario La Paz, Madrid, Spain
6Centro Nacional de Biotecnología, Consejo Superior de Investigaciones Científicas, Madrid, Spain

Objectives & Study: Hypothesis: Antigliadin antibodies in breast milk may have a protective effect on coeliac disease development.

Objectives: To study the presence of antibodies against gliadin (AGA) in breast milk (BM) and to analyse their relationship with maternal diet.

Methods: Samples of mature milk were obtained at different months of lactation (1-14) from 23 mothers: 12 on a normal diet (ND) and 11 on a gluten free diet (GFD) (coeliac mothers) and were analyzed for Secretory AGA-IgA (S-AGA) and AGA-IgA by indirect homemade ELISA. Total IgA (g/L) was measured in human milk whey using an ELISA kit from Bethyl Laboratories.

Results: AGA levels vary from one mother to another, but are stable in each mother from the first month of lactation onwards. S-AGA and AGA-IgA were detected in BM, both in mothers on a GFD and mothers on a normal gluten containing diet.

The comparison of the estimated kernel density curves for S-AGA showed a difference between both groups, with slightly lower values for mothers on GFD. Similar results were obtained for AGA-IgA. However differences between the 2 groups of mothers did not reach statistical significance (repeated measures ANOVA, S-AGA p-value=0.12, AGA-IgA p-value=0.16); analysis of these results suggests however this was related to the low sample size: 94 observations but only 23 different individuals.

Total IgA values varied between 0.1 and 1 g/L in most individuals, the median IgA value being 0.66 g/L and the interquartile range [0.44; 0.94]. We observed a great variability among mothers, some cases showing uncommonly high values.

To assess the relationship between IgA and the other variables, a linear mixed model approach was used. The model including S-AGA instead of AGA-IgA had a considerably higher AICC (Corrected Akaike Information Criterion) (229.2 vs. 235.7), indicating that a positive association exists between levels of AGA and total IgA. This association is higher between levels of AGA-IgA and total IgA than for S-AGA and total IgA.

Conclusion: AGA was present in all BM samples, independently of mother’s diet. Thus breastfeeding is a way of transferring antibodies to the baby, so this practice could be relevant for CD prevention in breastfed infants. A larger study is now ongoing so as to establish a potential protective effect of these antibodies on coeliac disease development.

Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0033

**MONITORING COELIAC DISEASE: VALUE OF ANTIBODIES IN PREDICTING MUCOSAL HEALING**

Hubert Kogler 1,*, Edith Vécsei 1, Stephanie Steinwendner 1, Albina Innerhofer 1, Karin Hammer 1, Oskar A. Haas 1, Gabriele Amann 2, Andreas Chott 3, Harald Vogelsang 4, Regine Schoenlechner 5, Wolfgang Huf 6, Andreas Vécsei 1

1 Paediatric Gastroenterology, St. Anna Children’s Hospital, Medical University Vienna, Vienna, Austria, 2 Clinical Department of Pathology, Medical University Vienna, Vienna, Austria, 3 Institute of Pathology and Microbiology, Wilhelminenspital, Austria, 4 Division for Gastroenterology and Hepatology, Department of Internal Medicine III, Medical University Vienna, Vienna, Austria, 5 Department of Food Science and Technology, Institute of Food Technology, University of Natural Resources and Life Sciences, 6 Center for Medical Physics and Biomedical Engineering, Medical University Vienna, Vienna, Austria

**Objectives & Study:** To compare the performance of antibody tests in predicting small-intestinal mucosal status in diagnosis vs. follow-up monitoring of coeliac disease (CD), a prospective cohort study at a tertiary care-center was conducted.

**Methods:** 148 children underwent oesophagogastroduodenoscopy with biopsies either for symptoms ± positive CD antibodies (group A; n=95) or monitoring CD diagnosed ≥ 1 year before study enrolment (group B; n=53). Group A comprised 32 children with newly diagnosed CD (group A1) and 63 children with non-coeliac dyspepsia (group A2). Using biopsy (Marsh ≥ 2) as the criterion standard, areas under ROC curves (AUCs) and likelihood-ratios were calculated to estimate the performance of antibody tests against tissue transglutaminase (TG2), deamidated gliadin peptide (DPG), and EMA.

**Results:** AUCs were higher when tests were used for diagnosing vs. monitoring CD: 1 vs. 0.86 for TG2-IgA, 0.85 vs. 0.74 for TG2-IgG, 0.97 vs. 0.61 for DPG-IgA, and 0.99 vs. 0.88 for DPG-IgG, respectively. Among group B children, 88.7% showed mucosal healing after a median of 2.2 years after primary diagnosis. Only the negative likelihood-ratio of EMA was low enough (0.097) to effectively rule out persistent mucosal injury. However, out of 12 EMA-positive children with mucosal healing, 9 subsequently turned EMA-negative.

**Conclusion:** Among the CD antibodies examined, negative EMA most reliably predict mucosal healing. In general, however, antibody testing after a median of 2.2 years after primary diagnosis is of limited value in predicting the mucosal status but may be sufficient after a longer period of time.

**Disclosure of Interest:** H. Kogler: None Declared, E. Vécsei: None Declared, S. Steinwendner: None Declared, A. Innerhofer: None Declared, K. Hammer: None Declared, O. Haas: None Declared, G. Amann: None Declared, A. Chott: None Declared, H. Vogelsang: None Declared, R. Schoenlechner: None Declared, W. Huf: None Declared, A. Vécsei Grant / Research Support for: The study was partially supported by Dr. Schäfer GmbH/Srl, Burgstall, BZ, Italy, and the St. Anna Fund, Vienna, Austria. Antibody kits were supplied free of charge by Inova Diagnostics, Inc., Werfen Group. The study sponsors were not involved in the study design, in the collection, analysis, interpretation of data and in writing of the report., Consultant for: Dr. Andreas Vécsei has served as a consultant and scientific advisor for Dr. Schäfer GmbH/Srl, Burgstall, BZ, Italy.
POSITIVE IGG DEAMIDATED GLIADIN PEPTIDES BUT NO VILLOUS ATROPHY A FALSE
POSITIVE TEST OR AN EARLY SIGN OF FUTURE COELIAC DISEASE?

Lars Browaldh 1,*, Yigael Finkel 1, Ola Olén 1
1Sachs Children and Youth Hospital, South General Hospital, Karolinska Institutet, Stockholm, Sweden

Objectives & Study: Background: We previously studied the diagnostic performance and actual costs in clinical practice of immunoglobulin (Ig)G/IgA deamidated gliadin peptide antibodies (DGP) as a complement to IgA antibodies against tissue transglutaminase (tTG) for the diagnosis of pediatric celiac disease (CD). We concluded that for diagnosing CD, tTG was superior to DGP, even in children younger than 2 years (Olen et al, JPGN 2012), but we also found a large proportion of false positive DGP results (i.e. “potential CD”). Children with “potential CD” are defined as having a normal small intestinal mucosa but an increased risk of developing CD as indicated by positive CD serology (Ludvigsson JF, et al 2012) Other studies have found that many children with potential CD (based on tTG-values) develop CD within a few years and other studies have found that DGP positivity precedes tTG positivity in children at risk for CD.

Aim: In order to verify the results of the above study we aimed to review the children with raised DGP who did not fulfill CD histopathology criteria in their duodenal biopsies to exclude later presentation of celiac disease.

Methods: 46 children investigated for suspected CD, who had a positive DGP, but a normal duodenal biopsy, were invited. 27 accepted repeated clinical investigation and tTG/DGP measurement, 10 were interviewed on the phone but declined further follow up because lack of symptoms and 9 were lost for follow-up. Methods for analyzing tTG and DGP have been described elsewhere (Olén et al JPGN 2012) and cutoff values as suggested by the manufacturers were used.

Results: 27 children (12 girls), median age 3 (range 1-15) years accepted our invitation. All reported good health without any remaining gastrointestinal symptoms. The repeated serology tests were taken 42 (median) months (range 4-53) after the first investigation. At follow up, all children were negative for both tTG and DGP. HLA DQ5 and 8 were analyzed in 18 patients, 10 of whom were negative for both HLA-classes.

Conclusion: Children with potential CD based on a positive DGP, a negative tTG, and normal duodenal biopsies, were negative for both DGP and tTG at follow up 3.5 years (median) later.

References: Olen et al, JPGN 2012;55: 695–700

Disclosure of Interest: None Declared
THE RELATIONSHIP BETWEEN TISSUE TRANSGLUTAMINASE ANTIBODY TITRES AND HISTOLOGICAL CLASSIFICATION IN COELIAC DISEASE

Nkem Onyeador 1, Naomi Jennings 1, Siba Prosad Paul 1,*, Bhupinder Kaur Sandhu 1
1Paediatric Gastroenterology, Bristol Royal Hospital for Children, Bristol, United Kingdom

Objectives & Study: Coeliac disease (CD) is an immune mediated systemic disorder elicited by the ingestion of gluten and related prolamines in genetically susceptible individuals. Diagnosis has been based on small bowel histology as per ESPGHAN guidelines. In 2012 ESPGHAN guidelines 1 were modified and recommend that in symptomatic patients a diagnosis of CD can be made without small-bowel biopsy if anti-tissue transglutaminase antibody (TTG) titre is greater than 10 times upper limit of normal (>10ULN), together with presence of HLA-DQ2 and/or DQ8.
This study aimed to examine the relationship between TTG levels and the corresponding histological features.

Methods: Data was collected prospectively at diagnosis of CD from 126 consecutive children between June’2011- May 2012. TTG was measured using ELISA technique. Histological samples were obtained from endoscopic small-bowel biopsies and interpreted by paediatric histopathologists. The relationship between the modified Marsh criteria histological findings and contemporaneous TTG levels was analysed.

Results: Out of 126 children, 13(10.5%) had positive TTG but no documented titres. In 12(10%) histological report did not specify Marsh classification. Complete data of histological report and TTG level were therefore available from 104 children (82%). The data (table) shows an association between TTG level and histological staging of CD. 58 (48%) children had TTG>10ULN (>100U/ml). 57/58 of these patients had biopsy proven CD. The sensitivity of the TTG level >100U/ml alone in correctly diagnosing CD in this cohort was 98.3%.

<table>
<thead>
<tr>
<th>Modified Marsh Criteria identified on histology</th>
<th>3a</th>
<th>3b</th>
<th>3c</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean TTG level (U/ml) (SD)</td>
<td>95.9</td>
<td>110.0</td>
<td>167.4</td>
</tr>
<tr>
<td>(95% confidence level)</td>
<td>66.8-124.9</td>
<td>87.5-132.3</td>
<td>143.0-191.7</td>
</tr>
</tbody>
</table>

Conclusion: 98.3% of children with TTG>100U/ml had histologically confirmed CD although total villous atrophy was associated more often with TTG level of >200U/ml. It is essential to report TTG titres by all laboratories. This study supports the new ESPGHAN guidelines for the selective use of high TTG levels in diagnosing CD in symptomatic children without a biopsy.


Disclosure of Interest: None Declared
COELIAC SEROLOGY TESTING IN IRISH CHILDREN - A SUBSTITUTE FOR BIOPSY?
Jayasree Satish Kutty 1,*, Michael McDermott 2, Maureen O’Sullivan 2, Shona Quinn 3, Billy Bourke 4, 5, 6, Annmarie Broderick 5, 6, 7, Seamus Hussey 3, 5, 6

1National Centre for Paediatric Gastroenterology, Our Lady’s Children's Hospital, 2Department of Pathology, 3National Centre for Paediatric Gastroenterology, OLCHC, Crumlin, Dublin12, Ireland, 4National Centre for Paediatric Gastroenterology, OLCHC, Crumlin, Dublin12, Ireland, 5School of Medicine and Medical Science, University College Dublin, Dublin, Ireland, 6National Children's Research Centre, OLCHC, Crumlin, Dublin12, Ireland, 7National Centre for Paediatric Gastroenterology, OLCHC, Crumlin, Dublin12, Ireland

Objectives & Study: Small intestinal biopsy remains the reference standard for diagnosing coeliac disease (CD) in children. Recent international guidelines suggest that for select patients, biopsy may not be necessary. The aims of this study were to: (a) correlate coeliac serology with histology findings in Irish children with a high pre test probability of the disease (b) determine if proposed changes to the CD diagnostic algorithm hold true in an Irish paediatric cohort.

Methods: A retrospective chart review of all cases of suspected CD that underwent endoscopy at the National Centre for Paediatric Gastroenterology, Our Lady’s Children’s Hospital from January 2004 to December 2011 was undertaken. Data retrieved included endoscopic and histologic findings, co-morbidities and serology results (where available).

Results: 596 patients (57% female) underwent endoscopy for suspected CD. Serology data were available for 544 (91%) patients. CD was confirmed on histology in 304 (51%) children. tTG (tissue transglutaminase) was positive in 405 (79%) patients, of whom 288 (71%) also had a positive biopsy and 7 patients (5%) with negative tTG had a positive biopsy. This result was highly significant with a p value of 0.0001. Of the available 195 positive EMA (endomysial antibody) results, 184 (94%) had a positive tTG as well. 110 of 117 children with tTG values > 20μg/ml plus a + EmA had CD on histology. 3 of 105 (2.8%) patients with tTG>100 μg/ml had a normal histology. The sensitivity, specificity, positive predictive value (PPV) and negative predictive value of tTG levels ranging from 2-99 were 97% (CI 95-98), 53% (CI 46-59), 71% (CI 63-75) and 95% (CI 90-98) respectively. The corresponding values for tTG levels >100 were 94% (CI 87-97), 98% (CI 93-99), 97% (CI 92-99) and 95% (CI 90-98). The PPV of tTG 2-10μg/ml was 37%, but at 100μg/ml, this was 97%.

Conclusion: Intestinal biopsy remains the reference standard for CD diagnosis. High titre serology correlates well but not perfectly with histology findings. Diagnostic accuracy rather than screening convenience is essential before prescribing a life-long gluten free diet.

References: Walker-Smith et al, Arch Dis Child, 1990;65:909-11
Husby et al, JPGN (2012)

Disclosure of Interest: None Declared
**IS THROMBIN GENERATION ELEVATED IN PAEDIATRIC PATIENTS WITH COELIAC DISEASE?**

**A PILOT STUDY**

Andrea Deutschmann 1,*, Axel Schlagenhauf 1, Bettina Leschnik 1, Karl Martin Hoffmann 1, Almuthe Christine Hauer 1, Wolfgang Muntean 1

1Department of Paediatrics and Adolescent Medicine, Medical University of Graz, Graz, Austria

**Objectives & Study:** Venous thromboembolism or stroke in childhood often has no identifiable underlying cause. Celiac disease (CD), an immune-mediated inflammatory enteropathy is associated with a modestly increased risk of venous thromboembolism (VTE) and stroke. The in-vitro measurement of thrombin generation using calibrated automated thrombography is the only test sensitive to hypercoagulable changes in plasma. Aim of our pilot study was to investigate thrombin generation in pediatric patients with celiac disease in comparison to pediatric controls.

**Methods:** Plasma samples were collected from 19 patients with celiac disease and 20 healthy controls. In the patient group thrombin generation, determined by means of calibrated automated thrombography was measured twice. The first measurement was undertaken when celiac disease was diagnosed and repeated after normalization of their transglutaminase antibody titers (TTG-Ab) following a strict gluten free diet.

**Results:** Patients with CD at diagnosis exhibited a significantly shorter lag time ($P < 0.001$) and a shorter time to peak ($P < 0.02$) compared to controls. These differences disappeared after normalization of the TTG-Ab. No significant differences were found in the endogenous thrombin potential (ETP) between any of the study groups.

**Conclusion:** We found a shorter lag time in patients with untreated celiac disease which is typically for an activated coagulation system. However ETP, the best predictive parameter for thromboembolic events was not elevated.

**Disclosure of Interest:** None Declared
OBJECTIVES & STUDY: Celiac disease is an autoimmune disease, characterized by inflammation localized to the small bowel but less is known about systemic signs of inflammation. The aim was to measure cytokines of the T helper 1 cell (Th1) and T helper 2 cell (Th2) pattern in children with screening detected celiac disease.

METHODS: Serum samples selected before start of a gluten free diet from 26 children diagnosed with biopsy-proven celiac disease at mean 3.4 (range 3.2-3.7) years and from 52 matched controls, were assayed in an multiplex ELISA for the 10 cytokines: IFN-γ, IL-1β, IL-2, IL-4, IL-5, IL-8, IL-10, IL-12p70, IL-13 and TNF-α.

RESULTS: Five of 10 of the cytokines were elevated among children with celiac disease compared to controls. In Th1 cytokines median value of IFN-γ was 29.8 (IQR 4.1-492.4) pg/mL as compared to 1.7 (IQR 0.5-13.3) pg/mL in controls (p<0.001) and for IL-12 median value was 14.1 (IQR 5.7-32.0) pg/mL as compared to 3.7 (IQR 1.0-9.7) pg/mL in controls (p=0.001). Similar findings were demonstrated for the Th2 cytokines IL-5 (median 81.7 pg/mL vs. 7.1 pg/mL, p<0.001), IL-10 (median 3.7 pg/mL vs. 0.8 pg/mL, p=0.001) and IL-13 (median 6.3 pg/mL vs. 2.5 pg/mL, p=0.002). No difference in cytokine levels between the two groups was found for TNF-α, IL-1β, IL-2, IL-4 and IL-8.

CONCLUSION: Children with celiac disease detected by screening demonstrate elevated levels of serum cytokines at time of diagnosis. A prolonged systemic inflammation due to untreated celiac disease may in turn contribute to long-term complications if not being diagnosed.

DISCLOSURE OF INTEREST: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0039

**THE RATE OF COELIAC DISEASE IN WV CHILDREN: THE VIEW FROM THE ENDOSCOPY SUITE**

Yoram Elitsur 1,*, Deborah Preston 1

1Paediatrics, Gastroenterology, Marshall University School of Medicine, Huntington, WV, United States

**Objectives & Study:** The rate of celiac disease in the United States in the general population has been estimated at about 1%. In a large epidemiological study, the rate of celiac disease in children was reported in 1:320 subjects (Fasano A et al. Arch Intern Med 2003). Those data were usually confirmed following positive serology. The rate of celiac disease suspected by histology data first vs. serology test first has never been investigated in symptomatic children.

**Aim:** 1. to investigate the overall rate of celiac disease in a cohort of West Virginian children who undergo upper endoscopy for various gastrointestinal symptoms. 2. To compare the rate of celiac disease in children who had positive histology result first vs. children who had positive serology test first.

**Methods:** Charts of all diagnostic upper endoscopy procedures performed between Jan. 2009- July 2013 were reviewed. Histological data of the small intestine and duodenal bulb biopsies were collected. At least 2 biopsies from both locations were available in all procedures, irrespective of the mucosal appearance. Subsequently, patients were divided according to the test that led to the final diagnosis; i.e.: Patients with positive histology followed by positive serology (group A), patients with positive serology followed by positive histology (Group B), patients with positive histology but negative serology (group C), and patients with negative histology but positive serology (Group D).

**Results:** A total of 698 upper endoscopic charts were reviewed. Sixteen children were confirmed with celiac disease (2.29%). No significant difference in the rate of celiac disease was observed between histology- lead vs. serology- lead celiac diagnosis (1.43% vs. 0.86%. p= 0.3145) (Table).

<table>
<thead>
<tr>
<th>Total</th>
<th>Group A</th>
<th>Group B</th>
<th>Group C</th>
<th>Group D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celiac disease (+)EGD/(+)Serol.</td>
<td>(+)Serol/(+)EGD</td>
<td>(+)EGD/(-)Serol.</td>
<td>(+)Serol/(+)EGD</td>
<td></td>
</tr>
<tr>
<td>16 (2.29%)</td>
<td>10 (1.43%)</td>
<td>6 (0.86%)</td>
<td>3* (0.42%)</td>
<td>2 (0.29%)</td>
</tr>
</tbody>
</table>

P= 0.3145 between group A and group B (Two tailed, Chi-square analysis); * All graded at Marsh 1.

**Conclusion:** 1. The rate of celiac disease in the cohort of children from WV was higher than the rate published in the general pediatric population (2.29%). 2. The rate of celiac disease was similar in our symptomatic children irrespective of which test led to the final diagnosis (positive histology or positive serology; p= 0.3145). 3. Celiac disease should be suspected in every upper endoscopic procedure thus, an appropriate number of biopsies is recommended.

**Disclosure of Interest:** None Declared
LACK OF EFFECT OF FTO COMMON VARIANT RS993960 ON WEIGHT GAIN IN COELIAC CHILDREN ON A GLUTEN-FREE DIET

Anna Grandone 1,*, Emanuele Miraglia del Giudice 1, Danila D’Ambrosio 1, Salvatore Tolone 2, Carlo Tolone 1

1Department of Paediatrics, 2Department of Surgery, Second University of Napoli, Napoli, Italy

**Objectives & Study:** Studies of adults and children with celiac disease have reported an increased risk of overweight during gluten-free diet (GFD). The FTO variant rs9939609 has been associated with a 31% increase in the risk of developing obesity in normal children and adults. In our study we aimed to analyze the effect of this variant on weight gain in a cohort of celiac children during the first years of GFD after diagnosis.

**Methods:** We studied 200 celiac children from southern Italy (5±3.9 years, 127 male). Anthropometric parameters were measured at diagnosis and at a mean follow-up time of 3±0.5 years of GFD. BMI z-score was calculated according standard references for age and sex. FTO genotype was defined by Taqman assay.

**Results:** Mean BMI z-score at diagnosis and at follow-up were respectively -0.04 ± 1 and +0.4 ±1 with a mean increase in BMI z-score of 0.4 ± 1. There was no influence of FTO genotype on all these parameters. Moreover 8% of patients was overweight or obese at diagnosis while at follow-up 21.5 % of children resulted overweight or obese. This increase in prevalence was statistically significant (p<0.05) but FTO genotype did not result having a role in determining it.

**Conclusion:** 1) we confirm that prevalence of obesity significantly increases after the GFD among celiac children. Therefore great attention is needed for nutritional counseling to these patients. 2) FTO gene seems not to have a role in determine this phenomenon. Our negative results could be explained by the fact that FTO gene seems not to be involved in metabolism or energy consumption but rather in food uptake behavior. On the other hand prolonging follow-up period could be useful to elucidate better FTO influence on weight gain in this kind of patients as our patients are quite young and FTO gene could not be yet involved in influencing body weight at that age.

**Disclosure of Interest:** None Declared
THYROID FUNCTIONALITY AND AUTOIMMUNITY IN COELIAC DISEASE

Irene Rutigliano 1, Nicola d’Altilia 1, Patrizia Cavaliere 1, Francesca Lotti 1, Mario d’Altilia 2, Michele Sacco 2, Massimo Pettoello-Mantovani 1, Angelo Campanozzi 1

1 Paediatrics, University of Foggia, Foggia, Italy, 2 Paediatrics, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy

Objectives & Study: Celiac Disease (CD) is an autoimmune enteropathy closely related to other autoimmune disorders, in particular autoimmune thyroid diseases. Some studies have suggested that the prevalence of autoimmune conditions in patients with CD increases with increasing age at diagnosis. AIM OF THE STUDY: We investigated thyroid functionality and autoimmunity in new diagnosed CD, trying to evaluate eventual age-related differences and correlations between CD and thyroid pathology.

Methods: We analyzed 246 children (mean age 5.2±3.6 yrs, median age 4.3 yrs), from two different Medical Centers, with biopsy-proven diagnosis of CD. Collected data included: sex and age at the diagnosis. Thyroid functionality and autoimmunity were assessed by measuring serum concentration of TSH, fT3, fT4, serum thyroperoxidase antibodies (TPO-Ab) and thyroglobulin antibodies (Tg-Ab) at the time of CD diagnosis. Histological grading of CD was evaluated according to Marsh-Oberhuber classification. Patients were divided in four groups according to age-quartiles obtained by statistical analyses.

Results: In our population 58/246 (23.6%) subjects presented values of thyroid autoimmunity above laboratory cut-off range (21 males, 37 female; p=0.615); but only 30/58 subjects (12.2% of the whole population) had TPO-Ab and/or Tg-Ab higher than 60 IU/ml (11 males, 19 females; p=0.778). Seven children had consensual positivity for both antibodies. No difference was recorded about the distribution of thyroid autoimmune positivity into the four quartiles of age (20% in the first quartile, 20% in the second, 36.7% in the third quartile, 23.3% in the fourth; p=0.476). Subjects with positive thyroid autoimmunity presented more frequent TSH levels above cut-off laboratory range: 24.6% vs 8.9% (p=0.002). No relationship was observed between thyroid antibodies positivity and histological grading of CD (p=0.095); but a “strange” inverse correlation was observed between Tg-Ab and Anti-gliadin IgA levels (rho= -0.248, p= 0.002) even after adjustment for age (r= -0.168, p= 0.040).

Conclusion: Our results suggest that thyroid autoimmunity does not increase with increasing age at the moment of diagnosis and is not related to histological grading of CD.

Disclosure of Interest: None Declared
**THE A-GLIADIN PEPTIDE 31-43 INDUCES NF-κB ACTIVATION AND MODULATE TYPE 2 TRANSGLUTAMINASE ACTIVITY IN AN INTESTINAL EPITHELIAL CELL LINE**

Ivana Caputo 1, 2, Maria Vittoria Barone 2, 3, Stefania Martucciello 1, Gaetana Paolella 1, Marilena Lepretti 1, Agnese Secondo 4, Riccardo Troncone 2, 3, Salvatore Auricchio 2, 3, Carla Esposito 1, 2

1Chemistry and Biology, University of Salerno, Fisciano (Salerno), Italy, 2ELFID, 3Paediatrics, 4Neurosciences, University of Naples Federico II, Naples, Italy

**Objectives & Study:** The A-gliadin peptide 31-43 is the prototype of peptides effective on the innate response in celiac disease, a complex intestinal inflammatory condition that develops in genetically susceptible individuals after exposure to dietary wheat gliadin. It has been demonstrated that NF-κB is constitutively activated in the inflamed mucosa of untreated celiac patients. Our aim was to investigated whether peptide 31-43 is able to induce NF-κB activation in Caco-2 cells. Since type 2 transglutaminase (TG2) can drive cross-linking and proteasome degradation of the NF-κB inhibitory protein, IκBa, we also aimed to investigate whether peptide 31-43 may lead to the activation of intracellular TG2.

**Methods:** We analysed NF-κB phosphorylation by western blotting. We performed functional studies on calcium homeostasis by Fura-2 AM single cell microfluorimetry. We performed *in situ* TG2 activity assay by using the substrate 5-(biotinamido)pentylamine and revealed activity by conventional microscopy and spectrophotometric analysis.

**Results:** We found that a brief treatment with peptide 31-43 induced an increase of NF-κB phosphorylation in total lysates and a higher level of phosphorylated NF-κB in nuclei. In the same experimental conditions, peptides 31-43 mobilized calcium ions from intracellular stores and also activated the enzymatic function of intracellular TG2.

**Conclusion:** Our findings suggest that peptide 31-43, by promoting NF-κB activation, could mediate a rapid local inflammatory response in celiac intestinal cells. Since peptide 31-43 also induces calcium mobilization with the consequent increase of TG2 activity, it is possible that NF-κB activation is mediated by the TG2-induced post-translational modification of the NF-κB inhibitor.

**Disclosure of Interest:** None Declared
Objectives & Study: Metabolic bone disease remains a significant and common complication of celiac disease (CD). Several studies have demonstrated low bone mineral density (BMD) at the time of CD diagnosis in both children and adults. Low bone density in children and adolescents is defined as an areal BMD (aBMD) less than 2 SD below the age-adjusted mean value (Z-score <−2 SD). The pathogenesis of bone loss in CD has not been completely elucidated: however, two major causal factors are malabsorption and inflammation. Calcium and Vitamin D might be poorly absorbed substances in celiac patients. It has been demonstrated an increased RANKL/OPG ratio in vitro and an increased osteoclastogenesis in untreated celiac patients due to chronic release of pro-inflammatory cytokines.

Aim of our study was to correlate Z-score value and anti-tissue transglutaminase type 2 (anti-tTG2) antibody title and Z-score value and Marsh-Oberhuber grade (MO) in children with CD at diagnosis.

Methods: We enrolled 99 celiac patients (M 35, F 64; age-range: 4-15 years). All patients had positive test results for anti-tTG2 antibodies; histological lesions were graded according to MO classification; all of them underwent lumbar DEXA performed by Lunar Prodigy Advance (GE Healthcare, USA). Bone mineral density was estimated by Z-score. The linear correlation between the anti-tTG2 title and Z-score value and between MO grade and Z-score was evaluated by the Pearson product-moment correlation coefficient (Pearson’s r).

Results: Anti-tTG2 antibody titers ≥10 times the upper limit of normal were found in 65 of 99 patients. 84 patients showed severe lesion degree (3c + 3b + 3a) in Marsh-Oberhuber classification, 3 patients showed MO2, 4 MO1, 4 no lesions and 4 didn’t undergo conventional upper GI (diagnosed according to the “biopsy-sparing” ESPGHAN 2012 criteria). Low BMD (Z-score ≤−2DS) was found in 13 (13.13%) patients; 20 (20.20%) patients showed −2< Z-score <−1; 43 (43.43%) patients showed -1≤ Z-score <0 and Z score ≥0 was detected in 23 (23.23%) patients. No correlations were found between Z-score value and anti-tTG2 title (Pearson’s r = -0.06) and between Z-score value and MO degree (Pearson’s r = 0.07).

Conclusion: Low bone mineral density does not correlate to the anti-tTG2 title and to Marsh-Oberhuber grading in a cohort of Italian children at CD diagnosis.

Disclosure of Interest: None Declared
**Objectives & Study:** Analyze in our pediatric population diagnosed of Coeliac Disease (CD) the incidence of hypertransaminasemia (HT) at diagnosis, the relationship with the clinical, serological and pathological patients and its evolution since the beginning of the GFD.

**Methods:** Retrospective descriptive study of coeliac children seen at our center between 1989 and 2012. Clinical variables at diagnosis were collected, serological (antitransglutaminase IgA antibodies (IgAATG Ab), antigliadin (AGA), antiendomysium antibodies (EMA)) and transaminases (ALT and AST) at diagnosis and one year after GFD. Preliminary data are presented relative to a total number of 1056 patients patients.

**Results:** Of the total registered (447) patients, 55% (n = 247) had transaminases at diagnosis, of whom 91 (37 %) had an increase in only one (ALT:19 % or AST:30 % ) or both ( 51 % , n = 47) . The increase was < 2 times the normal reference value ( 40UI / L ) for ALT in 72 % (n = 47) and AST in 86 % (n = 64) . 93% (n = 47) with follow-up diagnosis of elevated ALT was normalized one year after GFD , with 64 % (n = 48 ) in the case of the AST . None of the patients developed a severe liver disease. The HT group , 52 % (n = 47 ) were female , the average age at diagnosis was 44 months ( 9-149 ). 98 % (n = 89) had positive IgAATG Ab, 92 % positive AEM , 95 % positive HLA DQ2/DQ8, 100 % compatible with histopathology ( Marsh 2 or 3). Clinical diagnosis: chronic diarrhea ( 43%), failure to thrive (37 % ), abdominal distension ( 15%) and chronic (10 % ) anemia. In 94% of patients with HT ( n = 86) there is associated diseases. No significant differences in clinical and biochemical parameters evaluated for the total number of registered patients or in the group without elevated transaminase or in the group of patients without transaminases at diagnosis and also no significant differences were obtained according to the intensity of the lift are appreciated transaminases ( > or < x2 normal reference value) or the type of elevated transaminase.

**Conclusion:** The HT is a frequent finding in children with CD (similar to other series frequency). Although the origin is uncertain is usually not very important elevation and evolution during the first year after the start of the GFD is favorable, primarily ALT, without attaching cases of severe liver disease. Highlights the lack of statistically significant differences for different pathological anatomical clinical, laboratory and outcome measures.

**Disclosure of Interest:** None Declared
A STUDY OF THE IMPACT OF IMPLEMENTING THE NEW COELIAC GUIDELINES IN A SINGLE CENTRE

Anne Willmott 1,* Suchandra Pande 1
1Paediatrics, University Hospitals Leicester NHS Trust, Leicester, United Kingdom

Objectives & Study: The diagnosis of coeliac disease has changed over the years from one requiring several biopsies to one needing only blood testing and a single biopsy. The vastly improved accuracy of the blood tests led in 2012 to ESPGHAN and BSPGHAN agreeing new guidelines for the diagnosis of coeliac disease. In many cases this may avoid a biopsy altogether. The aim of this study was to look how practical the new guidelines were, to look at the impact of adopting them on endoscopy rates, and to audit our practice against the new standards.

Methods: All new diagnoses of coeliac disease in children under 16 in our centre in 2013 were analysed. These were recorded prospectively. As well as this each month all raised TTGs in children, processed by our immunology department were reviewed, to check that there was a record of all possible new patients, and this was also cross checked with the dietetic coeliac database. We recorded the blood tests done, the results and the speed of access to a definitive diagnosis (HLA result and repeat TTG, or biopsy result). We noted whether following the new pathway avoided endoscopy, and the cost implications involved in this.

Results: In 2013 34 patients were diagnosed with coeliac disease. Of these only 8 (24%) required endoscopy to confirm the diagnosis. After the initial screening test, diagnosis per patient with biopsy costs commissioners around £1400, (derived from tariff + top up) whereas diagnosis per patient without biopsy costs £130, thus there was a saving of approximately £36,000 in this year. It was hard to get accurate data regarding cost to the trust of an endoscopy as our PLICS data were clearly inaccurate. The HLA result did not change the diagnosis in any of our patients, as it was positive in all patients with significantly raised TTG.

In reviewing our practice we followed the new pathway correctly in 31/34 (91%) of pts. Three patients were wrongly started on gluten free diet after only one screening test. Two of these by a general paediatric colleague (identical twins), one in the private sector. All 3 had a repeat TTG test and HLA done within a few weeks of starting gluten free diet.

Conclusion: Following the new pathway was straightforward, and was correctly followed in 91% of cases. We avoided 26 endoscopies, saving £36,000 to commissioners, although the inaccurate PLICS data did not allow us to confirm cost implications to the trust of the reduction in endoscopy. The HLA result did not change the diagnosis, and it’s use in the context of TTG high enough to avoid biopsy needs to continue to be reviewed. Only three patients with raised TTG were not referred immediately to paediatric gastroenterology. All were discussed with the physicians concerned. We would recommend the new pathway, with continuing education of colleagues and cross checking with immunology extra safety measures to ensure all patients are correctly referred to gastroenterology.

Disclosure of Interest: None Declared
THE STRANGE TIMING OF COELIAC DISEASE

Irene Rutigliano 1,*, Nicola d’Altilia 1, Patrizia Cavaliere 1, Francesca Lotti 1, Mario d’Altilia 2, Michele Sacco 2, Massimo Pettoello-Mantovani 1, Angelo Campanozzi 1

1Paediatrics, University of Foggia, Foggia, 2Paediatrics, IRCCS Casa Sollievo della Sofferenza, San Giovanni Rotondo, Italy

Objectives & Study: Celiac disease (CD) is a genetically determined autoimmune disease with a recognized trigger. In current literature few studies have examined age-related clinical features of CD. AIM OF STUDY: To evaluate age-related clinical presentation of CD.

Methods: We analyzed 329 subjects with biopsy-proven diagnosis of CD. Collected data included: sex, clinical presentation (intestinal, extraintestinal and asymptomatic) and age at the diagnosis. Patients were divided in four groups according to quartiles of age.

Results: The first group was constituted by 82 children (age ≤2.059 yrs, 27 males and 55 females): 45.1% with extraintestinal symptoms, 52.4% with intestinal symptoms and 2.4% asymptomatic. The second group (82 children aged between 2.059 and 4.35 yrs, 29 boys and 53 girls) presented: 57.3% extraintestinal symptoms, 31.7% intestinal symptoms, 11% without clinical signs. The third group (83 children aged between 4.35 and 7.8 yrs, 31 boys and 52 girls): 44.6% complained extraintestinal symptoms, 41% intestinal and 14.4% were asymptomatic. The last group was constituted by 82 children (33 boys, 49 girls): 45.1% with atypical symptoms, 35.4% with typical symptoms and 19.5% asymptomatic subjects. The increasing in prevalence rate of asymptomatic form with age was significant (p=0.007).

Conclusion: Our results suggest age-related clinical presentation in CD: in particular asymptomatic form is more frequent in elder children and seems to increase with increasing age. These considerations confirm current evidences: CD is diagnosed at a later age with less apparent clinical manifestations. The reasons of this timing are not clear and further studies are requested to investigate this relationship.

Disclosure of Interest: None Declared
GENDERED EXPERIENCE OF LIVING AN EVERYDAY LIFE WITH COELIAC DISEASE SHOULD BE TAKEN INTO ACCOUNT WHEN THE HEALTH CARE IS ORGANIZING SUPPORT

Ethel Kauto1,2,*, Cecilia Olsson1, Anneli Ivarsson3, Hörmell Agneta1, Lena Aléx4
1Department of Food and Nutrition, 2Umeå Center for Gender Studies, Umeå, Sweden, 3Department of Public Health and Clinical Medicine, Epidemiology and Global Health, 4Department of Nursing, Umeå University, Umeå, Sweden

Objectives & Study: Objectives and study
In all societies, multiple norms of what is seen as masculine or feminine exist to construct a gender order. Previous studies have shown that women find it more troublesome to live with celiac disease than men do. This study examines aspects of that experiential differentiation. The objective of this study is to explore the daily experiences in relation to the gluten-free diet among young Swedish men and women diagnosed to celiac disease by screening in early adolescence.

Methods: Methods
Semi structured interviews were conducted with seven men and seven women, aged 17-18 years, about 5 years after they had been diagnosed with celiac disease through the screening study ETICS, (i.e. Exploring the Iceberg of Celiacs in Sweden). Interviews were transcribed verbatim, separated into those involving men and women, and thereafter inductive analysis was performed using qualitative content analysis techniques.

Results: Result
The preliminary analysis of the young men resulted in the main latent theme - conquering the disease and becoming a man. This was derived from three themes; i) a life changing event, ii) being one of the guys, and iii) adjusting the life according to the disease.
The analysis of the young women resulted in the main latent theme - an ongoing gendered endeavor in silence. This was derived from four themes; i) having little margin for personal maneuver, ii) being forced to be responsible, iii) blaming oneself, and iv) struggling with “normality”.
At first both the young men and the young women experienced the prescribed gluten-free diet as disgusting (especially the bread) but in time they learnt to differentiate among the gluten-free alternatives and to accept, and even appreciate, much of the gluten-free foods.

Conclusion: Conclusion
There are important gender differences in how young men and young women experience their everyday life with celiac disease, despite similarities in how they describe their thoughts about eating the actual gluten-free food product. Adhering to a strict diet means that you must be able to make demands on the environment and, be self-assured about what you will accept, characteristics that is compatible with the accepted norms of the dominant masculinity in our society. In contrast, the normative femininity involves caution and empathy which can make strict compliance to the gluten-free diet problematic for the young women. The health care system should take gender expectations in the society into account when organizing support in order to better meet the needs of the individual patient.

Disclosure of Interest: None Declared
GLUTEN-FREE DIET INFLUENCES PSYCHOSOCIAL ASPECTS OF LIFE OF CHILDREN WITH COELIAC DISEASE

Anna Rybak 1, Łukasz Obrzycki 1, Beata Oralewska 1, Anna Stolarczyk 1, Anna Szafarska-Poplawska 2, Barbara Iwańczak 3, Elżbieta Cyrt-Jarocka 4, Urszula Grzybowska-Chlebowczyk 5, Wojciech Cichy 6, Grażyna Czaja-Bulsa 7, Jerzy Socha 1, Piotr Socha 1

1Gastroenterology, Hepatology and Feeding Disorders, Children’s Memorial Health Institute, Warsaw, Poland, 2Department of Paediatrics, Allergology and Gastroenterology, Collegium Medicum Nicolaus Copernicus University, Bydgoszcz, Poland, 3Department of Paediatrics, Gastroenterology and Nutrition, Medical University of Wroclaw, Wroclaw, Poland, 4Department of Paediatrics, Gastroenterology and Allergology, Medical University, Białystok, Białystok, Poland, 5Department of Paediatrics, Medical University of Silesia, Katowice, Poland, 6Department of Paediatrics, Gastroenterology and Metabolic Diseases, University of Medical Sciences, Poznań, Poland, 7Department of Paediatrics, Gastroenterology and Rheumatology, Independent Specialist Public Health Care, Szczecin, Poland

Objectives & Study: It was proven that introducing life-long gluten-free diet (GFD) leads to impaired quality of life, decreased comfort and psychological distress in patients with coeliac disease (CD). Our study is a part of the project evaluating risk factors of atherosclerosis in children with CD. The aim of this study was to evaluate psychosocial aspects of life of children with CD and newly diagnosed children.

Methods: 277 patients were recruited in 7 clinics in Poland. We analyzed questionnaires from 210 children suffering from CD, treated for at least 5 years (group A), and 67 children included in the study on the day of CD diagnosis (group B). Questionnaires were fulfilled by the patients or their caregivers and they were analyzed with respect to the feelings of sadness or depression, contact with peers, occurrence of problems at school, smoking and alcohol consumption.

Results: The mean age of patients in group A was 14 years (3-23 years), in group B – 10 years (2-20 years). Over half of patients suffered from classical CD (n=156, 62%), 33% had an atypical CD and close to 5% (n=12) of patients presented with silent CD. Over 75% of patients (n=198) were compliant to GFD. We found no significant differences between the groups (A and B) with respect to feelings of sadness or depression. With respect to the contact with peers, they were assessed as very good or good in both groups (60% and 29% in group A; 41% and 39% in group B, respectively). We found significantly higher incidence of school problems in patients with >5 years celiac history (U=5 064,00; Z=-2,71; p=0,007). The question of worries related to home financial situation was confirmed as worrisome by a number of patients in both groups (22% and 42% respectively). We also analyzed the differences of all mentioned factors with the clinical presentation of CD and we found significant increase of worries related to home financial situation in patients with classical CD.

Conclusion: The psychosocial factors may have an vital impact on life, compliance to the treatment and presumably on comorbidities in patients with chronic diseases, including CD. We showed similar psychosocial problems among patients suffering from CD for more than 5 years and newly diagnosed patients. This may indicate stigmatizing by specific treatment (GFD) or disease itself, but also by symptoms, as the majority of presented patients suffered from the classical CD. Our results indicate need for early multidisciplinary approach in the care and treatment of children with CD.

Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0049

**MORPHOMETRIC CHANGES IN SMALL INTESTINAL BIOPSIES OF COELIAC CHILDREN DURING GLUTEN-FREE DIET**

Elena Roslavtseva 1,*, Yuri Lysikov 2, Tatiana Malitsyna 3, Tatiana Borovik 4

1Healthy and Sick Child Nutrition, Scientific Center for Children’s Health, 2Institute of Nutrition RAMS, 3Gastroenterology, Izmajlovskaya Children’s Hospital, 4Healthy and Sick Child Nutrition, Scientific Center for Children’s Health RAMS, Moscow, Russian Federation

**Objectives & Study:** Prescribing of a gluten-free diet for elevated anti-gliadin antibodies (IgG-AGA’s) or simply ex-juvantibus in children with chronic diarrhea, failure to thrive is now a usual practice in Russia, because of poor knowledge in pediatricians or lack of diagnostic facilities. The aim of our study was to evaluate when we could suspect celiac disease (CD), if the child already received gluten-free diet (GFD) for different terms

**Methods:** 307 biopsies from 234 children aged 0,5–16 years with CD, confirmed with ESPGHAN 2 Criteria (1989) were evaluated. Children non-compliant with gluten-free diet were excluded. Biopsies taken from the distal duodenum or proximal jejunum were fixed in 4% paraformaldehyde prepared in Hanks’ buffer and 1% OsO4, dehydrated in acetone and poured into epoxy resin Epon-Araldite mixture. Semi-thin sections for light microscopy were stained by toluidine blue. The thickness of mucosa, villous height, crypt depth were measured by morphometry in microns (μm) and intraepithelial lymphocyte count (IEL’s) in percent to the number of enterocytes

**Results:** 80% of celiacs had thin small intestinal mucosa, due to villous atrophy, recovering it’s normal thickness to the 18-36th months of the GFD. The villous height became significantly higher (p<0.001) in 6 months, the crypts’ depth lower in 6-12 months, (p=0.005), the villous/crypt’s ratio higher in 3 months (p<0.001), and IEL’s lower (p< 0.001) in 6-12 months of GFD. Nonetheless, in terms of 18-36 months of GFD, 60% of children had subatrophy of villi (<300 µm ) 52% - elongated crypts (> 200 µm ) and 62% elevated IEL’s (>30%).

**Conclusion:** Morphological remission develops slowly and irregularly in different patients, but we could confirm significant differences in the small intestinal morphometric parameters since the 6th month of GFD. Therefore there is a reason of performing a diagnostic biopsy of small intestinal mucosa in suspicion of CD even the child is already <6 months on the GFD; however in 50-60% of celiac histological symptoms of CD are reserved up to 3 years of GFD

**Disclosure of Interest:** None Declared
USEFULNESS OF THE RADIOIMMUNOLOGICAL TEST FOR ANTI-TRANSGLUTAMINASE AUTOANTIBODIES ON SALIVA IN COELIAC CHILDREN AND ADOLESCENTS: A MULTICENTER STUDY

Raffaella Nenna 1,*, Federica Lucantoni 1, Laura Petrarca 1, Monica Montuori 1, Maurizio Mennini 1, Maria Bavastrelli 1, Matteo Florio 1, Antonella Polimeni 2, Alessandra Maiorana 3, Magda Mensi 3, Domenico Compilato 4, Francesco Carroccio 4, Giuseppe Iacono 5, Claudio Tiberti 6, Margherita Bonamico 1

1 Department of Paediatrics, 2 Department of Odontostomatology, "Sapienza" University Of Rome, Rome, Italy. 3 Department of Surgical Specialities, Radiological Sciences, Public Health, University of Brescia, Brescia, Italy. 4 Department of Oral Medicine, University of Palermo, Italy. 5 Paediatrics, Di Cristina Hospital, Palermo, Italy. 6 Department of Internal Medicine, "Sapienza" University Of Rome, Rome, Italy

Objectives & Study: In a large series of six to eight years primary school-children, radioimmunological assay (RIA) for IgA anti-transglutaminase (TG2) in saliva has been demonstrated to be a sensitive screening method for coeliac disease (CD) (Nenna R. et al., JPGN 2013). Our aims was to evaluate the sensitivity and specificity of IgA TG2 RIA on saliva at CD diagnosis, in children and adolescents, divided in three age groups.

Methods: Over the period November 2011 - October 2013, 127 CD children and adolescents (35 males, age range 1-22 years, median 8.3 years) on a gluten-containing diet, positive to serum IgA TG2 RIA and/or ELISA, underwent a saliva collection to assay IgA TG2 by RIA. Moreover, 72 gastroenterological controls (GC) (35 males, age range 2-18 years, median 9.5 years) were enrolled.

Results: 101 out of 127 biopsy-proved CD children and adolescents (79.5%) showed high IgA TG2 RIA index in saliva. Particularly, 9 out of 14 children aged below 5 years (G1: 64.3%) (m±SD: 37.4±40.4), 51 out of 54 aged from 5 to 9 years (G2: 94.4%) (m±SD: 48.3±31.8) and 41 out of 59 children and adolescents aged more than 9 years (G3: 69.5%) (m±SD: 46.6±44.6) showed high TG2 Ab-Index. Significant differences were found among the three groups of patients (G1 vs G2: p=0.007; G1 vs G3: p=ns; G2 vs G3: p=0.001). All GC were IgA TG2 negative, but two weakly positive children.

Conclusion: The results of this preliminary report confirm a good sensitivity of the salivary test in primary school-children aged 5-9 years, while in younger, as well as older children and adolescents, blood tests show higher performance. In the small series the specificity of the test was good both in children and in adolescents.

Disclosure of Interest: None Declared
Objectives & Study: Shwachman-Diamond syndrome (SDS) is a rare genetic disorder characterized by exocrine pancreatic insufficiency, bone marrow dysfunction and skeletal abnormalities. This study is an overview of clinical experience of SDS in a National Clinic in the United Kingdom.

Methods: 44 children identified from the Hospital’s National SDS Clinic database. 13 excluded because of alternative diagnoses or incomplete data. 31 patients (15 male) with a clinical and/or genetic diagnosis of SDS were included. Their clinical symptoms, psychological and genetic characteristics were analysed from initial presentation until early adulthood or death.

Results: All 31 patients had genetic screening for the disease; 11/31 were compound heterozygotes for the common SBDS mutation (c.183_184TA>CT and C258+2T>C). Less common genetic profiles were identified in 13 patients.

8 patients had mild or transient neutropenia with no recurrent or serious infections. 19 had moderate to severe neutropenia and of those, 11 had transient or persistent pancytopenia with 2 progressing to bone marrow failure and bone marrow transplantation.

The majority of patients required long-term pancreatic enzyme and vitamin/trace element supplementation due to severe pancreatic insufficiency. 5 patients became pancreatic sufficient at follow up, including one with mild pancreatic lipomatosis on imaging. Transient transaminitis with absent/mild radiological features but no clinical implications was seen in 63%. A non specific enteropathy was identified endoscopically in 22%, with no clear correlation with pancreatic or genetic status.

Growth issues were a common denominator either due to feeding difficulties or skeletal dysplasia, the latter seen in 48%. No true endocrinopathies were identified. 21 patients had significant dental involvement.

18 patients had identifiable learning and behavioural difficulties, ranging from mild speech delay to severe hyperactivity and depression.

Congenital abnormalities such as cleft palate, congenital hydrocephalus, and congenital heart disease were seen in a minority. Renal manifestations included neonatal nephrocalcinosis, hyperoxaluria and late onset proteinuria.

Conclusion: This study of the largest cohort of SDS patients in Europe allows accurate phenotype and genotype descriptions and potential correlations. Better understanding of the spectrum of SDS manifestations will allow timely diagnosis and contribute to optimal management of this rare condition.

Disclosure of Interest: None Declared
THE CLINICAL COURSE OF CHRONIC PANCREATITIS IN CHILDREN WITH THE COINCIDENCE OF MUTATIONS IN THE CFTR AND SPINK1 GENES

Karolina Wejnarska 1,*, Jaroslaw Kierkus 1, Elwira Kolodziejczyk 1, Grzegorz Oracz 1, Jozef Ryzko 1
1Department of Gastroenterology, Hepatology and Feeding Disorders, The Children's Memorial Health Institute, Warsaw, Poland

Objectives & Study: Chronic pancreatitis (CP) is a rare disease diagnosed in children with increasing frequency. The causes of CP in children are varied. These include gene mutations, anatomic anomalies of the pancreatic duct and metabolic disorders. The aim of our study was to evaluate the clinical severity of chronic pancreatitis in children with the coincidence of mutations in the CFTR gene and SPINK1 gene.

Methods: 208 children with chronic pancreatitis hospitalized since 1988 to 2012 were enrolled into the study. Data were analyzed for age at diagnosis, severity of inflammatory lesions assessed on a Cambridge scale during ERCP and the frequency of intervention treatment - endoscopic or surgical. All the children had carried out the analysis of gene mutations that predispose to pancreatitis (PRSS1, CFTR, SPINK1).

Results: The coincidence of mutations in CFTR and SPINK1 genes was found in 9 children (4.3%) (three girls and six boys, with mean age 11.5 years, from 6 to 15 years). The coincidence of mutations N34S/- and delF508/- was detected in 3 patients, mutations N34S/- and IVS8-5T(TG)11/- in 5 children, mutation N34S/- and IVS3 +2 T> C/- and delF508/- in 1 patient. Family history was positive in 5/8 patients. In 3 children the first episode was preceded by the abdominal trauma. There was no significant difference in the age of the disease onset between the studied group and the rest of the patients (9 years vs. 8.9 years, NS). There was no difference in the severity of inflammatory lesions assessed on a Cambridge scale during ERCP (1.5 vs. 1.7, NS). The frequency of therapeutic procedures (endoscopic and surgical) (38% vs. 35%, NS), pancreatic duct stenting (38% vs. 35%, NS) and the frequency of ESWL were also similar in both groups of patients.

Conclusion: The clinical course of chronic pancreatitis in children with the coincidence of mutations in the CFTR and SPINK1 genes does not differ from the clinical course of disease caused by other etiological factors.

Disclosure of Interest: None Declared
GASTRIC EMPTYING AND GASTRO-OESOPHAGEAL REFLUX IN CHILDREN WITH CYSTIC FIBROSIS

Bruno Hauser 1,*, Kathelijn Keymolen 2, Ann Malfroot 1, Iris De Schutter 1, Elke De Wachter 1, Thierry Devreker 1, Elisabeth De Greef 1, Gigi Veereman 1, Yvan Vandenplas 1

1UZ Kinderziekenhuis Brussel, 2Center for Medical Genetics, UZ Brussel, Brussels, Belgium

Objectives & Study: According to the literature gastric emptying (GE) can be normal, decreased or increased in children with cystic fibrosis (CF). We studied GE in children with CF with symptoms suggestive for gastro-oesophageal reflux (GOR) (group 1) and children with CF without chronic gastro-intestinal symptoms (group 2).

Methods: Group 1 consisted of 24 children, 13 boys, age 5.8 ± 4.2 (0.5-17.1) years. Group 2 consisted of 22 children, 14 boys, age 8.8 ± 2.8 (5-14) years. Impedance-pH monitoring for detection of GOR (Sleuth, Sandhill Scientific Inc, Highlands Ranch, CO, USA) was performed in group 1. Acid reflux parameters were regarded as increased if the total oesophageal acid exposure was above the 95 th percentile of normal data obtained in healthy subjects (Vandenplas, 1991). 13C-octanoic acid breath test to measure GE of solids (pancake) using Non Dispersive Infrared Spectrometry (Wagner Analysen Technik, Bremen, Germany) was performed in both groups. GE was considered delayed if the gastric half emptying time was above the 95 th percentile of normal data obtained in healthy subjects (Hauser, unpublished data).

Results: Group 1: 11/24 children (45.8 %) had increased acid GOR ; 7/24 children (29.2 %) had delayed GE ; 3 patients had increased GOR and delayed GE (12.5 %), 8 patients had increased GOR and normal GE (33.3 %), 4 patients had normal GOR and delayed GE (16.7 %), and 9 patients had normal GOR and normal GE (37.5 %); delayed GE was present in 27.3 % of children with increased acid GOR and in 30.8 % of children with normal acid GOR. Group 2: 2/22 children (9.1 %) had delayed GE.

Conclusion: Increased acid GOR is present in about half of children with CF and symptoms suggestive of GOR. Delayed GE is documented in about 30 % of these children with or without increased acid GOR. Delayed GE is only present in about 10 % of children with CF without chronic gastrointestinal symptoms.

Disclosure of Interest: None Declared
**Gastroenterology**

**Cystic Fibrosis and Pancreatic Disorders**

PO-G-0054

**THE USE OF SOLUBLE TRANSFERRIN RECEPTOR AND HEPCIDIN IN THE ASSESSMENT OF IRON STATUS IN CHILDREN WITH CYSTIC FIBROSIS**

Lieke Uijterschout 1,*, Marjolijn Akkermans 1, Thom Zandstra 1, Marianne Nuijsink 1, Daniëlle Hendriks 2, Frank Brus 1

1Department of Paediatrics, Juliana Children's Hospital, The Hague, Netherlands, 2Department of Paediatrics, Juliana Children’s Hospital, The Hague, Netherlands

**Objectives & Study:** Iron deficiency (ID) is common in patients with cystic fibrosis (CF). Assessment of iron status in CF patients is complicated because most iron status indicators are influenced by infection or inflammation. We hypothesized that hepcidin and soluble transferring receptor (sTfR) may be more useful than ferritin (Fer) to distinguish between absolute and functional ID in children with CF.

**Methods:** We assessed iron status in 53 children with CF, using sTfR and hepcidin in addition to conventional iron status indicators. We analyzed the association between ID and age, dietary iron intake, the presence of infection/inflammation, erythropoietic activity and markers of CF disease progression such as pulmonary function, Pseudomonas Aeruginosa colonization, pancreas insufficiency and liver function.

**Results:** ID was present in 5 (11.9%) children respectively. Increased concentrations of sTfR were not observed in any of these children. Hepcidin concentrations were low and concentrations below the limit of detection were observed in 10 children (20.4%). Hepcidin was significantly associated with Fer.

**Conclusion:** We suggest that a low hepcidin in these children is an indicator of deficient iron stores. Hepcidin might provide more information on iron status in CF patients than Fer and sTfR. Future studies including more patients are necessary to reveal the role of hepcidin in the diagnosis and treatment of ID in CF patients.

**Disclosure of Interest:** None Declared
**NEW VARIANT OF CFTR GENE IN RECURRENT IDIOPATHIC PANCREATITIS**

Sabrina Cardile 1,*, Italia Loddo 2, Simona Valenti 1, Giuliana Morabito 1, Claudio Romano 1

1Paediatric Department, 2Department of Genetics, University of Messina, Messina, Italy

**Objectives & Study:** Acute and chronic pancreatitis in childhood cause occasional and significant morbidity, but our understanding of pancreatic inflammation is rudimentary. Genetic pancreatitis (GP) can be associated with mutations of cystic fibrosis transmembrane conductor regulator gene (CFTR), or cationic trypsinogen (PRSS1) gene, and/or serine protease inhibitor Kazal type 1 (SPINK1). In 1988, it was reported an association between idiopathic pancreatitis (IP) and CFTR mutations. Several mild pancreatic sufficient CFTR mutations were found to be associated with IP. Multiple range of loss-of-function CFTR variants have been reported to be associated with idiopathic pancreatitis but their functional effects remain to be clarified in most cases. The 5T variant is a stretch of five contiguous thymidines at the 3’ of the intron 8 of CFTR gene that exacerbates skipping of exon 9, resulting in reduced levels of functional CFTR protein. This process seems to be influenced by the number of TG repeats immediately adjacent to 5T. Individuals carrying 5T adjacent to either 12 or 13TG repeats was demonstrated are more likely correlated with a risk of IP.

**Methods:** We have investigated the cases of 4 children (aged 12, 10, 6 and 3 years) affected by IP. The diagnosis of pancreatitis was made by the presence of typical abdominal pain, serum amylase and/or lipase 3 times greater than the upper limit of normal and characteristic imaging findings detected by US e CT (volume increase of the pancreas, inhomogeneous structure and peripancreatic fluid collection). Sequence analysis of PRSS1, SPINK1 and CFTR genes was performed.

**Results:** Sequence analysis showed the absence of mutations in PRSS1 and SPINK1 genes. CFTR gene sequencing in three boys showed the presence of following IVS-8 polyT polymorphisms: 5T/5T 12TG/12TG; 5T/5T 11TG/12TG; 5T/9T 13TG/11TG. The 3-years old girl with the most severe form of IP showed 5T/7T 13TG/9TG. In this girl the 5T allele, in cis with 13TG, was associated in trans with F508del, a severe CFTR mutation.

**Conclusion:** Our results, in a limited number of cases, have shown the high prevalence of 5T carriers in CFTR can be considered a reliable predictor of the IP. The knowledge of TG repeat number in individuals with 5T can be of diagnostic value. Further studies are needed to comparing the prevalence of the 5T-poly(TG) in the general population without IP.

**Disclosure of Interest:** None Declared
Objectives & Study: PPP syndrome is characterized by the development of erythematous cutaneous nodules, poly or oligoarthritis and/or bone necrosis in the setting of an acute or chronic pancreatitis. We report about a patient who developed multiple osteo-necrotic lesions and panniculitis in consequence to a prolonged episode of pancreatitis. This has prompted us to look into the prevalence of PPP at the Hospital for Sick Children, Toronto. Investigations were extended to further explore the pathophysiology.

Methods: Retrospective chart review from 1992 to 2012 using “pancreatitis” and referral to Dermatology and/or Rheumatology. Histological examination of osseous tissue was performed. The periosteal fluid was analyzed for fatty acid and lipase activity. Immunoblot analysis was used to further specify the lipase type.

Results: A 6 year old boy presented with prolonged episode of pancreatitis following an abdominal handlebar injury with subsequent development of a pancreatic pseudocyst. The patient developed panniculitis in several digits of his right and left hand as well as 2 toes which resolved upon pseudocyst drainage following endoscopic cyst-gastrostomy. Rheumatological and microbiological investigations were negative. Bone biopsies revealed fat necrosis with saponification. Periosteal fluid showed high levels of free fatty acids and high lipase activity (4 times higher than serum levels). Protein immunoblotting specified lipase to be pancreas triglyceride lipase. In ten years only one other case of PPP occurred among 265 cases of pancreatitis, yielding an incidence of 7 per 1,000 pancreatitis cases.

Conclusion: The incidence of PPP syndrome is low, but clinical knowledge about it is important to avoid invasive and unnecessary treatments. High levels of pancreatic triglyceride lipase and free fatty acids in the periosteal fluid confirm that panniculitis is caused by local lipolysis due to high accumulation of pancreatic lipase leading to saponification of the tissue and secondary inflammation.

Disclosure of Interest: None Declared
Gastroenterology
Cystic Fibrosis and Pancreatic Disorders
PO-G-0057

GUT MICROBIOTA IN CYSTIC FIBROSIS (CF) PATIENTS: A COMBINED -OMIC TRANSLATIONAL WORKFLOW

Lorenza Putignani 1, Federico Alghisi 2,* and P. Vernocchi, F. Majo, F. Alghisi, M. Valerio, L. Casadei, F. Del Chierico, A. La Storia, F. De Filippis, C. Rizzo, E. Fiscarelli, C. Manetti, M. Muraca, V. Lucidi, D. Ercolini, B. Dallapiccola, L. Putignani
1Laboratories, Bambino Gesu' Children's Hospital and Research Institute, Rome, Italy, 2Paediatrics, Bambino Gesu' Children's Hospital and Research Institute, Rome, Italy

Objectives & Study: Cystic fibrosis (CF), is a disorder affecting the exocrine glands of the respiratory, digestive and reproductive systems and its lethality ranging from the first year of life to the third (and later) decade. This lethal hereditary disorder has known or suspected links to the gut microbiota, including a possible association with its dysbiosis. High-throughput meta-omics-based approaches may actually assist in unveiling this complex network of symbiosis modifications. The aim of this work was to investigate the gut microbiota composition and modulation of CF patients by metagenomic and metabolomic combined analyses in relation with healthy children.

Methods: Thirty faecal samples from either CF patients and healthy children (HC) (age range 0-6 years) were collected at Bambino Gesù Children's Hospital. The metabolomic analyses were performed by GC-MS/SPME and 1H-NMR, while metagenomic analysis was carried out by 454 pyrosequencing platform.

Results: About 200 volatile organic compounds (VOCs), 150 shared between HC and CF children and 50 belonged only to CF patients were detected and quantified by GC-MS/SPME and about 20 molecules characterized with 1H-NMR. The inter-individual variability of VOCs levels resulted high. Compared to HC, the level of esters, alcohols and aldehydes were higher in CF patients. On the contrary, SCFA were higher in HC than CF. 1H-NMR analysis, showed lower levels of amino acids and uracil in CF patients than HC. Metagenomic results on 60 CF and HC samples indicated Firmicutes as most abundant phyla, while the abundance of Bacteroidetes and Proteobacteria varied according to the sample analyzed. Moreover, this analysis identified a remarkable degree of variability of the operational taxonomic units (OTUs) confirming the high level of inter-individual metabolic variability.

Conclusion: By this integrated approach it's possible to generate personalized “-omics” charts that can be used for the monitoring of the nutritional state of the child and for the evaluation of gut absorption in CF patients, hence provide a translational medicine tool.

Disclosure of Interest: None Declared
**Gastroenterology**

**Cystic Fibrosis and Pancreatic Disorders**

PO-G-0058

**AUTOIMMUNE MARKERS IN CHILDREN WITH CHRONIC PANCREATITIS**

Grzegorz Oracz 1,*, Bozena Cukrowska 2, Jaroslaw Kierkus 1, Karolina Wejnarska 1, Elwira Kołodziejczyk 1, Jozef Ryzko 1

1Dep. of Gastroenterology, Hepatology and Feeding Disorders, 2Department of Pathology, The Childrens Memorial Health Institute, Warsaw, Poland

**Objectives & Study:** In the last decade we can observe gradual increase of autoimmune diseases. The etiology of CP in children is varied and includes gene mutations, anatomic anomalies, and others. The reported paediatric experience with chronic pancreatitis (CP) is small and little is known about the role of autoimmune pancreatitis (AIP).

The aim of the study was to assess the frequency of autoimmune markers in children with CP.

**Methods:** 129 children hospitalized at the Department of Gastroenterology, The Children’s Memorial Health Institute, between 2005 and 2012 were examined for the presence of AIP; the level of IgG4 was determined, and the tests for anti-tissue antibodies (ANA, ASMA, AMA, ANCA, AHA) were conducted. Clinical data were recorded and analyzed.

**Results:** Anti-tissue antibodies were detected in 75/129 children (58%), and 24/68 patients (35.3%) showed an increased IgG4 level. Based on the International Association of Pancreatology criteria, a suspicion of AIP was raised in six patients. In 32/75 (42.6%) patients with autoimmune markers we found gene mutations predisposing to CP. In 16/75 children (21.3%) anatomic anomalies were fund. There was no difference in the severity of the disease and clinical course between children with autoimmune stigmata and patients without autoimmune markers.

**Conclusion:** In children with CP, similarly to adults, there is a high frequency of biochemical markers of autoimmunity. It’s worth to remember that AIP can occur in children.

**Disclosure of Interest:** None Declared
**Objectives & Study:** To assess the current management of acute pancreatitis in our centre.

**Methods:** Retrospective review of clinical charts of the patients with a diagnosis of pancreatitis at the moment of discharge during the past 7 years, evaluating epidemiologic data, etiology, symptoms, laboratory and imaging results, treatment given and clinical outcome.

**Results:** A total of 84 patients were obtained (1.36‰ of the total of the in-patients during the studied period). 40 were males (47.6%). The mean age was 11 years. In 24 patients the cause of admission was pancreatitis, while in the other 60 the cause was another. 18 patients presented recurrent pancreatitis. 64 had a history of important co-morbidity, mainly hematologic malignancies (29), solid tumours (9), cystic fibrosis (6). The symptoms at the time of diagnosis were as follows: abdominal pain (43), vomiting (29), fever (13), diarrhoea (10), asthenia/discomfort (7), other (11), and 22 did not exhibit symptoms of pancreatitis (the diagnosis was made solely on laboratory results). Most cases presented more than one symptom. The mean value of serum amylase and serum lipase were 519 U/L and 440 U/L respectively. An abdominal ultrasound was performed in 78 patients (90%), with a normal result in 55 of these (65%). For those with altered results, the most frequent findings were changes in the echogenicity of the pancreas (10) and an increase in the size of the gland (5). In 65 cases, other complementary tests were performed (among which were 19 abdominal CT, 11 abdominal X-rays and 3 cholangio resonances). The most frequent causes of pancreatitis were as follows: toxic/pharmacological (26), idiopathic (7) and post-traumatic (7). 76 patients received analgesic treatment (being metamizol the most commonly used in 46 cases), and 62 received antibiotics, most because of their associated co-morbidity or as surgical prophylaxis. One patient required surgery (pseudocyst drainage). As for nutritional treatment, 68 patients received enteral nutrition (after a mean period of 3.8 days of fasting). Out of these 68, 47 received a low-fat enteral diet. 31 were fed by tube (18 transpiloric, 13 nasogastric). 37 received parenteral nutrition (22 low-fat). 43 required admittance to the Intensive Care Unit, principally due to their underlying disease. The mean duration of admittance to hospital was of 36 days (range 1 to 195 days). 10 patients perished, all because of their underlying disease. The only complication registered owing to pancreatitis was the case of a pancreatic pseudocyst, mentioned above.

**Conclusion:** Pancreatitis is a very rare disease in childhood. It appears mainly in patients with associated co-morbidity. The toxic/pharmacological cause is the main etiology found. Medical treatment (with a high emphasis on nutrition) remains the basic support.

**Disclosure of Interest:** None Declared
Objectives & Study: Endoscopic retrograde cholangiopancreatography (ERCP) is increasingly being used in the evaluation and management of bilo-pancreatic disorders in children. The aim of this study was to review the records of pediatric patients who underwent ERCP procedures in the last year and report eventual complications.

Methods: Medical records of the eight patients followed in our tertiary referral center, who underwent ERCP for any indication during the last year were retrospectively analyzed. Indication for ERCP and serious adverse events including bleeding, perforation, pancreatitis or death were reported.

Results: Twelve ERCPs were performed on 8 patients. Patient age was 6.6±4.6 years and the sex ratio was 1M/1F. The indications were: complications of pancreatic trauma (3 cases), choledochal cyst (1), pancreatic tumor (1), Wirsung duct lithiasis related to chronic pancreatitis (1) and biliary derivation (2). A therapeutic intervention was performed in 6 patients (62.5%), representing 10 ERCP procedures, and technical success was achieved in 7/10 ERCPs. Reason for therapeutic failure were biliary duct paucity (1 case) and impossibility to recanalize distal pancreatic duct after traumatic Wirsung disruption (2 cases). Two (2/8) patients presented a moderate adverse event as they developed uncomplicated acute pancreatitis after the intervention.

Conclusion: ERCP indications are rare in the pediatric population. However the technique is as efficacious as in adults with low rates of adverse events in the hands of experienced endoscopists working in high-volume centers.

Disclosure of Interest: None Declared
INDICATIONS AND EFFICACY OF ENDOSCOPIC ULTRASOUND IN CHILDREN
Barbara Bizzarri 1*, Elisabetta Manzali 1, Alessandro Fugazza 1, Antonino Salerno 1, Federica Gaiani 1, Benedetta Cavirani 1, Giorgio Nervi 1, Gian Luigi de'Angelis 1
1Endoscopy Unit, Parma, Italy

Objectives & Study: The role of Endoscopic Ultrasound (EUS) is well defined in adult disorders but still not in children. The aim of the study is to evaluate retrospectively EUS±FNA indications and clinical utility in children.

Methods: Fifty EUS were performed in 42 patients (20 male) aged 7-18 yrs (median 15 yrs). We considered indications, type of anesthesia, findings, complications.

Results: Thirty-nine upper and 11 lower EUS were performed: 32 upper EUS were performed in deep sedation and 7 in general anesthesia; 4 lower EUS under conscious sedation. Indications for upper EUS were: suspected choledocholithiasis in 13 patients (31%), acute (PA) or recurrent pancreatitis in 6 pts (15%), abdominal pain suggestive of pancreatobiliary (PB) origin in 6 pts (15%), abdominal trauma in 1 pt (2%), sclerosing cholangitis (SC) in 1 pt (2%), suspected neuroendocrine tumor (NET) in 1 pt (2%), postprandial hypoglicemia in 1 pt (2%), common bile duct (CBD) ectasia in 1 pt (2%), follow-up post-cholecystectomy in 1 pt (2%) and pancreatic cyst in 2 pts (5%). Of these suspected for serous cystoadenoma. This last pt underwent FNA which confirmed the suspect. EUS confirmed choledocolithiasis in 10 cases out of 13. In pts with recurrent pancreatitis EUS showed: 1 negative, 2 initial signs of chronic pancreatitis (PC), 3 PA (1 lithiasic, 1 alithiasic, 1 necrotic-hemorrhagic). In this last pt EUS, after 1 month, revealed a tail’s pseudocyst with gallbladder lithiasis. In all 6 pts with abdominal pain suggestive of PB origin, EUS showed pancreatitis signs with gallbladder microolithiasis; in pt with abdominal trauma EUS revealed intra-abdominal fluid; SC was confirmed in 1 pt; EUS confirmed the diagnosis of NET, and it was negative after surgical treatment. New diagnosis of PC was made in pt with hypoglycemia; and of PA in pt with CBD ectasia; post-cholecystectomy EUS was negative. Indications for lower EUS were: surgical anal follow-up in 4 pts (10%), suspected anal fistula in 2 pts (5%), Crohn disease in 2 pts (5%), and fecal incontinence in 1 patient (2%). In post-surgical pts, EUS was negative in 2 pts and it showed anal sphincter interruption in 2 pts, one with an associated transsфинcterial fistula. In pts with Crohn, EUS revealed in 1 pt external anal sphincter thinning and in the other an anal abscess and fistula; in 2 patients with suspected fistula EUS was normal and in the last one extrarectal cystic lesion was revealed. Overall, 30 pts (71%) received a new diagnosis by EUS, with subsequent clinical management. EUS was successfully completed in all of the patients with no immediate or delayed complications.

Conclusion: EUS is a low-risk procedure. EUS±FNA can be successfully performed in children and it has a fundamental role in suspected PB disorders, the main indication in our patients.

Disclosure of Interest: None Declared


**Gastroenterology Endoscopy**

PO-G-0062

**DIAGNOSTIC AND THERAPEUTIC YIELD OF choledochoscopy AND PANCREATOSCOPY (INTRADUCTAL ENDOSCOPY) IN PAEDIATRIC PATIENTS**

Douglas S Fishman 1,*, Sanjiv Harpavat 2, Mark V Mazziotti 3, Alberto Hernandez 4, Sheena A Pimpalwar 5, Isaac Rajman 6

1 Baylor College of Medicine-Texas Children's Hospital, Texas, United States, 2 Section of Paediatric Gastroenterology, Hepatology and Nutrition, Baylor College of Medicine, Texas, United States, 3 Paediatric Surgery, 4 Department of Radiology, 5 Texas Children's Hospital, 6 Digestive Associates of Houston, Houston, United States

**Objectives & Study:** Improvements in intraductal endoscopy (IE) have enabled both pediatric and adult endoscopists to offer diagnostic and therapeutic capabilities in patients with pancreaticobiliary disease. This includes: direct visualization of ductal mucosa, ability to biopsy, facilitate cannulation and laser lithotripsy. We evaluated the yield of IE in our complete series of pediatric patients.

**Methods:** Single-center retrospective analysis of 30 cases were performed in 26 unique patients, with age range 2 to 21 (mean 13.8). Eight cases were performed in orthotopic liver transplant patients. Of two cases of recurrent pancreatitis, pancreatic duct cannulation was only attempted in one. Two different endoscopes were used: Spygloss Spyroscope © (n=29) and Olympus SIF-180 (n=1) in a patient with Roux-en-y anatomy. Procedures were performed perorally (n=26) and percutaneous transhepatic catheter (n=4). All peroral cases had prior biliary sphincterotomy and percutaneous usage (10 or 11F) was performed independent of choledochoscopy. The Dornier H20 (Gyrus, Phoenix, AZ, USA) Yag-Holmium LASER was used with the Lumenis 365 micron probe (Sunnyvale, CA, USA). All patients received prophylactic antibiotics. Cases were defined as either diagnostic or therapeutic and further characterized based on the findings and maneuvers performed.

**Results:** The most common indication was choledocholithiasis (n=14), obstructive jaundice (n=9), abnormal imaging (n=7). Additionally, 6 patients had PSC, 2 patients each had: pancreaticobiliary tumors (lymphoma and rhabdomyosarcoma), Mirizzi syndrome and prior choledochal cyst repair. Adverse events included bacteremia (n=1), self-resolving abdominal pain (n=1), incomplete viewing due to limited angulation within scope (n=2) and inability to get probe beyond ampulla (n=2) in a 3 yr old and a 17 yr old patient. A diagnosis was either made or confirmed in 26/30 cases (87%) including biopsy (n=2). A therapeutic procedure was successfully performed in all 7 cases attempted. This included Yag-Holmium laser lithotripsy (n=5) and directed cannulation (n=2). In four additional cases, occult stones were identified and removed by standard balloon extraction.

**Image:**

![Image](image-url)
Conclusion: IE of the pancreaticobiliary tree is feasible and safe with an expanding role in children with therapeutic options in addition to diagnostic capabilities. Intraductal findings provided useful clinical data in the majority of patients and therapeutic maneuvers were successful when attempted.

ENDOSCOPIC USEFULNESS IN EARLY SUSPICION OF SUPERIOR MESENTERIC ARTERY SYNDROME IN CHILDREN

Jae Young Kim 1,*, Myung Seok Shin 2
1Paediatrics, Chungnam National University Hospital, Daejeon, Korea, Republic Of Korea
2Paediatrics, St. Mary’s Hospital, Daejeon, Korea, Republic Of Korea

Objectives & Study: Superior mesenteric artery syndrome (SMAS) is a symptom complex condition that caused by the vascular compression of the third portion of the duodenum between the aorta and superior mesenteric artery. Diagnostic delay of SMAS is common because of lack of index of clinical suspicion. The aim of the present study was to assess whether the esophagogastroduodenoscopy (EGD) can give the useful clues for suspecting SMAS or not.

Methods: From August 2002 to February 2013, we prospectively collected data on patients who underwent EGD and upper gastrointestinal (UGI) contrast study. The recruitment in the present study was limited to patients who had more than one of those EGD findings as below: (1) a vertical pulsatile compression and partial luminal opening less than one-third with aeration at least 15 seconds at the third part of the duodenum (partial opening of the duodenal third part with aeration), (2) a large amount of bile mixed fluid (bile lake) in the stomach, (3) the proximal duodenal dilatation from the pulsatile compression (proximal duodenal dilatation). Patients with more than one of those endoscopic findings underwent UGI contrast study to confirm SMAS. The patients were classified as 2 groups: SMAS group and non-SMAS group according to the result of UGI contrast study.

Results: Of 29 enrolled patients, 18 patients had SMAS and 11 had no-SMAS. There were no significant differences in baseline demographics, clinical features, and growth status between two groups. The three most common presenting symptoms were postprandial discomfort (61.1% in SMAS patients vs 54.5% in non-SMAS patients), abdominal pain (55.6% in SMAS patients vs 90.9% in non-SMAS patients), and early satiety (50.0% in SMAS patients vs 18.2% in non-SMAS patients). EGD findings were observed in both groups as bellows: (1) partial duodenal third part opening with aeration (0 vs 9.1%, p=0.38), (2) partial duodenal third part opening with aeration and bile lake (5.6 vs 18.2%, p=0.54), (3) partial duodenal third part opening with aeration and proximal duodenal dilatation (22.2 vs 45.5%, p=0.11), (4) partial duodenal third part opening with aeration, bile lake and proximal duodenal dilatation (72.2 vs 27.3%, p=0.027)

Conclusion: EGD is useful for early suspicion of SMAS in children.

Disclosure of Interest: J. Y. Kim Conflict with: no conflicts of interest, M. S. Shin Conflict with: no conflicts of interest
**Gastroenterology**

**Endoscopy**

PO-G-0064

**ENDOSCOPIC TREATMENT OF ESOPHAGEAL AND GASTRIC LEAKAGES USING FULLY COVERED STENT IN CHILDREN**

Marc Bellaiche ¹, Solene Ganousse ¹, Arnaud Bonnard ², Alexis Mosca ¹, Xavier Dray ³, Jerome Viala ¹,*

¹Paediatric Gastroenterology and Pneumology, ²Paediatric Surgery, Robert Debre Hospital, APHP, Paris, France, ³Gastroenterology, Lariboisiere Hospital, APHP, Paris, France

**Objectives & Study:** Upper digestive fistula is a life-threatening condition. In the absence of stents specifically designed for children, descriptions of fully-covered SEMS placement for treatment of esophageal or gastric fistula in pediatrics are scarce.

**Methods:** All cases of esophageal or gastric perforations needing an endoscopic treatment were reviewed from 2011 to 2013. Six children (median age of 10.5 years; 3.1-13.6) were treated. One child fell on a plumber tube which perforated the esophagus. During vomiting efforts, a gastric rupture occurred in a child with neurological disorders. After 2 surgical repairs, the leakage persisted in the peritoneal cavity. Two children had anastomosis leakages after a Gravriliu esogastroplasty performed to treat a severe caustic stenosis. The leakages stood at the anastomosis and along the gastric tube suture with fistulisation in mediastinum and the right pleura respectively. In the last case, the perforation occurred in the Toupet valve during its surgical disassembly due to dysphagia. The surgical drainage tube induced another perforation in the first duodenum.

**Results:** The fully-covered SEMS were placed using upper endoscopy under general anaesthesia and tracheal intubation. A wire-guide allowed to place the SEMS with radioscopic controls. In 2 cases, 2 SEMS needed to be placed one in the other in order to totally cover the length of the lesion. The migration of the SEMS needed replacement in 2 cases. The radiologic leakage was immediately controlled in all children. The SEMS were extracted after follow-through X-ray and endoscopic controls. After median treatment duration of 30 days (13-42), 100% of the perforations were closed. The actual median follow-up duration was 5.8 months (2.2-16.8). A gastric tube stenosis occurred after treatment of both Gravriliu esoplasty. One needed a single dilation with no recurrence and the leakage of the anastomosis induced a severe stenosis which was resistant to dilations.

<table>
<thead>
<tr>
<th>Sex</th>
<th>Age (years)</th>
<th>Medical history</th>
<th>Indication</th>
<th>Diameter/Length (mm)</th>
<th>Duration (days)</th>
<th>Evolution</th>
<th>Follow-up (months)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Girl</td>
<td>3</td>
<td>Gravriliu esogastroplasty</td>
<td>Esopleural fistula</td>
<td>Lifeurop 18/60</td>
<td>14</td>
<td>Stenosis</td>
<td>5,8</td>
</tr>
<tr>
<td>Boy</td>
<td>7</td>
<td>Gravriliu esogastroplasty</td>
<td>Anastomosis leakage with cutaneous and mediastinal fistulas</td>
<td>Taewong 18/80</td>
<td>13</td>
<td>Stenosis</td>
<td>2,2</td>
</tr>
<tr>
<td>Boy</td>
<td>12</td>
<td>Toupet procedure for a reflux disease</td>
<td>Perforations of the Toupet valve and the first duodenum</td>
<td>Lifeurop 18/90+20/140</td>
<td>38</td>
<td>Migration</td>
<td>16,8</td>
</tr>
<tr>
<td>Boy</td>
<td>14</td>
<td>Nissen procedure in a neurological child</td>
<td>Total gastric rupture</td>
<td>Cousin 18/150+18/100</td>
<td>30</td>
<td>Migration</td>
<td>3,4</td>
</tr>
<tr>
<td>Girl</td>
<td>10</td>
<td>Traumatism</td>
<td>Esophageal perforation</td>
<td>Lifeurop 18/90</td>
<td>42</td>
<td>0</td>
<td>7,6</td>
</tr>
</tbody>
</table>

**Conclusion:** Endoscopic treatment of esophageal or gastric fistula is possible in young patients, using the large choice of adult fully-covered SEMS. These endoscopic procedures are efficient and well-tolerated, allowing to avoid the surgery.
Disclosure of Interest: None Declared
OBJECTIVES & STUDY: Meckel’s diverticulum is not a rare condition but it is difficult to visualize with conventional endoscopy. An accurate preoperative diagnosis of bleeding Meckel’s diverticulum in children remains a great challenge to the pediatrician. In addition, reports on the diagnostic value of double balloon enteroscopy in pediatric Meckel’s Diverticulum are limited. The aim of the study was to evaluate the diagnostic value of double balloon enteroscopy in pediatric patients with obscure gastrointestinal bleeding.

METHODS: Obscure gastrointestinal bleeding is defined as bleeding from the gastrointestinal tract that persists or recurs without an obvious cause after primary endoscopy (upper endoscopy and colonoscopy) and imaging studies, including Meckel’s scan, of the small bowel. From December 2006 to April 2012, double balloon enteroscopy was performed on 28 patients with Obscure gastrointestinal bleeding, and the diagnostic value of double balloon enteroscopy in pediatric patients with obscure gastrointestinal bleeding was evaluated.

RESULTS: Double balloon enteroscopy were performed in 28 patients with obscure gastrointestinal bleeding, Meckel’s diverticulum were eventually detected preoperatively in 10 of them. No serious procedure-related complications were observed in any cases. All 10 children underwent laparoscopic excision of the diverticula and recovered uneventfully. Pathological examination of the excised diverticula confirmed the diagnosis of Meckel’s diverticulum.

CONCLUSION: For pediatric patients who have gastrointestinal bleeding with features highly suspicious of Meckel’s diverticulum, if radioisotope scans and primary endoscopy were negative, Double balloon enteroscopy is an efficacious and safe means of diagnosis.

Disclosure of Interest: None Declared
Gastroenterology
Enteropathy (other than Coeliac Disease)
PO-G-0066
LONG-TERM OUTCOME OF INTESTINAL EPITHELIAL CELL DYSPLASIA/TUFTING ENTEROPATHY
Iona Ashworth 1*, Alexander Wilson 2, Michael Hii 3, Sarah Macdonald 4, Susan Hill 5
1Great Ormond Street Hospital, London, United Kingdom, 2Great Ormond Street Hospital for Children, London, United Kingdom, 3Great Ormond Street, 4Dietetics, Great Ormond Street Hospital for Children, London, United Kingdom, 5Gastroenterology, Great Ormond Street Hospital For Children, London, United Kingdom

Objectives & Study: To review the very long-term outcome of children with tufting enteropathy and age at which enteral autonomy is gained. Children with epithelial cell dysplasia/tufting enteropathy are usually dependent on parenteral nutrition (PN) treatment for many months and years. In some cases intestinal transplant has been performed. However there is little information on the total length of time that PN is required for and when children gain enteral autonomy

Methods: Twenty children who had presented in infancy with watery diarrhoea and severe intestinal failure (IF) that required long-term PN treatment were reviewed. All cases had the histological appearance of enterocyte tufting on small intestinal +/- colonic biopsies. Age, sex, country of origin, dependence on PN, survival and age of weaning off PN were recorded.

Results: Of the 20 patients 11 were male and 9 female. Ten patients were Maltese, 4 White British, 5 Arab and one Afghan. One patient died aged 2 years. The patients had all presented with diarrhoea and severe faltering growth. They were all commenced on treatment with long-term PN. In 15 cases parents were trained and PN was continued at home. Five children remained on long-term hospital PN.
When reviewed the surviving 19 patients were aged from 3 – 27 (mean 13) years. Eight children were aged under 10 (3-9) years, 6 children were aged 10 – 20 years and 5 over 20 years. One of the 8 children under 10 years of age had weaned off PN. Two of the 6 children aged 10-20 years had weaned off PN and 3 of the 5 patients over 20 years of age had done so. All 13 children still on PN had some enteral intake as well. Six/13 children had 7 infusions/week, 3/13 had 6 infusions/week, 3 others had 5/week and one, 2 infusions/week. The two patients aged over 20 years still on PN were infusing 5 nights/week. The six children (30%) who had gained enteral autonomy had done so when aged from 3-22 years. They are now aged from 10-24 years (mean 16.5 years). No child had needed to restart PN after stopping it.

Conclusion: Children with tufting enteropathy have an increasing chance of weaning off PN with increasing age ranging from 2/20 or 10% chance of doing so before 10 years of age to 40% aged 10-20 years and 3/5 or 60% of those aged over 20 years. It is possible that an even greater number of children could wean with best possible medical care and psychological support. Given the good long-term outcome, intestinal transplant should be avoided if at all possible.

Disclosure of Interest: None Declared
SUBSTANTIAL DECREASES IN THE NUMBER AND DIVERSITY OF MICROBIOTA DURING CHEMOTHERAPY-INDUCED INTESTINAL MUCOSITIS IN A RAT MODEL

Margot Fijlstra 1,2, Mithila Ferdous 3, Anne M. Koning 3, Edmond H.H.M. Rings 1,*, Hermie J.M. Harmsen 3, Wim J.E. Tissing 2

1Paediatric Gastroenterology and Hepatology, 2Paediatric Oncology, 3Medical Microbiology, University Medical Center Groningen, Groningen, Netherlands

Objectives & Study: Earlier, we showed in pediatric acute myeloid leukemia (AML) patients and adult stem cell transplant (SCT) patients that the commensal intestinal bacterial populations (microbiota) change dramatically during anti-cancer treatment, coinciding with gastrointestinal mucositis. Therefore, interventions targeting the microbiota during mucositis might be interesting. However, studying the effects of prebiotics, probiotics and antibiotics on mucositis can better be done in animals than in vulnerable mucositis patients. Therefore, we first aimed to study the microbial changes during chemotherapy-induced intestinal mucositis in a well-established rat model, to study whether this model can be used for future microbial intervention studies.

Methods: After intravenous injection (day 0) with MTX (90mg/kg) to induce mucositis or with saline (controls), MTX-treated rats were sacrificed at days 2, 4, 6 or 10, and saline-treated rats at days 3 or 11. We measured food intake and body weight, determined plasma citrulline level and small intestinal histology to score intestinal damage, and measured the number and diversity of intestinal bacteria in feces using FISH.

Results: Mucositis was most severe on day 4 when food intake, plasma citrulline level and villus length were the lowest, compared with controls (P<0.05). Specific microbial changes between MTX-treated rats and controls differed per day, but there was an overall decrease in most bacteria (using a universal probe) on days 4 (705-fold), 6 (5-fold) and 10 (5-fold) after MTX-treatment, compared with controls (P<0.05). At day 4, there was an absolute and relative decrease of anaerobes (13-fold and 58% resp.) and streptococci (296-fold and 1% resp.), but a relative increase of bacteroids (49%), lactobacilli and enterococci (together 16%) and enterobacteriaceae (2%), compared with controls (P<0.05).

Conclusion: In our established mucositis rat model, we found substantial decreases in the number and diversity of microbiota. These findings resemble earlier found human findings. The model therefore seems well suited to study the effects of different microbial interventions on gastrointestinal mucositis, prior to performing selected human studies.

Disclosure of Interest: None Declared
FOOD PROTEIN-INDUCED ENTEROCOLITIS SYNDROME IS AN ENTEROPATHY DISORDER WITH ENTEROCYTE APOPTOSIS BY DISRUPTED TIGHT JUNCTION

Jin-Bok Hwang 1,*, Geun Soo Park 1, Sang Pyo Kim 2, Yu-Na Kang 2, Seong-Ryong Lee 3, Seong-II Suh 3, Taeg Kyu Kwon 3 and No 1
1Paediatrics, 2Pathology, 3Institute for Medical Science, Keimyung University School Of Medicine, Daegu, Korea, Republic Of Korea

Objectives & Study: Up-regulation of tumor necrosis factor (TNF)-α on the mucosa of the small intestine is observed in the patients with food protein-induced enterocolitis syndrome (FPIES). Also, TNF-α has been reported to induce apoptosis in the epithelial cells by disruption of barrier function. The purpose of this study was to analyze enteropathy quantitatively in FPIES and to determine the apoptosis and disrupted tight junction in its pathogenesis.

Methods: Fifteen infants diagnosed with FPIES using standard oral food challenge test and 5 controls were included. Quantitative morphometric analyses of duodenal mucosa were performed. Immunohistochemical stains of CD3 for intraepithelial lymphocyte; M30 for epithelial apoptosis; TNF-α expression; claudin-1, claudin-4, and occludin for tight junction were performed. Apoptotic cells of M30 was counted as cells/high power field (HPF). The expression of other immunohistochemical stainings was graded as 0–3 score according to the extent and intensity of staining.

Results: Villous atrophy was observed in all FPIES patients (50~210 μm vs 305~380 μm in controls, p=0.0001). CD3 (p=0.038), TUNEL (p=0.043), and M30 (p=0.042) were significantly higher expressed in the mucosa of FPIES patients than the controls. Claudin-1 (p=0.01), claudin-4 (p=0.001), and occludin (p=0.003) were considerably lower expressed than the controls.

Conclusion: FPIES is an enteropathy disorder. Villous atrophy is induced by enterocyte apoptosis which may be induced by up-regulation of TNF-α with disrupted tight junction.

Disclosure of Interest: None Declared
**Objectives & Study:** Thalidomide has anti-angiogenesis and anti-TNF-alpha pharmacological effects and is being used in the treatment of refractory Crohn's disease. It is the objective of this study to explore the role of thalidomide on the regulation of tight junction proteins in a TNBS-induced inflammatory bowel disease rat model; and further elucidate the mechanism of thalidomide’s effect on the intestinal mucosa barrier.

**Methods:** 80 Sprague-Dawley rats of 4-5 weeks old were divided into control group (24 rats), model group (28 rats, TNBS 150 mg/kg) and treatment group (28 rats, thalidomide 150 mg/kg). 8-12 rats were sacrificed in each group on the 7th day and 10th day; and specimens from blood and colon were studied: (1) electron microscopy, general scoring, histological injury scoring; (2) TNF-a levels in blood; (3) Western blot and PCR to evaluate the expression of occludin and claudin-1; (4) Immunohistochemistry and PCR to observe ZO-1 expression and location.

**Results:** Intracolonic administration of TNBS can cause TNF-a level elevated in blood, with severe inflammation in the mucosa and submucosa with infiltration of neutrophils. At the same time, the structure of tight junctions will be destroyed, with increased dephosphorylated occludin, reduced claudin-1 protein and zo-1 redistributed to the cytoplasm. Intracolonic administration of TNBS can cause increased expression of occluding and zo-1, and decreased expression of claudin-1. Treatment with thalidomide can significantly reduce the level of blood TNF-a, and reduce the inflammatory cellular infiltration; and improve the orderly arrangement of epithelial cells and intestinal tight junctions. Compared with the model group, dephosphorylated occludin was reduced, while claudin-1 protein was increased; and the quantity of zo-1 beside the cell membrane was increased. Furthermore, the level of TNF-a was consistent with the level of dephosphorylated occludin.

**Conclusion:** TNBS induced inflammation can cause tight junction destruction, with increase in dephosphorylated occludin and reduction in claudin-1 protein and zo-1 redistributed to the cytoplasm. Thalidomide can inhibit the inflammatory reaction and improve the functionability of the tight junction.

**Disclosure of Interest:** None Declared
Gastroenterology

Enteropathy (other than Coeliac Disease)

PO-G-0070

GUT AND MESENTERIC LYMPH NODE INVOLVEMENT IN HIV-INFECTED PAEDIATRIC PATIENTS

Cecilia Mantegazza 1,* Giovanni Maconi 2, Gianvincenzo Zuccotti 1, Dario Dilillo 1, Vania Giacomet 1, Chiara Mameli 1

1General Paediatrics, 2gastroenterology, Hospital Luigi Sacco Milano General Paediatrics, Milano, Italy

Objectives & Study: The gastrointestinal tract is a primary target for Human Immunodeficiency Virus (HIV). HIV infection causes a depletion of CD4+ T-lymphocytes in the gut-associated lymphoid tissue and affects gastrointestinal mucosal integrity and permeability. The gastrointestinal tract has also been suggested as the main reservoir of HIV despite highly active antiretroviral therapy (HAART). We performed a prospective case-control study to assess gut involvement in HIV-infected patients, either naïve or on HAART, using noninvasive methods such as bowel ultrasound and fecal calprotectin.

Methods: Thirty HIV-infected children and youth underwent the following tests: CD4+ T-cell count and HIV viral load, fecal calprotectin and bowel ultrasound; the latter evaluated bowel wall thickness and mesenteric lymph nodes. Fecal calprotectin and bowel ultrasound were also assessed in thirty healthy controls matched for age and sex. In particular faecal calprotectin was measured through a quantitative immunochromatographic point-of-care test (Buhlmann laboratories AG, Schonenbuch, Switzerland) and concentrations ranging from 0 to 200 µg/g were considered to be normal reference values in children.

Results: Fecal calprotectin was normal in 29 HIV-infected patients and was not statistically different from controls (respectively mean value 63.8 ± 42.5 µg/g and 68.3 ± 40.5 µg/g; p: 0.419); calprotectin did not correlate with HIV viral load, CD4+ T-cell absolute count and percentage and HAART treatment. No significant changes on bowel ultrasound were found except for enlarged mesenteric lymph nodes, which were observed in 7 HIV-infected patients (23.3%) and 2 controls (6.6%). This last data significantly correlated with high HIV viral load (p: 0.001) and low CD4+ T-cell percentage (p: 0.004).

Conclusion: HIV-infected children did not have significant biochemical or ultrasonographic signs of mucosal inflammation. Few patients showed enlarged mesenteric lymph nodes, which correlated with uncontrolled HIV infection.

Disclosure of Interest: None Declared
Objectives & Study: Nutritional support is a very important aspect of management of inflammatory bowel disease. In order to explore the efficacy of nutritional products of various composition in IBD, four formulas of different nutritional composition were used to feed rats with experimental IBD to explore their effect on IGF-1, IGFBP3 expression and proliferation of proximal tibial epiphyseal cartilage at different periods.

Methods: 4-5 weeks SD rats were randomly divided into 8 groups: including 4 model groups and 4 control groups. Model groups had infusion of trinitro benzene sulfonic through the anus after fasting for 24h. The control groups received the same dose 0.9%NaCl solution. 4 model groups and 4 control groups were given IBD-specific formula, short peptides formula, ordinary formula and normal diet enteral nutrition respectively after operation. The rats were sacrificed on the 7th day after operation. Blood and the right tibia were taken and their lengths measured. The proximal epiphyseal segments were harvested for histological examination for chondrocyte proliferation. GHR, IGF-1R expression were assayed with immunohistochemical methods. IGF-1 and IGFBP3 expression levels in the blood were tested by ELISA.

Results: 1. The average tibia length of short peptides formula group was apparently longer than IBD-specific formula group and normal diet group (3.21±0.10 vs 3.06±0.15, 2.98±0.11, P<0.05) at the 7th day. 2. The expression of IGF-1 and IGFBP3: (1) Average blood IGF-1 levels (ng / ml) of the peptides formula group was significantly higher than IBD-specific formula group, ordinary formula group and normal diet group (3.79±0.42 vs 2.93±0.89, 2.69±0.49, 2.58±0.50, P<0.05) at 7th day among 4 model groups. (2) Average blood IGFBP3 levels of the peptides formula group was significantly higher than normal diet group (21.28±4.52 vs 16.11±2.86, P<0.05) at the 7th day. 3. Tibial pathology and immunohistochemistry: (1) In 4 different enteral nutrition model groups, the thickness of epiphyseal growth plate of peptides formula group was the thickest and the thinnest of epiphyseal growth plate appeared in IBD-specific formula group at 7th day. (2) In 4 different enteral nutrition model groups, the average chondrocytes count of proliferation zone and hypertrophy zone in epiphyseal growth plate of proximal tibial of peptides formula group was significantly more than that of IBD-specific formula group and normal diet group at 7th day (66.0±16.1 vs 47.9±6.3, 51.2±6.6, P<0.05). (3)TGHR expressed in the entire epiphyseal growth plate area, but according to the immunohistochemical sections it mainly expressed in resting zone.

Conclusion: The peptide-based formula seems to be the best in promoting the expression of IGF-1 and IGFBP3, and accelerate the growth of long bones within 7 days after operation.

Disclosure of Interest: None Declared
**Gastroenterology**

**Enteropathy (other than Coeliac Disease)**

PO-G-0072

**INTRACTABLE DIARRHEA CAUSED BY A NOVEL MUTATION, N309K, OF THE PROPROTEIN CONVERTASE SUBTILISIN/KEXIN TYPE 1 (PCSK1) GENE**

Montaser Abbasi ¹, Elias Blanco ², Iris Lindberg ², Itai Berger ¹, David Zangen ¹, Martin Martin ³, Orly Elpeleg ¹, Michael Wilschanski ¹

¹Hadassah University Hospital, Jerusalem, Israel, ²University of Maryland-Baltimore, Baltimore, Maryland, United States, ³University of California Los Angeles, Los Angeles, California, United States

**Objectives & Study:** Four children were born to healthy first cousins. Patient A developed neonatal malabsorptive diarrhea requiring TPN until 5 years of age. Repeated small intestinal biopsies showed non-specific enteropathy only. She developed hypothyroidism, growth hormone deficiency and subsequently, obesity. The two subsequent sisters (B,C) died from intractable epilepsy at 5 months and 9 days of age respectively, B also suffered from recurrent episodes of severe diarrhea and hypothyroidism.Sibling D is a 10-month old male who presented with neonatal diarrhea now requiring home TPN. No endocrinopathies have been found thus far, and his small bowel biopsy showed a similar non-specific enteropathy.

**Methods:** 250K SNPs in patients A, B and C were genotyped, and 5 homozygous regions shared by patients A and B that includes 337 protein-coding genes. Whole exome sequencing of patient D sequenced to a coverage of X63, and 97.1%. Of the 1089 on-target variants only 46 variants were homozygous and only 4 were located at the linked regions. We focused on the N309K mutation in the **proprotein convertase subtilisin/kexin type 1 (PCSK1)** gene, which was predicted as disease-causing by Mutation Taster software.

**Results:** Using Sanger sequencing confirmed this mutation segregated as a homozygous variant in the family in patients A, B and D. The **PCSK1** mutation affected an evolutionarily conserved residue within the active site. The position of this mutation corresponds to a residue critical to proprotein maturation and enzyme activity, the oxyanion hole transition state-stabilizing amino acid N309. Unexpectedly, the N309K mutant protein exhibited normal prodomain removal and was efficiently secreted from both HEK293 and Neuro2A cells. However, the secreted enzyme showed no catalytic activity, and was not processed into the 66 kDa form in either cell line; the wild-type protein was processed in Neuro2A cells. It was shown that the N309K enzyme is able to cleave its own propeptide but is catalytically inert against *in trans* substrates.

**Conclusion:** Our findings confirm that the novel mutation N309K in the **PCSK1** gene caused the pathology in this family. The failure of enteroendocrine cells caused by mutations in **PCSK1** results in severe infantile diarrhea accompanied by multiple endocrine abnormalities.

**Disclosure of Interest:** None Declared
**Objectives & Study:** Eosinophilic esophagitis (EoE) and gastroesophageal reflux disease (GERD) are characterized by esophageal mucosal eosinophilic infiltration. Esophageal Atresia (EA) is a congenital malformation occurring in 1:2500 births; GERD is one of its most common complications. Association between EoE and EA is still unknown. We report 7 EA repaired patients with food refusal caused by EoE, without an anastomotic stricture.

**Methods:** Seven patients long gap EA repaired underwent upper endoscopy-biopsies for food refusal. They were diagnosed as EoE and started PPI therapy, followed by standard EoE therapy in those unresponsive to PPI. Nissen funduplication was performed in patients depending on PPI.

**Results:** All patients had long gap EA Type I. During follow up (mean age 1.7 years, range 0.9 mounths-4yrs; M4: F3) they presented food refusal, failure to thrive, dysphagia and vomiting. At endoscopy no strictures; all pts had white specks and longitudinal furrows. Histology confirmed EoE (mean peak count 50 eos/HPF; range 25-115). After PPI therapy, 5/7 children showed clinical and histological remission and mucosal healing; relapsing after PPI discontinuation. Surgery was performed in 4/7, depending on long term PPI with disappearance of EoE. The remaining 3 asymptomatic patients are in follow up with PPI cycles, one of them also with restriction diet.

**Conclusion:** In EA repaired, when patients have food refusal, anastomotic stricture could not be the unique cause; it is always important to perform endoscopy for ruling out EoE, possibly relating to GERD secondary to brachiesophagus and dismotility disorders or for casual association.

**Disclosure of Interest:** None Declared
Gastroenterology
Enteropathy (other than Coeliac Disease)

TWO CASES OF TRICHO-HEPATO-ENTERIC SYNDROME (SYNDROMIC DIARRHEA) COMPLICATED WITH CROHNS-LIKE DISEASE

Elena Roslavtseva 1,*, Anton Anushenko 2, Ekaterina Tsimbalova 2, Alexander Potapov 2

1Healthy and Sick Child Nutrition, 2Gastroenterology, Scientific Center for Children's Health, Moscow, Russian Federation

Objectives & Study: Tricho-hepato-enteric syndrome, THES is a rare bowel disorder caused by mutation in SKIV2L or TTC37, characterized by intractable diarrhea of infancy; facial dysmorphism; hair abnormalities; immune disorders; intrauterine growth restriction

Methods: Prospective study of two boys with THES

Results: Patient 1. I, born 2003. A boy delivered on the 36-th week of pregnancy (weight 2200 g, length 46 cm) from healthy non-consanguineous parents. Ventricular septal defect and aortic valve insufficiency diagnosed soon after birth. Chronic diarrhea since the 2-nd month of age; the 1st year of life -failure to thrive, several septic episodes. Jejunal biopsy: total villous atrophy, crypt’s hyperplasia, normal IEL count, microerosions. 1 year: weight 4800 g, height 65 cm. The symptoms of facial dysmorphism, mental retardation and hair abnormalities increased with age, as well as malabsorption. At 6, he developed haemocolitis, weight loss, symptoms of acute inflammation. Colonoscopy: terminal ileitis, colon: longitudinal cracks filled with detritus. Biopsy: Crohn’s disease. He received corticosteroids, courses of Infliximab and Adalidumab with inconstant effect. 6-10 years: dependant on TPN, receives 600-800 ml amino acid formula. 10 years: weight 12 kg, 8-12 stools per day. Patient 2. A, born 2008, from non-consanguineous parents (42-nd week, 2600 g, 50 cm). At 2 months referred to ICU with failure to thrive, abdominal distention and diarrhea. TPN was started with a positive effect but enteral feeding with hydrolyzed formula caused a relapse. 1 year: weight 3700 g, intractable diarrhea. Colonoscopy: aphthous lesions suggestive for Crohn’s disease. First seen in our clinic at the age of 2. Typical facial and hair dysmorphism, severe electrolyte imbalance, hyperIG-emia, hypoalbuminemia. Endoscopy: severe pancolitis. Small intestinal biopsy: villous subatrophy. No need in PN, enteral nutrition with extensive hydrolysed formula and anti-TNF-α therapy was started (5 mg/kg per infusion). Infliximab reduced PCDAI after initial course (3 infusions) more than 12,5 points. Now, at the age of 5, his weight is 11.5 kg, he has mild mental retardation, 3 bowel movements/day, without blood and mucus. However, ESR 79 mm/h, IgG 18,89 g/l, IgA 6,79 g/l. The colonoscopy shows moderate endoscopic activity of Crohn’s disease (SES-CD 6 points). The dose of Infliximab was evaluated to 8,5 mg/kg. Both patients have mutations in TTC37 gene

Conclusion: In 2 boys with THES, we describe Crohn’s like disease involving terminal ileus and colon and requiring biological treatment. In a comprehensive review 1 we could not find a mention about Chohn’s like disease in those patients

References: 1Fabre A, Martinez-Vinson C, Goulet O, Badens C. Syndromic diarrhea/Tricho-hepato-enteric syndrome. Orphanet Journal of Rare Diseases 2013, 8:5

Disclosure of Interest: None Declared
Gastroenterology

Enteropathy (other than Coeliac Disease)

PO-G-0075

INTEGRATING OF NEW RECOMMENDATION FOR PREVENTION AND TREATMENT OF PROTEIN LOSING ENTEROPATHY IN CHILDREN AFTER FONTAN AND OTHER COMPLEX CONGENITAL HEART DISEASE PROCEDURES SINGLE CENTRE EXPERIENCE

Ramush Bejiqi 1,*, Ragip Retkoceri 1, Naim Zeka 1, Hana Bejiqi 2, Shqipe Surdulli 2, Arber Retkoceri 2
1Department of Cardiology, University Clinical Center of Kosovo, Paediatric Clinic, Kosovo, 2Main Center of Family Medicine, Prishtina, Family Medicine, Prishtina, Albania

Objectives & Study: Protein-losing enteropathy is a disorder characterized by abnormal enteric protein loss. It’s relatively uncommon complication of Fontan and other complex congenital heart disease (CCHD) procedures. Aim of presentation is to describe single centre experience in diagnosis, evaluation, management and treatment children with protein-losing enteropathy after Fontan or other CCHD procedures, follows with a comprehensive review of protein-losing enteropathy publications, and concludes with suggestions for prevention and treatment.

Methods: Retrospectively we analyzed patients with CCHD and protein-losing enteropathy in our institution, starting from January 2000 to December 2012 which underwent cardiac surgery with CCHD.

Results: We evaluated 18 cases with protein-losing enteropathy, aged 6 to 19 years (mean 14± 9); three children had undergone Senning procedure for D-transposition, one Tetralogy of Fallot, and remaining 14 patients had undergone Fontan procedures; (anatomic diagnosis are: six with tricuspid atresia, seven with d-transposition, double outlet right ventricle and pulmonary atresia and two with hypoplastic left heart syndrome). The diagnosis of protein-losing enteropathy was made at median age of 5.6 years, ranging from 13 months to 15 years. Diagnosis was made using alpha 1-antitrypsin as a gold marker in stool. In 14 patients edema was found, in three ascites, and six patients had pleural effusion. Laboratory findings at the time of diagnosis are: abnormal enteric protein loss was documented in all 18 patients. At the time of diagnosis all patients receiving some form of anticoagulation, 17 patients receiving other medication: 17 diuretics and ACE inhibitors, 12 digoxin, 9 antiarrhythmics. Echocardiography was performed for all patients and different abnormalities were registered. In 14 patients also magnetic resonance was performed. Therapeutic approach was based on the non-specific medication (diet, diuretics, digoxin, ACE inhibitors, and anticoagulants) and specific treatment: heparin and corticosteroids therapy. Long-term response to this type of therapy was registered in three patients. Nine patients underwent treatment with heparin and corticosteroids and no one experienced long term benefit. Despite of needs for catheter therapy or surgical intervention in our study, in the absent of technical and human resources now any one had underwent those procedures. Six patients has been transferred abroad and in vive of them surgical intervention was perform.

Conclusion: Protein-losing enteropathy remains a devastating complication of Fontan procedure and despite in advantages in surgical and medical therapy there is no evidence that protein-losing enteropathy is less common in the current area.

Disclosure of Interest: None Declared
**Gastroenterology**

**Enteropathy (other than Coeliac Disease)**

**PO-G-0076**

**LOSS OF XX CAUSES VARIANT MICROVILLUS INCLUSION DISEASE**

Janneke Stapelbroek 1,*, S Middendorp 1, A Janecke 2, C Wiegerinck 1, K Schneeberger 1, J Escher 3, R Adam 4, C Thoni 2, D Haaften-Visser van 1, G Vogel 2, A Jordan 4, C Weis 4, I Nijman 1, G Monroe 1, H Clevers 5, E Cutz 6, M Hess 2, L Huber 2, E Nieuwenhuis 1, G Haaften van 1, R Houwen 1, T Muller 2

1University Medical Center Utrecht, Utrecht, Netherlands, 2Innsbruck Medical University, Innsbruck, Austria, 3Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands, 4University Medical Center Mannheim, Mannheim, Germany, 5Hubrecht Institute for Developmental Biology and Stem Cell Research, Utrecht, Netherlands, 6Hospital for Sick Children, Toronto, Canada

**Objectives & Study:** Microvillus inclusion disease (MVID) is characterized by severe and persistent congenital diarrhea. Patients are dependent on total parenteral nutrition (TPN) unless treated by intestinal transplantation. The pathological hallmarks are loss of brush border microvilli, secretory granules in the subapical cytoplasm of enterocytes and intracytoplasmic microvillus inclusions in villous enterocytes. It is caused by mutations in Myosin 5b (MYO5B). However a subset of patients presents with a variant, milder phenotype, which may allow for partial or complete weaning from TPN. Morphologically the frequency of microvillus inclusions bodies in these patients is low and microvilli can be found at the basolateral membrane.

**Methods:** We obtained DNA and intestinal biopsies from two patients with the clinical characteristics of variant MVID. Both patients were born from a consanguineous marriage and had no mutations in MYO5B. We performed whole-exome sequencing in combination with homozygosity mapping to identify the causative gene. In addition we established organoid cultures (mini-guts) from a duodenal biopsy of one of these patients.

**Results:** Biopsies from both patients had the pathological characteristics of variant MVID on light microscopy (LM) and electron microscopy (EM). Whole exome sequencing revealed homozygous mutations in XX in both patients (respectively a stop mutation and a frame shift mutation leading to a premature stop-codon). The protein encoded by this gene is an essential part of the pathway that is necessary for transport of proteins to the apical membrane of enterocytes. Moreover the organoids we have generated recapitulated the histological characteristics of variant MVID on both LM and EM.

**Conclusion:** Mutations in XX are a cause of variant MVID

**Disclosure of Interest:** None Declared
ULTRA SHORT BOWEL SYNDROME (USBS) IN CHILDREN: LONG-TERM PARENTERAL NUTRITION IN COMPARISON WITH INTESTINAL TRANSPLANTATION

Solène Artru, Florence Lacaille, Cécile Lambe, Christophe Chardot, Bénédicte Pigneur, Hélène Lengline, Swellen Gastineau, Cécile Talbotec, Frank Ruemmele, Virginie Colomb, Sabine Irtan, Olivier Goulet


Objectives & Study: After extensive small bowel resection in neonatal period, intestinal transplantation (ITx) or combined liver and intestinal transplantation (LITx) represent the final option for patients with cirrhosis or loss of venous access resulting from thrombosis. This study aims to compare survival, PN dependency and nutritional status of USBS children on long term parenteral nutrition (LTPN) with USBS children who have been transplanted.

Methods: This retrospective study includes 41 children and young adults followed since 1990. After extensive resection ultrashort bowel (USB) was defined according to the intraoperative measure of residual bowel length being ≤ 30cm with ileocaecal valve (ICV), or ≥ 40cm and ≤ 80 cm without ICV. Patients were enrolled in a LTPN program, 24 have received an intestinal graft.

Results: In the LTPN group (n=17), all children survived and are currently 14.6 ± 6 years old. Five children have been weaned from PN after 6.2 ± 5.5 years. For the 12 children still on LTPN, the average duration of PN is 10.6 ± 6.2 years, the average number of weekly infusion is 4.0 ± 1.8 days /7 while PN provides 49 ± 26 % of the recommended daily allowance (RDA). Nine children had an early onset of cholestasis and 10 still have hepatic biological disorders. The current BMI in this group is -1.14 ± 1.15 (standard deviations for age). In the ITx group (n=24), 15 children were transplanted for extensive vascular thrombosis (5 of them with colon) and 9 had a combined transplantation for severe liver disease (5 of them a combined bowel + liver and 4 a combined bowel + liver + duodenum + pancreas). The average age at transplantation was 4.7 ± 2.3 years. ITx group’s survival is 58% (67% for isolated ITx ± colon and 45 % in the combined transplantation group). Death occurred 10 ± 26 months after Tx. Among surviving transplanted children 100% have been weaned from PN, 69 ± 82 days after Tx. Mean follow up after transplantation is 9.2 ± 6.4 years. The BMI in this group is -0.7 ± 1.9 (standard deviations for age)

Conclusion: Even if 100% of the transplanted children who survived have been weaned from PN, survival rate is significantly lower in the ITx group (p<0.05). A multidisciplinary approach by a specialized medical team may allow a total weaning of PN before adulthood. For those children still remaining PN dependent, PN infusions provide less than 50% of RDA, while the reduced number of week’s days of infusions makes their quality of life more acceptable. These results make difficult the indication of ITx. Extensive vascular thrombosis and/or severe liver disease occur remain indications for transplantation.

Disclosure of Interest: None Declared
INTRAEPITHELIAL LYMPHOCYTOSIS IS COMMON IN CHILDREN WITHOUT COELIAC DISEASE AND IS NOT MEANINGFULLY INFLUENCED BY HELICOBACTER PYLORI INFECTION

Anat Guz-Mark 1,*, Noam Zevit 1, 2, Sara Morgenstern 2, 3, Raanan Shamir 1, 2

1Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children’s Medical Center of Israel, Petach Tikva, Israel, 2Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel, 3Department of Pathology, Rabin Medical Center- Beilinson Campus, Petach Tikva, Israel

Objectives & Study: Increased numbers of duodenal intra-epithelial lymphocytes (IELs) characterize celiac disease (CD), but have also been described in non-celiacs. Controversy exists regarding an association between increased IELs and infection with Helicobacter pylori (H. pylori), which is commonly found in children. This study aim was to assess the relationship between H. pylori infection and duodenal IELs in a large cohort of children, with and without CD.

Methods: We reviewed gastric and duodenal biopsies of children who underwent esophagogastroduodenoscopy between January 2006 and February 2013 because of either recurrent abdominal pain (RAP) or suspected CD at Schneider Children’s Medical Center of Israel, a referral center for Israel’s largest Health Maintenance Organization. The duodenal IEL count and HP presence in antral biopsies were determined for each specimen.

Results: Children with RAP (n=693) or CD (n=306) were included. Among children with RAP, H. pylori was present in 33.8%. The mean IEL count in the H. pylori positive RAP group was 17.8(±8.8) per 100 enterocytes, versus 15.8(±8.3) in the H. pylori negative patients (p=0.004). Increased IEL counts (≥25 IELs/100 enterocytes) were found in 15.7% of healthy, H. pylori negative, non-celiac children. Among children with CD, there was no significant difference in IEL counts according to H. pylori status: 73.1(±26.1) versus 72.6 (±26.5) in H. pylori positive and negative patients, respectively.

Conclusion: Our study suggests that slightly elevated duodenal IEL counts are common in the healthy pediatric population. H. pylori infection has no major influence on the IEL counts in children with RAP or with CD.

Disclosure of Interest: None Declared
EVALUATION OF A NOVEL NON-BIOPSY TECHNIQUE FOR THE DIAGNOSIS AND MONITORING OF EOSINOPHILIC OESOPHAGITIS

Harsita Patel 1, Eleanor Minshall 2, John Warner 2, Trevor Hansel 3, Robert Boyle 2, Jenny Epstein 4,

1 Imperial College London, School of Medicine, London, United Kingdom, 2 Department of Paediatrics, Imperial College London, United Kingdom, 3 National Heart and Lung Institute, Imperial College London, London, United Kingdom 4 Department of Paediatric Gastroenterology, Chelsea and Westminster Hospital, U.K., London, United Kingdom

Objectives & Study: Eosinophilic oesophagitis (EO) is an emerging disease characterised by oesophageal dysfunction and intra-epithelial infiltration of eosinophils. The gold standard for diagnosis is endoscopy and biopsy. No reliable, non-biopsy diagnostic method has been identified for use in children. The aim of our study was to evaluate the efficacy of a novel sampling method, oesophosorption, to sample mucosal lining fluid (MLF) and identify biomarkers which correlate with the presence and severity of EO in children.

Methods: A specially designed device employed a synthetic absorptive matrix attached to a plastic wire (Hunt Developments), introduced through the operating portal of an endoscope. A multiplex assay was used to assess levels of a panel of cytokines and chemokines in MLF. Levels of inflammatory mediators were compared between cases with EO and controls without, and correlated with histopathological findings.

Results: Nine children were recruited into the study (7 boys, median age 11). 5/9 had confirmed EO upon histological analysis. Cytokines and chemokines were commonly detected in oesophageal MLF, in both EO and non-EO, and levels were not correlated with those found in nasal secretions or saliva. Eotaxin-1 levels were raised in EO (median 49.3 pg/ml cases; 7.3pg/ml controls P=0.05), and correlated with eosinophil density per mm2 (R= 0.72, P=0.03) and number of degranulated eosinophils per mm2 (R= 0.82, P=0.01). Other inflammatory mediators were not significantly different between cases and controls.

Conclusion: Inflammatory mediators are detectable in the oesophageal MLF of children and do not appear to be from swallowed salivary or nasal secretions. These preliminary results suggest that oesophosorption should be further investigated as a tool for diagnosing and monitoring EO without the need for oesophageal biopsy.

Disclosure of Interest: None Declared
DEVELOPING A CLINICAL TRIALS NETWORK FOR PAEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION ACROSS EUROPE

Nick Croft 1,*, Varsha Tailor 1, Seamus Hussey 2, Lissy de Ridder 3, Julian Thomas 4 and Paediatric European Digestive Diseases Clinical Research Network

1Centre for Digestive Diseases, Barts And The London School Of Medicine, London, United Kingdom, 2University College Dublin, Dublin, Ireland, 3Erasmus University Medical Center, Rotterdam, Netherlands, 4Newcastle University Hospital, Newcastle, United Kingdom

Objectives & Study: Paediatric European Digestive Diseases Clinical Research Network (PEDDCReN) was established in April 2013 with the aim of supporting the development of large studies in paediatric patients in the speciality of Gastroenterology, Hepatology and Nutrition (GHN). The Project is supported by LINKS funding from the UEG (United European Gastroenterology) and is led by the British, Irish and Dutch Societies of Gastroenterology in collaboration with ESPGHAN and ENPR-EMA (The European Network of Paediatric Research at the European Medicines Agency). We report the preliminary results of an on line survey as a first step of PEDDCReN, identifying investigators’ resources, expertise and interest in the UK.

Methods: The survey was designed by the steering group of PEDDCReN and utilised the web based system REDCap. It takes 5 minutes to complete with 1 respondent per hospital. In October 2013 this was sent to paediatric gastroenterologists in the UK as members of the British Society of Paediatric Gastroenterology, Hepatology and Nutrition.

Results: After 2 weeks 12 units (including 25 investigators) had replied representing children’s services with a median of 140 beds (range 30-385), 4 were stand alone children’s hospitals, 5 were children’s hospitals co-located with adult hospitals, 2 were smaller children’s units in adult hospitals and one was a neonatal unit. 9/12 were paediatric gastroenterology services, there was one large liver service, one general paediatric service and one neonatal unit. All wished to be part of PEDDCReN and were happy for contact details to be passed on to both industry and non-industry investigators. The survey identified each units interest in recruiting into a range of GI and liver diseases (10/12 wished to recruit for IBD studies whereas only 4/12 for infant diarrhea). Less than 33% would also recruit to liver studies including infective hepatitis. Of the respondents 66% have been a principle investigator (in their hospital) and 25% had been chief investigators for the UK. 58% were willing to take on phase I or II studies but only 25% had done any in the last 3 years. 42% had a clinical research facility available on site and 75% have access to research nurses. Sites were also asked whether they currently followed up any patients with rare GI or liver diseases such as congenital enteropathy (5/12), congenital transport defect (1/12), polyposis syndromes (6/12), chronic intestinal pseudo-obstruction (7/12).

Conclusion: This shows the ability of PEDDCReN to identify interest, expertise and resources. This will shortly be extended to Ireland and the Netherlands and then the rest of Europe. The potential for investigators to utilise this network for feasibility data both for large scale clinical trials and rare diseases studies should be a major benefit.

Disclosure of Interest: N. Croft Conflict with: Abbot/Abbvie Shire Bristol Myers Squibb Danone MSD Ferring J&J DrFalk Schering Plough, V. Tailor: None Declared, S. Hussey: None Declared, L. de Ridder: None Declared, J. Thomas: None Declared
EFFECT OF OZONE ON INTESTINAL RECOVERY FOLLOWING INTESTINAL ISCHEMIA-REPERFUSION INJURY IN A RAT

Ron Shaoul 1,*, Yulia Pollack 2, Igor Sukhotnik 3

1Paediatric Gastroenterology and Nutrition, Rambam Medical Center, 2Laboratory of Intestinal Adaptation and Recovery, Technion, Faculty of Medicine, 3Paediatric Surgery, Bnai Zion Medical Center, Haifa, Israel

Objectives & Study: Growing evidence suggests that ozone (O3) protects the host against pathological conditions mediated by reactive oxygen species by increasing the activity of antioxidant enzymes. The purpose of the present study was to examine the effect of O3 on intestinal recovery and enterocyte turnover after intestinal ischemia-reperfusion (IR) injury in rats.

Methods: Male Sprague-Dawley rats were divided into four experimental groups: 1) sham rats underwent laparotomy, 2) sham-O3 rats underwent laparotomy and were treated with an ozone/oxygen mixture (0.7 mg/kg/day) intraperitoneally and intraluminally (50%/50%), 3) IR-rats underwent occlusion of both superior mesenteric artery and portal vein for 20 minutes followed by 48 hours of reperfusion, and 3) IR-O3 rats underwent IR and were treated with an ozone/oxygen mixture similar to group 2. Intestinal structural changes, Park's injury score, enterocyte proliferation and enterocyte apoptosis were determined 48 hours following IR. Western blot was used to determine ERK and Bax protein levels. A non-parametric Kruskal-Wallis ANOVA test was used for statistical analysis with P less than 0.05 considered statistically significant.

Results: treatment of IR rats with O3 resulted in a significant increase in mucosal weight in jejunum (70%) and ileum (32%), mucosal DNA (two-fold increase) and protein (35%) in ileum, villus height and crypt depth in jejunum (61% and 16%, correspondingly) and ileum (31% and 43%, correspondingly) compared to IR animals. IR-O3 rats also had a significantly lower intestinal injury score as well as a lower apoptotic index in jejunum and ileum compared and IR animals. A significant increase in cell proliferation rates in IR-O3 animals was accompanied by increased levels of ERK protein.

Conclusion: Treatment with ozone prevents intestinal mucosal damage, stimulates cell proliferation and inhibits programmed cell death following intestinal IR in a rat.

Disclosure of Interest: None Declared
CUGBP1 AND HUR COMPETITIVELY CONTROL THE EXPRESSION OF β-CATENIN AND MODULATE EPITHELIAL CELL PROLIFERATION DURING TPN TREATMENT

Tingxi Yu 1,*, Bei-Lin Gu 1, Jun-Kai Yan 1, Wei-Hui Yan 1, Wei Cai 1
1Shanghai Key Laboratory of Paediatric Gastroenterology and Nutrition, Xin Hua Hospital Affiliated to Shanghai Jiaotong University School of Medicine and Shanghai Institute for Paediatric Research, Shanghai, China

Objectives & Study: Total parenteral nutrition (TPN) significantly down-regulates E-cadherin and β-catenin expression, results in the decline of epithelial cell (EC) proliferation and epithelial barrier dysfunction. RNA binding protein, CUGBP1 and HuR, primarily bind to GU or AU-rich elements located in the 3’-untranslated regions (UTRs) of their target transcripts and regulate mRNA stability and translation. Based on the predicted CUGBP1 and HuR-hits in the β-catenin 3’-UTR, this study sought to determine if CUGBP1 and HuR jointly regulate β-catenin expression, thus contribute to TPN-associated loss of EC proliferation.

Methods: The binding of CUGBP1 and HuR with β-catenin mRNA was examined by biotin pull-down assays and ribonucleoprotein/IP analysis. CUGBP1 and HuR function was investigated by gene silencing and overexpression. EC proliferation was detected by Real Time Cell Analyzer or MTT method. The expression of HuR and CUGBP1 in intestinal villi in rat exposed to TPN treatment for 7 days was detected by immunohistochemical staining and western blot.

Results: CUGBP1 and HuR directly interacted with the β-catenin mRNA 3’-UTR. CUGBP1 overexpression increased the level of [CUGBP1/β-catenin mRNA] complex, repressed β-catenin protein expression (by ~75%), and decreased the cell proliferation; silencing CUGBP1 decreased CUGBP1/β-catenin mRNA association, enhanced β-catenin expression (by ~3 times) and increased cell proliferation. In contrast, overexpression of HuR increased β-catenin protein level (by ~4 times); silencing HuR decreased β-catenin protein expression (by ~80%). Furthermore, HuR overexpression prevented CUGBP1-induced repression of β-catenin expression. Importantly, there was increased expression of CUGBP1 in rat intestinal villi after TPN treatment while HuR remained unchanged or decreased.

Conclusion: These results indicate: 1) β-catenin mRNA is a target of CUGBP1 and HuR; 2) CUGBP1 and HuR jointly modulate the expression of β-catenin; and 3) CUGBP1 and HuR play important roles in the regulation of intestinal epithelial cell proliferation during TPN treatment.

Disclosure of Interest: None Declared
FOOD ALLERGY-INDUCED BEHAVIORAL ABNORMALITIES AND NEUROINFLAMMATION ARE PREVENTED BY A DIETARY INTERVENTION WITH BIFIDOBACTERIUM BREVE M-16V IN COMBINATION WITH NON DIGESTIBLE Oligosaccharides

Yulyia Borre 1, Sander de Kivit 2, Liz Morgan 2, Berend Olivier 2, Johan Garssen 2,*, Aletta Desiree Kraneveld 2

1Alimentary Pharmabiotic Centre, University College Cork, Cork, Ireland, 2Pharmaceutical Sciences, Division of Pharmacology, Utrecht University, 3584 CG Utrecht, Netherlands

Objectives & Study: The gut-immune-brain axis has been implicated in various neurodevelopmental disorders. The immune pathophysiology of food allergic reactions has been well characterized, however, little is known about its consequences on brain function. The aims of this study were to investigate whether food allergy affects brain function and to examine the effect of dietary supplementation with Bifidobacterium breve M-16V in combination with short chain galacto-oligosaccharides and long-chain fructo-oligosaccharides (Bb/GF) alleviates the food allergy-induced neuropathologies.

Methods: Balb/c mice were fed a control or Bb/GF diet for 2 weeks prior to and during a 5 week sensitization protocol to ovalbumin (OVA) by gavage. Around the oral challenge with OVA nesting behavior, open field and T maze tests were performed to assess behavior and cognition. For further analysis fecal and serum samples, ileal lamina propria cells as well as hippocampi were collected. Diarrhea, OVA-specific immunoglobulins, activated T cell subtypes and mRNA expression brain derived neutrophic factor (BDNF), FoxP3 (transcription factor specific for regulatory T cells) and p-glycoprotein (blood brain barrier marker) were examined.

Results: The food allergic reaction was confirmed by increased OVA-specific IgE levels in serum, diarrhea and enhanced number OVA-specific Th2 cells and reduced numbers of Th1 and regulatory T cells in the ileum. OVA-allergic mice demonstrated impaired nesting behavior, increased anxiety levels and spatial memory deficits. These aberrations were associated with decreased expression of mRNA of BDNF and p-glycoprotein in the hippocampi. FACS analysis of the hippocampal cells showed an increased number of activated macrophages and CD4+ T cells. Bb/GF diet normalized OVA-induced aberrant behavior and cognition and cellular and molecular changes in the brain.

Conclusion: The present data demonstrate that food allergic reaction modifies the brain inflammatory status (activated macrophages and T cells) and dampens the cognitive abilities suggesting that food allergy may play a role in the development and/or progression of neurodevelopmental disorders. In addition, targeting the gut-immune-brain axis with Bb/GF diet may have implications for treatment of patients suffering from neurodevelopmental disorders.

Disclosure of Interest: Y. Borre: None Declared, S. de Kivit: None Declared, L. Morgan: None Declared, B. Olivier: None Declared, J. Garssen Employee of: Nutricia Research Utrecht, The Netherlands, A. Kraneveld: None Declared
Objective & Study: There is evidence of an increased risk of infections in neonates treated with gastric acidity inhibitors (GAI). The aim of the study was to investigate the etiology of infections associated with the use of GAI in Very Low Birth Weight (VLBW) newborns.

Methods: Multicenter prospective observational study was conducted on VLBW neonates with birth weight between 401-1500 g or gestational age between 24 and 32 weeks, consecutively observed in Neonatal Intensive Care Unit. Information regarding the occurrence and microbiology of sepsis in subjects exposed or not exposed (controls) to treatment with gastric acidity inhibitors, were collected.

Results: We evaluated 274 VLBW infants: 91 have taken ranitidine and 183 have not. The main clinical and demographic characteristics did not differ between the two groups. Occurrence of infections was significantly higher in the group exposed to treatment with gastric acidity inhibitors (OR 5.5, 95% CI 2.9-10.4, p < 0.001). Gram-negative bacteria (Escherichia coli 10 vs. 2, p < 0.001; Klebsiella pneumoniae 8 vs. 1, p < 0.001; Pseudomonas aeruginosa 6 vs. 1, p = < 0.006) were prevalent in neonates exposed to ranitidine compared to controls.

Conclusion: The therapy with ranitidine in VLBW infants is associated with an increased risk of infections caused primarily by Gram-negative bacteria. Neonatologists need to consider this aspect in the antibiotic management of sepsis associated with the use of gastric acidity inhibitors.


Disclosure of Interest: None Declared
THE USE OF GUM ARABIC IN TREATMENT OF CHILDHOOD CONSTIPATION

Omayma MohyEldin Sabir 1,*, Mercy Mshelbwala 2, Mohamed Widaa 1

1Pediatrics, University of Al NLAIN, Khartoum, Sudan, 2Pediatrics, University of Al NLAIN, Stockton, United Kingdom

Objectives & Study: to evaluate the effect of gum arabic as an adjuvant to laxatives in the management of functional constipation in children

Methods: children less than 16 years old who attended Gaafar Ibnaouf specialist children hospital between June 2011 - May 2012 with constipation were randomly recruited into this study. They were divided in to two groups – with same age and severity of disease, children in the first group were treated with laxatives (lactulose and Senna), and those in the second group were treated with Gum Arabic and laxatives. Children were seen after 1, 3 and 6 months of treatment, they were rated as successfully treated when they had ≥3 bowel movements per week, soft stool, no soiling or abdominal pain in the last 3 weeks of treatment.

Results: 150 children with constipation were seen. 133 children with functional constipation. Successful outcome were obtained in those who were treated with laxative and Gum Arabic. 65% showed improvement at 1st month of treatment and 93.6% at 3rd month of treatment, while those who were treated with laxative alone showed 56.66% improved at 1 month of treatment and 80% at 3rd month. With p value <0.025

Conclusion: Functional constipation is the most cause of constipation in Sudanese children. Gum Arabic added to laxative achieved quicker recovery


Disclosure of Interest: None Declared
Gastroenterology
Gastroenterology Other
PO-G-0086
GASTROINTESTINAL INFLAMMATION IN MICE IN UTERO EXPOSED TO VALPROIC ACID AS A MODEL FOR AUTISM SPECTRUM DISORDERS
Caroline De Theije 1,*, Pim Koelink 1, Mechiel Korte 1, Berend Olivier 1, Joan Garssen 1, Aletta Kraneveld 1
1Pharmacology, Utrecht University, Utrecht, Netherlands

Objectives & Study: Autism spectrum disorder (ASD) is a cluster of neurodevelopmental disorders characterized by impairments in communication, social interest and stereotypical behaviour. Dysfunction of the intestinal tract is reported in patients with ASD and implicated in the development and severity of ASD symptoms. However, more research is required to investigate the association of intestinal problems with ASD and the potential underlying mechanisms.

Methods: The purpose of this study was to investigate comorbid symptoms of intestinal inflammation in a murine model of ASD induced by prenatal exposure to valproic acid (VPA). Pregnant BALB/c females were treated subcutaneously with 600 mg/kg VPA or phosphate buffered saline on gestational day 11. Offspring were housed with their mother until weaning on postnatal day 21 (P21). All pups were exposed to a social behaviour test on P28. Inflammatory correlates and activity of the serotonergic system were measured in brain and intestinal tissue.

Results: Here we demonstrate, in addition to reduced social behaviour and increased expression of neuroinflammatory markers in the brain, that VPA in utero-exposed male offspring showed epithelial cell loss and neutrophil infiltration in the intestinal tract. Furthermore, reduced levels of serotonin were not only observed in the prefrontal cortex and amygdala of VPA in utero-exposed males, but also in the small intestine. Interestingly, this intestinal phenotype was not observed in female offspring.

Conclusion: Overall, we demonstrate that gender-specific inflammatory conditions are present in the small intestines of VPA in utero-exposed mice and are accompanied by a disturbed serotonergic system in the brain as well as in the intestinal tract. These findings provide potential targets for new approaches in the treatment of gastrointestinal dysfunction and behaviour in patients with ASD.

Disclosure of Interest: C. De Theije Grant / Research Support for: Nutricia Research, P. Koelink: None Declared, M. Korte: None Declared, B. Olivier: None Declared, J. Garssen Employee of: Nutricia Research, A. Kraneveld: None Declared
**Objectives & Study:** Lactoferrin (LF) is the second most abundant protein in human milk, with many functions: protection from infections, immunomodulation, enhancement of gut barrier, promotion of the growth of bifidobacteria. Breast milk may represent the main source of LF found in the gut of newborns.

**Aim of the study.** a) To evaluate, in breast milk and newborn stools, LF levels, lactobacilli (LB) and bifidobacteria (BF) concentration; b) To evaluate relationship between LF levels, maternal milk microbiota and/or newborns gut microbiota.

**Methods:** Milk and stool samples were collected in mothers and newborns at birth (T0) and one month (T30) after delivery in order to assess the amount of lactobacilli and bifidobacteria, (Real time – PCR,) and LF (ELISA). Statistical analysis (SPSS software): χ² test, student t-test, linear regression.

**Results:** 46 mothers/newborns pairs were enrolled, 34 term newborns (TN) (mean Gestational Age, GA: 39.02 weeks) and 12 preterm newborns (PTN) (mean GA: 29.1 weeks). LF levels (mg/ml) were higher in colostrum than in mature milk as in TN (7.0 ± 5.1 vs 2.3 ± 0.8, p =0.001) as in PTN (7.3 ± 3.2 vs 2.3 ± 0.4) with linear positive relation between colostrum and mature milk (p=0.0074). In the infant stools LF levels (µg/ml) increased during the first month of life as in TN (T0: 994 ±1828, T30: 3052 ±4323, p=0.001) as in PTN (T0 :1631 ± 2206; T30: 7633 ± 9960) with a statistical significant association with breast milk LF concentration at T30 (p= 0.03). Similar amounts of LB and BF were detected in colostrum and mature milk without significant differences between groups (term or preterm delivery) and time. In TN and PTN the amount of fecal LB and BF significantly increased from T0 (TN: LB 7.0x10⁴ ± 1.7x10⁵, BF 1.4x10⁶ ± 7.3x10⁷ ; PTN LB 2.6x10⁵ ± 6.5x10⁵, BF 1.8x10⁶ ± 5.0x10⁶) to T30 (TN: LB 1.2x10⁶ ± 2.4x10⁸, p<0.001, BF1.2x10⁶ ± 2.5x10⁸, p= 0.001 ;PTN LB 2.5x10⁵ ± 4.9x10⁵, p=0.03, BF 3.3x10⁷ ± 6.9x10⁷, p=0.013). In PTN, at T0 the concentration of fecal BF and LB resulted associated with the concentration of fecal LF at birth (p=0.026 and p=0.017, respectively).

**Conclusion:** 1) Fecal LF level in newborns are significantly associated with breast milk LF concentration. 2) Breast milk and fecal LF are not associated with the amount of protective microorganisms in breast milk nor in the feces of term infants. 3) Fecal levels of lactobacilli and bifidobacteria are significantly associated with the concentration of fecal LF at birth in preterm infants. Lactoferrin could have in PTN an important role in development of an “healthy microbiota”.

**Disclosure of Interest:** None Declared
INFLIXIMAB FOR MANAGEMENT OF PERSISTENT INFLAMMATION AND ULCERATION WITH OR WITHOUT ACUTE CELLULAR REJECTION IN PAEDIATRIC INTESTINAL TRANSPLANT RECIPIENTS

Marie O'meara 1, 2,*, Anil Dhawan 1, Babu Vadomalayan 1, Jonathan Hind 1
1Paediatric Liver, GI and Nutrition Centre, 2Pharmacy, Kings College Hospital NHS Foundation Trust, London, United Kingdom

Objectives & Study: The use of infliximab in Inflammatory bowel disease is well described. TNFα upregulation correlates with severity of acute cellular rejection (ACR) in animal models of intestinal transplant (IT). Conventional immunosuppressive agents do not effectively suppress TNFα. Infliximab has been used for treatment of ACR in small numbers of patients post IT. We report our experience of infliximab as therapy in persistent ulceration and inflammation with/without ACR post Isolated small bowel transplant (ISBT).

Methods:
3 patients, 2 female; underlying diagnoses: gastroschisis (patients 1&2) and chronic intestinal pseudo-obstruction, received an ISBT at 4, 5 and 16 years of age respectively. Immunosupression was Basiliximab induction, Tacrolimus and prednisolone maintenance. Sirolimus was added 1 month post transplant but was not tolerated in all 3 patients due to lymphopaenia.
Infliximab was given at 7, 11 and 29 months post transplant for pyrexia and increased stoma losses accompanied by ongoing graft mucosal ulceration with biopsy proven inflammation. Two patients had histological features of acute cellular rejection, one of which was steroid resistant but showed an initial response to Anti-Thymocyte globulin. Patients received 2, 7 and 7 doses of infliximab respectively.

Results: Infliximab was well tolerated and no adverse effects were noted. Symptoms and histology improved in all patients. In patient 1 infliximab was given for 2 doses. After the second dose histology showed well-preserved mucosal architecture without inflammation or apoptosis. Follow up is 22 months post initiation of infliximab. The patient is fully enterally fed, clinically well and with normal graft histology.
In patient 2 infliximab was given for 7 doses. Histology of the graft was improved but continued to show ulceration. Treatment was discontinued after the 7th dose due to norovirus infection which was treated with immunoglobulin, and required recommencement of parenteral nutrition (PN). Follow up is 17 months post initiation of infliximab. The patient is currently regrading onto enteral feeds.
In patient 3 infliximab was given for 7 doses. Histology was normal at four weeks post the 7th infliximab dose. There was no further evidence of inflammation, ulceration or rejection. Follow up is 17 months post initiation of infliximab. The patient required PN post ACR. The patient is now fully enterally fed and clinically well with normal graft histology.

Conclusion:
Infliximab may be a promising agent in the treatment of persistent inflammation and ulceration in this patient group. The optimum dose, level and treatment duration is not yet established. Further prospective work is indicated to confirm efficacy and safety.

Disclosure of Interest: None Declared
AMINO-ACID-BASED FORMULA VERSUS EXTENSIVELY HYDROLYSED FORMULA IN RELIEVING THE SYMPTOMS OF INFANTS WITH SUSPECTED NON-IGE COW’S MILK ALLERGY: A RANDOMISED PROSPECTIVE, CONTROLLED, DOUBLE BLIND STUDY

David Gil Ortega 1,* , Marcos Antonio Giménez Abadía 1 , María Navalón Rubio 1 , Inmaculada Vives Piñera 1 , José María Nadal Ortega 1
1 Unidad de Gastroenterología, Hepatología y Nutrición Pediátrica., Hospital Universitario Virgen de la Arrixaca, El Palmar (Murcia), Spain

Objectives & Study:

When non-IgE cow milk protein allergy (CMPA) is suspected, an elimination diet is indicated as a diagnostic tool. An extensively hydrolyzed formula (eFH) is then recommended in recent guidelines as a first option although these eHF may fail up to a 5% in managing CMPA. Aminoacid based formulas (AAF) may have a higher efficacy in controlling symptoms in certain CMPA patients, especially those with non-IgE CMPA

Methods: Randomized controlled, double blind, prospective interventional trial to compare efficacy of eFH and AAF in controlling symptoms in infants with non IgE CMPA suspected. 105 infant younger than 9 months with symptoms appearing in relation with formula feeding suggesting CMPA were referred and 90 randomized to receive eFH or AAF (25 excluded: IgE-CMPA test positive, previous eHF/AAF treatment or breast feeding more than twice a day). A Symptom Score, previously validated, and a 24 h Symptoms Record were compared on inclusion visit and + 15 and + 30 days after elimination diet

Results: Both groups had similar age, gender and body composition and without significant differences in Symptoms Score or SCORAD. After 4 weeks on diet no differences between both groups were detected in formula acceptance. Both groups improved in weigh, length or BMI, episodes of vomiting, depositions, time of sleeping per day in similar rate. Symptoms Score on day +30 was significantly lower in AAF group than in eHF (7.8/60 vs 12.9/60, p<0.05) with a higher reduction from the initial visit (72% vs 52%, p<0.01). AAF group also showed a higher reduction of crying minutes oer day on day +15 (-86% vs -51%, p<0.05)

Conclusion: This study supports the previously observed evidences about a superior efficacy of AAF in relieving symptoms of infants with non-IgE CMPA. AAF should be considered as a first option in 2-4 weeks elimination diets who indicated for this group of patients

Disclosure of Interest: D. Gil Ortega Grant / Research Support for: An unconditional grant from Nutricia was received by the Fundación para la Formación e Investigación Sanitaria de la Región de Murcia (FFIS) to develop this study, M. A. Giménez Abadía: None Declared, M. Navalón Rubio: None Declared, I. Vives Piñera: None Declared, J. M. Nadal Ortega: None Declared
S100A12 AND HBD2 CORRELATE WITH THE COMPOSITION OF THE FECAL MICROFLORA IN ELBW INFANTS AND EXPANSION OF E. COLI IS ASSOCIATED WITH NEC
Andreas Jenke 1,*, Jan Postberg 1, Kai Hensel 1, Stefan Wirth 1
1HELIOS Children’s Hospital, Witten/Herdecke University, 42283 Wuppertal, Germany

Objectives & Study: To describe the development of the gut microbiota in extremely low birth weight (ELBW) infants with and without necrotizing enterocolitis (NEC).

Methods: Fecal microflora were prospectively analyzed in fecal samples of all ELBW infants using 16S ribosomal real time PCR assays. In addition fecal inflammatory markers fecal Calprotectin (fCP) and S100A12 and the antimicrobial peptide hBD2 were measured.

Results: Fecal microflora established early in ELBW infants and microbiota composition remained stable over the following first 28 days of life except for the prevalence of C. difficile which decreased with decreasing antibiotic use. Infants who subsequently developed NEC had an increase of total bacterial count (9.8fold) 24h prior clinical symptoms mainly due to the expansion of E. coli species (21.6fold) whereas microbiota composition did not differ from healthy ELBW infants five days before onset of NEC. Importantly, S100A12 and hBD2 positively correlated with the total and E. coli bacterial CFU/g feces ($r^2$ 0.4 and 0.64 respectively) whereas we found no correlation between the fecal microbiota and fCP levels.

Image:
**Conclusion:** In summary, we found evidence for a disturbed homeostasis between the intestinal microbiome and host immunity in ELBW infants with NEC. Moreover, S100A12 and hBD2 correlate with the fecal microbiota thus linking the intestinal innate immune response to the bacterial colonization possibly thus providing a diagnostic tool in the future.

**Disclosure of Interest:** None Declared
**Objectives & Study:** To analyse the clinical characteristics of child-onset systemic lupus erythematosus (SLE) patients with gastrointestinal manifestations, especially the acute and severe abdominal pain cases.

**Methods:** Medical records of 119 patients with SLE under the age 16 years old in Peking Union Medical College Hospital from January 2010 to March 2013 were reviewed and retrospectively analysed with gastrointestinal manifestations. All patients were diagnosed as SLE according to 1997 American College of Rheumatology (ACR) revised classification criteria.

**Results:** Gastrointestinal involvement was recorded in 24 (20.2%) children. The median (range) age at the time of initial gastrointestinal manifestations was (13.5±2) years. The ratio of female to male was 7:17. And in 4 cases, gastrointestinal manifestations occurred as the initial symptoms. Abdominal pain was the most frequent symptom, present in 13 (13/24) patients. 11 (11/24) cases had nausea and vomiting, 4 cases (4/24) had abdominal distension and 3 (3/24) cases had diarrhea. Acute and severe abdominal pain included 9 cases, of which 6 patients were diagnosed as intestinal pseudo-obstruction (of which 2 cases had bilateral ureterohydrenephrosis), once case had acute peritonitis with surgery, once case was diagnosed as protein losing enteropathy and one case had acute pancreatitis. Also liver impairment could also occur in SLE. All cases got alleviated with the treatment of steroids and immunosuppressive drugs.

**Conclusion:** Gastrointestinal manifestations can be initial symptoms of SLE. Intestinal pseudo-obstruction, protein losing enteropathy, and acute pancreatitis are uncommon but important gastrointestinal manifestations in SLE patients which respond well to steroids and immunosuppressive drugs. It is important for pediatric physicians to make early recognition and timely treatment.

**Disclosure of Interest:** None Declared
THE EFFECTS OF OZONE ON INTESTINAL EPITHELIAL HOMEOSTASIS IN A RAT
Ron Shaoul 1,*, Yulia Pollak 2, Igor Sukhotnik 3
1Paediatric Gastroenterology and Nutrition, Rambam Medical Center, Haifa, Israel, 2Laboratory of Intestinal Adaptation and Recovery, Technion, Faculty of Medicine, 3Paediatric Surgery, Bnai Zion Medical Center, Haifa, Israel

Objectives & Study: The positive effects of ozone therapy on gastrointestinal disorders have been previously described. Ozone preconditioning decreases tissue damage and increases antioxidant enzyme activity in an experimental model of methotrexate-induced intestinal injury and decreases inflammation, edema, and oxidative stress during experimental colitis. The mechanisms of these positive effects are poorly understood. The purpose of the present study was to investigate whether the use of ozone may potentiate the gut intestinal mucosal homeostasis in a rat model.

Methods: Adult rats weighing 250-280g were randomly assigned to one of three experimental groups of 8 rats each: 1) Control rats were treated with oral 2cc (by gavage) and intraperitoneal (IP) 2cc water for 5 days; 2) OZ-PO rats were treated with oral 2 cc of ozone/oxygen mixture (by gavage) and IP 2cc water for 5 days; 3) OZ-IP rats were treated with oral 2cc water (by gavage) and IP 2cc of ozone/oxygen mixture for 5 days. Rats were sacrificed on day 6th. Bowel and mucosal weight, mucosal DNA and protein, villus height and crypt depth, cell proliferation and apoptosis were determined at sacrifice.

Results: OZ-IP rats demonstrated a greater jejunal and ileal villus height and crypt depth, greater enterocyte proliferation index in jejunum, and lower enterocyte apoptosis in ileum compared to control animals. Oral administration of ozone/oxygen mixture resulted in a less significant effect on cell turnover.

Conclusion: Treatment with ozone/oxygen mixture stimulates intestinal cell turnover in a rat. Intraperitoneal administration of ozone exerted more prominent effect compared to oral administration.

Disclosure of Interest: None Declared
COLONISATION OF ANTIBIOTIC RESISTANT E. COLI BACTERIA IN HEALTHY INFANTS' GUT DURING THE FIRST YEAR OF LIFE

Benjamin Hetzer 1,*, Dorothea Orth-Höller 2, Reinhard Würzner 2, Martina Prelog 3, Peninnah Oberdorfer 4, Thomas Müller 1

1Department of Paediatrics, 2Division of Hygiene and Medical Microbiology, Medical University of Innsbruck, Innsbruck, Austria, 3University Children’s Hospital, University of Würzburg, Würzburg, Germany, 4Department of Paediatrics, Chiang Mai University, Chiang Mai, Thailand

Objectives & Study: Increasing resistance against antibiotics is a serious emerging problem worldwide. Especially in neonates infections with resistant E. coli bacteria are a life-threatening hazard. The aim of this study, conducted in the region of Northern Thailand, was to record the development of antibiotic resistant E. coli in healthy infants’ gut during the period from birth until one year of life.

Methods: Stool samples were collected during the first 48 hours after birth, after two weeks, two months, four to six months and after one year and screened for resistant E. coli bacteria against ampicillin, tetracycline, trimethoprim and cefazolin. Furthermore prevalence of antibiotic resistant E. coli was evaluated in parents (one stool sample was collected at the beginning of the study). Altogether 142 families completed the study.

Results: 35.2% (50 out of 142) neonates’ meconium samples already contained resistant E. coli in meconium. The highest frequency of resistant E. coli was shown against tetracycline (32.2%) followed by ampicillin (28.7%), trimethoprim (21%) and cefazolin (8.4%). Increasing prevalence of antibiotic-resistant E. coli was found at every point of sample collection. During the study period all infants showed resistance to at least one of the antibiotics tested. Prevalence of resistance in infants after one year of life (tetracycline 81.3%, ampicillin 73.4%, trimethoprim 66.2% and cefazolin 34.5%) almost matched the prevalence of resistant E. coli in parents (tetracycline 86.4%, ampicillin 82.1%, trimethoprim 63.1% and cefazolin 32.3%).

Conclusion: Thus, a high prevalence of antibiotic-resistant E. coli was observed in neonates in Thailand which increased during the first year of life. Based on the prevalence rates found in infants and parents it can be assumed that resistant E. coli are transmitted from the mothers to their newborns during birth, but also from parents to children during the first year of life via household contact. However this hypothesis has to be verified by molecular comparison of the resistant strains which will be done in a further study. Awareness concerning this problem and selective application of antibiotic drugs is an urgent need to avoid progression of resistance.

Disclosure of Interest: None Declared
ESOPHAGEAL EOSINOPHILIA: A 13-YEAR RETROSPECTIVE ANALYSIS IN CHILDREN
Kleoniki Roka 1,*, Paraskevi Papadogeorgou 1, Smaragdi Fessatou 1, Amalia Patereli 2, Kalliopi Stefanaki 2, Ioanna Panagiotou 1, Eleftheria Roma 1, Giorgos Chouliaras 1
11st Department of Paediatrics, University of Athens, Athens, Greece, 2Pathology Department, Agia Sophia Children’s Hospital, Athens, Greece

Objectives & Study: Esophageal eosinophilia is becoming increasingly common. We aimed to study the prevalence of esophageal eosinophilia in children who underwent first esophagogastroduodenal endoscopy (EGD) and its evolution over the study period.

Methods: All children who underwent EGD between 2000-2012 were retrospectively included. Clinical, endoscopic and histological findings were studied. Children with presence of at least 15 eosinophils per HPF in oesophagus were analyzed.

Results: We studied 1989 patients (median age 7.5 years, range 1mo-18y, 1010 boys). Esophageal eosinophilia was found in 124 children (6.2%, 83 boys). Statistical difference was observed only in gender (p<0.001). Celiac disease, H.pylori gastritis and inflammatory bowel disease coexisted in 12.9%, 8.1% and 2.4% of the patients with esophageal eosinophilia respectively. A 24hour esophageal pH study was performed in 30 patients with esophageal eosinophilia and acid reflux was found in 21 subjects (16.9% overall). Children with retrosternal pain were 3.2 times more likely to have esophageal eosinophilia compared to those without (OR=3.2, 95% CI: 1.66-6.41, p=0.0006). Children with epigastric pain were 2.0 times less likely to have esophageal eosinophilia compared to those without epigastric pain (OR=2.0, 95%CI: 1.34-3.2, p=0.001). Children with endoscopic presence of esophageal rings were 49.15 times more likely to have esophageal eosinophilia compared to those without rings (OR=49.16, 95% CI: 13.3-181.1, p<0.0001). Children with endoscopic presence of nodules in esophagus were 2.48 times more likely to have esophageal eosinophilia compared to those without nodules (OR=2.48, 95% CI: 1.56-3.96, p=0.0001). No statistical difference for the presence of celiac disease in children with esophageal eosinophilia compared to controls was observed in our study (12.9% vs 16.8% respectively, p=0.11). The new cases with esophageal eosinophilia between periods 2001-2006 and 2007-2012 have been doubled (7.9% vs 4.0%, p<0.01).

Conclusion: A significant increase of esophageal eosinophilia was observed during the recent years. Retrosternal pain and endoscopic presence of rings or nodules in esophagus enhance the suspicion of esophageal eosinophilia in paediatric patients.

Disclosure of Interest: None Declared
PAEDIATRIC EOSINOPHILIC OESOPHAGITIS A TERTIARY GASTRO-ALLERGY EXPERIENCE

Katherine Fawbert 1,*, Eleanor Minshall 2, Nicholas Francis 3, John Warner 2, John Fell 1, Jenny Epstein 1

1Department of Paediatric Gastroenterology, Chelsea and Westminster NHS Trust, London, United Kingdom, 2Department of Paediatric Allergy, 3Department of Histopathology, Imperial Healthcare NHS Trust, London, United Kingdom

Objectives & Study: Eosinophilic oesophagitis (EoO) is a chronic immune-mediated condition characterised by oesophageal dysfunction and eosinophilic infiltration. It is a clinically heterogeneous condition with proton pump inhibitor (PPI)-responsive and non-atopic subtypes. Approaches to its diagnosis and management vary, although steps toward their standardisation are underway.

Methods: We performed a retrospective case review of 34 patients with EoO under the care of a Paediatric Gastroenterology and a Paediatric Allergy Centre focussing on presentation and management.

Results: Case notes were reviewed in 34 patients with EoO. Age at diagnosis ranged from 0.83-16 yrs (mean 7.3 yrs). Of our cohort 24 were male and a minority were white British (43%). Most were referred from Hospital Paediatricians (38%). Z scores for weight ranged from -3.31 to +2.71 SD, with two patients below -2 SD and one below -3 SD. Z scores for height ranged from -2.67 to 2.05 SD. BMI Z scores ranged from -3.73 to 2.51 SD. The commonest presenting symptoms were vomiting (62%), abdominal pain (47%), dysphagia (38%), and regurgitation (21%). Twenty two patients were atopic, six had a neurological diagnosis, three co-existent eosinophilic colitis and two had IgA deficiency. At presentation, ten patients were on no treatment. Treatments included a PPI (n=20; 63%) and montelukast (n=18; 53%). The circulating eosinophil count was elevated in 62% of patients (mean 0.74 x10^9/L) and the majority had a raised total IgE (85%; median 435 kU/L). Specific IgE was determined in 71% (24/34) with positive tests to egg (71%), milk (63%), wheat (52%), and soy (50%). Skin prick tests were performed in 23 children, with 15 (65%) positive to foods, and 14 were positive to aeroallergens (61%). At endoscopy, macroscopic abnormalities were seen in 59%, with the most common finding being linear furrowing (n=8;24%). On histological examination, the mean eosinophil count was 26/hpf (range 15-50/hpf). Intraepithelial lymphocytes were seen in 53%, and chronic inflammation in 44%. After diagnosis, 26 commenced dietary restriction, 19 started PPI therapy and 14 continued on a PPI. Nine were commenced on topical or systemic steroids.

Conclusion: Our cohort was predominantly male, with a high rate of atopy in concordance with previously published data. The most widely reported symptoms were vomiting, abdominal pain, dysphagia and regurgitation, most had an eosinophilia with raised total and specific IgE. Clinical heterogeneity was reflected in the presentation and wide variety of drug and dietary treatments commenced before referral. Allergy testing was often useful in guiding treatment, although management strategies varied. Work is on-going to determine treatment efficacy, optimal monitoring of disease progression and therapeutic response within the EoO clinical spectrum.

Disclosure of Interest: None Declared
Silvia Salvatore 1,*, Giovanni DiNardo 2, Saverio Mallardo 2, Valentina Mancini 3, Chiara Moretti 4, Osvaldo Borrelli 5, Paolo Lionetti 6, Costantino DeGiacomo 4, Salvatore Cucchiara 2, Patrizia Latorre 7
1University of Insubria, Varese, Italy, 2Università La Sapienza, Roma, Italy, 3Pediatria, Parma, Italy, 4Ospedale Niguarda, Milano, Italy, 5Great Ormond Street Hospital for Sick Children, London, United Kingdom, 6Ospedale Meyer, Firenze, Italy, 7Ospedale di Circolo, Varese, Italy

Objectives & Study: The association between gastroesophageal reflux (GER) and laryngeal inflammation is controversial. However, in many patients acid inhibitors are started based on laryngeal investigation. The aim of the study was to examine the correlation between laryngeal findings and acid/weakly acid GER.

Methods: All children underwent laryngoscopic examination and multichannel esophageal impedance/pH-monitoring (MII-pH). The time window between the two investigations was within 1.5 months in all patients and no treatment was started in between. Laryngoscopy was considered as positive if it showed interarytenoid erythema and/or edema and/or vocal cord nodules. MII-pH analysis was focused on the reflux index (R.I. = the percentage of time in the entire investigation during which the pH is less than 4.0) for acid GER, and on the bolus exposure index (BEI = the percentage of time during which liquid or mixed GER was present) for total (acid plus weakly acid) GER. We analyzed the laryngeal data according to RI > 5% and >10% for acid, and to BEI > 1.4% and >2% for total GER.

Results: 84 children (range 1-180 months, median age 50 months) were analyzed. Nearly 90% of the patients were referred by the ENT specialist because of abnormal laryngeal findings suspected of GER in children with different respiratory manifestation. The most common symptoms were chronic cough in children and ALTE/apnea in infants. 73 patients (87%) had positive laryngoscopy: the association between laryngeal findings and MII-pH results are reported in the following table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>EDEMA</th>
<th>ERYTHEMA</th>
<th>NODULES</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>29</td>
<td>57</td>
<td>7</td>
</tr>
<tr>
<td>RI &gt; 5%</td>
<td>4</td>
<td>13</td>
<td>1</td>
</tr>
<tr>
<td>RI &gt;10%</td>
<td>3</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>BEI &gt; 2%</td>
<td>10</td>
<td>25</td>
<td>4</td>
</tr>
<tr>
<td>BEI &gt;1.4%</td>
<td>8</td>
<td>10</td>
<td>1</td>
</tr>
</tbody>
</table>

The presence of edema and erythema was not mutually exclusive. In the only 11 patients with negative laryngoscopy 3 had R.I. > 5% and 3 (2 different ones) BEI > 1.4%.

Conclusion: The correlation between laryngeal inflammations (reported as GER related) detected at laryngoscope and acid GER is poor. The empiric use of acid inhibitors in these patients is not recommended. When both acid and weakly acid GER were considered we found a positive association in nearly 60% of children.

Disclosure of Interest: None Declared
**Gastroenterology**

**GERD, Peptic Disease and Helicobactor Pylori**

PO-G-0097

**IMPEDEANCE BASELINE, AGE AND ESOPHAGITIS IN CHILDREN**

Silvia Salvatore 1,*, Alessandro Salvatoni 1, Dario Unmarino 2, Rachel Van Der Pol 3, Maurizio Fuoti 4, Fabio Meneghin 5, Marc Benninga 3, Yvan Vandenplas 6

1University of Insubria, Varese, Italy, 2Università Federico II, Napoli, Italy, 3AMC, Amsterdam, Netherlands, 4Spedali Civili, Brescia, 5Ospedale Sacco, Milano, Italy, 6Universitair KinderZiekenhuis Brussel, Brussels, Belgium

**Objectives & Study:** Esophageal impedance baseline is an impedance parameter recently related to esophageal integrity. The aim of this study was to assess the relationship between impedance baseline and endoscopic findings in children.

**Methods:** Children with symptoms of gastro-esophageal reflux submitted to both endoscopy and impedance were included. Esophagitis was graded according to the Los Angeles classification. Mean impedance baseline was automatically calculated over 24-hours tracings. Data were adjusted for age through z-score transformation using normalized percentiles. Non parametric Mann-Whitney and Kruskal-Wallis tests, multiple and stepwise regression were used. P value <0.05 was considered as statistically significant.

**Results:** A total of 298 impedance tracings were analysed. Endoscopic and histological esophagitis were detected in 30% and 29% patients, respectively. Median impedance baseline z-score was significantly decreased both in proximal (p=0.02) and distal (p=0.01) esophagus in patients with endoscopic (but not histological) esophagitis. Patients with more severe esophagitis showed the lowest z-score. Bolus exposure index and the number of reflux episodes were the variables that were significantly associated with the impedance baseline z-score.

**Conclusion:** Impedance baseline z-score is significantly decreased in infants and children with endoscopic esophagitis. Severity of esophagitis, bolus exposure index and number of reflux episodes are factors influencing impedance baseline.

**Disclosure of Interest:** None Declared
Objectives & Study: Whether there is a correlation between reflux symptom severity (SS) and esophageal histological grade (EHG) is still under debate. The inherent pediatric literature is scarce and inconclusive and most studies scored symptoms using unvalidated tools. The primary aim of the study was to assess the relationship between SS and EHG in children investigated for GERD. The secondary objective was to assess the possible relationship between specific symptoms complained and a higher EHG.

Methods: We enrolled every child aged between 2 and 17 years referred from January 2012 to July 2013 to perform upper GI endoscopy because of symptoms suspected to be GERD-related. Once enrolled, patients were asked to complete the PGSQ validated questionnaire, scoring the main symptoms complained and their impact on daily life and school activities (range 0-40). During the upper GI endoscopy 4 distal esophageal biopsies were taken. Mucosal samples were scored according to the Yerian-Fiocca classification ranging from 0 (normal mucosa) to 8 (severe esophagitis).

Results: 164 children (males/females: 74/90, mean age ± SD: 123.1 ± 49.4 mths) were included in the study. The mean symptomatic score was 11.3. The mean EHG was 2.64. No significant association between SS and EHG was found (rs:0.05; p:0.49). When considering only the patients with heartburn or chest pain, SS and EHG did not show any positive correlation as well (rs:0.03; p:0.75). Analyzing data from age-stratified population, we found a lack of positive association between SS and EHG in both children and adolescents. Intercellular space diameters (ISD) were normal in 28%, mildly dilated in 47% and highly dilated in 25% patients. No correlation was found between ISD and SS, either when considering the global population or the patients with heartburn and respiratory symptoms alone.

Conclusion: The main finding of this multicenter, prospective study on children with suspected GERD-related symptoms is the lack of correlation between SS and EHG, even when considering the different age groups and the patients with different clinical presentations separately. Medical literature about this topic is not univocal. This is the first study to have used validated symptomatic scores, especially for the age group between 9 and 17 years.


Disclosure of Interest: None Declared
**Objectives & Study:** Several studies evaluate the efficacy of the H₂ breath test as a non-invasive study with high sensitivity and specificity to diagnose lactose intolerance. Moreover, it has been reported that an increase in breath CH₄ excretion occurs in children with lactose intolerance. Breath CH₄ excretion in normal children averages 1.6 parts per million (ppm) from 0 to 120 minutes. The aim of the study is to evaluate the importance of CH₄ measurements in the diagnosis of lactose intolerance.

**Methods:** We evaluated 134 children with symptoms suggestive of lactose intolerance. All patients underwent a Lactose H₂ (H₂) and CH₄ (CH₄) Breath Test (LHMBT). Lactose was administered orally (dose of 2 mg/kg, max 50 mg) diluted in max 250 ml of water. The expired air was collected in specific syringes with a capacity of 20 ml. One breath sample was taken before the intake of lactose and breath samples were taken after the ingestion of lactose every 15 min for 3 hours. The expired H₂, CH₄ and CO₂ was measured with a specific analyzer (Microlyzer DP; Quintron Instruments, Milwaukee, Wis.). The result was considered positive when a H₂ peak exceeded 20 ppm over the baseline value and/or CH₄ exceeded 12 ppm over the baseline value, observed in two or more samples. A clinician, blinded for the results of the breath test, registered the symptoms of the patients during the test. Statistical evaluation was considered statistically significant for a p<0.05).

**Results:** Fifty-two children out of 134 (38.8%) had a positive breath test. Twenty-seven patients out of 52 (51.9%) were positive for H₂ and CH₄ (H₂+CH₄+), while the remaining were positive only for the H₂ (H₂+CH₄-). No patient had CH₄ positivity only. The peak level of H₂ in H₂+CH₄+ patients was significantly higher than in H₂+CH₄- patients (P<0.0001). Forty-two children out of 134 (31.3%) had symptoms during the breathtest. Of these, 16 children had a negative breath test, 18 were H₂+CH₄+ and 8 were H₂+CH₄-. No statistical difference was found in the comparison of the highest level reached by the gas and the difference between these values and the baseline values in patient with positive breath test with and without symptoms. (p=0.538).

**Conclusion:** Our results show that CH₄ had no added value to a simple H₂ breathtest.

**Disclosure of Interest:** None Declared
**Objectives & Study:** The role of Helicobacter pylori (HP) as a cause of iron deficiency anemia (IDA) in childhood is controversial. ESPGHAN recommended to consider testing for HP in children with IDA refractory to oral iron when other causes for IDA are ruled out, and to perform an upper gastrointestinal endoscopy (UGE). The impact of HP eradication on IDA is controversial as well. **Aims:** 1. To evaluate the HP prevalence in children undergoing UGE due to IDA compared to children without IDA. 2. To evaluate the impact of HP eradication on IDA parameters compared to non-eradication.

**Methods:** A retrospective study of children ≤ 18 yrs referred for UGE during 2004-2010 in 2 medical centers in Israel. After an initial chart screening of indications for UGE, patients with diagnosis of celiac disease, IBD, interventional procedures, evidence of bleeding, and incomplete records were excluded. The remaining patients were divided into study group - children referred with IDA with or without other symptoms and control group - children referred to UGE with other indications. Data extraction included: IDA parameters (hemoglobin, serum iron and ferritin, TIBC, MCV, RDW), presence of HP by rapid-urease test or intestinal biopsy, treatment and evidence of HP eradication, and F/U of IDA parameters. Endpoints: 1. Prevalence of HP in the study compared to control group. 2. Within study group - IDA parameters in patients with HP compared with patient with IDA and no HP. 3. Within the HP group with IDA - improvement of IDA parameters in patient with HP eradication compared to non-eradication.

**Results:** The study and control groups included 104 and 787 patients, with 52% and 44% males, and age 9.0±5.5, and 9.7±5.0, respectively. HP was found in 38/104 (36.5%) of the study, and in 147/787 (18.7%) of the control groups, respectively (p<0.01). Within the study group - Baseline ferritin levels were significantly lower in HP-positive than in HP-negative patients (p=0.02). However, no difference was found in baseline hemoglobin level between the groups. During follow-up (6-18 months) of the 38 HP-positive patients, 26 had HP eradication, 5 had no eradication and 7 were lost to F/U. A significantly higher rate of eradicated patients achieved an increase in hemoglobin of more than 2 gr% than non-eradicated (14/26 vs 0/5, p=0.02).

**Conclusion:** HP is a significant cause of IDA in patient referred for upper endoscopy with this indication, and is more prevalent than in patients without IDA. The degree of iron deficiency is higher in HP than in non-HP infected patients with IDA. A better improvement of hemoglobin levels is achieved in patients with HP eradication than non-eradicated patients.

**Disclosure of Interest:** None Declared
THE EFFECT OF HELICOBACTER PYLORI INFECTION ON THE TIGHT JUNCTION PROTEIN EXPRESSION OF GASTRIC MUCOSA AND ITS SIGNIFICANCE IN CHILDREN

Mizu Jiang 1*, Wei Li 2, Xiaoli Shu 2, Weizhong Gu 2, Kerong Peng 2
1 Gastroenterology, 2 Children’s Hospital, Zhejiang University School of Medicine, Hangzhou, China

Objectives & Study: To understand the junction protein expression of gastric mucosa including occlusal proteins (occludin), closed protein (claudin), zonula occludens (ZO-1), epithelial cadherin (E-cadherin), and β ring protein (β-catenin) and the clinical significance in children with Helicobacter pylori (Hp) infection.

Methods: The patients performed by gastric endoscopy because of nausea, vomiting, abdominal pain, bloating, acid reflux, melena, and other gastrointestinal symptoms were enrolled in this study from May to November in 2011 in Children's Hospital affiliated Zhejiang University School of Medicine. Informed consent was signed by their parents, and the study was in accordance with the principles of medical ethics. Three gastric antrum specimens were biopsied; one for rapid urease test (RUT), one for a fixed in 10 % formalin submission pathology, and the last one was preserved at -80 °C after cryopreservation in liquid nitrogen refrigerator. The mRNA levels and protein expression of tight junction protein of gastric mucosa was measured by RT-PCR and western blot respectively. The location and semi quantitative of E-cadherin and β-catenin in gastric mucosa were detected by immunohistochemistry staining method.

Results: Forty one cases aged 3.5-16 years old (male 28 cases, female 13 cases) had complete clinical and pathological data were analyzed in this study. Of them, 27 cases were Hp positive and 14 cases were Hp negative according to the result of RUT and gastric mucosa pathology detection. In the Hp positive group, 13 cases were diagnosed with peptic ulcer, and 14 cases without peptic ulcer. The mRNA level of ZO-1, E-cadherin, β-catenin in the Hp positive group regardless of peptic ulcer was significantly lower than that in the Hp negative group (all P <0.01). The expression of claudin-4 in Hp positive gastric ulcer group increased obviously, the difference was statistically significant (P<0.01), while the difference of occludin levels was no statistical significance among the three groups. Immunohistochemistry results showed that E-cadherin, β-catenin levels in the Hp positive patients were also significantly lower than that in the Hp negative group (P<0.01 and <0.05, respectively).

Conclusion: Our results revealed that the tight junction protein ZO-1, E-cadherin, β-catenin expression of gastric mucosa were decreased in children with Hp infection, while claudin-4 expression was increased in patients with peptic ulcer, suggesting that gastric epithelial barrier function damage may be the main pathogenesis of Hp associated gastric diseases in children.

Disclosure of Interest: None Declared
A HIGH PREVALENCE OF HELICOBACTER PYLORI INFECTION AMONG CHILDREN WITH INFLAMMATORY BOWEL DISEASE

Michal Kori¹*, Reut Klein-Daniel², Jacob Yahav¹

¹Paediatric Gastroenterology, ²Paediatrics, Kaplan Medical Center, Rehovot, Israel

Objectives & Study: Inflammatory Bowel Disease (IBD) is a growing worldwide health burden in which the etiology remains elusive. Helicobacter Pylori (HP) infection is prevalent worldwide and acquired in early childhood. HP prevalence is lower in developed countries especially among children. In contrast, IBD prevalence is higher in developed countries. Epidemiologic data suggests a protective effect of HP infection against disease with an autoimmune component. There is preliminary evidence in adults to suggest that patients with IBD are less frequently infected with HP. The objective of this study is to examine the prevalence of HP infection among Israeli children with IBD compared to non-IBD children.

Methods: We retrospectively studied the infection rate of HP infection based on endoscopic and pathology reports in children newly diagnosed with IBD at the Pediatric Gastrointestinal Unit at Kaplan Medical Center between 2000-2013. The rate of HP infection was compared to two control groups. Group A - children who underwent upper and lower endoscopy for suspected IBD who had normal ileo-colonoscopy and the diagnosis of IBD was deferred. Group B - children diagnosed with celiac disease who had biopsy specimen taken from the stomach during endoscopy. Age at diagnosis and gender were documented.

Results: Data from 334 endoscopic and pathologic reports were collected. 112 patients were diagnosed with IBD, 96 with crohn's disease, 12 with Ulcerative Colitis and 4 with IBD-U (undefined). 78/112 (69.6%) children with IBD, mean age 13.5±3.3 were HP positive. 49/82 (59.7%) children without IBD, mean age 13.7±3.1 were HP positive. 94/140(67.1%) children with Celiac disease, mean age 8±5.0 were HP positive. The prevalence of HP infection was exceptionally high in all three groups and not statistically different between the groups. There was no difference in the mean age of children with and without HP infection (11.34 vs 11.14 years). The mean age of the celiac patients was statistically lower than the mean age of the other two groups. Celiac disease was more prevalent among females (1:1.63) but there was no difference in HP prevalence between boys and girls.

Conclusion: The prevalence of HP infection is high among children with newly diagnosed IBD in Israel. This data is in contrast to previous studies in adults demonstrating an inverse association between HP and IBD.

Disclosure of Interest: None Declared
Gastroenterology

GERD, Peptic Disease and Helicobacter Pylori

PO-G-0103

REFLUX ESOPHAGITIS PREVALENCE AND EVOLUTION IN H.PYLORI-POSITIVE VS. -NEGATIVE CHILDREN

Dorin Farcau 1,* and Pop Daniela, Farcău Mihaela, Ichim Gabriela, Fufezan Otilia

1IIIrd Paediatric Department, "Iuliu Hatieganu" Medicine & Pharmacy University Cluj-Napoca, Cluj-Napoca, Romania

Objectives & Study: There are many controversies regarding the development/worsening of reflux esophagitis (RE) after H.pylori (HP) eradication. Only few data exists in pediatric patients. The aim of the study was to assess a possible protective role of H.pylori infection for RE development/evolution.

Methods: We included in a prospective study 144 dyspeptic children (56 males, age range 5-18 years) admitted in our department between 2002 and 2012. They were previously diagnosed for RE (Savary-Miller endoscopic criteria) and also checked for the presence of HP infection (rapid urease test and/or histology). All RE patients received therapy with omeprazole for 3 months, those HP positive also receiving clarithromycin and amoxicillin (b.i.d., in addition to the first week of omeprazole therapy). The patients having only HP infection received a triple therapy (omeprazole, clarithromycin and amoxicillin, b.i.d., 1 week). The patients who completed the study were re-evaluated after 3 months for RE and HP status according to the initial diagnostic protocol. Regarding the RE assessment, we considered a better endoscopic grade or endoscopic healing as favourable evolution and the same/worse endoscopic grade as unfavourable evolution, respectively.

Results: At the initial diagnostic work-up HP infection was present in 74/144 (51.38%) patients, of which 44 had RE. RE was also present in 43/70 of HP negative cases. There was no significant difference (p>0.05) in RE prevalence between HP positive vs. – negative patients. The study was completed by 72 patients initially diagnosed with RE and 25 initially HP positive patients without RE. Among the RE patients who completed the study, 36/72 (50%) were initially HP positive, with an eradication rate of 61.11% (22/36 patients). According to HP status the RE patients were assessed in three groups, as follows: Group A (persistent positive, n=14), Group B (initially positive, n=22) and Group C (initially negative, n=36). Regarding the RE status after 3 months of omeprazole therapy, a favourable endoscopic evolution was present in: 10/14 patients from group A, 16/22 patients from Group B and 25/36 patients in Group C, respectively. There were no statistical differences between RE favourable evolution in the above mentioned groups (p>0.05). In the initially HP positive cases without RE the eradication rate was 56% (14/25 patients). None of them developed endoscopic findings of RE at re-evaluation.

Conclusion: RE prevalence/evolution in dyspeptic children is not related to HP status.

Disclosure of Interest: None Declared
REGURGITATION AND GASTROESOPHAGEAL REFLUX DISEASE IN 6 - 9 MONTH OLD INDONESIAN INFANTS

Yvan Vandenplas 1,*, Badriul Hegar 2
1Paediatrics, UZ BRUSSELI, Brussels, Belgium, 2Department of Child Health, Faculty of Medicine, University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia

Objectives & Study: Regurgitation is known to peak at the age of 3-4 months, with a sharp decrease around the age of 6 months. Little is known about the natural evolution of infants who still regurgitate after the age of 6 months.

Methods: 131 infants older than 6 months regurgitating more than once a day were followed for a period of 3 months.

Results: Most of the subjects regurgitated 3 or more times/day and did spit up an estimated volume of more than 15 mL. The frequency and volume of regurgitation decreased during follow-up. At the end of follow-up, there were no subjects that regurgitated more than once a day, more than 4 days/week and or large volume of regurgitation (15 mL).

Considering the risk factors for persistence of regurgitation, we did a bivariate and multivariate analysis for sex, age, exclusively breastfeeding, smoke exposure, family history of GER, and non-pharmacotherapy. No significant difference was found for any of these variables in bivariate or multivariate analysis. Twenty-two infants still regurgitated ≥ 3 times/day after 3 months follow-up; 3/22 (14 %) had complied with non pharmacotherapy education, whereas 19/22 (86%) infants that still regurgitated at the end of follow-up did not comply with the educational advice given. According to our data, gastro-esophageal reflux disease is seldom at this age. Conservative treatment (reassurance, dietary treatment, behavioral advice) resulted in a significant better outcome than natural evolution.

Conclusion: Regurgitation that persisted after the age of 6 months, strongly decreased during a 3-month follow-up with conservative treatment. Gastro-esophageal reflux disease is rare in this age group; therefore, anti-reflux medication is seldom needed.

Disclosure of Interest: Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals, B. Hegar: None Declared
**Objectives & Study:** Endoscopic presence of nodules in antrum seems to be associated with *H. Pylori* infection in small series of paediatric patients with epigastric pain. We aimed to study the prevalence of nodular gastritis in children who underwent first esophagogastroduodenal endoscopy (EGD).

**Methods:** All children who underwent EGD between 2002-2011 were retrospectively included. Clinical, endoscopic and histological findings were studied. *H. Pylori* infection was defined by positive culture or by positive histology and CLO-test. Those children with negative or not available culture and only one positive test (histology or CLO) were further evaluated by urea breath test and the positives were also included in the infected group.

**Results:** We studied 1674 patients (median age 7.5 years, range 1mo-18y, 851 boys). *H.Pylori* (+) gastritis was found in 11.9%, while 5.4% of the patients had endoscopic and histological findings within normal limits (controls). Antral nodular gastritis was endoscopically found in 77.0% of patients with *H.Pylori* (+) gastritis, 10.0% of *H.Pylori* (-) gastritis and only 6.0% of controls. Presence of nodular gastritis achieved a specificity of 90.0% and a sensitivity of 77.0% in distinguishing between *H.Pylori* (+) from *H.Pylori* (-) patients. Children with endoscopic presence of nodules in antrum were 32.3 times more likely to have *H.Pylori* (+) gastritis compared to children without (OR: 32.3, 95% ci: 22.2-46.9, p<0.001). Those children were also 2.8 times less likely to have *H.Pylori* (-) gastritis compared to children without nodular gastritis (OR: 2.8, 95% ci: 2.1-3.6, p<0.001). Finally, patients with endoscopic presence of nodules in antrum were 4.0 times less likely to belong in the control group (OR: 4.0, 95% ci: 2.5-6.5, p<0.001).

**Conclusion:** Endoscopical presence of nodules in antrum enhances with statistical significant difference the suspicion of *H.Pylori* infection in paediatric patients.

**Disclosure of Interest:** None Declared
?.PYLORI(-) GASTRITIS IN CHILDREN: COMPARISON OF CLINICAL, ENDOSCOPIC AND HISTOLOGICAL FINDINGS WITH ?.PYLORI(+) GASTRITIS

Kleoniki Roka 1, Kalliopi Stefanaki 2, Smaragdi Fessatou 1*, Ioanna Panagiotou 1, Eleftheria Roma 1, Giorgos Chouliaras 1

11st Department of Paediatrics, University of Athens, Athens, Greece, 2Pathology Department, Agia Sophia Children's Hospital, Athens, Greece

Objectives & Study: H. Pylori (-) gastritis is significantly more common in children compared to adults, while only few data concerning etiology, time of acquisition and grade in children exist. Our purpose was to study clinical, endoscopic and histological characteristics of H. Pylori(-) gastritis in children who underwent first esophagogastroduodenal endoscopy (EGD) as well as to compare these characteristics with those of H. Pylori(+) gastritis.

Methods: All children who underwent EGD between 2002-2011 were retrospectively included. Clinical, endoscopic and histological findings were studied. H. Pylori infection was defined by positive culture or by positive histology and CLO-test. Those children with negative or not available culture and only one positive test (histology or CLO) were further evaluated by urea breath test and the positives were also included in the infected group.

Results: We studied 1578 patients (median age 7.5 years, range: 1mo-18y, 851 boys). H. Pylori(-) και H. Pylori(+) gastritis were found in 88.1% and 11.9% respectively. Statistical significance was observed only in age (7.6 versus 9.7 years respectively, p<0.001). Children with epigastric pain were 5.0 times more likely to have H. Pylori(+) gastritis compared to those without epigastric pain (OR=5.0, 95% CI:3.6-6.8, p<0.001). Endoscopic findings within normal limits were observed in 23.8% of patients with H. Pylori(-) gastritis versus only 5.7% of those with H. Pylori(+) gastritis (p<0.001). Concomitant esophagitis or/and duodenitis were observed in 41.9 % of H. Pylori(-) subjects and only 2.0% of H. Pylori(+) ones (p<0.001). Finally, histological findings of medium-severe activity and chronicity were less common in H. Pylori(-)-group (7.4% and 51.0% respectively in children with H. Pylori(-) gastritis versus 85.6% και 92.8% in those with H. Pylori(+) gastritis).

Conclusion: H. Pylori(-) gastritis was significantly more common. The absence of pathological endoscopic findings as well as the concomitant presence of pathologic findings from esophagus or/and duodenum enhances diagnosis of H. Pylori(-) gastritis, which is more commonly found in younger ages and histologically characterized by lesser grade of activity and chronicity.

Disclosure of Interest: None Declared
HELICOBACTER PYLORI INFECTION IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE
Nevzat Aykut Bayrakt 1,*, Engin Tutar 1, Burcu Volkan 1, Esra Polat 1, Birol Öztürk 1, Çiğdem Çelikel 2, Deniz Ertem 1
1Department of Paediatric Gastroenterology, Hepatology and Nutrition, 2Department of Pathology, Marmara University School of Medicine, Istanbul, Turkey

Objectives & Study: A potential protective effect of Helicobacter pylori (Hp) infection against the development of inflammatory bowel disease (IBD) has been suggested in some of the adult studies. However, most of these studies were retrospective, previous treatment of Hp infection and antibiotic use usually has not been mentioned, and serology was commonly used to detect Hp infection. The data regarding children are scarce. The aim of this study was to evaluate the association between Hp and IBD prospectively in children with IBD.

Methods: Newly diagnosed ulcerative colitis (UC) and Crohn’s disease (CD) patients were included into the study. Disease activity was determined by using the pediatric UC activity index (PUCAI) and pediatric CD activity index (PCDAI). Otherwise healthy individuals who underwent gastroscopy in the same period were enrolled as controls. The presence of Hp infection was investigated by histopathology and the rapid urease test. Children who previously received eradication for Hp were not included into the study.

Results: A total of 72 IBD patients (33 CD, mean age: 11.6±3.4 years, 52.7% girls) and 416 controls (mean age: 12.4±4.9, 51.9% girls) were included in the study. Overall Hp infection rate was 43.1% in IBD patients (39.3% in CD, 46.1% in UC) and 33.4% in the control group (p>0.05). Hp infection was not correlated with the activity of IBD (CD r²:-0.02 and UC r²:0.2, p>0.05). Fourteen (42.4%) patients with CD had gastric involvement and the rate of Hp infection was lower compared to the remaining 19 CD patients without gastric involvement (14.2% vs. 57.9%, respectively, p=0.01). While 21 UC patients (53.8%) had pancolitis, the remaining 18 patients (46.2%) had distal colitis, and the rate of Hp infection was higher in patients with pancolitis compared to the ones with distal colitis (52.3% vs. 38.8%, respectively, p>0.05).

Conclusion: The frequency of Hp infection was not different between IBD patients and the control group in this cohort. A much lower rate of Hp infection in CD patients with gastric involvement may suggest a lesser affinity of Hp for unhealthy gastric mucosa. The suggestion regarding protective role of Hp infection against IBD needs further investigation not only in children but also in countries with a higher endemicity.

Disclosure of Interest: None Declared
Objectives & Study: We reviewed our patient population on proton pump inhibitor (PPI) for > 6 months with an aim to characterize this patient population regarding potential risks of this class of medication.

Methods: We reviewed our electronic medical record to assess all patients < 21 years of age exposed to PPI for greater than 6 months seen by one of our 26 Pediatric Gastroenterology providers in the year 2012. We assessed common lab values believed to be related to adverse effects of (chronic) PPI use. Where possible, we report serum iron (Fe) levels, hematocrit (Hct), serum B₁₂ levels, serum Magnesium (Mg) levels, and serum creatinine (Cr) levels in this patient population. Based on our institution’s laboratory average normals for age, Fe deficiency was defined as Fe <50 mcg/dL, anemia was defined as Hct <34%, Hypomagnesemia as a Mg < 1.4 MEq/L and B₁₂ deficiency as a level <250 pg/ml.

Results: A total of 1434 patients on PPI for >6 months were seen by our group in 2012. Average length of exposure to PPI was 606 days (range of 180 – 2954 days). The average age at assessment was 10.4 years (range 6 months – 21 years). Sixty one per cent were female. Omeprazole was the preferred PPI - 63% were on omeprazole, 27% on lansoprazole, 5% on esomeprazole, 4% on pantoprazole, and less than 1% on rabeprazole and dexlansoprazole. Of this patient population, 774 (54%) had a Hct performed while on PPI and 109 were anemic (7.3%). Iron deficiency was noted in 31 patients (20%). A Cr was performed in 779 (54%) patients, and no one had an elevated Cr. A Mg level was measured in 291 (18%), and only 3 patients had low values. Vitamin B₁₂ was measured in 158 (11%) patients, and only 1 (0.6%) was low. The Hct, Fe, Cr, B₁₂, and Mg levels were not correlated with length of time exposed to PPI. We then examined the 446 patients of the cohort (31%) who had been exposed to PPI for a minimum of 2 years. The Hct was measured in 309 (70%) patients, and 46 (10%) were anemic. Serum Fe was measured in 114 (26%) patients, and 35 (8%) were deficient. The Vitamin B₁₂ and serum magnesium levels were measured in 81 (18%) and 125(28%) patients, respectively, and none were low. The serum Cr was assessed in 238 (53%) patients, and none had an elevated value. None of these parameters were correlated with the length of PPI exposure. The risk of anemia was no different than in American pediatric hospitalized patients ².

Conclusion: In our large cohort of patients exposed to PPI for > 6 months, we did not find an increased rate of anemia, B₁₂ deficiency, hypomagnesemia, Fe deficiency, or elevated Cr. Length of PPI exposure in this cohort did not increase the risk of abnormalities in the measured parameters.


Disclosure of Interest: None Declared
PITFALLS IN MONITORING GASTRO-ESOPHAGEAL REFLUX AND COUGH ASSOCIATION
Tsili Zangen 1,*, Dorit Ater 2, Shlomzion Frank 2, Arie Levine 1, Avigdor Mandelberg 2
1Paediatric Gastroenterology and Nutrition, 2Paediatric Pulmunology, Wolfson Medical Center, Holon, Israel

Objectives & Study: A main indication for reflux testing is to correlate reflux with cough. Gastro-esophageal reflux (GER) monitoring has greatly improved with the use of pH multi-channel intra-luminal impedance (pH-MII) but we still lack the possibility to measure cough and respiratory symptoms objectively. Parents' report of cough during reflux testing has a risk of missing events and a lag time between the event and its report. Furthermore, the sequence of events, reflux-cough or cough-reflux, is important to understand the patho-physiology and to optimize treatment. Our aim is to investigate the advantage of objective recording of cough over parents' report during GER monitoring.

Methods: We used simultaneous and synchronized recording of esophageal pH- MII and an external respiratory sounds monitor (RSM) that recorded the respiratory sounds using small flat microphones placed on the child's upper chest. The data was compared to the parents' reports. We studied 9 children with chronic cough who were referred for PH-MII evaluation. The respiratory sounds were analyzed one minute before and one minute after each GER episode.

Results: There were 205 GER episodes. The RSM recorded cough in 92 (45%) and parents reported cough in only 20 GER episodes (22%). The mean lag time between RSM recording of cough and the parental report was 47 seconds. In 10 out of the 20 (50%) cough events reported by the parents in proximity to GER the lag between the cough recorded by RSM and the parent’s report caused inversion of the sequence: the RSM recorded cough before the reflux and the parent's report shifted the cough after the reflux.

Conclusion: Parents missed many cough events, and the lag between the actual cough and the parents' report changed significantly the sequence of events. Objective simultaneous recording of cough and GER is mandatory for a better understanding of the GER-cough association and to identify the patients that will benefit from anti reflux treatment.

Disclosure of Interest: None Declared
Objectives & Study: Previously published studies have indicated that gastroesophageal reflux disease (GERD) is very common in patients with cystic fibrosis (CF), also in paediatric population. However, it hasn’t been well characterized so far. The aim of the study was to characterize gastroesophageal reflux episodes (GER) in children with cystic fibrosis.

Methods: This was a multicentre, prospective study of children with cystic fibrosis. All children underwent 24 hour multichannel intraluminal pH-impedance (MII-pH) monitoring. The characteristic of GER was made with BioVIEW analysis software and manual revision made by single investigator.

Results: 44 consecutive patients (22 boys, median age 10.33) were enrolled into the study. GERD was diagnosed in 26/44 (59.1%) patients. A total of 1585 reflux episodes were detected by MII-pH. 1199 (75.6%) of them were acid, 382 (24.1%) - weakly acid and 4 (0.3%) - weakly alkaline. 691 (43.6%) GER episodes reached the proximal oesophagus. In only 31.8% (14/44) patients typical GERD symptoms were present.

Conclusion: It was the largest study characterising reflux events in children with CF with a use of MII-pH published so far. The frequency of GERD in this population was very high, similar to previously raised. Acid GER were prevalent in children with CF. Number of proximal reflux events was relatively high which may indicate an increased risk for aspiration. In children with CF GERD should be diagnosed regardless of presence of its typical symptoms.

Disclosure of Interest: None Declared
**Gastroenterology**

**GERD, Peptic Disease and Helicobacter Pylori**

PO-G-0111

**COULD MORE ATOPY CORRESPOND TO MORE REFLUX?**

Marcella Pedullà 1,*, Vincenzo Fierro 1, Francesco Capuano 1, Ester Del Tufo 1, Valeria Papacciuoli 2, Salvatore Tolone 3, Carlo Tolone 1

1Department of Paediatrics, Second University of Naples, Naples, Italy, 2Department of Pathology, Federico II, Naples, Italy, 3Department of Surgery, Second University of Naples, Naples, Italy

**Objectives & Study:** Eosinophilic esophagitis (EoE) is an antigen-driven immunologic process that involves multiple pathogenic pathways, often related to IgE sensitization. Because it has been recently described that refractory gastroesophageal reflux disease can represent an initial stage of EoE, we have hypothesized that atopy could interfere also with gastroesophageal reflux (GER) and gastroesophageal reflux disease (GERD) expression in infants and children.

**Methods:** From January, 2011 to October 2013, 163 infants, children and adolescents referred to Day Hospital of Pediatric Department of SUN for GER or GERD symptoms were consecutively enrolled for the study. GER and GERD diagnosis and the selection of three aged based groups (Group I: 0-12 months, Group II: 13-144, Group III: >145) were assessed according to the NASPGHAN guidelines. Because a suspicion of EoE, 2 patients affected by refractory GERD were excluded by the study. In all the patients the diagnosis of atopy - based on clinical history - was confirmed by skin prick test (SPT) as well as by measuring serum total IgE (normal value from 0 to 12 months <21; from 12 to 24 months <41; from 25 to 60 months < 81 kU/l; from 61 to 156 months < 101 kU/l) (ImmunoCAP total IgE). A t-test was used to compare the difference between mean values and a c² test was used to analyze the difference between proportion. A p value < 0.05 was considered significant.

**Results:** The results were described in table.

<table>
<thead>
<tr>
<th>Group</th>
<th>GER Atopic</th>
<th>GER Not Atopic</th>
<th>GERD Atopic</th>
<th>GERD Not Atopic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group I: 0-12 months n.13</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GER atopic n.4</td>
<td>Age in months (mean±SD)</td>
<td>7±2.8*</td>
<td>9</td>
<td>8.14±2.6*</td>
</tr>
<tr>
<td>GER not atopic n.1</td>
<td>Gender Male %</td>
<td>50%*</td>
<td>100%</td>
<td>71%*</td>
</tr>
<tr>
<td>GERD atopic n.7</td>
<td>IgE tot (mean±SD)</td>
<td>28.3±8.52*</td>
<td>15.2</td>
<td>63.7±25.9*</td>
</tr>
<tr>
<td>GERD not atopic n.1</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p=0.71</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group II: 13-144 months n.141</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GER atopic n.28</td>
<td>Age in months (mean±SD)</td>
<td>53.35±32.99</td>
<td>41.7±27.4</td>
<td>58.12±29.23</td>
</tr>
<tr>
<td>GER not atopic n.23</td>
<td>Gender Male %</td>
<td>50%</td>
<td>48%</td>
<td>67%</td>
</tr>
<tr>
<td>GERD atopic n.58</td>
<td>IgE tot (mean±SD)</td>
<td>97.46±92.15*</td>
<td>10.9±10</td>
<td>225.3±307.8*</td>
</tr>
<tr>
<td>GERD not atopic n.32</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>p=0.26</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group III: &gt;145 months n.6</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>GER atopic n.0</td>
<td>Age in months (mean±SD)</td>
<td>/</td>
<td>/</td>
<td>155±7</td>
</tr>
<tr>
<td>GER not atopic n.0</td>
<td>Gender Male %</td>
<td>/</td>
<td>/</td>
<td>0</td>
</tr>
<tr>
<td>GERD atopic n.2</td>
<td>IgE tot (mean±SD)</td>
<td>/</td>
<td>/</td>
<td>123±31.8</td>
</tr>
<tr>
<td>GERD not atopic n.4</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

**Conclusion:** Nevertheless we didn’t releved significant difference of GER and GERD diagnosis frequencies between atopic and not atopic patients, noteworthy we found significant differences between the total serum IgE values in atopic GER vs atopic GERD both in infants and children groups. So that we hypothesized that in
atopic children IgE sensitization i.e. atopy could drive a common progressive inflammation from GER to GERD and EoE.

**Disclosure of Interest:** None Declared
ANTIBIOTIC SENSITIVITY IN HELICOBACTER PYLORI INFECTION: A RETROSPECTIVE STUDY IN A QUEBEC TERTIARY PAEDIATRIC CENTER
Jessica Ezri 1,*, Colette Deslandres 1
1Division of Paediatric Gastroenterology, Hôpital Sainte-Justine, Montreal, Canada

Objectives & Study: Helicobacter pylori infection is frequently acquired during childhood. Canadian and more recent ESPGHAN / NASPGHAN guidelines recommend mucosal biopsies with H. pylori culture and antibiotic sensitivity testing before undergoing first-line antibiotic therapy in children with suspected infection. The aim of the study was to review H. pylori antibiotic sensitivity in a tertiary pediatric center. To our knowledge, no data on H. pylori antibiotic sensitivity in children has been published in Quebec.

Methods: A retrospective study of all the patients who underwent antral biopsies for H. pylori culture and antibiotic sensitivity was conducted between April 2010 and April 2012. Antral samples were immediately carried to microbiology laboratory to proceed to bacterial culture. Sensitivity to usual antibiotics such as amoxicillin, clarithromycin, metronidazole and tetracyclines was tested in those samples positive for H. pylori. H. pylori culture and antibiotic sensitivity were not performed routinely even when H. pylori infection was highly suspected upon macroscopic examination.

Results: 1548 upper endoscopies were performed during the study period. 53 subjects (3.4%; 29 females; median age 13.5 years, range 1.7-18.7) had antral biopsies for H. pylori culture. Indications for H. pylori culture were nodular antritis (27) and/or gastric/bulbar ulcers or erosions (12) and/or nodular bulbitis (6); moderate-to-severe gastritis (5); persistent anemia (1) and no documented reason in 7 subjects. H. pylori culture was positive in 20 subjects (37.7%), including 17 with nodular antritis, one with bulbar ulcer, one with nodular bulbitis and one with severe gastritis. H. pylori bacteria were all sensitive to amoxicillin (100%) and tetracycline (100%). Twelve were sensitive to clarithromycin (60%) and 13 to metronidazole (65%).

Conclusion: Nodular antritis was associated with a greater proportion of positive Hp infection. Furthermore our results confirmed excellent sensitivity of H. pylori to amoxicillin and tetracyclines. Unfortunately tetracyclines are contraindicated below 12 years of age. Resistance of H. pylori to clarithromycin and metronidazole in children vary across the world. However we found a surprisingly high resistance rate to these two antibiotics compared to the data reported in the literature. A prospective study will be carried on in order to confirm our preliminary data as H. pylori culture and antibiotic sensitivity will optimize eradication of the bacteria.

Disclosure of Interest: None Declared
Objectives & Study: Wireless pH-monitoring provides a more accurate assessment as compared to conventional methods when diagnosing adults for gastroesophageal reflux (GERD). There are no studies on investigating children for 48 hours before and after medication with proton pump inhibitors and in terms of evaluating safety, tolerability and feasibility. The aim was to compile these outcomes from a single pediatric gastroenterology unit of diagnosing children for GERD.

Methods: A 48-hour pH monitoring were performed in 106 children (50 males, 56 females) at a median age of 11.5 (range 1.4-18.3) years using the BRAVO capsule wireless system. The capsule was inserted under general anesthesia during upper endoscopy. The guardians of the included children were asked to fill in a diary on symptoms, food intake and body position during the study period. On the second day of investigation they were to medicate with high dose proton pump inhibitors. The definition of GERD was based on a reflux index of >5% and DeMeester score >14.7, respectively.

Results: A total of 46 children had signs of esophagitis on endoscopy whereas 26 had histological features of esophagitis of whom 76 had agreeable findings in both (p=0.004). Application of the capsule was successful in 103 and interpretable in 99 of the children. Medical records on reflux index were available in 90 children at a median reflux index 4.7 (range 0.3-63.4) and median DeMeester score 17.6 (range 2.2-207.6) of whom 43/90 (47.8%) and 51/90 (56.7%) had GERD according to reflux index >5% and DeMeester score >14.7, respectively. After medication with proton pump inhibitor at mean dose 1.5 mg/kg (SD ±0.6 mg) on the second day of investigation, reflux index decreased to median 2.2% (0-58%) and DeMeester score to median 8.2 (0.3-178.6) respectively, p<0.0001. No severe adverse events was reported.

Conclusion: Using the wireless Bravo capsule system pH monitoring is both a safe and tolerable method and is recommended when investigating children for GERD. The use of proton pump inhibitors on the second day of assessment provides additional information on response to treatment suggesting the pH monitoring preferrably should be extended to 48 hours.

Disclosure of Interest: None Declared
Objectives & Study: The rate of Eosinophilic esophagitis (EoE) in children is increasing while the rate of Helicobacter pylori (Hp) infection has been decreasing in children living in the developed countries. EoE is closely related to allergy, while Hp infection is closely related to low socioeconomic status and poor hygienic conditions. Interestingly, in countries with poor hygienic conditions the rate of allergy is low (hygienic theory) while the rate of Hp infection is high. Thus, the opposite epidemiological data of both diseases may suggest a “protective” effect between them. Indeed, a negative association between esophageal eosinophilia and Hp infection was documented (Dellon ES. Gastro. 2011). The relationship between Hp infection and EoE disease has never been investigated in the pediatric population.

Objective: To investigate the relationship between Hp infection and EoE in children.

Methods: A retrospective analysis of all first diagnostic endoscopic procedure (2007-2012) performed in our gastroenterology clinic was reviewed. Chronological data and histologic diagnoses were collected. Biopsies from the esophagus and stomach (antrum, body) were available in all the charts irrespective of mucosal appearance. Hp diagnosis was determined by histology (H&E, Giemsa, CLO-test). EoE diagnosis was established after patients failed adequate PPI therapy and when high number of eosinophils (>15Eos/HPF) was documented at the distal/mid esophageal biopsy.

Results: A total of 966 charts were available for review. The mean age and M:F ratio was 11.3 y and 1:1.18, respectively. Esophagitis, idiopathic gastritis, EoE, and Hp infection was detected in 268 (28%), 480 (50%), 62 (6%), and 31 (3%) patients, respectively. The association between Hp infection and esophageal GER, gastritis, and EoE is described in the following Table.

<table>
<thead>
<tr>
<th>Count (%)</th>
<th>Hp infection and</th>
<th>EoE</th>
<th>Gastritis</th>
<th>GER</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (3%)</td>
<td>Fisher’s Exact Test p-value</td>
<td>0.716</td>
<td>&lt;0.0001</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>32 (100%)</td>
<td>Phi Coefficient (p-value)</td>
<td>-0.024 (0.461)</td>
<td>0.183 (&lt;0.0001)</td>
<td>0.294 (&lt;0.0001)</td>
</tr>
</tbody>
</table>

Conclusion: No significant association (Phi Coefficient) was noted between Hp infection and EoE disease (p= -0.024). Positive association was found between Hp infection and gastritis (p= 0.183) and between Hp infection and GER (p= 0.294). We hypothesize that the low rate of EoE and Hp infection in our population is responsible for the lack of association between both diseases.

Disclosure of Interest: None Declared
EFFECT OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY ON GASTROESOPHAGEAL REFLUX IN CHILDREN

Matjaž Homan 1,*, Rok Orel 1

1University Childrens Hospital, Ljubljana, Slovenia

Objectives & Study: The development or an increase of gastroesophageal reflux (GER) is considered to be one of the possible complications after percutaneous endoscopic gastrostomy (PEG). Only a few studies were performed to date to explore that issue and the conclusions were controversial.

Methods: In a prospective study we included 21 pediatric patients with feeding problems (median age, 5.5 years; range, 0.6-18 years; 57.1% male), most of them had cerebral palsy. Before, and 2-16 months after the insertion of PEG, continuous 24-hours pH monitoring (PH) or combined pH and multiple intraluminal impedance (PH/MII) was performed.

Results: The median acid exposure index (%) measured by pH monitoring was 3.87 before and 6.05 after PEG placement (not statistically significant). Median number of total refluxes, weakly acid refluxes and non acid refluxes in 24 hours pre and post PEG insertion were (35.43/ 64.5, 14.24/30.56, and 4.74/30.56, respectively). Although, all reflux parameters were higher after the procedure, the differences were not statistically significant. Interestingly, mean time needed for a bolus to be cleared from the esophagus decreased significantly after insertion of the PEG (P<0.05).

Conclusion: According to our results, GER probably increases and bolus clearens time decreases, after insertion of PEG. However, higher number of patients should be studied to confirm these assumptions as our results did not get statistical significance.

Disclosure of Interest: None Declared
DIFFERENT TYPES OF GASTRITIS AND THEIR EVOLUTION IN CHILDREN OVER THE LAST DECADE

Kinga Cristina Slavescu 1,*, Radu Razvan Slavescu 2, Costica Sarban 3, Alexandru Pirvan 1, Camelia Margescu 3, Dan Gheban 4, Nicolae Miu 1

1Second Pediatric Clinic, University of Medicine and Pharmacy “Iuliu Hatieganu”, Cluj-Napoca, Romania, 2Computer Science, Technical University of Cluj-Napoca, Cluj-Napoca, Romania, 3Second Pediatric Clinic, 4Department of Pathology, Children’s Hospital, Cluj-Napoca, Romania

Objectives & Study: In the last decades there was a change in the etiology of gastritis in the western world. In the early 1990s most cases of gastritis were attributed to H. pylori infection. More recently the number of H. pylori-negative chronic active gastritis and H. heilmannii infection has increased. Regarding reactive gastritis there are no studies that assess their prevalence within the gastritis and their evolution in the pediatric population. The aims of this study were to assess the prevalence of different types of gastritis (infectious, reactive or other types) in the studied group and their evolution during the study, their relevancy in each of the age groups. We also evaluated the histological parameters which influence the prognosis of various types of gastritis.

Methods: This study has been performed over a 13-year period, in the Second Pediatric Clinic in Cluj-Napoca, Romania, in children presenting with gastrointestinal symptoms or with malabsorption and those who have been known with hepatic or gastrointestinal diseases. A total of 3257 patients have been included (2058 females) with a median age of 13 (9-16) years.

Results: 2765 (84.89%) patients had characteristic changes for gastritis in the histopathological examinations. 173 children had macroscopic ulcerative lesions, 93 (53.76%) of them acute forms. Throughout the study, there was a decrease in the prevalence of H. pylori gastritis (r =-0.39, p=0.19) and an increase in the prevalence of reactive gastritis (r=0.71, p=0.006) and specific forms of gastritis (r=0.36, p=0.23). Regarding the infectious etiology there was a significant increase of H. heilmannii gastritis (r=0.75, p=0.003). During the study there was an increased rate of gastric (r=0.30, p=0.33) and duodenal ulcers (r=0.41, p=0.16). H. pylori gastritis (p=0.0003) and reactive gastritis (p=0.0043) were more frequent in spring-summer period compared to autumn-winter. 23.48% of reactive gastritis has been cured compared to 11.84% of H. pylori gastritis (OR=2.29, CI95%=1.21 to 4.31, p<0.05). 2.7 times more children were healed of those with no activity on the histopathological exam (CI95%=1.41 to 5.32, p=0.003).

Conclusion: During the study the prevalence of H. pylori gastritis decreases and the reactive and H. heilmannii gastritis increases. Related to age groups there was an increase of H. pylori gastritis with age and a decrease of reactive gastritis. Reactive gastritis has more favorable evolution compared with H. pylori gastritis. The absence of activity on the histopathological exam was associated with a positive evolution of gastritis.

Disclosure of Interest: None Declared
CHRONIC NONSPECIFIC DIARRHEA OF CHILDHOOD: DOES OLIGOFRUCTOSE AND INULINE COMBINATION REALLY WORK?

Cristina Becheanu 1,*, Iulia Tincu 1, Roxana Smadeanu 1, Ana Maria Bradeanu 1, Gabriela Lesanu 1
1Gastroenterology, “Grigore Alexandrescu” Emergency Children’s Hospital, Bucharest, Romania

Objectives & Study: Chronic nonspecific diarrhea is a common cause of persistent diarrhea in the first years of life. Its causes are not clear, and they might include mechanisms such as bowel motility disorders or dietary factors (low fat diet, osmotic fluids, very high fluid intake). If the symptoms are mild, no treatment is needed. Prebiotics might improve symptoms in these patients acting through gut microbiota. The aim of the study was to evaluate the number and severity of acute episodes of diarrhea in children with chronic nonspecific diarrhea who received a combination of oligofructose and inulin (Bifido Baby).

Methods: In a randomized, placebo control and parallel trial we included patients aged 1 to 5 years old, with at least 5 episodes of diarrhea in the last 6 months fulfilling the criteria of chronic nonspecific diarrhea. All subjects were randomized to receive a combination of oligofructose and inuline (Bifido Baby), 4 g/day, included in group A, or only dietary recommendations (according to actual guideline) for a 3 months period, included in group B. The number and duration of acute episodes were noted in 2 visits (at the end of the treatment and 3 months after).

Results: A total of 54 patients were initially included (n=31 group A, n=23 group B). After 6 months, 29 Bifido Baby patients and 20 controls completed the study. At the beginning of the study, all patients had similar characteristics regarding number of acute episodes of diarrhea and duration of the episodes as well, while after 3 months of treatment there was a significant improvement in the treatment group, as shown in the table below. The symptoms were substantially relieved for group A patients after another period of 3 months without treatment.

<table>
<thead>
<tr>
<th>Group A (N=29)</th>
<th>Group B (N=20)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>number of acute episodes (±SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit 1</td>
<td>5,2 (±2,1)</td>
<td>3,9 (±1,1)</td>
</tr>
<tr>
<td>Visit 2</td>
<td>1,17 (±1,2)</td>
<td>4,5 (±1,6)</td>
</tr>
<tr>
<td>Visit 3</td>
<td>0,58 (±0,7)</td>
<td>1,2 (±1)</td>
</tr>
<tr>
<td>duration of the acute episodes: days (±SD)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Visit 1</td>
<td>6,4 (±4)</td>
<td>4 (±1,1)</td>
</tr>
<tr>
<td>Visit 2</td>
<td>2,7 (±3,4)</td>
<td>8,9 (±2,9)</td>
</tr>
<tr>
<td>Visit 3</td>
<td>1,2 (±1,8)</td>
<td>3,6 (±4,8)</td>
</tr>
</tbody>
</table>

Conclusion: A combination of oligofructose and inuline (Bifido Baby) supplementation in patients with chronic nonspecific diarrhea is effective in reducing the discomfort associated with an increased number of daily stools and thus “it improves the quality of life”. Further studies need to be performed.

Disclosure of Interest: None Declared
GUT DIRECTED HYPNOTHERAPY IN CHILDREN WITH IRRITABLE BOWEL SYNDROME OR FUNCTIONAL ABDOMINAL PAIN: A RANDOMIZED CONTROLLED TRIAL ON SELF EXERCISES AT HOME USING CD VERSUS INDIVIDUAL THERAPY BY QUALIFIED THERAPISTS

Juliette Rutten 1, Arine Vlieger 2*, Carla Frankenhuis 1, Elvira K George 3, Michael Groeneweg 4, Obbe F Norbruis 5, Walthier Tjon a Ten 6, Herbert van Wering 7, Marc Benninga 1

1Paediatric Gastroenterology, Emma Children’s Hospital AMC, Amsterdam, Netherlands, 2Paediatrics, St Antonius Hospital, Nieuwegein, Netherlands, 3Paediatrics, MCA, Alkmaar, Netherlands, 4Paediatrics, Maasstadziekenhui, Rotterdam, Netherlands, 5Paediatrics, Isala Clinics, Zwolle, Netherlands, 6Paediatrics, Maxima Medical Center, Veldhoven, 7Paediatrics, Amphia Hospital, Breda, Netherlands

Objectives & Study: Gut-directed hypnotherapy (HT) has been shown to be effective in children with irritable bowel syndrome (IBS) and functional abdominal pain (syndrome) (FAP(S)). It is however unavailable to many children, because HT is costly, requires a significant parental time investment and there is a shortage in qualified therapists. We conducted a multi-center RCT comparing the effectiveness of individual hypnotherapy by a therapist to home-based treatment using an audio CD with standardized hypnotic exercises.

Methods: These preliminary analyses include 234 children aged 8-18 years with IBS or FAP(S). Children were randomized to individual HT (n=115) or home-based HT with a CD (n=119). Individual HT was given by 12 different qualified therapists and consisted of 6 sessions over a 3-month period. Children in the CD-group were instructed to listen to the hypnosis CD, containing the same exercises used in the individual sessions, at least 5 times a week for a 3-month period. Pain frequency (PFS) and pain intensity (PIS) were measured using standardized abdominal pain diaries at baseline and after treatment. Treatment success was defined as a reduction in both pain frequency and intensity of at least 50%. Additionally, adequate relief was reported by parents.

Results: PFS scores decreased significantly from 15.0 to 6.5 in the HT-group (p=0.00) and from 14.6 to 9.1 in the CD-group (p=0.00). PIS scores in the HT-group decreased from 15.1 to 6.9 (p=0.00) and from 14.7 to 9.5 in the CD-group (p=0.00). However, reduction in PFS and PIS scores was significantly greater in the HT-group (p=0.02; p=0.01) compared to the CD group. In the HT-group 51.4% was successfully treated versus 36.8% in the CD-group (p=0.03). There was a trend towards a higher percentage of adequate relief in the HT-group (82.1% vs. 71.3%: p=0.07).

Conclusion: These preliminary analyses show that short-term efficacy of gut-directed HT performed by different qualified therapists is superior to home-based treatment with a hypnosis CD with respect to pain frequency and intensity scores. Nevertheless, home-based treatment seems to be a valuable treatment option, given the high percentage of parents reporting adequate relief.

Disclosure of Interest: None Declared
**Objectives & Study:** Full term newborn are expected to have the ability to coordinate the sucking-swallow-breath process whereas preterm infants have uncoordinated swallowing prior to 34 weeks of postconceptional age. This study aimed to assess the coordination of S-S-B pattern of full term newborn infants on exclusive breastfeeding within the early post-natal period and compare with preterm infants at bottle-feeding by using a microphone through a cervical digital auscultation.

**Methods:** Thirty-two full term infants on exclusive breastfeeding and 32 preterm infants were assessed. All infants underwent digital cervical auscultation whilst being fed by using a microphone connected to the neck. Audiosignals were recorded. Mean values of 3 audiosignals recordings of 30s each were used for each infant. SSS was considered as either sucking or swallowing. The following variables were analyzed: total number of SSS in 30s; total duration of SSS in 30s; total number of respiratory pauses >2.5s in 30s; total duration of respiratory pauses >2.5s.

**Results:** Total duration of SSS was higher in preterm (19.38±4.30s) than full term infants (12.58±5.68s), p<0.001. Number of pauses in 30s was higher in full term (2.50±0.81) than preterm infants (1.96±0.83), p=0.01. Total duration of pauses was significantly higher in full term (17.41±5.68s) than preterm infants (10.23±4.20s), p<0.001.

**Conclusion:** Full term breastfed infants within the first days of life have prolonged respiratory pauses during the S-S-B process. This may reflect the development of the mature pattern of swallowing process with lifelong consequences.

**Disclosure of Interest:** None Declared
DO DISTINCT DYSPEPSIA SUBGROUPS EXIST IN CHILDREN?

Marina Russo 1,* Rossella Turco 1, Rosa Castiello 1, Marialuisa Andreozzi 1, Eleonora Giannetti 1, Annalisa Alessandrella 1, Erasmo Miele 1, Annamaria Staiano 1

1Translational Medical Sciences, Section of Paediatrics, University of Naples "Federico II", Naples, Italy

Objectives & Study: The heterogeneity of the dyspepsia symptom complex is well known. Several attempts to classify functional dyspepsia (FD) into subgroups have been proposed as a basis for diagnosis and therapy, but data are conflicting. The adult committee on Functional Gastrointestinal Disorders distinguish two different subgroups of symptoms: Post-prandial distress syndrome and Epigastric pain syndrome. There is no evidence in pediatrics on this distinction. Our study aimed to assess the prevalence in a pediatric population of these different subgroups.

Methods: Eighty-five pediatric patients (Median age: 10 years; range: 4 to 17 years; M/F: 38/47) with a diagnosis of FD were enrolled between April 2013 and November 2013. Diagnosis was based on Rome III criteria for children. After enrolment all patients completed a gastrointestinal symptoms questionnaire adapted from the adult Rome III criteria and a questionnaire measuring physical, mental and social aspects of quality of life. Severity and incidence of gastrointestinal symptoms were measured by Likert scale.

Results: Through the analysis of the filled questionnaires, two different symptomatic subgroups were identified. Fourteen out of 85 patients (16.5%) reported exclusive upper abdominal pain (Group1), while seventy-one out of 85 (83.5%) patients reported upper abdominal pain associated with early satiety and/or nausea (Group2). Prevalence of nausea was 55%. Symptoms such as alitosis, insomnia anxiety and headache were not associated with any of the two groups (p=0.1; p=0.5; p=0.4; p=0.5 respectively). Patients in Group 2 were significantly more often under anti-acid and anti-spastic therapies (p=0.07; p=0.05, respectively). Thirty-eight out of 85 (45%) patients met the criteria for abdominal migraine; the presence of nausea significantly correlated with abdominal migraine (p=0.0001). No associations with gender were found. Eighty-one out of 85 (96%) patients met criteria for anxiety disorders.

Conclusion: Two different dyspepsia subgroups were identified in our pediatric population, applying Adult Rome III criteria, suggesting that nausea and early satiety are highly prevalent symptoms in patients with upper abdominal pain. Considerations need to be made in order to redefine diagnostic criteria for pediatric dyspepsia.

Disclosure of Interest: None Declared
Objectives & Study: Esophageal food impaction (EFI) is present when a bolus of food becomes lodged in the esophagus. EFI in children is not generally associated with underlying esophageal anatomic abnormalities. To date, there has been little data published describing the etiology of EFI in children. Esophageal motility abnormalities, as measured by conventional manometry (CM), are non-specific in the majority of patients presenting with bolus impaction. The aims of the present study were: (i) to assess the esophageal patterns in patients by a topographic analysis of high-resolution manometry (HRM) data; and (ii) to establish a relationship between motility abnormalities and endoscopy findings both macroscopically and histologically.

Methods: All children that had undergone endoscopy for removal of a food bolus between September 2012 and September 2013 were evaluated in a prospective observational field study. Water perfused HRM system with 22 circumferential pressure sensors with an outer diameter of 4.2 cm was used to produce esophageal pressure topography plots. 12 patients fulfilled the inclusion criteria.

Results: Based on the reviewed Chicago classification of the 12 patients, 2 (17%) fulfilled the criteria for type 2 achalasia, 3 (25%) showed pan-esophageal pressurization, 3 (25%) showed compartmentalized pressurization and 4 (33%) showed peristaltic dysfunction. Patients with failed peristalsis or hypotensive peristalsis in ≥ 30% but <70% of test swallows were classified as mild peristaltic dysfunction whereas those with ≥ 70% of swallows with these patterns had severe peristaltic dysfunction. A macroscopically unremarkable upper gastrointestinal tract without any predisposing conditions for foreign body impaction was detected in 58% of the patients (7/12 patients). Endoscopic changes of the distal esophagus (erythema, friability, mucosal edema) suggestive of reflux esophagitis were seen in 3 patients (25%). One patient had typical macroscopic appearance of eosinophilic esophagitis in the mid esophagus, which include circular rings and linear furrows. Finally, in a 10-year old boy the endoscopic procedure revealed an esophageal stricture. Of 12 patients biopsied, one had esophageal stricture as the cause, three patients had EE identified histologically. In 4 patients (33%) the histologic findings were suggestive of reflux esophagitis whereas the biopsies were normal in 4 patients (33%).

Conclusion: The prevalence of EFI has increased over the last 15 years. Endoscopic, histologic and motility studies are needed to evaluate the etiology of food impaction. High-resolution manometry displayed as esophageal pressure topography is becoming a widely accepted technique for evaluating and categorizing esophageal motility disorders.

Disclosure of Interest: None Declared
DYSAUTONOMIA AND FOREGUT DYSMOTILITY IN THE JOINT HYPERMOBILITY SYNDROME

Protima Amon 1*, Rebecca Irvine 2, Patricia Taraborrelli 3, Phang Boon Lim 3, Nigel Meadows 1, Nelly Ninis 2, David Rawat 1

1 Paediatric Gastroenterology, The Royal London Hospital, London, United Kingdom, 2 Paediatrics, St Mary’s Hospital, 3 Imperial College Syncope Diagnostic Unit, Hammersmith Hospital, London, United Kingdom

Objectives & Study: The joint hypermobility syndrome (JHS) is a multi-system inherited connective tissue disorder. In addition to the skin and musculoskeletal manifestations, gastrointestinal (GI) symptoms and autonomic nervous system-related symptoms are commonly seen which can cause significant debilitating disease. Postural orthostatic tachycardia syndrome (POTS) is a form of dysautonomia which is well recognised to be associated with JHS in adults but there is very little data in children. POTS can be difficult to diagnose. A tilt table test is vital in the diagnosis of POTS, although all symptoms must be considered before a final diagnosis is made. The presentation may be so varied and subtle that clinicians often fail to recognize autonomic disturbance as an individual clinical entity within the disorder leading to inadequate management.

The purpose of this study was to investigate the presence of cardiovascular autonomic dysfunction in paediatric patients with JHS and describe the association with foregut symptoms.

Methods: We conducted a retrospective review of the medical notes and electronic patient records for all children diagnosed with JHS (Beighton score >4/9) referred to the syncope service based at Hammersmith Hospital. The study period was June 2011 to October 2013. Cardiovascular autonomic function was evaluated using the tilt table test.

Results: A total of 53 children were recruited with a median age range of 15.2 yrs (range 8.1yrs-18.7 yrs). The gender distribution was 28 females (53%) and 25 males (47%). All patients had autonomic nervous system-related symptoms including postural dizziness or syncope (53%), palpitations (40%), migraine (25%) and chest pain (19%).

<table>
<thead>
<tr>
<th>GI symptoms</th>
<th>Tilt test result</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nausea/Bloating</td>
<td>35 POTS</td>
</tr>
<tr>
<td>Reflux</td>
<td>28 POTS and vasovagal syncope</td>
</tr>
<tr>
<td>Abdominal pain</td>
<td>25 Vasovagal Syncope</td>
</tr>
<tr>
<td>Constipation</td>
<td>21 Test not completed/inconclusive</td>
</tr>
<tr>
<td>Diarrhoea</td>
<td>8 Normal</td>
</tr>
<tr>
<td>Feeding difficulties</td>
<td>8</td>
</tr>
<tr>
<td>No GI symptoms</td>
<td>5</td>
</tr>
</tbody>
</table>

Of the 53 JHS patients with autonomic symptoms, 48 (91%) patients had GI-related symptoms. 45 (85%) of these patients had confirmed cardiovascular autonomic dysfunction on tilt testing. All these patients also complained of foregut symptoms, predominantly nausea and bloating. Foregut dysfunction was a co-morbid presentation in all JHS patients with cardiovascular dysautonomia.
Conclusion: Children with JHS presenting with foregut symptoms are likely to have associated cardiovascular autonomic dysfunction. Recognition of these symptoms by paediatricians is important as formal evaluation and treatment of the dysautonomia may improve the quality of life for these patients. Further studies are required to evaluate the objective improvement of GI symptoms following treatment for dysautonomia.

Disclosure of Interest: None Declared
**Objectives & Study:** Functional constipation (FC) often begins in the first year of life. Complaints consist of infrequent, painful and hard defecation. Although standard definitions and criteria have been formulated to describe FC, these are not always used in research and clinical practice. Our primary aim is to systematically assess how definitions and outcome measures are defined in therapeutic randomized controlled trials (RCTs) of infants with FC.

**Methods:** We searched PubMed, EMBASE and Cochrane databases. Studies were included if (1) it was a (systematic review of) therapeutic RCT; (2) children <12 months old; (3) they had functional constipation; (4) a clear definition of constipation was provided; (5) were written in English.

**Results:** Out of 1155 articles, only 3 met our inclusion criteria. Two trials investigated new infant formulas and the third RCT evaluated the efficacy of Lactobacillus reuteri. After excluding duplicates (n=8), reasons for exclusion were a lack of relevance to our research question (n=1113), study design (n=11) and not fulfilling inclusion criteria (n=20). A total of 181 infants were included, of whom 53.8% were male, sample sizes ranged between 41-95 infants. Infants in 2 studies were treated in secondary and tertiary centers, in 1 study only in primary care. The 3 included RCTs used different definitions for infant constipation. Constipation was defined in the first study as having a stool frequency <1 per day. In the second trial as the presence of ≥ 1 of the following symptoms: frequency of defecation <3/week, painful defecation (crying) and abdominal/rectal palpable mass. The third RCT used the ROME III criteria for infant functional constipation. All three trials used frequency of defecation and stool consistency as primary outcome. 1 RCT used the absence of abdominal/rectal palpable mass and the absence of painful defecation, and one RCT the presence of inconsolable crying episodes as additional primary outcomes. Only in one study treatment success was defined, namely ≥ 3 defections per week.

**Conclusion:** Three different definitions for infant constipation were used in the 3 different trials, of which one used the current accepted Rome III criteria for infant constipation. Defecation frequency and stool consistency were used as primary outcome measures in the 3 included trials. There is a clear lack of well-designed clinical trials evaluating the efficacy of laxative treatment in infants with constipation. In order to make comparison between future trials possible, there is a need to come to consensus for (1) standard definitions, (2) standard core outcomes and (3) instruments to support core outcomes that are valid and reliable.

**Disclosure of Interest:** None Declared
THE OUTCOME AND COMPLICATIONS OF PERCUTANEOUS TRANSPYLORIC AND POSTPYLORIC FEEDING DEVICES

Eunice Goto¹,*, Mohith Shamdas², Grant Mallon¹, Grace Audu¹, Muhammad Choudhry³, Simon Clarke³, Jenny Epstein¹, John M Fell¹, Krishna Soondrum¹

¹Paediatric Gastroenterology, Chelsea and Westminster Hospital, London, United Kingdom, ²School of Medicine, Imperial College, ³Paediatric Surgery, Chelsea and Westminster Hospital, London, United Kingdom

Objectives & Study: Trans- and postpyloric tube feeding (TPF) is used in children unable to tolerate gastric feeding. Nasojejunal tubes can be used short term; more permanent devices are transgastric jejunal tubes (PEG-J) or a surgical jejunostomy. This study aimed to evaluate the outcome of children on TPF and assessing associated complications.

Methods: In this retrospective study we reviewed all patients who had a percutaneous device for TPF inserted in our tertiary GI unit in the time from December 2007 to November 2012. Demographics, underlying pathology and outcome data were obtained by reviewing the case notes. The outcome of TPF at one year was measured and when available further yearly outcomes documented.

Results: 40 children were identified (16 girls). 90% had faltering growth. The indication for TPF was: a) severe gastro-oesophageal reflux (GOR) with acid reflux time >12% +/- acute life threatening respiratory event (n = 5); b) foregut dysmotility with neurological and/or neuromuscular disorder (n = 22); c) foregut dysmotility post neonatal GI surgery (necrotising enterocolitis: n = 3, long gap oesophageal atresia: n = 3, tracheo-oesophageal fistula: n = 2, small bowel atresia: n = 2); d) GI dysmotility with underlying enteropathy (n = 3); e) delayed gastric emptying (n = 1).

17 patients had a surgical jejunostomy inserted, 23 had radiological placed PEG-J tubes through an existing gastrostomy. The median age at insertion 40.3 months (range: 3 months to 16 years).

Outcome: In the first year vomiting improved in 70%. 32 patients demonstrated weight gain (24 children reaching their expected weight for age). 10 patients were partially weaned TPF receiving a minimum of 20% of feeds orally or gastrically. One patient was weaned off TPF within a year, further 3 patients were weaned off within the second year (all had a jejunostomy). 3 patients had PEG-J converted to surgical jejunostomy. Seven children failed to respond and progressed to parental nutrition.

Complications: Skin infections and overgranulation was seen in 40%. 12 patients (6 PEGJ) had problems with tube migration, blockage or displacements with frequent tube reinsertions. Two patients had bowel perforation (surgical jejunostomy). One perioperative death (jejunostomy insertion) due to sepsis was noted. Four patients died in the second year due to their underlying comorbidity.

Conclusion: TPF is a well-established tool in the management of upper GI dysmotility but is not without complications. The majority of patients showed improvement of symptoms and demonstrated weight gain. Complications of TPF were skin infections, tube blockage and displacement. A high mortality rate (12.5%) in this study reflects the vulnerable nature of this population which has multiple co-morbidities

Disclosure of Interest: None Declared
DAO LOW LEVELS AND PAEDIATRIC GASTROINTESTINAL PATHOLOGY

Gemma Colomé Rivero 1,*, Ramon Tormo Carnicer 1, Antonio Rosell Camps 2, Hegoi Segurola Gurrutxaga 1, Gillermo Cárdenas Lagranja 1

1Paediatric Gastroenterology, Hospital Quirón, Barcelona, Spain, 2Paediatric Gastroenterology, Son Espases Hospital, Palma De Mallorca, Spain

Objectives & Study: Histamine intolerance (HI) is an underestimated gastroenterology pathology associated with predominant digestive complaints. HI is a pathology that occurs where there is an imbalance between excessive intake of histamine through food or a deficit in the degradation of this by detoxification systems in the intestine and liver; this resulting in an excess of histamine which may cause numerous symptoms, mimicking an allergic reaction. The goal of this study is to describe HI cases diagnosed in a paediatric gastroenterology unit during one year and to know the response to treatment.

Methods: Observational, retrospective study of patients under 15 years, diagnosed with HI during one year in our paediatric gastroenterology unit. Diagnosis of HI is performed by presentation of 2 or more characteristic digestive complaints (multiple secondary food vomiting, diarrhoea and/or abdominal pain) for more than 3 months, low diamino oxidase (DAO) serum activity and response to a low histamine diet with negative IgE-mediated food allergy tests.

Results: Thirty one patients fulfilled the diagnostic criteria. Mean age of symptoms onset was 6 years (6 months vs 13 years and 6 months) and mean age at diagnosis was 10 years and 1 month (17 months vs. 15 years). Predominant symptoms include diffuse abdominal pain (31/31), headache (16/31), intermittent vomiting (9/31). Growth rate was normal. In all cases IgA serum antitransglutaminase determinations were performed and were negative. The diagnosis was established by detecting DAO plasma levels, in 27 cases was less than 10 KU/l (normal value > 10kU/l) and disappearance of symptoms the first week of onset of diet low in histamine. In 4 cases DAO values were normal but responded well to diet.

Conclusion: Although HI is not a well known disease, paediatricians need to think about it in patients with gastroenterology symptoms typical of HI. Predominant complaints include diffuse abdominal pain, headache and chronic intermittent vomiting; also had extra intestinal symptoms, mainly headache (16/31).

Disclosure of Interest: None Declared
**Gastroenterology**

**GI Motility and Functional GI Disorders**

PO-G-0126

ARE FUNCTIONAL ABDOMINAL PAIN (SYNDROME) AND IRRITABLE BOWEL SYNDROME IN CHILDREN DIFFERENT CLINICAL ENTITIES? A COMPARISON OF PATIENT CHARACTERISTICS

Arine Vlieger 1,*, Juliette Rutten 2, Marc Benninga 2

1Paediatrics, St Antonius Hospital, Nieuwegein, Netherlands, 2Paediatric Gastroenterology, Emma Children’s Hospital AMC, Amsterdam, Netherlands

**Objectives & Study:** It has been suggested that different subcategories of childhood abdominal pain related functional gastrointestinal disorders (AP-FGIDs) in childhood are not separate clinical entities, but instead represent variable expressions of the same functional disorder. The aim of this study was to compare clinical and psychological characteristics of children with functional abdominal pain (FAP), functional abdominal pain syndrome (FAPS) and irritable bowel syndrome (IBS).

**Methods:** Two-hundred and sixty children, aged 8-18 years fulfilling Rome III criteria for FAP(S) or IBS were included in a randomized controlled trial evaluating the effect of hypnotherapy. At inclusion, questionnaires were used to assess demographics, clinical features, abdominal pain frequency and intensity, depression and anxiety, somatization, health related quality of life, pain beliefs and coping strategies.

**Results:** No differences were found between children with IBS and FAP(S) with respect to the main outcomes frequency and intensity of abdominal pain, symptoms of depression and anxiety, somatization, health related quality of life, pain beliefs and coping strategies. A significantly higher percentage of IBS-patients had a positive family history for abdominal pain related FGIDs (56.8% vs. 37.8%; p=0.00). Moreover, characteristics of patients with IBS subtypes did not differ. Patients with FAP or FAPS only differed with respect to problem focused coping strategy (2.21 ± 0.61 vs. 2.52 ±0.49; p=0.00)

**Conclusion:** Pediatric IBS and FAP(S) patients do not differ with respect to clinical and psychosocial characteristics. These results support the hypothesis that these different AP-FGIDs are not separate entities, but can be considered different expressions of one underlying functional disorder.

**Disclosure of Interest:** None Declared
INFLUENCE OF NEONATAL PERIOD ON FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS
Silvia Salvatore 1,*, Enzo Dattoli 2, Francesco Tandoi 3, Mariella Baldassarre 4, Fabio Meneghin 5, Dario Dilillo 5, Loredana Bellantuomo 6, Gian Vincenzo Zuccotti 5, Massimo Agosti 7
1Paediatrics, 2University of Insubria, 3Neonatal Unit, Ospedale "F. Del Ponte", Varese, 4Neonatology Unit, Università di Bari, Bari, Italy, 5Ospedale Sacco, Milano, Italy, 6Università di Bari, Bari, 7Ospedale "F. Del Ponte", Varese, Italy

Objectives & Study: Functional gastrointestinal disorders (FGIDs) are common in infants. Underlying mechanisms, risk and protective factors still need to be clarified. Objectives: To assess the influence of different neonatal factors on the incidence of FGIDS in the first months of life.

Methods: Preterm and at term babies born in 3 Italian hospitals (with Neonatal Intensive Care Units) were recruited. Exclusion criteria were represented by: malformations, (any kind of) surgery, neurological, immune, metabolic, cardiac or renal diseases. FGIDs were evaluated through a specific form according to Rome III criteria at 1,3,6,12 months. Gestational age, mode of delivery, feeding pattern, antibiotic administration in neonatal period, and duration of hospitalization at birth were considered. Review of hospital charts, out-patient clinic database and/or a standardized phone interview were also used for missing data.

Results: 450 infants have currently completed the follow-up. The incidence of FGIDs was significantly higher in preterm compared to at term newborns (85% vs. 48%, p<0.0001) with significant difference for regurgitation (44% vs. 20%), colic (58% vs. 29%), dyschezia (32% vs. 11%) and constipation (26% vs. 12%). Both preterm (68%) and at term (26%) newborns treated with antibiotics in the perinatal period showed a significant increased incidence of FGIDs compared to the ones not treated with antibiotics (90% vs. 73%, p=0.0008 and 67% vs. 48%, p=0.024, respectively). FGIDs were significantly more frequent in infants born by caesarean section compared to vaginal delivery (83% vs. 59%; p=0.0088; OR 1.66), formula fed compared to (exclusively) breast fed (75% vs. 63%; p=0.0018; OR=2.19), and with longer hospital staying at birth (p=0.001; OR 2.7).

Conclusion: FGIDs are common disorders at any age, including early infancy. Preterm delivery and neonatal use of antibiotic are significantly associated with an increased incidence of FGIDs in the first months of life. Caesarean section, formula feeding and longer hospital staying at birth are also more frequently reported in infants with FGIDs. To clarify the role of different factors during neonatal period may provide new insights in the pathogenesis of FGIDs and indicate possible protective strategies.

Disclosure of Interest: None Declared
Gastroenterology
GI Motility and Functional GI Disorders
PO-G-0128

GASTROINTESTINAL DISORDERS IN CHILDREN WITH AUTISM SPECTRUM DISORDERS
Luis Guerra 1, Elena Rubio 1, César Sánchez Sánchez 1,*; Guillermo Alvarez-Calatayud 1, Jimena Pérez Moreno 1, Mar Tolin 1, Blanca Hernandez-Macho 1, Caridad Benavides 2, Mara Parellada 2
1Paediatric Gastroenterology Unit, 2Department of Psychiatry, Hospital General Universitario Gregorio Marañón, Madrid, Spain

Objectives & Study: Gastrointestinal disorders and associated symptoms are common in patients with autism spectrum disorders (ASDs) although their prevalence is not well established. The aim of this study is to describe the frequency of gastrointestinal disorders in these patients.

Methods: Retrospective review of clinical records of patients with ASDs who were admitted in Paediatric Gastroenterology Service (PGES) from January 2005 to August 2013. We collected epidemiological variables represented by the median and average, and clinical variables represented by frequencies and percentages.

Results: There were 73 patients with ASDs attending to PGES. Of these, 72.6% were males. At first clinical assessment patients age ranged from 2 to 15 years old (median age 7 years old), weight-for-age z-score average was 0.88 and height-for-age z-score average was 0.79. We found that 63% of patients were under concomitant psychiatric medication (41% neuroleptics, 15.1% antiepileptics, 13.7% benzodiazepines). Common presenting complaints were constipation (21 patients; 30.15%), abdominal pain (28.8%) and diarrhea (16.4%). Other presenting complaints were food intolerance (12.3%) and behavioral changes or irritability (6.8%). Constipation (29 patients; 39.7%), abdominal pain (13.7%) and gastroesophageal reflux disease (GERD) (12.3%) were the most prevalent specific gastrointestinal disorders. Ten patients had some kind of food intolerance (13.7%), four of them were IgE-mediated food allergy and just one was coeliac disease (1.4%). We found 3 cases of obesity (4.1%) and 3 cases of mild malnutrition (4.1%). Five patients had encopresis (6.8%), four of them associated with constipation. Diet and lifestyle changes were recommended in 54.8% of patients. Laxatives were the most prescribed drugs (41.1%). Other medications prescribed were antimicrobials (21.9%) in parasitic disease and bacterial overgrowth syndrome and proton-pump inhibitors (19.2%) in GERD and gastritis. Of those patients with abdominal pain as presenting complaint, twelve of them (57.1%) had constipation as specific gastrointestinal disorder. Twenty of them (68.9%) were under concomitant psychiatric medication, fifteen received neuroleptics (51.7%).

Conclusion: Constipation and abdominal pain were the most common presenting complaints. Constipation was the most common specific gastrointestinal disorder. More than 50% of the patients with constipation were under concomitant psychiatric medication that can lead to or worsen this problem (with potential astringent effect). Just one patient had celiac disease.

Disclosure of Interest: None Declared
FUNCTIONAL GASTROINTESTINAL DISORDERS AND THE ASSOCIATION TO COELIAC DISEASE A POPULATION BASED SCREENING STUDY IN CHILDREN

Ola Olén 1, Olof Sandström 2, Anna Myléus 3, Anna Rosén 4, Annelie Carlsson 5, Lotta Högb erg 6, Hans Stenlund 3, Magnus Simrén 7, Anneli Ivarsson 3

1Department of Internal Medicine, Karolinska Institutet, Stockholm, Sweden, 2Department of Clinical Sciences, Paediatrics, 3Department of Public Health and Clinical Medicine, Epidemiology and Global Health, 4Department of Medical Biosciences, Medical and Clinical Genetics, Umeå University, Umeå, Sweden, 5Department of Clinical Sciences, Paediatrics, Lund University, Lund, 6Department of Clinical and Experimental Medicine, Paediatrics, Linköping University, Linköping, Sweden, 7Department of Internal Medicine & Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Gothenburg, Sweden

Objectives & Study: In adults, testing for celiac disease (CD) is recommended in subjects with symptoms compatible with a functional gastrointestinal disorder (FGID). There are few studies of CD prevalence in children with a suspected FGID, and evidence supporting CD testing in these children is lacking. We aimed to describe the prevalence of children meeting diagnostic criteria for FGIDs in Swedish 12-year olds and the association to undetected or previously detected CD.

Methods: A population-based sample of 5,424 Swedish 12-year-olds underwent serological CD screening with tissue-transglutaminase-IgA of whom 5,268 also answered the Rome III diagnostic questionnaire for FGIDs before knowledge of the screening results. Children with a positive serology underwent a duodenal biopsy to rule out or confirm the CD-diagnosis. Screening and diagnostic criteria for CD have been previously described (Ivarsson et al).

Results: The prevalence of the FGIDs evaluated in this study (irritable bowel syndrome (IBS), functional abdominal pain (FAP), functional dyspepsia (FD) and functional constipation (FC)) was 3% (n=133), 4% (n=218), 1% (n=57) and 3% (n=157), respectively. The prevalence of undetected CD or previously detected CD was 1.6% (n=89) and 0.6% (n=32), respectively, as previously reported (Ivarsson, et al). The prevalence of undetected CD was similar (p=0.98) in children without FGID (1.7%, n=82) as in those with FGID (1.6%, n=9) with the following pattern: IBS (1.7%, n=1), FAP (1.8%, n=4), FD (1.7%, n=2) and FC (1.3%, n=2). Previously detected (and treated) CD was equally common (p=0.98) in children without FGID (0.6%, n=29) as in children with FGID (0.5%, n=3) with the following pattern: IBS (1.5%, n=2), FAP (0.5%, n=1), FD (0%, n=0), FC (0%, n=0).

Conclusion: Children fulfilling the Rome III criteria for the FGIDs IBS, FAP, FD or FC did not have an increased risk of undetected CD. Also, children with treated CD did not have an increased risk of FGID symptoms.


Disclosure of Interest: None Declared
Efficacy of a Probiotic Mixture in the Treatment of Children with Chronic Abdominal Pain and Small Intestinal Bacterial Overgrowth; A Randomized Controlled Trial

Judith Korterink¹,*, Lize Ockeloen², Marc Benninga³, Judith Deckers-Kocken¹
¹Paediatrics, Jeroen Bosch Hospital, ’s Hertogenbosch, Netherlands, ²Paediatrics, Emma’s Children’s Hospital, Amsterdam, Netherlands, ³Paediatric Gastroenterology & Nutrition, Emma Children’s Hospital / Academic Medical Center, Amsterdam, Netherlands

Objectives & Study: It has been hypothesized that excessive coliform bacteria reside in the small bowel secondary to motility abnormalities in patients with functional gastrointestinal disorders (FGID), well recognized as small intestinal bacterial overgrowth (SIBO) (1). Modifying the intestinal microbiota with probiotics seems a potential treatment for SIBO and may lead to symptom improvement (2). Therefore the aim of this pilot study is to investigate the effect of a mixture of probiotics on chronic abdominal pain and SIBO compared to placebo.

Methods: Children aged 8-18 years with SIBO and abdominal pain-related FGID according to the ROME III criteria were enrolled. Patients with a positive glucose hydrogen breath test (GBT); i.e. a fasting breath hydrogen concentration > 20 ppm or an increase of H2 levels of > 12 ppm over the baseline value after ingestion of glucose, were diagnosed as SIBO. Abdominal pain intensity and frequency were measured at baseline using an abdominal pain dairy for four weeks. Patients were randomized in a double-blind fashion to receive a probiotic mixture (4 x 10⁹ cfu Bifidobacterium and Lactobacillus) or placebo for eight weeks. GBT and abdominal pain diary were repeated after the intervention.

Results: 152 children with abdominal pain-related FGID underwent a GBT, 20 children were diagnosed as having SIBO (13.2%). Therefore, only 15 children (out of the powered 70) were randomized. Children were aged 10-18 years (mean 13.9 yrs), nine received the probiotic mixture (60%), six children received placebo (40%). Two children of the probiotic group dropped out and one child of the placebo group. No significant differences were found between the probiotic and placebo group with respect to the improvement of the pain intensity score (p= 0.327, CI 95% -3.02-8.14), or the pain frequency score (p= 0.575, CI 95% 4.09-6.92). GBT normalized in 71.4% of the probiotic group and in 80% of the placebo group after treatment, p=1.000.

Conclusion: No significant effect in reducing abdominal pain in children with SIBO was seen after treatment with a probiotic mixture. However, this should be interpreted cautiously, because of the small sample size. Furthermore, the normalization of the GBT after placebo is remarkable. Additional investigations in order to establish the relation between GBT and SIBO in children with functional abdominal pain is warranted.

References:
¹Lin MD. Small Intestinal Bacterial Overgrowth A Framework for Understanding Irritable Bowel Syndrome. JAMA 2004;292(7)

Disclosure of Interest: J. Korterink Industry of: Winclove Probiotics Bio Industries BV, Amsterdam, the Netherlands and MCO Health BV, Almere, the Netherlands, L. Ockeloen: None Declared, M. Benninga: None Declared, J. Deckers-Kocken: None Declared
A COMPARISON OF POLYETHYLENE GLYCOL AT A DOSE OF 0.7 G/KG VERSUS 0.3 G/KG FOR THE MAINTENANCE TREATMENT OF FUNCTIONAL CONSTIPATION IN CHILDREN: A RANDOMIZED OPEN LABEL TRIAL

Piotr Dziechciarz 1,*, Andrea Horvath 1, Hania Szajewska 1

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

Objective & Study: Several randomized controlled trials have shown that polyethylene glycol (PEG) is superior to placebo, lactulose, and milk of magnesia for the treatment of functional constipation in children. However, there is a paucity of data regarding the most effective dose of PEG. The aim of this study was to evaluate the efficacy and safety of two different PEG doses for the maintenance treatment of functional constipation in children.

Methods: We conducted an open label, randomized controlled trial in which children with functional constipation diagnosed according to the Rome III criteria who were aged 1 to 18 years were randomly assigned to receive PEG 4000 at a dose of either 0.7 g/kg (high-dose group; n=45) or 0.3 g/kg (low-dose group; n=47) for 6 weeks. In the event of less than 3 bowel movements per week, the dose of PEG was increased and/or an additional laxative was administered. The primary outcome measure was therapeutic success, defined as ≥3 bowel movements per week with no fecal soiling during the last week of the intervention.

Results: Of the 92 children, 90 (98%), with a mean age of 3.7 ± 2.1 years, completed the study. The primary outcome measure (therapeutic success) was similar in the high-dose PEG group and the low-dose PEG group (43/44 vs. 41/46, respectively, relative risk, RR 1.10, 95% CI 0.98 to 1.22). However, in the high-dose PEG group compared with the low-dose PEG group, there was a reduced need for therapy adjustment (4/44 vs. 17/46, respectively, RR 0.25, 95% CI 0.09 to 0.67); a similar number of stools per week (6.5 ± 1.1 vs. 5.2 ± 1.5, respectively, mean difference, MD 1.3, 95% CI 0.8 to 1.8); a reduced number of patients with painful defecation (0/44 vs. 11/46, respectively, RR 0.05, 95% CI 0.0 to 0.75), and a similar number of patients with abdominal pain (44/46 vs. 11/46, RR 0.38, 95% CI 0.13 to 1.11). Both doses were well tolerated, and the risk of adverse events was similar in both groups (5/44 vs. 9/46, RR 0.58, 95% CI 0.2 to 1.6). Parental satisfaction with the treatment assessed using a 10-cm visual analog scale (VAS) was similar in both groups (9.4 ± 1.1 vs. 8.1 ± 1.9, MD 1.3, 95% CI 0.7 to 1.9).

Conclusion: Both doses of PEG were equally effective in the treatment of children with functional constipation. However, the use of low-dose PEG was associated with an increased need for additional therapy, which could have contributed to the treatment success in that group.

Disclosure of Interest: None Declared
**Gastroenterology**  
**GI Motility and Functional GI Disorders**  
PO-G-0132

**DIENTAMOEBA FRAGILIS AND ABDOMINAL PAIN-RELATED FUNCTIONAL GASTROINTESTINAL DISORDERS IN CHILDREN: A CASE-CONTROL STUDY**

Judith Korterink 1,* Marin de Jong 1, Marc Benninga 2, Mirrian Hilbink 3, Judith Deckers-Kocken 1

1Paediatrics, Jeroen Bosch Hospital, ’s Hertogenbosch, Netherlands, 2Paediatric Gastroenterology & Nutrition, Emma Children’s Hospital / Academic Medical Center, Amsterdam, Netherlands, 3Jeroen Bosch Academy, Jeroen Bosch Hospital, ’s Hertogenbosch, Netherlands

**Objectives & Study:** The role of *Dientamoeba* (*D.*) *fragilis* in functional gastrointestinal disorders (FGID) in children is not completely known. A possible role has been described for this protozoan in the aetiology of FGID (1-3). The aim of this study is to investigate the clinical relevance of *D. fragilis* in children with FGID.

**Methods:** From April 2011 until April 2013, a total of 132 patients, aged 8-18 years, with abdominal pain-related FGID according the ROME III criteria, referred to a non-academic hospital and 77 patients, aged 8-18 years, without gastro-intestinal symptoms referred to a psychiatric hospital, were included in the study. *D. fragilis* was diagnosed by real-time PCR in fecal samples. Clinical data were retrospectively analyzed by examining patients’ hospital records from the Jeroen Bosch Hospital and the psychiatric hospital Herlaarhof in The Netherlands.

**Results:** *D. fragilis* was detected in 57 patients with abdominal pain-related FGID (43.2%) and in 39 controls (50.6%) (p=.255). In the group of children with abdominal pain-related FGID, no significant differences in symptomatology were found between those with or without a *D. fragilis* infection, except for other functional complaints (i.e. headache, back pain or neck pain) and eosinophilia. Parasitological eradication was achieved in 61.7% of patients after treatment with Metronidazole or Clioquinol, while clinical improvement occurred in 40.4% of patients only. No association was found between clinical and microbiological response after treatment for *D. fragilis* (p=.435).

**Conclusion:** This retrospective case study showed that *D. fragilis* is very common in asymptomatic children and makes the potential etiological role for *D. fragilis* in children with abdominal pain-related FGID questionable.

**References:**


**Disclosure of Interest:** None Declared
Objectives & Study: European Clinical Practice Guidelines (CPG) for Acute Gastroenteritis (AGE) are poorly applied with an excess of unnecessary interventions. E-learning is a potentially ideal tool for CPG implementation due to its versatility and universal access. The project called TEEN-AGE(Train European Network on AGE) was specifically conducted to implement ESPGHAN/ESPID pediatric CPG for AGE through e-learning. TEEN-AGE aimed at assessing the impact on both knowledge and clinical practice of a 5-modules course on CPG for AGE loaded on United European Gastroenterology (UEG) website and freely accessible (http://www.e-learning.ueg.eu/courses/take-course.html?no_cache=1&st0%5Baction%5D=enrol&cprs%5Br%5D=18362).

Methods: Physicians from 11 European countries were invited to register in the course and personal data, pre-and post-course questionnaires and clinical data about 3 to 5 patients managed before and after the course were obtained. Adherence was measured by comparing medical interventions reported with those listed in CPG (adherence score of >90%).

Results: Fifty-nine physicians completed the course and enrolled a total of 545 children with AGE (281 before and 264 after the course). The course improved knowledge scores (pre-course 8.6±2.7 vs post-course 12.8±2.1 points, p<0.001), average adherence (87.0±7.7% to 90.6±7.1%, p=0.001) and the number of patients managed in full adherence (33.6±31.7% to 43.9±36.1%, p=0.037). A multilevel logistic regression analysis showed that bloody diarrhea [OR=5.75 (95%CI=1.39-23.89), p=0.016], abdominal pain [OR=1.88 (95%CI=1.1-3.24), p=0.02] and frequent vomiting [OR=4.07 (95%CI=1.39-11.89), p=0.01] were associated to non-adherence and this trend was reduced by e-learning. The course reduced inappropriate interventions in all the domains.

Conclusion: E-learning increases knowledge and improves clinical practice in pediatric AGE as judged by the increase of adherence to CPG and is an effective tool for CPG implementation.

Disclosure of Interest: None Declared
**Gastroenterology**

**GI-Infections**

**PO-G-0134**

**PREDICTIVE VALUE OF CERTAIN INFLAMMATORY MARKERS IN ROTAVIRUS ENTEROCOLITIS IN CHILDREN**

Luminita Dobrota 1, 2*, Mihai-Leonida Neamtu 1, 2

1Paediatric Clinic, 2CCMRP, Paediatric Clinic Hospital, Sibiu, Romania

**Objectives & Study:** Rotavirus enterocolitis is perhaps the most atypical intestinal infection in children. In a while is discussed about increased levels of serum transaminase and/or decreased levels of mean platelet value (MPV) related with rotavirus infection (RVI). Observed in due time, these analyses could reduce the incidence of nosocomial infection.

To demonstrate the predictive value of certain inflammatory markers in early etiologic suspected diagnosis of RVI.

**Methods:** Prospective study performed between January-September 2013 in hospitalized pediatric patients. Inclusion criteria were: at least one of the following signs/symptoms (fever, vomiting, loss of appetite, abdominal pain, dehydration), diarrhoea in the first 48 hours of admission. Exclusion criteria were: patients RV previus vaccinated, patients with blood, pus or mucus in stools.

All patients were assigned a severity grade of diarrhoea and were investigated in terms of transaminase, C-reactive protein, and platelet values. The rapid immunochromatographic test were performed in the first 48 hours of admission to confirm the diagnosis.

**Results:** The study group comprised 582 patients: 98 tested positive for rotavirus and 484 tested negative.

The RV positive group had the following features: mean age 10 months (range 1 month – 47 months), mean length of hospitalization 6 days, higher incidence (45 cases - 45.91 %) of atypical symptoms (fever and extradigestive signs – cough, edema); 7 cases presented adenovirus coinfection, 8 cases were considered nosocomial infection; 24 cases presented elevated levels of serum transaminase, 42 elevated C-reactive protein and 16 decreased levels of MPV. According with Vesikari score, 43 cases were mild infection, 45 moderate and 10 severe.

The results showed a very high significance between RV enterocolitis and elevated serum transaminase (p < 0.0002). At the age group 0-12 months, the inflammatory syndrome – RV enterocolitis association had a high statistical significance (p < 0.01), at the other age groups, the statistical significance (p < 0.05) was only for severe cases.

The adenovirus coinfection not altered the length of hospitalization (p < 0.82), the values of transaminase (p < 0.1) and MPV (p < 0.79).

**Conclusion:** The elevated serum transaminase and the inflammatory syndrome can guide a rapid suspicion of RV enterocolitis, even in the absence of typical symptoms.

**References:**

**Disclosure of Interest:** None Declared
**Objectives & Study:** Cryptosporidiosis is now recognized a major public health problem. It is usually characterized by acute symptoms of watery diarrhea and malabsorption accompanied by abdominal cramps, vomiting and loss of appetite. The aim of this study was to review notified human cryptosporidiosis cases in France between 2006 and 2012 with specific emphasis in the pediatric population, and to identify risk factors for human cryptosporidiosis infection.

**Methods:** The ANOFEL Cryptosporidium National Network which includes 39 hospital Parasitology laboratories was set up in France in 2004 upon request of health public authorities to provide them with information on the incidence and epidemiology of human cryptosporidiosis in France. Each member is committed to notify new cases of human cryptosporidiosis, collect stool samples for genotyping and related clinical/epidemiological data.

**Results:** From January 2006 to December 2012, a total of 669 cases of cryptosporidiosis were notified. No group cases were identified during this period in metropolitan France. Children were the second at-risk population (n = 145 cases with 23 cases in 2006, 18 in 2007, 14 in 2008, 36 in 2009, 20 in 2010, 17 in 2001 and 17 in 2012) after immunocompromised adult subjects. As previously reported, the highest rate (66.2%) was reported among young children (0-4 years).

In this population, a seasonal peak was observed in summer-autumn. In contrast to adult population, data analysis according to immune status showed that 73% of patients had no immune deficiency. The remaining patients were immunocompromised with transplantation and immune deficiency being the most prevalent causes of immunosuppression. Genotyping of isolates revealed a major proportion of *C. parvum* and *C. hominis* both in adult and pediatric patients but other zoonotic species such as *C. meleagridis* and *C. cuniculus* were also identified in the pediatric population.

**Conclusion:** These data confirm the relative high prevalence of cryptosporidiosis in young children, compared with adults. A specific attention should thus be paid in young children with acute symptoms of diarrhea, especially during the summer season when prevalence of enteric viral infection is low.

**Disclosure of Interest:** None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0136

INFLIXIMAB THERAPY IN CHILDREN WITH IBD: BETTER LONG TERM OUTCOMES WITH CONCURRENT IMMUNOSUPPRESSION

Juliana Cheng 1, Collin Barker 1, Kevan Jacobson 1,

1Paediatric Gastroenterology, Hepatology and Nutrition, British Columbia Children’s Hospital, Vancouver, Canada

**Objectives & Study:** infliximab (IFX) has been used in the treatment of pediatric IBD since 2000. However, few studies have reported long-term outcomes, and none have evaluated IFX monotherapy compared to concomitant therapy with IFX plus immunomodulator (IM: azathioprine, 6MP, or methotrexate) in this population. The aim of the study was to determine the 1-year outcome of IFX monotherapy compared to IFX + IM in children with IBD.

**Methods:** A retrospective chart review was undertaken on all children receiving IFX for IBD at British Columbia Children’s Hospital, Canada from January 2002 to July 2013. Continued response at 1-year (reduction in PCDAI score by at least 15 points from baseline) was evaluated using a multiple logistic regression model, adjusted for IBD type, age at induction, disease location, behaviour, and induction corticosteroids. Remission outcomes (PCDAI ≤ 10) were evaluated using a Kaplan-Meier curve. Poisson regression was used to model the association between IFX monotherapy and IFX + IM, and IFX failure rates over time, with the rate ratio being a measure of this association, adjusted for the above confounders.

**Results:** 181 children with IBD treated with IFX were identified. 148 patients met inclusion criteria (81 males; age at diagnosis/age at IFX start mean±SD: 11.92±3.03 and 14.08±2.57 respectively), 114 Crohn disease and 34 colitis (UC or IBD-U). Ongoing response at 1-year was strongly associated with concomitant therapy (OR=3.10, 95% CI 1.20-8.06, p<0.05). Forty-five patients failed IFX (15 primary non responders, 30 secondary loss of response) during a total of 258 patient-years follow-up, giving an incidence failure rate of 17 per 100 person-years. Long-term outcomes are depicted by the Kaplan-Meier curve (Figure 1). Significantly fewer IFX failures were evident in patients on concomitant therapy (RR=0.44, 95% CI 0.24-0.79, p<0.01). Only corticosteroid use at induction was a statistically significant predictor of IFX failure over time (RR=2.33, 95% CI 1.22-4.46, p=0.01).

**Image:**

![Kaplan-Meier Curve](image.png)

*Log-rank test: Chisq= 7.6 on 1 degrees of freedom, p=0.00593*
Conclusion: Concomitant therapy with IFX and IM in children with IBD provides superior one-year outcomes compared to IFX use alone. Ongoing post marketing studies are required and further research into long-term outcomes of children treated with IFX who receive corticosteroids at induction may be warranted.

**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0137

**CALCIUM-SENSING RECEPTOR AGONISTS ALTER GUT PERMEABILITY AND REDUCE DIARRHEA IN MODELS OF INDUCED COLITIS**

Sam Xianjun Cheng, Lieqi Tang, Yaima Lightfoot, Tao Yang, Mansour Mohamadzadeth

University of Florida, Gainesville, United States

**Objectives & Study:** Fluid movement in the gut is controlled by trans- and para-cellular processes; both contribute to diarrhea formation when disturbed. While bacterial and viral toxins cause diarrhea via the transcellular process, inflammation induces diarrhea primarily via alterations of the paracellular process. We have previously shown that extracellular calcium-sensing receptor (CaSR) agonists can reduce toxin-stimulated diarrhea by modulating the transcellular pathway (AJP’02; Gastroenterology’04; PNAS’06 & AJP’12). In this study, we examined if CaSR agonists can also close the paracellular pathway and reduce inflammatory diarrhea.

**Methods:** 4-6 wk-old Sprague-Dawley rats and C57BL/6 mice were employed and effects of CaSR on intestinal barrier function, innate and adaptive immune responses, inflammation & clinical diarrhea scores were examined, either at basal or under challenge of dextran sulfate sodium (DSS), a known inflammatory stressor. Whereas CaSR activation was achieved nutritionally by raising calcium, spermine or tryptophan in the diet (2.5 x RDA) or pharmacologically by daily gavaging Cinacalcet (3mg/kg), a specific CaSR agonist, its inactivation was accomplished genetically through the use of intestine-specific CaSR knockout.

**Results:** DSS induced breakdown of the epithelial barrier resulting in inflammatory diarrhea. Activation of CaSR either nutritionally by oral calcium, spermine or tryptophan or pharmacologically by cinacalcet rescued the intestinal integrity induced by DSS and attenuated diarrhea. Consistent with active control of epithelial barrier and gut inflammation by CaSR, genetic knockout of intestinal CaSR diminished the barrier function, altered microbiota balance, and skewed local and systemic innate and T cell immune responses from a status characterized by regulation to one that is highly stimulated. Following DSS challenge, CaSR-/mice had significantly more severe colitis and diarrhea than their wild type littermates.

**Conclusion:** We conclude that the CaSR plays a critical role in the regulation of gut homeostasis, the disruption of which results in pathogenic intestinal inflammation. Thus, the CaSR may serve as a potential therapeutic target for not only infectious diarrhea but also auto inflammatory diseases, including IBD.

**Disclosure of Interest:** None Declared
CROHN DISEASE LOCALIZATION DOES NOT CONTRIBUTE TO RESPONSE FOR INDUCTION THERAPY WITH INFlixIMAB IN CHILDREN

Maciej Dadalski 1,*, Agnieszka Wegner 2, Jaroslaw Kierkus 1
1Gastroenterology, Hepatology and Feeding Disorders, Children’s Memorial Health Institute, Warsaw, Poland. 2Gastroenterology, Hepatology and Feeding Disorders, Children’s Memorial Health Institution, Warsaw, Poland

Objectives & 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 ileal or colonic localization can contribute response for biological therapy. The aim of the study was to explore the contribution of CD gut localization to response for induction therapy with infliximab in children.

Methods: 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 in each ileocolonic segment were used as five 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 0,91 and specificity 0,08.

Conclusion: Crohn Disease localization does not contribute to response for induction therapy with infliximab in children.

Disclosure of Interest: None Declared
STUDY OF ABNORMAL LIVER FUNCTION TESTS AT DIAGNOSIS OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE (pIBD) IN A LARGE COHORT IN SOUTHERN ENGLAND

Cathelijne Van Der Feen 1,*, Emma Grainger-Allen 1, James Ashton 1, Vanessa Hewertson 1, Akshay Batra 1, Robert Mark Beattie 1, Mark Wright 2, Sanjay Bansal 3, Nadeem A Afzal 1
1Paediatrics, 2Hepatology, University Hospital Southampton, Southampton, United Kingdom,
3Paediatric Hepatology, King's College Hospital, London, United Kingdom

Objectives & Study: To study the proportion of children with abnormal liver function tests at diagnosis of pIBD in a large consecutive cohort from the South Coast of England (Wessex region). Secondary aims are to assess the clinical outcome particularly from development of autoimmune liver disease point of view.

Methods: A full review of the prospectively maintained pIBD database in University Hospital Southampton was conducted. This is a database of a consecutive cohort of children diagnosed with IBD between January 2002 and September 2013. Details of clinical presentation and blood results at diagnosis were recorded in all and those with abnormal liver function tests (ALT, Bilirubin, Albumin and GGT) at presentation were identified. The individual records of these children were further reviewed for biochemical and disease outcome.

Results: 504 patients were identified with a new diagnosis of pIBD (Mean±SD age at diagnosis was 12.5±3.0 yrs); 313 patients were diagnosed with Crohn’s disease (CD), 137 patients with Ulcerative colitis (UC) and 54 with IBDU.

At presentation liver enzyme tests were abnormal in 6.9% of all patients (n=35). 11.7% of the children with UC (16/137) had abnormal LFT’s compared to 5.1% of the children with Crohn’s disease (16/313) at diagnosis. Children with abnormal liver tests were more likely to have UC than CD (OR 2.46 [95%CI 1.19–5.07; p=0.013]). See table.

Spontaneous normalisation of liver tests occurred in 40% of patients within 3 months of diagnosis, a further 9% by 6 months and 54% by 12 months (Mean follow up 28.8 months ± 6.02). Liver disease was diagnosed in 11 (out of 35) with abnormal LFTs (31%) with imaging and/or biopsy; 9 with autoimmune sclerosing cholangitis (AISC), 1 autoimmune hepatitis (AIH) and 1 patient was diagnosed with nonalcoholic steatohepatitis(NASH). A further 5 children who were clinically well followed showed a self-remitting course without any serologic evidence of autoimmunity.

<table>
<thead>
<tr>
<th>Outcome at follow up (N=35)</th>
<th>Crohn’s disease</th>
<th>Ulcerative colitis</th>
<th>IBDU</th>
</tr>
</thead>
<tbody>
<tr>
<td>pIBD recruited in study</td>
<td>313</td>
<td>137</td>
<td>54</td>
</tr>
<tr>
<td>Abn LFT’s at Dx</td>
<td>16 (5.1%)</td>
<td>16 (11.7%)</td>
<td>3(5.6%)</td>
</tr>
<tr>
<td>Normalised</td>
<td>8</td>
<td>8</td>
<td>3</td>
</tr>
<tr>
<td>AISC</td>
<td>4</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>AIH</td>
<td></td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>NASH</td>
<td>1</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Undx/nonspecific</td>
<td>3</td>
<td>2</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: This is the largest study to date of the assessment of abnormal liver function in a large cohort of children diagnosed with pIBD. Abnormal liver function tests at diagnosis are more common in children with UC which resolve in more than 50% of patients. About one third of patients progress to develop autoimmune liver disease.

Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0140

**FECAL CALPROTECTIN IS A GOOD BIOMARKER OF MUCOSAL HEALING IN MONITORING OF CHILDREN WITH IBD**

Michał Szczepanski¹, Maciej Dadalski¹, Jarosław Kierkus¹

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

**Objectives & Study:** Fecal calprotectin concentrations of patients with inflammatory bowel diseases (IBD) are much higher than those of healthy controls or patients with functional disorders or other gastrointestinal diseases. Thus fecal calprotectin is a good biomarker of gut inflammation in differential diagnosis of IBD as well as mucosal healing in monitoring of IBD in adults. There is shortage of data concerning predictive value of fecal calprotectin in mucosa status assessment in children with IBD. The aim of the study was to assess the usefulness of fecal calprotectin as a biomarker of endoscopy proven mucosal healing in monitoring of children with IBD.

**Methods:** 46 patients (25M, 21F; aged 13.7±3.8) with IBD (24 ulcerative colitis (UC) and 22 Crohn’s disease (CD)) were involved to the study and had elective colonoscopy performed and fecal calprotectin within a week before endoscopy measured. Mucosa status during endoscopy were assessed with SES-CD in case of CD and with Baron score in case of UC. Full mucosal healing was defined as SES-CD=0 or Baron score=0. The ROC curves was used as a statistical method to establish cut off points and AUC (area under curve) was regarded as assessment of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation present.

**Results:** The AUC was 0.95. The optimal cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation present was 233ug/g with sensitivity 1 and specificity 0.79. When specificity was outweighed over sensitivity the cut-off point was 54ug/g with sensitivity 0.77 and specificity 0.97.

**Conclusion:** Fecal calprotectin is a good biomarker of mucosal healing in monitoring of children with IBD. Values below 54ug/g enable to select 77% patients with full mucosal healing.

**Disclosure of Interest:** None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

**PO-G-0141**

**PREVALENCE AND COURSE OF ANEMIA IN PAEDIATRIC IBD PATIENTS DATA OF THE GERMAN-AUSTRIAN REGISTRY CEDATA-GPGE**

Jan Laffolie ¹, Martin Laass ², Claudia Wendt ¹, Dietmar Scholz ¹, Stephan Buderus ³, Klaus-Peter Zimmer ¹ and CEDATA-GPGE Study Group

¹General Paediatrics and Neonatology, University Giessen, Giessen, Germany ²Paediatric Gastroenterology, University Dresden, Dresden Germany, ³Paediatric Gastroenterology, Marien Hospital, Bonn, Germany

**Objectives & Study:** Anemia is one of the most common extraintestinal manifestations in inflammatory bowel disease (IBD) and may negatively impact quality of life. In the present study we analysed data from the pediatric IBD registry “CEDATA-GPGE” of Germany and Austria to determine prevalence, risk factors and course of anemia in a large cohort with pediatric IBD.

**Methods:** Data from pediatric patients from 90 centers - registered in CEDATA-GPGE between 2004 and 2010 - was analyzed for the time at disease manifestation and after one, two, three, four and five years. Anemia was defined using age-adjusted values (haemoglobin, hematocrit, mean corpuscular volume) from the German KiGGS study. Patient self-assessment was quantified on a Likert scale from 1 to 5 (1=very good, 5=very bad). Disease activity was measured by physicians general assessment on a 4 point scale (1=remission, 4=severe activity) and by Pediatric Crohn’s Disease Activity Index (PCDAI) or Pediatric Ulcerative Colitis Activity Index (PUCAI). Testing was performed using t-test or Mann-Whitney U test.

**Results:** 3554 patients (age 0–18 years) with Crohn’s disease (CD), ulcerative colitis (UC) and IBD unclassified (IBD-U) were registered in CEDATA-GPGE. 3303 patients (2020 CD, 1061 UC, 222 IBD-U) with at least one follow-up visit were regarded as confirmed IBD and included in the final analysis. Of these patients 1925 (58.3%) had an anemia - most common microcytotic. Anemia was more frequent in CD (60.6%) than in UC (54.5%) and in IBD-U (55.4%). Iron therapy (oral or intravenous) was prescribed for 765/1925 (39.7%) of anemic patients. Anemic CD patients (mean±standard deviation; 2.9±0.9 vs. 2.4±0.9; p<0.0001, t-test) and anemic UC patients (2.8±0.9 vs. 2.2±0.9; p<0.0001) showed significantly worse self-assessment than non-anemic patients. Physician’s assessment was significantly worse in anemic vs. non-anemic patients in all three diseases. PCDAI in CD (25.9±14 vs. 18.1±12.0; p<0.0001) and PUCAI in UC (34.4±25.0 vs. 16.8±19.9; p<0.0001) were significantly higher in anemic than in non-anemic patients. Younger age was associated with more severe anemia.

**Conclusion:** Almost two thirds of all CEDATA-GPGE registered pediatric IBD patients were anemic at the time of disease manifestation but only 39.7% of anemic patients received iron therapy. Patients with severe disease are more likely to present with anemia. Pediatric gastroenterologists should be aware of this problem and iron supplementation should strongly be considered for the therapeutic regime. Further longitudinal analyses are needed to show if we treat our patients properly and inflammation as well as anemia improves in the long term.

**Disclosure of Interest:** None Declared
THE TYROSINE PHOSPHATASE SHP-2 PROTECTS AGAINST INTESTINAL INFLAMMATION

Corentin Babakissa 1,*, Genevieve Coulombe 2, Ariane Langlois 2, Nathalie Rivard 2

1Paediatrics, University of Sherbrooke, Sherbrooke, Canada, 2Anatomy and Cell Biology, University of Sherbrooke, Sherbrooke, Canada

Objectives & Study: SHP-2 (Src homology-2 domain containing protein tyrosine phosphatase-2) is a tyrosine phosphatase associated with human diseases such as the Noonan syndrome and various cancers. Recently, polymorphisms in the PTPN11 gene coding for SHP-2 have been found in patients with ulcerative colitis. Even though SHP-2 is highly expressed in intestinal epithelial cells (IECs), its role has never been characterized.

Methods: Mice with an intestinal epithelial cell-specific deletion of SHP-2 were generated (SHP-2IEC-KO mice). Western blots and qRT-PCR analyses were performed with murine intestinal mucosal enrichments. Tissue architecture was observed by hematoxylin-eosin staining. Cytokines and chemokines were quantified using an antibody array. SHP-2 localization was analyzed by immunohistochemistry in Children with inflammatory bowel disease.

Results: 1- Western blots confirmed the loss of SHP-2 expression in the intestinal epithelium of mutant mice (n=100). 2- SHP-2IEC-KO mice rapidly showed growth retardation compared to control littermates. 3- Notably, one month-old mutants exhibited severe colitis with diarrhea, anal bleeding and blood in stool. Colon architecture was markedly altered with infiltration of immune cells, longer colonic crypts and presence of crypt abscesses with neutrophil accumulation. 4- Levels of immune response modulators were significantly increased in SHP-2IEC-KO mice (CXCL1, CXCL5, CCL5 and CCL11). 5- Preliminary data showed that SHP-2 expression was reduced in intestinal biopsy from children with inflammatory bowel disease (n=3).

Conclusion: These results indicate that, in the absence of epithelial SHP-2 expression, mice spontaneously develop colitis. Also, decreased SHP-2 expression is noticed in children with inflammatory bowel disease. Thus, our results suggest that SHP-2 protects intestinal epithelial cells against the development of inflammation.

Disclosure of Interest: None Declared
THE FIRST SUCCESSFUL FECAL TRANSPLANTATION IN A ONE-YEAR-OLD GIRL WITH EARLY ONSET COLITIS

Yvan Vandenplas 1,*, Gigi Veereman 1, JN Samsom 2, JC Escher 2
1Paediatrics, UZ BRUSSEL, Brussels, Belgium, 2Laboratory of Paediatrics, Division Gastroenterology and Nutrition, Sophia Children’s Hospital-Erasmus Medical Center, Rotterdam, Netherlands

Objectives & Study: An 10 monhs old girl presented with an early onset colitits (“ulcerative colitis like”), which did not improve with classic therapy (mesalazine, azathioprine, prednisolone, infliximab). She had an adverse reaction to rapamune. Several probiotics, including VSL-3, proved unsuccessful. An adverse reaction to rapamune made further administration impossible. Intravenous large spectrum antibiotics and total parental nutrition were administered for severe flares.

Methods: Because of LB’s young age at onset, an immunodeficiency was suspected. A thorough and complete work-up could not show a deficiency.

Results: The first fecal microbiota transplantation was attempted at the age of 18 months. The first four fecal transplantations, with fresh stools from an age-related niece, led to a transitory improvement and normal stools for seven to 14 days. The last three fecal transplants were with fresh stools from the patient’s older brother. Interestingly, LB tolerated the fecal transplants from the niece well, but reacted to the fecal transplant from the brother with profuse sweating, vomiting, paleness, tachycardia (blood pressure remained at 70/40) and transitory fever. She recovered spontaneously within one hour; no active intervention was needed. Normalization of the stools lasted for one month. After the third fecal transplantation with the stools of her brother, she remained asymptomatic. Six months later LB still had normal stools and all medication had been discontinued. A colonoscopy performed six months after the last transplant, showed no lesions and normal histology, consistent with a resting phase of inactive UC.

Conclusion: To the best of our knowledge, this is the first report of a successful fecal transplant in a child with early onset colitis. Our findings suggest that alternate donors may be indicated if results are unsatisfactory. Any decision should consider whether fecal transplant is a better option than continuing an ineffective treatment strategy that might be detrimental to the patient. Careful monitoring is warranted in these patients.

Disclosure of Interest: None Declared
LOOKING BEYOND MUCOSA: EFFECT OF BIOLOGIC THERAPY ON TRANSMURAL HEALING EVALUATED BY ULTRASONOGRAPHY IN PAEDIATRIC CROHN'S DISEASE

Fortunata Civitelli 1,*  Manuel Murciano 1, Federica Nuti 1, Salvatore Oliva 1, Giovanni Di Nardo 1, Lorena Messina 1, Marina Aloi 1, Franca Viola 1, Salvatore Cucchiara 1

1 Paediatric Gastroenterology and Liver Unit, Sapienza University, Rome, Italy

Objectives & Study: Therapeutic goals for Crohn’s disease (CD) have evolved from a mere control of symptoms to the concept of deep remission (DR), including clinical and biomarker remission and mucosal healing (MH). Biologic therapy with anti-TNFα is effective in achieving MH. Yet, CD is a transmural disease, characterized by a progressive bowel damage leading to complications. This is the first pediatric study prospectively evaluating the efficacy of anti-TNF therapy in inducing clinical remission, MH and TH in CD.

Methods: Pediatric CD patients (pts) starting biological therapy with Infliximab or Adalimumab were prospectively enrolled. All pts were naïve to biologics. Clinical activity (Pediatric Crohn’s Disease Activity Index, PCDAI), laboratory tests (CRP, ESR), endoscopic activity (simple endoscopic score, SES-CD) and transmural disease assessed by small intestine contrast ultrasonography (SICUS) were evaluated before starting (T0) and after 9-12 months of therapy (T1). Complete MH was defined as a SES-CD of 0-1, partial MH as 50% decrease vs T0. At US the evaluated parameters were: extension of disease(cm), bowel wall thickness >3 mm(BWT), BW vascularity (BWV), stratification of the BW (BWS), presence of stricture, fistulae and abscess. Wilcoxon signed rank test was used for pair comparison (T1–T0).

Results: 26 pts (mean age 13.3 ± 4.2 males) were included. The mean PCDAI, SES-CD, CRP, ESR, BWT and disease extension values significantly decreased at T1 (table). Increased BWV was present in 80% of pts at T0 and in 24% at T1 (p<0.0001). In pts with complete and partial MH the extension of disease and the mean BWT at US were significantly reduced at T1 (p<0.02); in pts without endoscopic response the US parameters didn’t change significantly, despite clinical response. Presence of strictures and stratified aspect of the BW didn’t modify during therapy in any group.

<table>
<thead>
<tr>
<th></th>
<th>T0</th>
<th>T1</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>PCDAI</td>
<td>33.7 ± 18.2</td>
<td>13.1 ± 12.8</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>SES-CD</td>
<td>15.8 ± 8.1</td>
<td>6.1 ± 6.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>CRP (µg/l)</td>
<td>30609 ± 24539</td>
<td>8744 ± 16330</td>
<td>≤0.001</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>69 ± 35</td>
<td>35 ± 26</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>BWT (mm)</td>
<td>5.9 ± 1.6</td>
<td>4.3 ± 1.7</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Extension of ileal disease (cm)</td>
<td>15.6 ± 6</td>
<td>9.08 ± 5.7</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Conclusion: Biologics are effective in inducing clinical and laboratory remission and in achieving MH in pediatric CD. Transmural inflammation significantly improves during therapy, however when a substantial bowel damage (stricture) is present, the effect on TH might be poorer. Further studies are needed to evaluate the impact of TH on the long term outcome of CD.

Disclosure of Interest: None Declared
DOES INFLAMMATORY BOWEL DISEASE (UNCLASSIFIED) EVOLVE INTO CROHNS DISEASE OR ULCERATIVE COLITIS?

Siba Prosad Paul 1,*, Christine Spray 1, Dharamveer Basude 1, Sarah Sandmann 1, Pramila Ramani 1, Bhupinder Kaur Sandhu 1

1Paediatric Gastroenterology, Bristol Royal Hospital for Children, Bristol, United Kingdom

Objectives & Study: In 5–15% of children diagnosed with inflammatory bowel disease (IBD), the histological picture at diagnosis doesn’t fit in with either ulcerative colitis (UC) or Crohn’s disease (CD) and is classified as unclassified-IBD (IBDU) or indeterminate colitis 1. The aim of this prospective study is to determine whether IBDU evolves into UC or CD.

Methods: Prospective data has been collected on all the newly diagnosed children with IBD at the only regional paediatric gastroenterology centre covering southwest of England. All patients suspected of IBD had upper and lower gastrointestinal endoscopy and MRE scan or barium meal as recommended by BSPGHAN 2. Patients diagnosed with IBDU during 2004–2011 were included in the study and followed up for a minimum of 2 years (range 2–9 years). The patient notes were reviewed in 2013 and any changes in diagnosis recorded.

Results: 333 children were diagnosed with IBD between 2004–2011: 193 (58%) had CD, 115 (34.5%) UC and 25 (7.5%) IBDU. Age (mean) at diagnosis: 10.2 years (IBDU), 11.5 years (CD) and 11.6 years (UC). 7/26 (27%) IBDU had pan-colitis and 19/26 (63%) had patchy or left-sided colitis on lower gastrointestinal endoscopy. After 2 to 9 years, IBDU evolved into CD in 5 patients (22.8%), UC in 3 (13.6%) and remained IBDU in 14 patients (63.6%). Latest data was unavailable for 3 (11.6%) because of transfer to distant adult services. ANCA was positive in 3 out of 4 patients whose diagnosis was revised as CD.

Conclusion: This large prospective study has documented that over 2–9 years, 22.8% IBDU evolved into CD, 13.6% into UC and 63.6% remained IBDU. IBDU patients tended to be younger at diagnosis. Positive ANCA was not an useful predictive marker. This has implications for management of IBDU patients especially where surgical treatment is considered.

References: 1.


2.


Disclosure of Interest: None Declared
INFLIXIMAB THERAPY IN PAEDIATRIC CROHN’S DISEASE: RESULTS FROM DEVELOP, A MULTICENTER PROSPECTIVE INFLAMMATORY BOWEL DISEASE REGISTRY


1Cedars-Sinai Med Cntr, Los Angeles, United States, 2Sapienza U Rome, Rome, Italy, 3Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands, 4Mayo Clinic, Rochester, United States, 5Chelsea & Westminster Hospital, London, United Kingdom, 6Children's Cntr Digestive Healthcare Paediatric Gastro, Atlanta, United States, 7Hosp Sick Children, Toronto, Canada, 8Connecticut Children's Med Cntr, Hartford, United States, 9Ludwig Maximilians University , Munich, Germany, 10Emory U Sch of Med, Atlanta, United States, 11KCE-Belgian Health Care Knowledge Cntr, Brussels, Belgium, 12MassGeneral Hosp for Children, Boston, 13U Vermont, Burlington, 14Children's Hosp Philadelphia, Philadelphia, United States, 15Hopital Necker-Enfants Malades, Paris, France, 16Janssen Services, LLC., Spring House, 17Cohen Children's Med Cntr, New Hyde Park, United States

Objectives & Study: To describe the utilization of infliximab [IFX] for the treatment of pediatric Crohn’s Disease (CD) patients participating in the DEVELOP registry.

Methods: DEVELOP is an ongoing, international, multi-center, prospective, observational long-term registry, started in 2007, describing the natural history of pediatric inflammatory bowel disease (IBD) and the safety of current and emerging therapies. We focused on CD patients who received their first IFX dose during or within 4wks of entry into the registry. Data collected include: disease duration, time to first IFX infusion after diagnosis, average IFX dose and interval, dose changes, and discontinuations.

Results: Of the 4485 patients enrolled as of June 30, 2013, 2736 (61%) were exposed to IFX at any time point; 706 CD patients (60% male, median age 14 yrs, disease duration mean 2.2 yrs) met study criteria. Average first IFX dose was 5.1 mg/kg (range: 4.87-5.54mg/kg) and was unrelated to age/gender. Average initial maintenance dose interval reported at registry visit was q7.2 wks; 86% received doses between q >6wks and ≤8wks. Median IFX-exposure was 18.8 months with a median of 11 infusions received. 586 patients remained on IFX (median 20.9 months); of the 120 patients who discontinued infliximab (17%), median exposure was 10.2 months and 37% [44/120] discontinued due to “loss of efficacy”. Average dose of IFX during the registry for CD patients was 5.9 mg/kg (median 5.3 mg/kg; IQR: 5.0-6.7 mg/kg) and average frequency was q7.3wks (median 8 wks; IQR: 6.8-8.0 wks). 529/706 patients had both initial and last dose and dose interval reported. 20.6% of these patients did not change dose or interval, 31% increased dose only and 1.5% decreased dose interval. 32.5% adjusted both dose and interval; of these patients 17.8% increased dose and shortened interval, 2.8 % decreased dose and shortened interval.

Conclusion: In the DEVELOP registry, initiated in 2007, >80% of pediatric CD patients who initiated IFX during or within 4wks of entry into the registry maintained IFX therapy through June 2013. 80% received dose adjustments and 32.5% adjusted both dose and dose interval.

**Objectives & Study:** The aim of this study was to assess the safety of infliximab in patients with Crohn's disease in clinical practice.

**Methods:** The medical records of 157 patients treated with infliximab since 10 years were reviewed for severe adverse events. The patients received a median of 26 infusions and had a median follow-up of 4 years.

**Results:** 34 patients (21.6%) developed severe adverse effects. 8 patients developed severe psoriasis (5%), 4 (2.5%) developed arthritis which improved with infliximab discontinuation. Two patients who received combined therapy (infliximab and immunosuppressors) (1.2%) developed systemic Lupus erythematosus with auto-antibodies which recovered after IFX discontinuation. One patient (0.6%) developed chronic active hepatitis B which contraindicated the treatment. Severe folliculitis occurred in three patients (1.9%). Two patients (1.2%) convulsed in the hours after the infusion and required anti-epileptic treatments. Among the 157 patients, 10 (6.4%) had allergic reaction twenty minutes after the beginning of the infusion with tachycardia and dyspnea (all patients were receiving premedication with hemisuccinate hydrocortisone and antihistaminics, scheduled infliximab, 4 received combined therapy and 6 infliximab monotherapy). 3 patients (1.9%) required hospitalisation for severe infection (rotavirus gastro-enteritis, H1N1 influenza, herpes stomatitis). One patient (0.6%) developed chronic myeloid leukemia; he received combined therapy infliximab and 6-mercaptopurine for a severe Crohn's disease and received 13 infusions. The infliximab therapy and the 6-mercaptopurine were stopped and a treatment by Imatinib and mesalazine has been started which maintained the leukemia and the Crohn's disease in remission.

**Conclusion:** Long-term follow-up of patients with Crohn's disease who were treated with infliximab showed an acceptable safety profile. No significant difference were seen between infliximab alone or associated with immunosuppressors in severe adverse events, despite the fact that chronic myeloid leukemia and lupus occurred in patients receiving a concomittant immunosuppressive therapy.

**Disclosure of Interest:** None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0148

ANTI-GLYCAN ANTIBODIES ARE ASSOCIATED WITH DISEASE PHENOTYPE, NOD2 AND NEGATIVELY ATG16L1 BUT NOT IL23 VARIANTS IN PAEDIATRIC CROHNS DISEASE PATIENTS

Malgorzata Klementyna Sladek 1,*, Adam Cmiel 2, Marek Sanak 3

1Department of Paediatrics, Gastroenterology and Nutrition, Jagiellonian University Medical College, Krakow, Poland, 2Department of Applied Mathematics, University of Science and Technology, 3Department of Internal Madicine, Jagiellonian University Medical College, Krakow, Poland

**Objectives & Study:** This study was designed to investigate the association between panel of anti-glycan antibodies and Crohn’s disease (CD) phenotype and variants in genes involved in bacterial sensing (NOD2), autophagy (ATG16L1) and interleukin-23 (IL-23) signaling pathway.

**Methods:** 134 unrelated, well characterized CD pediatric patients from a tertiary referral hospital were evaluated. Sera were analyzed for anti-*Saccharomyces cerevisiae* antibodies IgA and IgG (ASCA) by indirect immunofluorescence technique and for anti-chitobioside antibodies IgA (ACCA), anti-laminaribioside antibodies IgG (ALCA), anti-mannobioside antibodies IgG (AMCA) by enzyme-linked immunosorbent assay (ELISA). DNA was tested for three CD-associated NOD2 variants (G908R, R702W, 3020insC), variant in ATG16L1 (T300A) gene and variant in IL-23R (R381Q) gene.

**Results:** Cumulative seroreactivity assessed by quartile sum scores for ACCA, ALCA, AMCA was associated with older age (10 to 17 yrs) of CD diagnosis (P=0.046) and disease location in large bowel with terminal ileum (L3) involvement (P=0.029). In multiple regression analysis presence of any anti-glycan antibody was independently associated with extensive disease location (L3) (P=0.01) and complicated disease behavior. When compared with CD patients without NOD2 mutations, the presence of at least one NOD2 variant (G908R, R702W, 3020insC) more frequently lead to ASCA positivity (41, 5% vs. 22, 7%; P=0.036). G908R variant was associated with the cumulative seroreactivity to ACCA (P=0.03) and 3020insC NOD2 variant was associated with cumulative seroreactivity to ALCA (P=0.02). ATG16L1 variant was negatively associated with seroreactivity to any glycan epitopes while IL-23R variant did not contribute to development of anti-glycan antibodies.

**Conclusion:** Reactivity to microbial components was associated with disease phenotype and variants in innate immune receptor gene (NOD2) further supporting the role of altered microbial sensing in the pathogenesis of CD. It is intriguing that an opposite effect of ATG16L1 variant was observed. IL23R signaling pathway was found to not influence antibody formation against glycan epitopes.

**Disclosure of Interest:** None Declared
INVESTIGATING DNA METHYLATION AND GENE EXPRESSION PROFILES OF HUMAN INTESTINAL EPITHELIAL CELLS IN INFLAMMATORY BOWEL DISEASE AND DURING GUT DEVELOPMENT

Alexander Ross 1,*, Judith Kraiczy 1, Komal Nayak 1, Matthias Zilbauer 1

1 Paediatric Gastroenterology, Cambridge University Hospitals, Cambridge, United Kingdom

Objectives & Study: DNA methylation is an important epigenetic mechanism involved in regulation of gene expression. Increasing evidence suggests a major role of epigenetic mechanisms such as DNA methylation in the development of inflammatory bowel diseases (IBD). The objectives of our study were to assess the role of DNA methylation during human gut development in health and its potential implication in IBD pathogenesis.

Methods: Foetal gut samples were obtained from medically terminated foetuses, and paediatric samples from biopsies. Epithelial cells were isolated using enzyme digestion and magnetic bead separation, with RNA and DNA subsequently extracted. Genome-wide methylation analysis was performed using Illumina HumanMethylation-450kBeadArray, whilst gene expression was assessed by Affymetrix Gene ST1.1 microarrays. Data analyses and statistical testing were performed using Bioconductor packages in R statistical software.

Results: The majority of unmethylated CpGs were found in CpG islands, whilst methylated sites were mainly located away from CpG islands (i.e. “open sea”). Multidimensional scaling analysis (MDS plots) of DNA methylation and gene expression revealed a similar grouping pattern separating samples by age, gut location, and disease state. Approximately 10% of annotated differentially methylated regions (DMR) were found to overlap with differentially expressed mRNA transcripts. Gene ontology (GO) analysis performed on DMRs overlapping differentially expressed genes showed enrichment for immune and defence functions in both development and inflammatory bowel disease.

Conclusion: Intestinal epithelial cells display a distinct DNA methylation profile according to age group, gut location, and inflammatory bowel disease state. Gene expression profiles display a clustering pattern similar to methylation, with 10% of genes containing DMRs were also found to be differentially expressed, suggesting a functional association between DNA methylation and gene expression. GO analysis on regulatory DMRs indicate a potential role of DNA methylation in the development of intestinal epithelial immune function in health while alterations contribute to the development of inflammatory bowel disease state.

Disclosure of Interest: None Declared
EVOLUTION OF PAEDIATRIC ONSET CROHN'S DISEASE PHENOTYPE: A POPULATION BASED COHORT STUDY

Firas Yaser Rinawi 1,*, Amit Assa 1, Yoram Rosenbach 1, Corina Hartman 1, 2, Noam Zevit 1, 2, Yael Mozer Glassberg 1, Ari Silberman 1, Rivka Shapiro 1, 2, Vered Nachmias Friedler 1, Raanan Shamir 1, 2

1Institute of Gastroenterology, Nutrition and Liver Diseases, Schneider Children's Medical Center of Israel, Petach-Tikva, Israel, 2Sackler Faculty of Medicine, Tel-Aviv University, Tel-Aviv, Israel

Objectives & Study: Crohn's disease (CD) behavior and location may change over time, affecting therapeutic decisions. Our aim was to investigate the phenotypic evolution of pediatric onset Crohn's disease over a prolonged follow-up.

Methods: Records of 105 pediatric onset CD patients with at least 10 years follow-up were reviewed retrospectively. Disease behavior and location according to accepted pediatric classifications were determined at diagnosis and at the end of follow-up. The proportions of the different disease behaviors and locations were calculated at these time points.

Results: The mean age at diagnosis was 12.5±3.1 years and the median follow-up period was 13.5 years (range, 10-21.5 years). Disease location at diagnosis and at the end of follow-up was, respectively: ileal in 53 (50.5%) and 44 (41.9%), colonic in 13 (12.4%) and 10 (9.5%), ileocolonic in 35 (33.3%) and 47 (44.8%), isolated upper gastrointestinal involvement in 4 (3.8%) and 2 (1.9%). Overall, 58.1% of patients had a change in disease location (p<0.001). This includes changes from colonic or ileal to ileocolonic and vice versa. Disease behavior at diagnosis and at the end of follow-up was, respectively: non-stricturing non-penetrating in 84 (80%) and 51 (48.6%), stricturing in 17 (16.2%) and 28 (26.7%), penetrating in 4 (3.8%) and 26 (24.8%). Overall, there was an increase of 31.5% in complicated disease behavior over time (p<0.001). Perianal involvement increased from 18.1% of cases at presentation to 30.5% at the end of follow-up (p<0.05).

Conclusion: Long-term follow-up of pediatric onset CD demonstrated a substantial change in both disease location and behavior over time.

Disclosure of Interest: None Declared
Objectives & Study: The role of commensal gut microbiota is essential to induce and preserve a balanced intestinal immune response. Several bacteria strains, such as Bifidobacterium species, have been reported to reduce inflammation and contribute to the maintenance of intestinal homeostasis. However, the interaction between these bacteria and the gut immune system remains largely unknown. Because of the central role played by dendritic cells (DCs) in regulating immune responses and inducing tolerance, we examined in vitro the effects of a probiotic mixture, composed from three different Bifidobacterium species (B. Longum, B. Breve, B. Infantis), on the phenotype and function of monocyte-derived DCs from children with inflammatory bowel disease (IBD).

Methods: DCs obtained from peripheral blood monocytes of pediatric patients with Crohn’s disease (CD; N=16), ulcerative colitis (UC; n=17), and healthy controls (HC; n=9) were incubated with fluorescein labeled bacteria (E.coli) particles or DQ-Ovalbumin (DQ-OVA) after a 24 hours pre-treatment with the probiotic mixture, in order to evaluate DC phenotype, antigen sampling and processing by flow cytometry. Moreover, after each incubation, supernatants from cells were collected to measure TNF-alfa, INF-gamma and IL-17 cytokine secretion by ELISAs.

Results: DCs generated from both CD and UC pediatric patients showed significant higher bacteria particles uptake after incubation with the probiotic mixture (p=0.0009 and p=0.009, respectively for CD and UC). Also DQ-OVA processing improved after the exposure to the probiotic mixture, showing a significant increase, but only in CD patients (p=0.03). In contrast DCs from HC showed no significant changes in bacterial uptake and DQ-OVA processing upon incubation with the probiotic mixture. No effect was observed on DCs expression of the activation markers HLADR and CD86, or on TNF-alfa production induced by antigens. By contrast, INF-gamma and IL-17 resulted almost undetectable in cellular medium upon bacteria particles incubation independently of probiotic exposure.

Conclusion: In IBD patients an altered capacity to capture and process luminal bacteria antigens can lead to intestinal inflammation. Bifidobacteria significantly improve E.coli-derived particles uptake by DCs from both CD and UC patients. Interestingly, in DC from HC, in which autophagic mechanism is not altered, no prominent effect of probiotic mixture was observed. This improvement of antigen sampling and processing could partially solve the impairment of intestinal innate immunity reducing uncontrolled microorganism growth in the intestine of children with IBD.

Disclosure of Interest: None Declared
**Objectives & Study:** Anti-neutrophil cytoplasmic antibodies (ANCA) are found in up to 50% of patients with ulcerative colitis (UC). Antibodies against proteinase-3 (PR3), one of the ANCA specificities, are serological markers for small vessel vasculitis such as granulomatosis with polyangiitis. Proteinase 3 (PR3) is a neutrophil serine protease and activates - similar to caspase-1 - pro-interleukin-1β to interleukin-1β, a proinflammatory cytokine. Anti-PR3 antibodies are occasionally found in patients with UC, but exact prevalence and pathogenic importance of these findings are unknown. The aim of this study was to analyze prevalence and clinical correlation of anti-PR3 antibodies in pediatric patients with inflammatory bowel disease (IBD).

**Methods:** We collected sera and recorded clinical data from 165 pediatric IBD patients (87 Crohn's disease (CD), 73 UC, 4 IBD unclassified) at the time of disease manifestation and 64 healthy pediatric controls from 2005 to 2012. All samples were tested for ANCA by indirect immunofluorescence (IIF) and for anti-PR3 antibodies on a novel chemiluminescence assay - using native purified PR3 coated paramagnetic beads. For statistical analysis we used the chi-square test of the SPSS 21.0 package.

**Results:** Mean age at diagnosis of IBD was 12.3 years (range 1.7 to 17.8). PSC (confirmed or highly suspected) was diagnosed in 22 patients with UC but in none of the CD or IBD unclassified patients. ANCA by IIF were found in 52% (38/73) of UC patients but only in 15% (13/87) of CD patients (Chi-square=51.1; p<0.05). Anti-PR3 antibodies were found to be significantly more often positive in UC (36/73, 49%) then in CD (8/87, 9%) or IBD unclassified (0/4) (Chi-square=34.0; p<0.0001). All controls were negative for anti-PR3 antibodies. 64% (14/22) of IBD patients with PSC were anti-PR3 positive in contrast to 27% (30/112) of IBD patients without PSC (Chi-square=17.5; p<0.05). No correlation was found with age of diagnosis or disease extent of UC according to Paris classification.

**Conclusion:** We detected anti-PR3 antibodies in a significant proportion of pediatric IBD patients with PSC. Anti-PR3 is able to induce vasculitis by recognizing membrane-bound PR3 in granulomatosis with polyangiitis. Mucosal vasculitis is also seen in inflamed tissue in histological specimens of IBD. Anti-PR3 antibodies may therefore play a role in the pathogenesis of inflammation of bile ducts and their small vessels. Our findings support the assumption of an autoimmune genesis of PSC. More detailed analysis will assess further associations between anti-PR3 positivity and clinical phenotype of IBD.

**Disclosure of Interest:** None Declared
MENTAL HEALTH OF MOTHERS OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE

Helene Werner 1,*, Markus A. Landolt 1, Patrick Buehr 1, Rebekka Koller 1, Andreas Nydegger 2, Johannes Spalinger 3, Klaas Heyland 4, Susanne Schibli 5, Christian P Braegger 1 and the Swiss IBD Cohort Study Group

1University Children's Hospital, Zurich, Switzerland, 2University Children's Hospital, Lausanne, Switzerland, 3Children's Hospital, Lucerne, Switzerland, 4Children's Hospital, Winterthur, 5University Children's Hospital, Berne, Switzerland

Objectives & Study: Children and adolescents with inflammatory bowel disease (IBD) are faced with the challenges of a life-long chronic disease associated with periods of remission and relapse of gastrointestinal symptoms such as diarrhoea and abdominal pain, as well as extra-intestinal manifestations such as anorexia, weight loss, fatigue, and skin and joint symptoms. For the adaptation to these challenges, the quality of parental support and mental health is crucial. The objective of the present Swiss multi-centre cohort study was to describe parents’ mental health problems of children with IBD, to compare the level of these problems with a normative sample and to examine the influence of child and parent factors on mental health problems.

Methods: 124 mothers of children with an IBD diagnosis (56% Crohn’s disease, 44% ulcerative colitis/indeterminate colitis) were included in the study. Mothers completed the standardized and well-validated Symptom Check List (SCL-27) and Strengths and Difficulties Questionnaire (SDQ); medical data were extracted from the patients’ hospital records.

Results: Mothers of children with IBD had more dysthymic symptoms (p=.000, Cohen’s d=.38) and had more symptoms of social phobia (p=.03, Cohen’s d=.19) compared to age-matched female references. Furthermore, multivariate regression analysis indicated that a shorter disease duration of child’s IBD, more child behaviour problems and the presence of an IBD diagnosis in a mother significantly predicted higher overall mental health problems of the mothers (F=4.32, p<.001, R^2adj=.23).

Conclusion: This study is the first to present data on mental health problems in mothers of children with IBD in Switzerland. Our study indicates that mothers of children with IBD are most strongly affected in terms of troubles concentrating, remembering, and low in energy and that the level of these problems was significantly higher than in age-matched female references. Thus, child’s IBD might be a significant burden for many mothers. Furthermore, our study showed that mental health problems of the mothers are determined by child medical, child behavioural and mother characteristics. Mothers with an own IBD diagnosis may have the greatest need for professional interventions in order to support their child in his/her adaptation process to the challenges of the disease.

Disclosure of Interest: None Declared
EFFICACY AND SAFETY OF INFliximAB MONOTHERAPY IN PAEDIATRIC CROHN'S DISEASE - A MULTICENTER STUDY

Martinez-Vinson Christine 1, Frank Ruemmele 2, Olivier Mouterde 3, Alain Lachaux 4, Alain Dabadie 5, Patrick Tounian 6, Alexis Mosca 7, Jane Languepin 8, Jean-Pierre Hugot 1, Jean-Pierre Cézard 1 and Groupe Francophone d'Hépato Gastro et Nutrition Pédiatriques


Objectives & Study: Combination therapy with infliximab plus immunosuppressors is associated with an increase risk of opportunistic infection and lymphomas. This prospective observational and multicenter study assessed the efficacy and safety of Infliximab Monotherapy in Pediatric Crohn’s disease.

Methods: Seventy one patients with severe inflammatory bowel disease were included. All patients were treated with infliximab for the first time and received three-dose induction followed by scheduled maintenance therapy. The immunosuppressors were stopped after the third infliximab injection (day 45). The primary and secondary endpoints were remission rates and occurrence of severe adverse events, every 2 months during one year after the immunosuppressor is stopped. Remission was defined as Harvey Bradshaw<4, C-reactive protein (CRP) <0.3 mg/dL, Sedimentation Rate<10.

Results: At 12 months, 70.5 % of patients were in remission. Infliximab therapy had to be intensified as either an increase in the dose of infliximab (from 5mg/kg to 10 mg/kg) in 26.3 % or a decrease in the infusion interval (less than every 8 weeks) in 42.6 %. Concurrent corticosteroid use was necessary in 13.1 %. No patient required surgery. Infusion reactions were seen in 4.2 %. During one year follow-up no severe adverse events occurred (notably infections and cancers).

When patients still received an immunosuppressors during the first six weeks of infliximab treatment, 6.1 % had anti-infliximab antibodies, 6.1 % had not, and 87.9 % had still circulating infliximab.

One year after the interruption of the immunosuppressors and during infliximab treatment, 17.2 % had anti-infliximab antibodies, 10.3 % had not, and 72.4 % had remaining circulating infliximab.

Conclusion: This prospective observational and multicenter study assessed the efficacy and safety of Infliximab Monotherapy in Pediatric Crohn’s disease, with a remission rate of 70 % and no difference in severe adverse effects as compared to previous published studies where Immunosuppressors were associated.

Disclosure of Interest: None Declared
LONG-TERM OUTCOME OF PAEDIATRIC-ONSET ULCERATIVE COLITIS: EARLY YEARS ARE SHAPING THE FUTURE

Dominique Turck, Corinne Gower-Rousseau, Hélène Sarter, Mathurin Fumery, Anaïs Peneau, Claire Spyckerelle, Jean-Eric Laberenne, Francis Vasseur, Laurent Peyrin-Biroulet, Jean-Frederic Colombel, Guillaume Savoye

1Paediatrics, 2Public Health, CHU, Lille, France, 3Gastroenterology, CHU, Amiens, France, 4Paediatrics, GHICL, Lille, France, 5Gastroenterology, CH, Seclin, France, 6Gastroenterology, CHU, Nancy, France, 7Gastroenterology, CHU, Lille, France, 8Gastroenterology, CHU, Rouen, France

Objectives & Study: Data on long-term outcome of paediatric-onset ulcerative colitis (UC) are scarce.

Methods: All patients recorded between 1988 and 2004 with a diagnosis of UC before the age of 17 years were included. The cumulative risks of receiving immunosuppressants (IS, including azathioprine and/or methotrexate and/or cyclosporine) and anti-TNFα therapy, as well as undergoing colectomy were estimated via the Kaplan-Meier method.

Results: 159 paediatric-onset UC patients with a follow-up ≥ 2 years were identified (5% of all cases of UC), including 92 females. Twenty-two children (14%) had less than 10 years at UC diagnosis. Median age at diagnosis was 14.5 years [IQR: 11.4-16.1] and median duration of follow-up was 11.5 years [8.2-15.8]. At diagnosis 25% of children had proctitis (E1), 38% left-sided colitis (E2) and 37% extensive colitis (E3). Disease course was characterised by disease extension in 50% of patients (50 among 101 E1 and E2). Cumulative risks of colonic extension were 11% at 1 year, 48% at 5 years, 54% at 10 years and 57% at 15 years. At diagnosis 12 (7.6%) patients had extra intestinal manifestations and 40 (25%) at maximal follow-up including articular manifestations (n=27). Cumulative probabilities of receiving IS and anti-TNFα therapy were respectively 20% and 0.5% at 2 years, 28% and 4% at 5 years, 32% and 7% at 10 years and 35% and 13% at 15 years. Cumulative probabilities of colectomy were 6% at 1 year, 20% at 5 years, 21% at 10 years and 24% at 15 years.

Conclusion: In this large population-based cohort of paediatric-onset UC disease the rate of disease extension and colectomy rapidly increased within the first 6 years after diagnosis and then remained stable. These data emphasize the need for early intervention to modify the natural history of paediatric UC.

Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0156

**INDUCTION OF REMISSION IN CROHN'S DISEASE IN CHILDREN AND YOUNG ADULTS USING A CROHN'S DISEASE EXCLUSION DIET (CDED)**

Rotem Sigall Boneh 1, Tamar Pfeffer Gik 1, Idit Segal 1, Arie Levine 1

1Paediatric Gastroenterology Unit, E. Wolfson Medical Center, Holon, Israel

**Objectives & Study:** Exclusive enteral nutrition is an effective method for inducing remission in active pediatric Crohn's disease. Success appears to depend primarily on exclusion of free diet. Multiple dietary components may alter the microbiome, induce intestinal permeability affect the mucous layer or allow translocation of bacteria in animal models or cell lines. We hypothesized that the effect of EEN is due to exclusion of dietary components that may alter the microbiome or generate an acquired bacterial clearance defect. We developed a diet based on exclusion of these dietary components (Crohn's Disease Exclusion Diet).

**Methods:** Children and young adults with luminal active disease defined as a pediatric Crohn's disease activity index (PCDAI) >7.5 and <40 in children, or Harvey Bradshaw index (HBI) >3 received a 12 week structured diet that allowed free access to specific unprocessed fresh foods and restricted exposure to all other foods. Patients received 50% of calories from a polymeric formula. PCDAI, HBI, CRP and ESR were reevaluated at 6 weeks. The primary endpoint was clinical remission at 6 weeks defined as PCDAI<7.5 in children or HBI <3. Children and young adults with luminal active disease defined as a pediatric Crohn's disease activity index (PCDAI) >7.5 and <40 in children, or Harvey Bradshaw index (HBI) >3 received a 12 week structured diet that allowed free access to specific unprocessed fresh foods and restricted exposure to all other foods. Patients received 50% of calories from a polymeric formula. PCDAI, HBI, CRP and ESR were reevaluated at 6 weeks. The primary endpoint was clinical remission at 6 weeks defined as PCDAI<7.5 in children or HBI <3.

**Results:** We treated 41 patients (28 pt ≤18 yrs, mean age at treatment 16 ± 5.7, range 9-32 yrs) the mean disease duration was 2 years. Mean PCDAI decreased from 24.2 ± 8.3 to 5.8 ± 8.4 (p<0.001) mean HBI from 5.7 ± 2.8 to 1.4 ± 2.7 (p<0.001). Remission was obtained in 27/41 patients (66%). Normalization of CRP occurred in 18/27 (66.6%) patients in remission. Five patients did not use any formula, 4/5 obtained remission just with CDED.

**Conclusion:** Dietary therapy involving exclusion of components hypothesized to affect the microbiome or intestinal permeability to bacteria, appears to lead to high remission rates with improvement in inflammation in early mild to moderate luminal Crohn's disease.

**Disclosure of Interest:** None Declared
OBJECTIVES & STUDY: Part of a larger prospective study supported by the Swiss National Science Foundation focusing on energy metabolism in children with IBD, the present study is aimed at assessing the accuracy of Schofield’s equation in order to predict resting energy expenditure (REE) in children with inflammatory bowel disease (IBD) and in healthy controls compared to REE measured by indirect calorimetry (QUARK RMR).

METHODS: Twenty-one patients (11 girls; mean age: 14.3 years, range 12-16 years) with IBD (Crohn’s disease n=15, ulcerative colitis n=6) and twenty-nine healthy controls (12 girls; mean age: 12.7 years, range 10-16.5 years) were enrolled. Estimated REE was calculated using Schofield equation and compared to the value measured by indirect calorimetry. Paired t-tests were performed and P-values < 0.05 were considered statistically significant.

RESULTS: Schofield’s equation has a tendency to overestimate REE in children with IBD compared to healthy controls (1429kCal/j ± 161 vs. 1362kCal/j ± 154, respectively; P<0.02), whilst it is very accurate in healthy controls (1505kCal/j ± 262 vs. 1521kCal/j ± 273, respectively; P: NS).

CONCLUSION: Schofield’s equation can accurately predict REE in healthy children, but is not reliable in assessing REE in children with IBD. This may be explained by changes in metabolism and body composition in children with IBD.

DISCLOSURE OF INTEREST: None Declared
THE COMPARISON OF CHILDREN WITH INFLAMMATORY BOWEL DISEASE WITH AND WITHOUT IL-10 RECEPTOR MUTATION

Omer Faruk Beser 1,*, Kaan Boztug 2, Didem Gulcu 1, Tufan Kutlu 1, Fugen Cullu Cokugras 1, Tulay Erkan 1
1Paediatric Gastroenterology, Hepatology and Nutrition, Istanbul University Cerrahpasa Medical Faculty, Istanbul, Turkey, 2Molecular Genetic, Research Center for Molecular Medicine of the Austrian Academy of Sciences, Vienna, Austria

Objectives & Study: Interleukin-10 (IL-10) receptor consists of two alpha molecules (IL10-R1) and two beta molecules (IL10-R2) (1). It is known that severe enterocolitis may develop in humans in whom defect in IL-10 or receptors is found, since this signal pathway which inhibits inflammation does not function and inflammation can not be controlled (2). In our study, we aimed to determine the presence of IL-10 receptor resistance gene mutations as a cause of inflammatory bowel disease (IBD) in children aged between 0 and 18 years with a diagnosis of IBD by genetic analysis and compare the follow-up findings of the patients who had IL-10 receptor mutation in terms of demographic, clinical, laboratory and treatment response properties with the patients who had no mutation.

Methods: Genotype analysis was performed to determine the presence of IL-10 and/or IL-10 receptor mutations in 53 patients with a diagnosis of IBD. Based on previous genetic studies, the potential gene regions where mutations were found were seperated and selected. Mutation screening was done in these selected regions in IL-10, IL-10RA and IL-10RB genes. Gene-specific and protein-specific tests were done to determine the functional effects of the mutations defined on the interleukin-10 signal pathway.

Results: Consanguinity in the parents, early age of onset and a course of Crohn’s disease were statistically significantly different in the patients who were found to have mutation on the IL-10 pathway compared to the patients who were not found to have mutation (p=0.014, p=0.005, p <0.001, respectively). While perianal fistula was found in 100% of the patients who had mutation, it was found in only 14.9% of the patients who had no mutation (p <0.001). It was found that weight and height-for-age Z scores were statistically significantly lower in the IL-10 (+) group (p <0.001, p <0.001, respectively). We observed that azathioprine and anti-TNF antibody treatments were used more frequently in the patients who were found to have mutation compared to the patients who were found to have no mutation and remission times were statistically significantly longer in the IL(+) group compared to the IL-10 (-) group (p <0.001).

Conclusion: We think that genetic mutations including mainly IL-10 may have a greater impact in occurence of the disease in early onset IBD in the childhood age group. When there is mutation on the IL-10 signal pathway, the disease onset is at an earlier age, the prognosis is severe and response to treatment is not well.


Disclosure of Interest: None Declared
Objectives & Study: Growth failure is well-recognised in children with severe IBD. Anti-TNF therapies have been shown to improve linear growth in evidence usually from case series (single or multiple centres). We aimed to examine whether anti-TNF therapy improves growth in a population-based cohort of children with IBD.

Methods: A retrospective case note review was performed in all paediatric IBD treatment centres in Scotland of children <18 years with IBD who received infliximab (IFX) from 2000-2012. Anthropometric measurements (height, weight and BMI) taken at T-12, start of IFX (T0) and 12 (T+12) months after treatment. Height values were converted into standard deviation scores and height velocity calculated in cm/year.

Results: 194 patients were included with a median age at diagnosis of 11.2 years (2.7-17.2); 116 (60%) male with follow up for a median of 1.9 years (0.1-8.8). At T+12, 94 IBD cases had growth data, 56 (60%) males and 87 (93%) CD; 83 (87%) received immunomodulators and 53 (56%) corticosteroids at T0. Mean height SDS T-12 was -0.64 +/-1.1, a significant improvement was then seen from T0 -0.8 +/-1.1 to T+12 -0.72 +/-1.1 (p=0.039). Mean Δ height SDS improved from -0.16 +/-0.38 at T0 to T+12 was 0.08 +/-0.36 (p<0.001) with height velocity improving from 3.9 +/-2.5 at T0 to 4.9 +/-2.9 (p=0.006).

51 (54%) CD entered remission with improvement in height SDS from T0 -0.81 +/-1.1 to -0.58 +/-1.1 at T+12 (p<0.001), Δ height SDS, T0 -0.16 +/-0.37 to 0.23 +/-0.31 at T+12 (p<0.001) and height velocity 3.9 +/-2.5 at T0 to 5.8 +/-2.9 at T12 (p<0.001). In those who did not achieve remission (n=36), a significant decrease was seen in height SDS from T-12 to T0, T-12 -0.78 +/-1.0 to -0.94 at T0 (p=0.018). No improvement was then seen in height, mean height SDS at T0 -0.94 +/-0.91 to T+12 -1.1 +/-0.93 (p>0.05), or Δ height SDS or height velocity.

Data for UC showed no significant difference in height SDS, T-12 0.17 +/-0.67 to 0.16 +/-0.91 at T0 then 0.12 +/-0.85 in those that achieved remission (n=4) whilst those that did not achieve remission (n=3) showed decreased height SDS at T-12 0.03 +/-1.96, then -0.27 at T0 and -0.44 at T+12 (p>0.05), no change in Δ height SDS or height velocity was observed at T-12, T0 or T+12 (p<0.05).

Conclusion: Improvement in height SDS and height velocity at 12 months was seen in those who achieved remission on IFX in CD, but worsened in those who did not. No improvement was seen in height for UC patients irrespective of gain of remission, but numbers were small. Further follow up needs to be carried out to determine if growth improvement is maintained in those who achieve remission and ascertain the mechanism by which IFX improves growth.
MUCOSAL HEALING IN CHILDREN WITH CROHNS DISEASE ON LONG TERM MAINTENANCE TREATMENT

Hemant Bhavsar 1,*, Theodoric Wong 1, Susan Protheroe 1, Stephen Murphy 1, Ronald Bremner 1, Rafeeq Muhammed 1

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

Objectives & Study: The conventional goal of treatment in Crohn’s disease is to induce and maintain clinical remission. However achieving clinical remission alone may not change natural history of Crohn’s disease. Emerging evidence suggest that achieving and maintaining mucosal healing is associated with more sustained clinical remission and reduced rate of hospitalisation and surgery. The aim of our study is to identify the mucosal healing status of patients with Crohn’s disease on long term maintenance treatment.

Methods: We have prospectively assessed the endoscopic severity of Crohn’s disease in children who had undergone reassessment colonoscopy from October 2012 to September 2013. We have used Crohn’s Disease Endoscopic Index of Severity (CDEIS) for children who did not have bowel resection and Rutgeerts endoscopic grading scale for children who had right hemicolectomy.

Results: 59 colonoscopic examinations were done in 57 children in the time period from October 2012 to September 2013. In 51 children, we have used CDEIS to assess mucosal healing. 20 children had achieved complete mucosal healing (CDEIS score 2). 31 children did not achieve complete mucosal healing and their CDEIS score varied from 3 to 25. Significantly higher proportion of children in the complete mucosal healing group had received treatment with anti-Tumour Necrosis Factor (anti TNF) agents compared to the children in the other group (65% v 32% p value0.04). The anti TNF agents used in the children in both groups were Infliximab. There were no significant difference in disease distribution, peri-anal involvement, Haemoglobin, CRP, ESR, platelets and Azathioprine use when comparing children in both the groups. Hospitalisation rate was higher for children who have not achieved complete mucosal healing (35% v 10%). No children needed surgery in the group with complete mucosal healing compared to 5 children needing right hemicolectomy in the group with incomplete mucosal healing.

7 children had reassessment colonoscopy after their right hemicolectomy and we have used Rutgeerts endoscopic grading scale to assess their mucosal healing status. 4 children had complete mucosal healing (Rutgeerts score i0), 3 were on treatment with Infliximab and Azathioprin, one was on Azathioprine alone.

Conclusion: In our experience 42% (24/57) children with Crohn’s disease on maintenance treatment have achieved complete mucosal healing. Treatment with Anti TNF agents was a significant factor in achieving mucosal healing. Children who had achieved complete mucosal healing did not need bowel surgery.

Disclosure of Interest: H. Bhavsar: None Declared, T. Wong: None Declared, S. Protheroe Conflict with: MSD, Tillotts Pharma, S. Murphy Grant / Research Support for: from MSD, R. Bremner: None Declared, R. Muhammed Grant / Research Support for: from MSD, Abbvie, Falk Pharma and Tillotts Pharma, Speakers bureau of: MSD
INTESTINAL IRON ABSORPTION IN PEDIATRIC INFLAMMATORY BOWEL DISEASE: A PROSPECTIVE, SINGLE-CENTER STUDY

Massimo Martinelli 1,*, Caterina Strisciuglio 1, Annalisa Alessandrella 1, Felice Crocetto 1, Silverio Perrotta 2, Bruno Nobili 2, Annamaria Staiano 1, Erasmo Miele 1
1Translational Medical Sciences, University of Naples "Federico II", Naples, Italy, 2Paediatrics, Second University of Naples, Naples, Italy

Objectives & Study: Anemia in patients with Inflammatory Bowel Disease (IBD) is a common problem of multifactorial origin, including blood loss, iron malabsorption (IM), and anemia of chronic inflammation (ACI). Due to difficulties in distinguishing blood loss anemia from ACI, it is still controversial if oral iron supplementation should be used. We sought to elucidate alterations in iron absorption in pediatric patients with a diagnosis of IBD.

Methods: Fifty-nine subjects affected by IBD (Ulcerative Colitis: 36; Crohn’s disease: 23; M/F 33/26; Median age: 13.4 years) were prospectively enrolled between December 2012 and June 2013. After an overnight fast, full blood count, serum iron, ferritin, transferrin, soluble transferrin receptor, inflammatory indexes [C-reactive protein (CRP), erythrocyte sedimentation rate (ESR)] and fecal calprotectin were obtained. In order to evaluate the efficacy of iron absorption an iron load test (ILT) was performed to those patients who signed informed consent. Ferrous sulfate (dosed as 1 mg/kg elemental iron with a 60-mg maximum) was then administered orally as a liquid preparation, followed by determination of serum iron after two hours. PUCAI, PCDAI, localization of disease, disease duration and IBD therapy were also evaluated.

Results: Anemia was diagnosed in 10 out of 59 patients (16.9%). Forty-five out of 59 patients (76.2%) performed ILT. Thirteen out of 45 (26.8%) patients showed a pathologic ILT. Patients with iron malabsorption showed significant higher values of ERS and CRP compared with patients with normal iron absorption (p=0.03 and p=0.06). PUCAI and PCDAI were significantly increased in patients with a pathologic ILT (p=0.001 and 0.005). Baseline iron level, hemoglobin and transferrin values were significantly lower in patients with IM (p=0.001, p=0.03 and 0.02). No specific type of IBD resulted to predispose to IM (p=0.7). Localization of disease and IBD therapy were not associated with IM (p=0.2, 0.6 and 0.3 respectively). Although, baseline ferritin and fecal calprotectin resulted to be higher in patients with IM, these differences were not statistically significant (p=0.1 and p=0.2).

Conclusion: Iron oral absorption is inversely correlated with inflammatory indexes in pediatric IBD. Patients affected by active IBD have impaired oral iron absorption compared with patients with inactive disease. These findings suggest that oral iron administration may be of limited benefit to these patients. Future studies are needed to further elucidate the molecular basis of anemia and iron malabsorption.

Disclosure of Interest: None Declared
USE OF FUNCTIONAL PLATELET INDICES IN INFLAMMATORY BOWEL DISEASE: ARE THEY HELPFUL AS OTHER INFLAMMATORY MARKERS?

Nevzat Aykut Bayrak 1,*, Emel Uyar 1, Engin Tutar 1, Burcu Volkan 1, Esra Polat 1, Deniz Ertem 1

1 Paediatric Gastroenterology, Hepatology and Nutrition, Marmara University School of Medicine, Istanbul, Turkey

Objectives & Study: Platelets are involved in the pathogenesis of inflammatory bowel disease (IBD) and increased platelet count (PLTc) has been associated with disease activity. Functional platelet indices (FPI) such as mean platelet volume (MPV), plateletcrit (PCT) and platelet distribution width (PDW) might have a correlation with disease activity in IBD. Despite available in complete blood count (CBC) analysis, FPI are not interpreted and usually overlooked by physicians. The aim of the study was to assess the correlation between PLTc with FPI and disease activity in children with IBD.

Methods: Newly diagnosed ulcerative colitis (UC) and Crohn’s disease (CD) patients and age and sex matched healthy subjects were recruited. Disease activity was assessed by pediatric UC activity index (PUCAI) and pediatric CD activity index (PCDAI). CBC including FPI, C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) were obtained at diagnosis and 6 months after the diagnosis for IBD cases and at the first visit for healthy subjects.

Results: A total of 68 patients with IBD (37 UC, 31 CD) and 92 healthy subjects were enrolled. At diagnosis, PLTc (445±175 x10^3/mm^3 vs. 286±82 x10^3/mm^3), MPV (7.27±1.4 fL vs. 8.4±1.9 fL) and PCT (0.31±0.12 vs. 0.23±0.06) were significantly different in IBD patients compared to the healthy subjects (p<0.01 PUCAI and PCDAI were significantly decreased 6 month after the diagnosis (p<0.05). When the same parameters were compared 6 month after the diagnosis, there was no significant difference between IBD and control group after the maintenance of remission (p>0.05). Disease activity was correlated with PLTc, MPV and PCT in UC (r^2:0.49, r^2:0.65 and r^2:0.59, respectively, p<0.01) as well as in CD (r^2:0.47, r^2:0.62 and r^2:0.58, respectively, p<0.01). Disease extent was not correlated with PLTc, FPI, CRP and ESR in UC or CD (p>0.05). Receiver operating characteristic curve was used to identify optimal cut off values of suggested parameters, sensitivity, specificity, positive (PPV) and negative (NPV) predictive value and accuracy ratios were calculated (table 1).

<table>
<thead>
<tr>
<th>Parameter (normal values)</th>
<th>Cut off value</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
<th>Accuracy (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>PLTc (150 – 400 x10^3/mm^3)</td>
<td>&gt;400</td>
<td>67.4</td>
<td>77.2</td>
<td>86.1</td>
<td>53.1</td>
<td>69.4</td>
</tr>
<tr>
<td>MPV (7.4 – 10 fL)</td>
<td>&lt;7.3</td>
<td>71.7</td>
<td>72.7</td>
<td>84.6</td>
<td>55.2</td>
<td>71.9</td>
</tr>
<tr>
<td>PCT (0.18-0.3 %)</td>
<td>&gt;0.26</td>
<td>65.2</td>
<td>63.6</td>
<td>78.9</td>
<td>46.7</td>
<td>64.8</td>
</tr>
<tr>
<td>CRP (0.5 mg/L)</td>
<td>&gt;10</td>
<td>56.5</td>
<td>45.4</td>
<td>68.4</td>
<td>33.3</td>
<td>54.2</td>
</tr>
<tr>
<td>ESR (0-20 mm/hr)</td>
<td>&gt;20</td>
<td>65.2</td>
<td>40.9</td>
<td>69.8</td>
<td>36</td>
<td>60.1</td>
</tr>
<tr>
<td>PLTc - MPV - PCT Combination</td>
<td>Above specified</td>
<td>84.8</td>
<td>50.1</td>
<td>86.5</td>
<td>46.7</td>
<td>77.5</td>
</tr>
</tbody>
</table>

Conclusion: Functional platelet indices are altered in IBD. Lower MPV value and higher PCT and PLTc are associated with active disease with higher sensitivity and specificity compared to routinely used inflammatory markers. Therefore, platelet count and functional platelet indices might be helpful for practical assessment of disease activity in outpatient IBD clinics.
Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0163

**ORAL ANTIBIOTIC COCKTAIL (MADOV) FOR TREATMENT OF REFRACTORY SEVERE COLITIS**

Dan Turner¹, Arie Levine², Ron Shaoul³, Kolho Kaija-Leena⁴, Yelena Rachman¹, Raffi Lev Tzion¹, Oren Ledder¹,*

¹Shaare Zedek Medical Centre, Jerusalem, Israel, ²Wolfson Medical Centre, Holon, Israel, ³Rambam Medical Centre, Haifa, Israel, ⁴Helsinki University Central Hospital, Helsinki, Finland

**Objectives & Study:** Results of previous studies on the effectiveness of antibiotics in ulcerative colitis (UC) are contradicting but seem more effective when used orally. In this retrospective, multicenter cohort study, we aimed to report our experience using a combination of antibiotics in moderate-severe refractory pediatric UC and “UC-like” Crohn’s colitis (metronidazole, amoxicillin, doxycillin, and, if an inpatient, also vancomycin (MADOV)). The combination has been selected following previous published evidence in adults.

**Methods:** 14 consecutively enrolled children [mean age 13.1±5.5 years], median disease duration 1.3 years (IQR 3.0); 11 (79%) pancolitis], were treated with a 2-week MADOV cocktail for refractory colitis in the three participating centers. Doxycillin was substituted with oral gentamycin or oral ciprofloxacin in children younger than 8 years or when an allergy to one of the drugs was suspected. All patients [10 UC, 1 “UC-like” Crohn’s colitis, and 3 IBD-U] had severe disease; 13 (93%) were corticosteroid dependent or refractory and 11 (79%) were refractory to anti-TNF.

**Results:** 8 children (57%) entered complete remission (PUCAI<10 points) and 2 children (14%) showed clinical improvement; mean PUCAI decreased from 70.5±14.6 to 11±17.8 (P<0.001) and mean CRP dropped from 3.3±2.5mg/dL to 1.2±1.2 mg/dL (P=0.018) within 2 weeks of treatment. Another 4 children (27%) did not respond to oral antibiotics. Imminent colectomy was avoided in one child (7%) with acute severe colitis refractory to steroids and infliximab due to the cocktail.

**Conclusion:** The use of wide-spectrum oral antibiotic cocktail in pediatric UC seems promising in 57-71% of patients who were refractory to other salvage therapy. A pediatric trial to assess this intervention in the randomized controlled setting is underway.

Involvement of a pro-inflammatory cytokine TL1A in pathogenesis of inflammatory bowel disease in children

Piotr Landowski 1, 2*, Tomasz Ślebioda 3, Barbara Kamińska 4, Zbigniew Kmieć 3, Piotr Wierzbicki 3, Marcin Stanisławowski 3

1Department of Paediatrics, Paediatric Gastroenterology, Hepatology and Nutrition, 2Department of Histology, Medical University of Gdańsk, Poland, 32Department of Histology, 4Department of Paediatrics, Paediatric Gastroenterology, Hepatology and Nutrition, Medical University of Gdańsk, 80-803 Gdańsk, Poland

Objectives & Study: TL1A is a pro-inflammatory cytokine and the ligand for death receptor 3 (DR3). Both of these proteins are strongly up-regulated on activated cells of the immune system. TL1A/DR3 interaction provides co-stimulatory signals for activated T cells, inducing production of several pro-inflammatory cytokines involved in the pathogenesis of IBD, especially IL-17A. Several studies show that elevated expression of TL1A and DR3 is associated with pathogenesis of Crohn’s disease and ulcerative colitis, although their exact pathological role has not been entirely elucidated yet.

Methods: Colon mucosa biopsies used for IHC and qPCR assays were collected from newly diagnosed paediatric (CD n=15; UC n=16) patients during colonoscopy. Control group consisted of age-matched patients (children: n=29) negatively diagnosed for colon inflammation. Following RNA isolation and reverse transcription, mRNA expression level of selected genes was determined by qPCR and normalised to the expression level of HPRT1.

Results: Interestingly, we have also observed a lower levels of TL1A, DR3 and IL-17A mRNA expression in patients with milder CD determined according to Paediatric Crohn’s Disease Activity Index (PCDAI). We did not find a similar dependence in UC which severity was determined according to Paediatric Ulcerative Colitis Activity Index (PUCAI), although this could have been caused by relatively small number of patients with moderate and severe stages of the disease. Our observations suggest that TL1A contributes to the development of CD and UC via induction of IL-17A expression, especially in the mild stage of CD.

Conclusion: Elevated expression of TL1A and DR3 proteins suggests that not only mononuclear cells but also colonic epithelial cells contribute to the development of IBD via induction of IL-17A expression. Therefore we speculate that TL1A/DR3 interaction may contribute to pathomechanisms of IBD via induction of IL-17A expression. Further studies are required to explain suggested role of TL1A and DR3 in pathogenesis of IBD.


Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0165

**NEUTRALIZATION OF ANTI-INFLAMMATORY IL-37 DOES NOT MODULATE SEVERITY OF ACUTE DSS-INDUCED COLITIS IN IL 37TG MICE**

Rahel Schwaiger 1,*, Andrea Ringleb 1, Ana-Maria Bulau 1, Doris Mayr 2, Philip Bufler 3

1Department of Paediatrics, Dr. von Hauner Children's Hospital University of Munich, Munich, Germany, 2Institute of Pathology, University of Munich, Munich, Germany, 3Department of Paediatrics, Dr. von Hauner Children's Hospital University of Munich, Munich, Germany

**Objectives & Study:** Interleukin-37 (IL-37) is a natural suppressor of innate immune responses with intra- and extracellular mechanisms of action. We showed that IL-37 protects mice from severe, acute Dextran Sodium Sulfate (DSS)-induced colitis and that hematopoietic cells originating from IL-37tg mice are sufficient to exert the anti-inflammatory effect of IL-37. To gain more insight into the relevance of extracellular IL-37, we treated IL-37tg mice with a neutralizing antibody against IL-37 during the induction of mild colitis by DSS.

**Methods:** Acute colitis was induced in Bl6 and IL-37tg mice by 2% DSS in drinking water. On day 1, 3 and 5 mice received 100µg of either anti IL37-IgG, that enhanced inflammation in IL-37tg mice after LPS challenge, or control rat IgG via intra-peritoneal injection. Clinical score including weight, stool consistency and hemoccult testing was evaluated each day. Mice were sacrificed at day 7. Colonic tissue was collected for histology and ex vivo culture. Heparinized whole blood cultures were stimulated overnight with LPS. Levels of cytokines were measured by Elisa and multiplex assay.

**Results:** Mild acute colitis was established in all DSS-treated mice (clinical activity score 0.7–1.5/4) with shortening of the colon (mean 5.5 vs. 7.8 cm, p<0.01). Colonic lymphocyte infiltration and mucosal erosions were slightly worse in IL-37tg mice (p=0.03) with no difference between the anti IL-37-IgG or control IgG treated groups. In parallel, serum IL-6 was significantly elevated in IL-37tg compared to Bl6 mice (p<0.01). Spontaneous release of IL-1ß, IL-6, IL-10, IL-17, IFNy and TNFa from colon cultures was higher in DSS-treated vs. untreated mice with maximum levels in the distal part of the colon. Distal colon cultures of IL-37tg mice treated with anti IL-37-IgG released more IL-6 than mice treated with control IgG (p=0.03). Similarly, IL-6 levels in LPS-stimulated whole blood cultures were increased (p=0.01) in anti IL-37-IgG compared to control IgG treated IL-37tg mice.

**Conclusion:** The increased severity of acute DSS-induced colitis in IL-37tg mice was unexpected and likely due minor disease activity compared to our previous study. Despite the fact that neutralizing anti IL-37-IgG enhanced release of IL-6 from ex vivo colon and LPS-stimulated whole blood cultures, we did not observe an overall increased severity of DSS-induced colitis in IL-37tg mice treated with anti IL-37-IgG. Future studies are needed to establish the relevance of extracellular IL-37 in a more severe model of acute colitis.

**Disclosure of Interest:** None Declared
Objectives & Study: Perianal fistulas are a common and often debilitating manifestation of Crohn’s disease (CD) in pediatric population, fistulae are often complex and their treatment is difficult and unsatisfactory. Therapeutic strategies for fistulizing CD involve both medical and surgical approaches. Infliximab (anti-TNFa) has been used for the treatment of fistulizing Crohn’s disease with variable efficacy. Surgical options include conventional fistulotomy, long-term seton drainage and advancement flap repair.

The aim of this study was to evaluate the efficacy of a combined management approach with a specific surgical procedure (cone-like fistulectomy) and medical therapy in complex perianal fistulizing pediatric CD.

Methods: We conducted a retrospective study of 15 pediatric patients with perianal complex fistulas in CD. Our patients underwent a specific surgical fistulectomy: cone-like technique combined with antiTNFa therapy in 10 patients and immunosuppressive therapy (6 mercaptopurine) in 5 patients. Cone-like fistulectomy consists in a cone-shape excision of the fistulous tract which allows healing by secondary intention with a lower risk of relapse.

We evaluated the rate and time of healing of perianal fistulas, the rate of recurrences and time to relapse at a median follow-up of 24 (standard deviation [SD] 14.4, range 6–47) months.

Results: Fifteen patients (10 male, 5 female, mean age 11.8 years) received combined therapy, overall median follow-up was 24 months. 13/15 patients (87%) had a complete remission at the end of follow-up. 2 patients (13%) relapsed with a recurrence perianal fistula after an initial response. In patients underwent cone-like fistulectomy the time to healing of fistula was 8.07 months (standard deviation [SD] 5.70, range 1-24). Six patients (40%), with a time interval of 9-24 months, presented a luminal disease relapse with no evidence of perianal fistula involvement.

Conclusion: Cone-like fistulectomy surgical technique combined with either antiTNFa or immunosuppressive therapy resulted in complete healing of complex perianal disease in 13/15 (87%) pediatric CD patients. Conventional surgery, such as drainage of sepsis and loose seton insertion, has an important role in treatment but is associated with a significant risk of recurrence of fistulation in such condition.

Our study results indicate that specific perianal surgery, a cone-like fistulectomy can significantly improve the rate and duration of fistula response in Crohn’s disease patients subsequently treated with antiTNFa or immunosuppressive therapy.

Disclosure of Interest: None Declared
RAPID INFliximab INFUSION IN CHILDREN: A SINGLE CENTER EXPERIENCE

Raffi Lev Tzion 1,*, Yelena Rachman 1, Oren Ledder 1, Yael Greenberg 2, Dan Turner 1, 3

1Pediatric Gastroenterology, 2Pediatric Day Hospital, Shaare Zedek Medical Center, Jerusalem, Israel, 3The Hebrew University of Jerusalem, Jerusalem, Israel

Objectives & Study: Infliximab was the first biologic therapy to be used for Crohn’s disease, and it continues to be an important staple of the inflammatory bowel disease (IBD) therapy armamentarium. A significant drawback of infliximab administration is the requirement that the patients spend 3-4 hours in a dedicated infusion center. Recent adult studies have questioned the need for prolonged administration, but pediatric data is exceedingly scarce. We report our experience with a 1-hour rapid infusion protocol, prescribed in our unit for IBD patients, over a 6-month period.

Methods: 1-hour infliximab infusions were offered 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) The time interval from the previous infusion was shorter than 10 weeks. Standard duration infusions were administered over the course of approximately 3 hours for the first 3 infusions, and approximately 2 hours for subsequent infusions. All patients received acetaminophen before the infusion without other premedication.

Results: Between 5-11/2013, 26 children with IBD received infliximab infusions (20 CD, 2 UC and 4 IBD-U); mean age 16±3 years, 50% males, and median disease duration 32±33.8 months. 6 children qualified for the rapid infusion protocol. 69 standard duration infusions and 11 rapid infusions were administered. Concomitant immunomodulators were administered with 35/69 (50.1%) standard duration infusions and 4/11 (36.4%) rapid infusions. One infusion reaction occurred during a standard duration infusion and none occurred during the rapid infusions.

Conclusion: Consistent with adult data, our preliminary results indicates that 1-hour infliximab infusions in selected pediatric IBD patients offer a safe alternative to traditional 2-3 hour infusions.

Disclosure of Interest: R. Lev Tzion: None Declared, Y. Rachman: None Declared, O. Ledder: None Declared, Y. Greenberg: None Declared, D. Turner Grant / Research Support for: for research from Janssen and MSD, Consultant for: Janssen and MSD, Speakers bureau of: Janssen and MSD, Conflict with: Travel support from Janssen and MSD
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0168

**STANDARD VERSUS RAPID FOOD REINTRODUCTION AFTER EXCLUSIVE ENTERAL NUTRITIONAL THERAPY IN PAEDIATRIC CROHNS DISEASE**

Abi Faiman 1*, Mohamed Mutilib 1, Alexander Moylan 1, Natalie Morgan 1, Daniel crespi 1, Mark Furman 1, Ajmal Kader 1

1Paediatrics, Royal Free Hospital, London, United Kingdom

**Objectives & Study:** In paediatric Crohn’s disease (PCD), 6-8 weeks of exclusive enteral nutritional (EEN) is effective for inducing remission in 60-80% of cases. EEN is followed by gradual food reintroduction over variable (1-5 week) periods. Currently there is no recommended duration or method for food reintroduction. The rationale for slow reintroduction is unclear and may be due to concerns about food intolerance or to maintain longer remission. Achieving a usual diet faster after EEN is important to prevent malnutrition.

**Aims:**
1. Compare relapse rates following standard and rapid reintroduction of food after EEN
2. Duration of maintained remission after EEN in two groups of PCD patients.

**Methods:** Only patients with a new diagnosis of PCD were included. Group A had standard food reintroduction over 5 weeks and group B had rapid reintroduction over 3 days. Data was collected over two consecutive time periods. Those with strictures and those on steroids or biologics during EEN were excluded. Minimum duration of follow up was 1 year.

**Results:**
- Group A had 20 and B had
  - EEN achieved clinical remission in 80% of
  - At six months 1/3rd patients from each group had relapsed.
  - In the first year after EEN 50
  - Time to first relapse was 188 days (A) and 136 days (B).
  - None of the above results were statistically significant

**Conclusion:** In PCD, rapid food reintroduction following 6 week EEN is safe and equally effective as longer food reintroduction. Rapid reintroduction is well tolerated and better accepted by patients. Relapse rate and duration of remission is uninfluenced by type of food reintroduction. These findings are important as they advocate for reintroduction of a usual diet faster in PCD patients which may improve quality of life and help prevent nutritional deficiencies in a patient group who are at greater risk of malnutrition.

**Disclosure of Interest:** None Declared
Objectives & Study: Anemia is a common manifestation of inflammatory bowel disease (IBD). Growth and development is still underway in childhood, and anemia has well-known negative effects on mental and physical development. Thus, early diagnosis and therapy of anemia is even more important in children. Despite the existence of efficient therapeutic options, treating anemia seems to remain a lower priority for pediatric gastroenterologists. The aim of the study is to describe the prevalence and type of anemia as well as treatment outcome.

Methods: Newly diagnosed ulcerative colitis (UC) and Crohn’s disease (CD) patients were enrolled, and disease activity was determined by using the pediatric UC activity index (PUCAI) and pediatric CD activity index (PCDAI). Hemoglobin (Hb), iron, total iron binding capacity, transferrin saturation (TfS), ferritin and C-reactive protein as well as body mass index (BMI) z scores were recorded at diagnosis and every 6 months during 2 year follow-up. IBD associated anemia was classified as described in adult IBD guidelines: Iron deficiency (ID), ID anemia (IDA), anemia of chronic disease (ACD) and combination of ID and ACD (cID-ACD). All anemic patients were given oral iron.

Results: A total of 68 cases were enrolled (31 CD). The prevalence of anemia was 66.2% (62.1% in UC and 70.9% in CD), and an additional 17.6% of patients had ID at diagnosis. Of anemic 45 patients, 26.5% had ACD, 22.1% had IDA, and 17.6% had cID-ACD. Forty anemic patients received oral iron therapy for 13.4±4.9 months with a cumulative dose of 3.2±1.4 mg/kg/day (range:1.4-5.7 mg/kg/d). At the end of 12 months, both Hb and TfS significantly increased (p<0.01). At the end of 2-year follow-up, the prevalence of anemia decreased to 33.3%, and improvement was most prominent in patients with cID-ACD and ACD. The number of patients with ID and IDA were not significantly changed. PUCAI and PCDAI scores significantly decreased 6 months after the initiation of treatment, and it was correlated with the improvement of anemia (r²=0.73, p<0.0001). Furthermore, BMI z scores increased in accordance with the improved hematological parameters and the control of disease activity at 6th month (r²=0.745, p<0.0001) and 6th month vs. 12th month (r²=0.7, p<0.0001).

Conclusion: The use of age and sex specific cut-offs for the definition of IBD associated anemia usually overlooks the problem. Classification of anemia (ACD, IDA, ID and, cID-ACD) as described in adult IBD guidelines might be necessary in children as well. While the ACD improves with treatment of IBD, IDA and ID are usually overlooked or persist despite oral iron supplementation. Even iron deficiency per se has a negative impact on growth in children; early recognition of anemia and effective treatment of iron deficiency states in IBD seems essential apart from the specific treatment of IBD.

Disclosure of Interest: None Declared
DIAGNOSIS OF INFLAMMATORY BOWEL DISEASES (IBDS) BY ANALYSIS OF VOLATILE ORGANIC COMPOUNDS (VOCS) PRESENT IN THE ALVEOLAR AIR OF PAEDIATRIC PATIENTS

Chiara Pierobon 1*, Stefano Martelossi 1, Luigi Perbellini 2, Andrea Princivalle 2, Francesco Pasini 2, Lorenzo Monasta 1

1 Institute for Maternal and Child Health – IRCCS “Burlo Garofolo”, Trieste, Italy, 2 Department of Public Health and Community Medicine, University of Verona, Verona, Italy

Objectives & Study: The aim of this case-control study is to develop a model for the non-invasive diagnosis of IBDs by analysing the differences in the patterns of VOCS in the alveolar air between IBD patients and controls subjects.

Methods: Patients aged 10-17 years affected by IBD (33 ulcerative colitis and 34 Crohn’s disease), other gastrointestinal disease (n=65) and subjects without gastrointestinal problems (n=102) were enrolled in this study during a one year period. All subjects were fasting at air sampling, and information was collected on their medical history and ongoing therapies. Patients with IBD were also evaluated with a pediatric activity index (CDAI or PUCAI) and the Paris disease classification. VOCS in alveolar breath were analysed by an ion molecule reaction mass spectrometry. Five models were built starting from 83 VOCS and the variable age, adopting a penalizing LASSO logistic regression approach.

Results: The first model, created to distinguish IBD patients from controls, was based on 18 VOCS plus age (sensitivity=91%, specificity=76%, area under the ROC curve (AUC)=0.925). The second model built to separate Crohn’s disease (CD) from controls (gastroenterological and healthy), was based of 13 VOCS plus age (sensitivity=91%, specificity=84%, AUC=0.964). The third model tried to distinguish CD from ulcerative colitis (UC), and was based on 14 VOCS plus age (sensitivity=94%, specificity=76%, AUC=0.933). The fourth model, which tried to discriminate between IBDs and gastroenterological controls, was based on 15 VOCS plus age (sensitivity=91%, specificity=84%, AUC=0.918). The last model, based on 13 VOCS plus age, was built to separate UCs from controls (both gastroenterological and healthy) (sensitivity=94%, specificity=71%, AUC=0.906). We have already identified 14 out of the 38 molecules involved. The remaining 24 are at present only known for their molecular weight.

Conclusion: This study demonstrates that paediatric patients affected by IBDs (in particular CD patients) have a specific alveolar air VOCS pattern that can distinguish them from healthy subjects and gastroenterological controls. CD and UC also present different patterns, which remarks the different pathogenesis and manifestation of the two diseases. This study could be the first step for developing new diagnostic tools based on alveolar air analysis and to start investigating, through the identification of the molecules which help discriminate between cases and controls, the specific flora characterising these patients, in order to gain information on the aetiology of IBD.

Disclosure of Interest: None Declared
**Objectives & Study:** The clinical presentation of children with inflammatory bowel disease (IBD) is often non-specific and overlaps with functional gastrointestinal disorders. Non-invasive tests may assist the general practitioner with this diagnostic dilemma. This systematic review provides summary estimates of the diagnostic accuracy of non-invasive tests for the diagnosis of IBD in children presenting with chronic gastrointestinal symptoms.

**Methods:** A literature search was conducted in Medline and Embase until November 2013 and citation search of references were performed. Two independent reviewers screened titles and abstracts, assessed quality of selected studies and extracted data. Included were studies with cross-sectional, cohort or case-control design that reported data for extraction or calculation of a two by two table of non-invasive tests (clinical assessments, blood or fecal tests or abdominal ultrasonography) for IBD, confirmed by endoscopy and histopathology or clinical follow up of minimal 12 months, in children with chronic gastrointestinal symptoms, aged 0-18 years. Methodological quality of the included studies was assessed with the Quality of Diagnostic Accuracy Studies checklist (QUADAS-2). Meta-analysis was performed using a bivariate model in case of clinical homogeneity.

**Results:** (Here we present preliminary results. Final results will be available in February 2014.) Nineteen studies met our inclusion criteria. Fecal calprotectin showed a pooled sensitivity and specificity of respectively 0.98 (95% confidence interval 0.92-0.99) and 0.78 (0.61-0.89). Pooled sensitivity of C-reactive protein, hemoglobin, erythrocyte sedimentation rate and platelet count were respectively 0.60 (0.43-0.76); 0.41 (0.26-0.57); 0.63 (0.52-0.73); 0.56 (0.33-0.76) and the specificity were respectively 0.93 (0.82-0.97); 0.89 (0.80-0.94); 0.91 (0.80-0.96); 0.92 (0.87-0.95). The performance of clinical assessments varied substantially. The sensitivity for rectal bleeding ranged from 0.48 to 0.82 and specificity from 0.50 to 0.92. Only one study presented test characteristics of ultrasonography with a sensitivity of 0.74 and specificity of 0.78.

**Conclusion:** Fecal calprotectin and blood tests demonstrated a high diagnostic accuracy for IBD in children with gastrointestinal symptoms in secondary or tertiary care setting. Results indicate that the high sensitivity of fecal calprotectin combined with the high specificity of the blood tests may represent a good diagnostic combination. None of the studies were performed in primary care; further research is required to investigate the diagnostic accuracy of non-invasive tests in this setting.

**Disclosure of Interest:** None Declared
REINDUCTION TREATMENT FOR LOSS OF RESPONSE TO TWO BIOLOGIC AGENTS IN CROHNS DISEASE

Nir Fireman 1,*, Arie Levine 1
1Paediatric Gastroenterology and Nutrition unit, Wolfson Medical Center, Holon, Israel

Objectives & Study: Background - Loss of response (LOR) to a single biological agent (i.e. Infliximab (IFX) or Adalimumab (ADA)) after previous failure of immunomodulators is a frequent event complicating the treatment of severe Crohn’s disease. Some patients may also lose response to a second biological agent, often exhausting all current medical therapies despite active disease. A new strategy for LOR is Reinduction of a previously failed biologic along with Methotrexate. Reinduction guarantees higher trough levels than decreasing dose intervals, and Methotrexate acts as a second agent for remission which might also impair formation of anti drug antibodies.

Methods: Methods - Retrospective analysis of Crohn’s disease patients in a pediatric IBD center, who developed LOR to two biologic agents and relapsed despite dose or interval changes. All patients had lost response to both Infliximab and Adalimumab and all had received a prior immunomodulator. All underwent a second induction (Reinduction treatment) with Adalimumab combined with Methotrexate (doses 10-15 mg/m²) one patient received Infliximab for reinduction treatment. Response to treatment was defined as decrease in clinical and laboratory disease activity whereas remission was defined as complete absence of clinical symptoms (PGA). Data on mucosal healing was collected for those who underwent a colonoscopy after reinduction.

Results: Results - 12 Crohn’s patients with LOR underwent a reinduction treatment. Mean age at presentation was 16.5 years (12-26), mean age of diagnosis was 12.7 years (7.5-17). 8 males and 4 females. Overall response to treatment was achieved in 9 patients (75%), while 7 (58.3%) reached a complete clinical remission. 3 (25%) patients failed to respond. 6 patients out of the remission group underwent a colonoscopy demonstrating a complete mucosal healing in 3 patients.

Conclusion: Conclusion - Reinduction of a previously failed biologic along with Methotrexate is a promising strategy for treatment of patients who lose response to two biological agents and exhaust all current medical therapies.

Disclosure of Interest: None Declared
DURATION OF REMISSION IN CHILDREN WITH CROHNS DISEASE TREATED INITIALLY WITH CORTICOSTEROIDS OR EXCLUSIVE ENTERAL NUTRITION

Ondrej Hradsky 1,*, Kristyna Zarubova 1, Jan Ohem 1, Radana Kotalova 1, Jiri Nevoral 1, Jiri Bronsky 1
1Paediatric, University Hospital Motol, Prague, Czech Republic

Objectives & Study: Exclusive enteral nutrition (EEN) has been repetitively shown to be at least equally effective as corticosteroids (CS) in induction of remission in pediatric patients with Crohn’s disease (CD). Data on duration of remission in these patients when treated with immunomodulators are scarce. Recent study has shown positive long-term outcomes of treatment with EEN over CS, however immunomodulators had not been primarily used. The aim of the study was to determine difference in duration of remission between patients treated initially with EEN or CS and parallely treated also with azathioprine (AZA).

Methods: Among 95 newly diagnosed patients from 2009 to 2012 with CD and follow-up at least 12 months (43 girls, median age at diagnosis 14 years) we identified 41 patients initially treated with CS and 26 with EEN. All patients were simultaneously started with AZA (2 mg/kg/day) immediately at the time of diagnosis. Nineteen patients treated with biologics (infliximab, adalimumab), three with mesalasine and six who underwent initial surgery (ileoceacal resection after conditioning) were excluded. Two patients from EEN group with intolerance to AZA have been also excluded.

Results: Among patients treated initially with CS resp. EEN, 46% (19/41) respectively 42% (10/24) had relapse in the first 12 months. There was no statistically significant difference between those two groups (p-value = 0.73). Survivor curve analysis has shown no difference over the full follow-up period (p-value = 0.74).

Conclusion: The benefit in long-term outcome of EEN over CS was not detectable when AZA was started at the time of diagnosis.
Supported by research grant VZ FNM 64203/6001.

Disclosure of Interest: None Declared
SURGERY FOR PAEDIATRIC CROHN’S DISEASE A SINGLE CENTRE EXPERIENCE

Jiri Bronsky 1,*, Richard Skaba 2, Lucie Pos 2, Jan Ohem 1, Blanka Rouskova 2, Ondrej Hradsky 1, Kristyna Zarubova 1, Jiri Nevoral 1, Vladimir Mixa 3, Martin Kyncl 4, Lenka Mrazkova 4
1Department of Paediatrics, 2Department of Paediatric Surgery, 3Department of Anaesthesiology, 4Department of Imaging Methods, University Hospital Motol, Prague, Czech Republic

Objectives & Study: Surgery has become part of routine medical treatment in paediatric patients with Crohn’s disease (CD). Resection of terminal ileum and ascending colon is the most common surgical procedure done in these patients. The aim of the study was to review the spectrum of indications and results of surgical procedures in our group of paediatric patients with CD.

Methods: A single-centre retrospective study of patients with CD who underwent surgical procedures between January 2008 and December 2012.

Results: In total, 37 patients (20 girls) underwent 53 operations within 5 year period. There were 26 local surgeries of perianal disease, 19 ileocecal resections (ICR), 1 right hemicolecotomy, 2 laparotomies and ileostomies, 3 laparotomies and drainage of intra-abdominal abscesses, 1 appendectomy and one partial gastric resection. The median age at the time of operation was 16.2 years (range 12.7 – 18.3 years) and the median time of duration of the CD before the first surgery was 15.5 months (0 - 60 months). ICR was the most common resection procedure done in our group. Indications of ICR were abscess and fistula in 10, stricture of terminal ileum in 4, bowel obstruction in 3 and high disease activity localized in terminal ileum non-responding to medical therapy in 2 patients. ICR with end-to-end anastomosis was performed in 18 patients, ICR with ileostomy and mucous colonic fistula in 1. The median hospital stay was 9 days (6 – 21 days). There were 4 complications (21%) – one anastomotic leak which required re-laparotomy and formation of an ileostomy, 1 intestinal obstruction due to peritoneal adhesions 9 months after primary operation and 2 intermittent intestinal obstructions responding well to conservative treatment. There were no anastomotic strictures that have required dilation and/or resection so far. Median follow-up after the ICR was 2 years (0.4 – 4.7 years). The disease reactivated (verified in endoscopy) in 4 patients (21%) - 2, 4,7 and 11 months after the first operation. There is one patient with ileostomy awaiting its closure. Current postoperative medication was Azathioprine in 8, Infliximab and Azathioprine in 8, Glucocorticoids and Azathioprine in 1 and Mercaptopurine in 1 and no medication in 1 patient (this patient refused any medication and he has been without problems since the surgical procedure).

Conclusion: Even though there is a risk of early disease relapse following surgery in paediatric patients with CD, surgical treatment of CD is well tolerated, has a relatively low rate of complications and contributes to achieve normal growth and development, decreased morbidity and satisfactory quality of life. Supported by research grant VZ FNM 64203/6001.

Disclosure of Interest: None Declared
THE CHANGING BEHAVIOUR OF NEW ONSET IBD IN IRISH CHILDREN FROM 2000-2011

Aoife Carey,1,2,3,*, Billy Bourke1,2,3,4, Anne Marie Broderick1,2,3, Shona Quinn1,2, Mary Hamzawi1,2, Karen Gleeson1,2, Rebecca Wylde1,5, Seamus Hussey1,2,3,4
1Our Ladys Hospital for Sick Children (OLCHC), 2National Centre for Paediatric Gastroenterology (NCPG), 3National Childrens Research Centre (NCRC), 4School of Medicine and Medical Science, University College Dublin, Dublin, Ireland, 5Leiden University Medical Centre, Leiden, Netherlands

Objectives & Study: The rise in the incidence of paediatric inflammatory bowel disease (IBD) in Ireland from 2000 to 2010 has been recently documented. The aim of this current study was to examine the phenotypic attributes of IBD among children diagnosed with new onset IBD in 2010 to 2011.

Methods: A retrospective review of paediatric IBD was undertaken using nationally representative data from the National Centre for Paediatric Gastroenterology, Hepatology and Nutrition (NCPGHN) in Ireland. IBD was phenotyped using the Paris classification and compared against previous Irish data from 2000 and 2008 and international figures. Data was analysed using the Statistical Package for Social Sciences (SPSS).

Results: The incidence of IBD from October 2010 to October 2011 was 7.5/100,000/year. Seventy nine children were diagnosed with IBD during the defined review period (49 boys, 32 girls, median age of diagnosis 12.7 years). The phenotype of new onset IBD has changed significantly from historic cohorts. There is a marked increase in the incidence of combined upper and lower gastrointestinal CD (32%>52%). Furthermore, there is a distinct increase in complex disease behaviour, such as stricturing and penetrating disease, from 2000 to 2011 (12%>27% respectively). The incidence of UC (n=29) has increased three-fold in 10 years (16 boys, median age of diagnosis 13.1 years). Additionally, 59% of children were reported to have moderate to severe disease activity, similar to previously reported data. At one year, 21 (46%) children with CD and 19 (66%) children with UC children were in remission, with 91% of children steroid free.

Conclusion: The incidence of IBD in Ireland remains high. The phenotypic behaviour of CD is changing with more complex disease behaviour evident at presentation. The prevalence of UC has tripled over 10 years. Future prospective longitudinal studies are needed to fully elucidate the factors underlying IBD in Irish children.

Disclosure of Interest: None Declared
EPIDEMIOLOGY OF INFLAMMATORY BOWEL DISEASE IN THE PAEDIATRIC POPULATION IN WESTERN AUSTRALIA

Alicia Ai Wei Lim 1,*, Catherine Mews 1, Forbes David 1, Zubin Grover 1, Anslie Lopez 1, Angela De Nardi 1, Madhur Ravikumara 1

1Gastroenterology, Princess Margaret Hospital for Children, Western Australia, Australia, Subiaco WA 6008, Australia

Objectives & Study: Inflammatory bowel disease (IBD) is a chronic inflammatory condition of the gastrointestinal tract characterised by a relapse-remission pattern and is associated with significant morbidity. Over the last 2 decades, there has been an increase in incidence of IBD globally. We present the epidemiological trend in paediatric IBD (<16 years of age) in Western Australia in the last 10 years.

Methods: This was a retrospective chart review of all patients diagnosed with IBD from year 2004 to present. Classification of IBD included are Crohn’s disease (CD), ulcerative colitis (UC) and inflammatory bowel disease - unclassified (IBDU). Princess Margaret Hospital is the only tertiary hospital in Western Australia offering paediatric endoscopic service which is necessary for the diagnosis of IBD.

Results: Over the 10 year period, 181 children were diagnosed with IBD. Hundred and one children (56%) were diagnosed with CD, 65 (36%) with UC and 15 (8%) with IBDU. The number of newly diagnosed IBD increased each year. There were 3 children diagnosed with IBD in 2004, 19 in 2009 and to date in 2013, we have 35 newly diagnosed IBD. We found no difference in rates of IBD with gender. The median age of diagnosis of IBD was 12 years of age (range 2.0 years - 16 years 11 months). Majority of the UC and IBDU had pancolitis at diagnosis while a more patchy distribution with CD. There are 52 children on biologics at present (38 CD, 7 each from UC and IBDU). Fourteen children required surgical intervention. Thirteen children from our cohort were also diagnosed with either sclerosing cholangitis (primary or autoimmune) or autoimmune hepatitis, known extra-intestinal manifestation of IBD.

Conclusion: There has been a significant increase in the incidence of paediatric IBD in recent years, in accordance to the global data. The estimated incidence rate is approximately 6.5 per 100,000 children population in Western Australia, which is one of the highest incidence rate of paediatric IBD to the best of our knowledge. This creates significant implications on the workforce and resource placement.

Disclosure of Interest: None Declared
OUTCOME MEASURES IN PAEDIATRIC IBD: DATA FROM A TERTIARY LEVEL CENTER IN UK

Simona Gatti 1,*, Mary Brennan 2, Franco Torrente 2, Matthias Zilbauer 2, Robert Heuschkel 2

1Department of Paediatrics, Università Politecnica delle Marche, Ancona, Italy, 2Department of Paediatric Gastroenterology, Hepatology and Nutrition, Addenbrookes Hospital, Cambridge, United Kingdom

Objectives & Study: Evaluation of a proposed outcome panel, including self-reported outcomes and patient perception of health in a tertiary paediatric IBD setting

Methods: The panel of outcome measures was designed based on a detailed literature review of currently available quality measures both within IBD and related immune mediated diseases. Patients, consecutively enrolled between November 2012 and February 2013, were asked to fill in a patient’ satisfaction questionnaire (adapted from QUOTE-IBD). Data were collected from medical notes and electronic records (e-MR) and the self-reported outcomes were extrapolated from the questionnaire. The project was registered as an audit. Eighty-one questionnaires were handed out, 76 patients returned the questionnaire (96%) and were prospectively included in the study (mean age: 12.89 ± 2.5; M/F: 1.1/1). The following measures (% of children) were considered: 1. six months steroid free remission, 2. satisfactory growth and nutritional status, 3. unplanned admissions in the last 12 months, 4. school attendance in the last 12 months, 5. self reported health status.

Results: Forty-three patients (63%) had Crohn’s disease (CD), 17% had Ulcerative Colitis (UC) and 20% had Inflammatory Bowel Disease Unclassified (IBDU). Overall 39% (CI95%; 28-50) were found to be in remission, with 31.66% being in 6 months steroid free remission (CI 95%: 19.9-43.4), with no differences between CD, UC and IBDU patients. Patients with a satisfactory growth status (height > 10° percentile) were 83.4% (CI 95%: 74-92.8) and those with satisfactory nutritional status (BMI > 10° percentile) were 93.6% (CI 95%: 87.4-99.8). A quarter of the IBD patients (23.8%; CI 95%: 11-36.6) had at least one unplanned admission in the previous year, with a median length of stay of 2.5 days (IQR: 2.75). Regarding the school attendance only 38.1% (CI 95%: 23.3-52.9) achieved the average national school attendance (95%). Only 33.3% of patients reported their well-being as “very good or excellent” in the previous 3 months with 70.7% reporting their health as being much better or better compared to the previous year. The reported well-being was found to correlate significantly with disease activity index (r= -0.4133, p= 0.0007). The awareness of own disease status was found to be significantly higher (p= 0.042) in patient in remission (72.4 %) compared to those not in remission (36.9 %)

Conclusion: This study represents the first effort to test a set of proposed outcome and quality measures in the management of children with IBD. We found the vast majority of the tested measures to be useful for assessing the quality of care delivered to children with IBD in a local setting. Further studies are now required to be performed in other UK centers ultimately allowing to set a national standard and thereby continuing to improve the quality of care

Disclosure of Interest: None Declared
INCREASING INCIDENCE OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE (PIBD) IN SOUTHERN ENGLAND

James John Ashton 1,*, Anthony E Wiskin 1, Sarah Ennis 2, Akshay Batra 1, Nadeem A Afzal 1, Robert Mark Beattie 1
1Paediatric Medical Unit, University Hospital Southampton, Southampton, United Kingdom, 2Human Genetics and Genomic Medicine, University of Southampton, Southampton, United Kingdom

Objectives & Study:
There has been a significant increase in the incidence of Paediatric inflammatory bowel disease over the last 25 years although this is no recent data from England. We aimed to analyse changes in incidence within a defined English population over the last decade and compare this to recent and historical incidence data from comparable studies

Methods:
The new diagnosis incidence of PIBD (age less than 16 years) was recorded from a prospective database for a geographically-defined area of southern England (2002-2012). Data was analysed for two separate time periods (cohort 1- 2002-2006 and cohort 2- 2008-2012) and compared to data from the British Paediatric Surveillance Unit survey in 1998/9(1). Data was analysed by age, sex and disease type.

Results:
There has been an increase in incidence of PIBD from 6.39/100,000/year during cohort 1 to 9.37/100,000/year during cohort 2 (P=0.0002). This compares with the BPSU incidence data in England (1998-99) of 5.2/100,000/year. The Male to Female ratio of overall PIBD incidence was comparable in both cohorts (cohort 1- 1.35:1, cohort 2- 1.5:1). There was no significant difference between median age of diagnosis in the two cohorts (p=0.46)

<table>
<thead>
<tr>
<th>Overall incidence rates of PIBD in Wessex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Incidence per 100,000/year</td>
</tr>
<tr>
<td>BPSU data for England (1998-99)</td>
</tr>
<tr>
<td>PIBD</td>
</tr>
<tr>
<td>5.2</td>
</tr>
<tr>
<td>Cohort 1 (2002-2007)</td>
</tr>
<tr>
<td>PIBD</td>
</tr>
<tr>
<td>6.39</td>
</tr>
<tr>
<td>Cohort 2 (2008-2013)</td>
</tr>
<tr>
<td>PIBD</td>
</tr>
<tr>
<td>9.37</td>
</tr>
</tbody>
</table>

Conclusion:
The incidence of PIBD continues to increase with a rise of almost 50% in the last decade in Southern England. The reasons for this increase are unclear and, although they may partly reflect earlier diagnosis and improved referral patterns, are likely also to reflect a genuine rise in new cases.

References:

Disclosure of Interest: None Declared
ELEVATED CRP AND PCDAI ARE ASSOCIATED WITH THE NEED FOR IMMUNOMODULATORS AND BIOLOGICALS AT ONE YEAR FOLLOW-UP IN PAEDIATRIC CD: RESULTS FROM A NATIONWIDE PAEDIATRIC IBD INCIDENT COHORT (HUPIR)

Katalin Eszter Müller 1,*, Gabor Veres 1 and HUPIR Group

11st Department of Paediatrics, Semmelweis University, Budapest, Hungary

Objectives & Study: Predicting short-term relapses and long-term prognosis would be indispensable in pediatric inflammatory bowel disease (IBD). The relationship of initial disease activity indices [PCDAI (Pediatric Crohn Disease Activity Index), PUCAI (Pediatric Ulcerative Colitis Activity Index)] and prognosis has not been deeply analyzed yet. Our aim was to evaluate the association of initially elevated CRP and disease activity with short-term prognosis in a nationwide pediatric incident cohort from Hungary.

Methods: From January 1, 2008 to December 31, 2010 demographic data and clinical characteristics of newly diagnosed pediatric IBD patients younger than 18 years were prospectively registered. Association of disease phenotype (Paris Classification) and CRP, disease activity indices (PCDAI, PUCAI) were analyzed. In addition, relationship of PCDAI, elevated CRP (higher than 10 mg/L) and the need for aggressive therapy (immunomodulators, biological therapy) at the end of the first year if the disease course.

Results: A total of 420 patients were identified [Crohn’s disease (CD): 266 (63.2%); ulcerative (UC) 124 (29.4%)]. Initially, 48% (124/256) of CD patients had moderate to severe disease (PCDAI>30), and this rate decreased to 2.1% by the end of the first year. Proportion of UC patients with moderate to severe disease (PUCAI>35) at diagnosis declined from 57.5% (69/120) to 6.8% after 1-year follow-up. The median activity index in CD was 30 (PCDAI, IQR 20-42.5) and the median of PUCAI was 35 (PUCAI, n=69; IQR 25-50).

In CD, PCDAI of children younger than 10 years (A1a) was lower than PCDAI of children older than 10 years (A1b) (p=0.007). Terminal ileal involvement was correlated with higher CRP (p=0.021) and PCDAI (p=0.026). Patients with strictureting/penetrating phenotype had elevated CRP (p=0.01) significantly more often than patients with inflammatory phenotype. In UC, elevated CRP (p<0.001) and PCDAI (p=0.015) at diagnosis in patients with CD were significantly associated with the need for immunomodulators and biologicals at one year. Frequency of elevated CRP level in patients with UC was related to the need for azathioprine (p=0.064), while PUCAI was not associated with the need for immunomodulators.

Conclusion: At diagnosis half of the patients with IBD had moderate to severe disease and this rate decreased to less than 10% after one year. Elevated CRP seemed to be predictive for the need of aggressive therapy in CD and UC. However, elevated PCDAI but not PUCAI were related to more aggressive disease course. This discrepancy is probably due to the different methods of the activity index.

Disclosure of Interest: None Declared
COMPARISON BETWEEN PAEDIATRIC CLASSICAL ULCERATIVE COLITIS AND ULCERATIVE COLITIS ASSOCIATED WITH AUTO-IMMUNE DISEASES

Chloé Guinet-Charpentier 1,*
1Children Hospital, Nancy, Vandoeuvre-Les-Nancy, France

Objectives & Study: Ulcerative colitis (UC) is a chronic inflammatory condition. Up to 25 % of IBD patients present in childhood. Previous reports suggested that UC may have a worse prognosis when associated with auto-immune diseases. We compared characteristics at diagnosis and natural history of the disease between classical UC (CUC) and UC associated with auto-immune diseases (UCAI) in children.

Methods: 67 children followed for UC were included in the study. Medical charts of patients from 1993 to 2012 were reviewed. Forty-nine patients (73 %) were included in the classical UC group (CUC) versus 18 (27 %) in the UC associated with auto-immune diseases group (UCAI). Characteristics at diagnosis and natural history of UC were analyzed.

Results: Median follow-up was 4.8 years. Median age at diagnosis was 11.6 years [2.4 - 14.7 years] in the UCAI group compared with 9.8 years [1.8 - 16.3 years] in the CUC group (p = 0.25). Time between symptoms onset and diagnosis was significantly shorter in the UCAI (2.4 months) than in the CUC (2.8 months) (p = 0.0001). Median delay between onset of digestive extra-intestinal auto-immune diseases (auto-immune hepatitis, primary sclerosing cholangitis or auto-immune pancreatitis) and UC diagnosis was less than 2 months [0.08 - 2 months] in the UCAI group. Family history of auto-immune diseases was twice more frequent in the UCAI group (77.8 %) than in the CUC one (36.9 %) (p = 0.001). There were no significant differences regarding biological (fecal calprotectin, hemoglobin or C-reactive protein) and histological (crypt abscesses, neutrophilic and eosinophilic infiltrates, basal plasmacytosis) findings between the two groups. No proctosigmoiditis was observed in the UCAI group. At five years, the need for corticosteroids did not differ between the two groups (80.4 % in the UCAI group versus 74.2 % in the CUC one ; p = 0.95). Eighty-six percents of UCAI patients had received azathioprine at one year as compared with 70.9 % in CUC group (p = 0.34). There was also no significant difference between the 2 groups for infliximab treatment at one and five years.

Conclusion: In this pediatric study, UCAI shows different characteristics at baseline compared to CUC, including time between symptoms onset and diagnosis and family history of auto-immune disease. However, the course of UCAI does not seem to be influenced by the presence of concomitant auto-immune diseases.

Disclosure of Interest: None Declared
**Objectives & Study:** Small bowel (SB) imaging is involved in the diagnosis, surveillance and reassessment of Crohn’s Disease (CD). Both Ultrasound (USS) and Magnetic Resonance Imaging (MRI) are used in the assessment of the SB in children with CD.

**Aim:** To compare efficacy of SB USS and SB MRI in identifying small bowel CD.

**Methods:** We reviewed data retrospectively from 34 children < 18 years old with diagnosis of CD, between January 2009 and October 2013. Clinical data was obtained from case notes. Imaging data included bowel wall thickness (abnormal if > 3mm) and disease activity, measured by contrast enhancement in MRI and vascularity on USS Doppler. Other features noted were lymph nodes (LN), collections, fistulae, strictures and inflammatory masses. We specifically looked at thickness in 3 anatomical sites “Jejunum, Ileum and Terminal Ileum (TI)”.

We included patients who had SB USS done by an experienced gastroenterology (GI) radiologist, and SB MRI done within 30 days of each other. A subgroup of patients was selected to compare imaging techniques against histology as a criterion standard for detecting TI disease. This subgroup included those who had endoscopy with biopsies within 30 days of either imaging modality.

**Results:** Our cohort included 34 patients (11 F, 23 M) median age 14.4 years, 19 newly diagnosed and 15 reassessments. On MRI, 38/102 (37.2%) sites had abnormal thickness and on USS 36/93 (38.7%) sites were abnormal. Of the 93 comparable sites, 30 (32.3%) were identified as abnormal in both MRI and USS, 14 sites (15%) were identified by only one modality and 50 sites were deemed as normal by both (53.7%). Anatomical site agreement occurred in 85% of cases.

In our subgroup (n=21) the sensitivity for detecting any abnormality compared to histology for MRI and USS was 87.5% and 81.3% respectively. The accuracy was 80% for both modalities. In addition to this, when assessing specifically bowel thickness alone in TI compared with histology, we found that MRI was 71.4% sensitive as compared to USS sensitivity of 66.7%.

**Conclusion:** MRI and USS are comparable in detecting abnormality of SB disease when the latter is performed by an experienced GI radiologist.

USS SB is less time consuming, more accessible and may be a comparable alternative to MRI in monitoring children with SB CD.

**Disclosure of Interest:** None Declared
THE BELGIAN REGISTRY OF PEDIATRIC CROHNS DISEASE (BELCRO): GROWTH STATUS AFTER 3 YEAR FOLLOW UP

Elisabeth De Greef 1*, Jestinah M Mahachie John 2, Ilse Hoffman 3, Françoise Smets 4, Stephanie Van Bievliet 5, Patrick Bontems 6, Isabelle Paquot 7, Philippe Alliet 8, Kristel Van Steen 2, Gigi Veereman 1 and IBD Working Group of Bespghan and Bird

1Pediatric Gastroenterology, UZ Brussel, Jette, 2Systems and Modeling Unit, Montifiori Institute, ULG, Liege, Belgium, 3Pediatric Gastroenterology, UZ Gasthuisberg, Leuven, Belgium, 4Pediatric Gastroenterology, UCL St Luc, Woluwe, Brussels, Belgium, 5Pediatric Gastroenterology, UZ Gent, Gent, Belgium, 6Pediatric Gastroenterology, HUDERF, Brussels, Belgium, 7Pediatric Gastroenterology, CHC espérance, Liege, Belgium, 8Pediatric Gastroenterology, Jessa Hospital, Hasselt, Belgium

Objectives & Study: The BELCRO cohort was initiated in 5/2008 to prospectively study newly diagnosed pediatric Crohn’s disease patients. Here we report on growth outcome at 3y follow up.

Methods: Data from the BELCRO database were evaluated at diagnosis (M0), after 24 (M24) and 36 months (M36). Cross sectional analysis at M36, longitudinal analysis and cluster profile analysis from M0 to M36 were performed on the growth data obtained. Hypothesis were tested at 5% significance.

Results: At M 36, consecutive data for BMI and height z-scores was available in 67 and 75 patients respectively. Disease severity went from 5% inactive, 19% mild and 76% moderate to severe at M0 to 70% inactive, 24% mild and 6% moderate to severe at M36. Median BMI z-score was -0.11 (range -3.38 to 2.01) and median height z-score was 0.13 (range -2.03 to 2.3). Five patients (7%) had height z-score and 19 patients (28%) BMI z-score < -2SD at M0. At M36, 0/5 and 5/19 remained < -2SD. Even though 75% of BMI z-scores and 93% of height z-scores remained within normal ranges (> -2SD < 2SD) at diagnosis, 66% of patients improved their BMI z-score and 43% their height z-score over 36M resulting in 91% of BMI z-scores between normal ranges at M36 and 97% for height z-scores. Patients diagnosed and followed by adult physicians had significantly better height z-scores at M0 which remained at M36 (P=0.027). L3 or L4A involvement imply a worse height z-score at M 36 (p= 0.02 ; p= 0.02). Only BMI z-score and height z-score at diagnosis and M24 predicted respectively the BMI z-score and height z-score at M36. Patients with inactive disease at M36 on Immunomodulator monotherapy had a better height z-score at M 36 (p= 0.006).

Conclusion: The majority of patients had severe disease at diagnosis, but few of them had severe growth retardation. An increase in z-scores for BMI and height is noticed in a large group of patients. Disease location and growth status at diagnosis seems to influence height z-scores at M36.

Disclosure of Interest: None Declared
**INFLIXIMAB IS AN EFFECTIVE INDUCTION THERAPY IN CHILDREN WITH PERIANAL FISTULIZING CROHNS DISEASE**

Agnieszka Wegner 1,*, Maciej Dądalski 2, Jarosław Kierkuś 2

1Departament of Gastroenterology, Hepatology and Eating Disorders, 2Department of Gastroenterology, Hepatology and Eating Disorders, Children's Memorial Health Institute, Warsaw, Poland

**Objectives & Study:** Infliximab is applied in the treatment of Crohn’s Disease (CD) in pediatric patients, who do not respond to conventional therapy or/and in case of perianal fistulizing CD. Overall efficacy of induction therapy with infliximab in children with CD is up to 80%, whereas in adult subgroup with perianal fistulizing CD induction therapy is successful in about 60% cases. The aim of this study was to assess the efficacy of induction therapy with infliximab in children with perianal fistulizing Crohn’s Disease.

**Methods:** This is a subanalysis of CIMIT study. The subgroup of 25 patients (19M, 6F; age 14,2±3,1 years; CD duration 1,8±1,8 years; PCDAI48,4±12 [mean±SD]) with PCDAI>30 and perianal fistula present 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 total PCDAI<30) and remission (PCDAI≤10) were assessed at Week 10 as well as fistulas’ healing.

**Results:** 1 patient had induction therapy stopped due to VZV infection. 21 out of 25 (84%) pts had clinical response, and 16 out of them (64%) had clinical remission at the end of induction therapy. Fistula closure was found in 16 of 25 patients (64%) at 10 weeks study. 3 out of 4 patients with no response still had active fistulas at Week 10 and among 9 patients with active fistulas at Week 10, 4 had clinical remission (fistula was the only symptom of CD) and 7 had clinical response.

**Conclusion:** Infliximab is an effective induction therapy in children with perianal fistulizing Crohn’s Disease with successful fistulas closure in 64% cases. The majority of patients with no fistula healing had also clinical benefit with such a therapy.

**Disclosure of Interest:** None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0184

**COMPLICATED CROHNS DISEASE, BETWEEN SURGERY AND GASTROENTEROLOGY**

Simona Faraci 1,*, Erminia Romeo 1, Francesca Rea 1, Giovanni Federici di Abriola 1, Tamara Caldaro 1, Filippo Torroni 1, Giuseppe Magazzù 2, Fiammetta Bracci 3, Luigi Dall'Oglio 1, Paola De Angelis 1

1Digestive Surgery and Endoscopy Unit., Bambino Gesù Children’s Hospital, IRCCS, Rome, Italy,

2Clinical and Biomolecular Hepato-Gastroenterology of Pediatric and Adult Age, University Hospital, Messina, Messina, Italy,

3Epatogastroenterology Unit, Bambino Gesù Children’s Hospital, IRCCS, Rome, Italy

**Objectives & Study:** Post-surgical recurrence of Crohn’s disease (CD) is common (65–90% within 12 months and 80–100% within 3 years). Clinical recurrence without therapy is about 20–25%/year; treatment of complications of CD and prevention of postoperative disease remain debated in pediatric patients, while in adults better codified. Evaluation of postsurgical treatment in pediatric CD.

**Methods:** From 1999, 36 patients (range 4-20 years, F/M:12/24), with complicated CD, divided into low, moderate, high-risk groups according to risk factors (smoking, disease behavior, previous surgery, family history, anastomotic type) underwent surgery. Age at diagnosis, location, extension and activity of CD, complications, indications for surgery, type of surgery, postoperative clinical course, pre and post surgical treatment and endoscopic recurrence were assessed.

**Results:** At diagnosis, localization of disease was ileo-colic (33 patients, 92%), ileal (2.5%) and jejunoileal (1 patient, 3%). Behaviour was inflammatory in 14 patients (39%), stenosing in 16 (44%) and stenosing/fistulizing in 6 (17%). Eleven patients underwent ileal resection or ileo-colonic resection, 3 patients strictureplasty and resection, 22 patients strictureplasty alone (9 Mikulicz and 13 modified Michelassi). All patients had therapy after surgery. Nine patients lost to endoscopic follow up (mean: 4.4 years). Ten, of the remaining 27 patients, relapsed. In low-risk group, one patient treated with AZA relapsed 4 years after surgery. In moderate-risk group 3 patients, treated with AZA and 5ASA relapsed one year after surgery, one patient treated with 5ASA alone relapsed one year after surgery and one patient treated with AZA 5 years later. In high-risk group 3 patients treated with 5ASA, relapsed at 1,2,4 years and one patient treated with AZA and 5 ASA relapsed 1 year after surgery. In moderate and in high risk group patients treated with biological (4) or immunosuppressant(4) therapy didn’t relapse. Mean follow-up of the 27 patients was 4.4 years (range: 1 month-14 years)

**Conclusion:** Literature suggests in adults therapy with high doses of mesalamine in isolated ileal resections in very low risk; with azathioprine in the disease with medium/ high risk; infliximab in penetrating and perianal disease. Prophylactic therapy should be initiated within 2 weeks of surgery and the duration must be at least two years. In children, there are no prospective study to individuate high and low-risk groups; the age already represents a high risk factor for recurrence. In our retrospective study we observed that early treatment is effective in pediatric operated CD, as in adults. We can consider adults guidelines applicable to pediatric population until prospective studies about more aggressive therapy after surgery will be done.

**Disclosure of Interest:** None Declared
Gastroenterology
Inflammatory Bowel Disease
PO-G-0185

GROWTH PATTERN AND GROWTH FAILURE IN PAEDIATRIC CROHN DISEASE ARE RELATED TO INFLAMMATORY STATUS BUT NOT TO DURATION OF STEROID THERAPY

Delphine Ley 1,*, Hélène Béhal 2, Corinne Gower-Rousseau 3, Alain Duhamel 2, Francis Vasseur 3, Mathurin Fumery 4, Laurent Michaud 1, Isabelle Rousseau 3, Guillaume Savoye 5, Dominique Turck 1
1Paediatric GI Unit, 2Biostatistics Unit, EA 2694, 3Epidemiology Unit, EA 2694, CHU Lille; Lille-2 University, Lille, France, 4Gastroenterology Unit, CHU Amiens; Amiens University, Amiens, France, 5Gastroenterology Unit, CHU Rouen; Rouen University, Rouen, France

Objectives & Study: Growth failure is the main complication of pediatric-onset Crohn disease (CD). The respective role of disease activity and steroid therapy in growth faltering is still a matter of debate. The aim of the present study was to investigate whether the growth pattern of children with CD was correlated with the evolution of inflammatory status during the disease course, whatever the cumulative duration of steroid therapy.

Methods: 107 patients (63 boys and 44 girls) with a diagnosis of CD made <17 years of age, followed in the same unit during ≥2 years and for whom ≥2 height measures were available during follow-up, were identified between 1998 and 2010. Height, C-reactive protein (CRP), orosomucoid and information on steroid therapy were collected at each visit. Growth velocity was compared to the evolution of inflammatory status during follow-up in a longitudinal multivariate analysis using a mixed model.

Results: Median age at CD diagnosis was 11.7 years (Q1-Q3: 9.8-13.5). According to the Paris classification, location of CD at diagnosis and at maximal follow-up was respectively as follows: L3 (70%; 86%); L2 (16%; 5%); L1 (14%; 9%); L4a (39%; 52%); L4b (11%; 22%). Behaviour at diagnosis and at maximal follow-up was respectively as follows: B1 (90%; 62%); B2 (7%; 28%); B3 (3%; 10%). Mean Height (H)/Age (A) Z-score at diagnosis was 0.1±1.3. Growth failure (H/A Z-score < –2) was present in seven (8%) patients at diagnosis and in five (5%) at maximal follow-up (median: 4.9 years; Q1-Q3: 3.8-6.4). Among the 75 patients who had reached their final height at maximal follow-up, mean H/A Z-score was 0.1 ± 1.2. Twenty (29%) patients had a final height that was at least 4 cm below their targeted height. Growth velocity was not influenced by the cumulative duration of steroid therapy (median: 7.1 months; Q1-Q3: 4.9-12.5), but was negatively correlated with the evolution of CRP (coefficient of the equation of regression (e) = –0.16; p<0.0001) and orosomucoid (e = –0.60; p<0.0001) during follow-up.

Conclusion: CD children with uncontrolled inflammatory status have a lower growth velocity and a higher risk for growth failure, regardless of cumulative duration of steroid therapy. The inflammatory status should be kept as close to normal as possible in pediatric-onset CD patients in order to optimize their growth pattern.

Disclosure of Interest: None Declared
COHORT STUDY OF CHILDHOOD OBESITY AND INFLAMMATORY BOWEL DISEASE IN UK

Anna Mccorquodale 1, Harween Dogra 1, Sandhia Naik 2,*, David Rawat 2

1Gastroenterology, 2Paediatric Gastroenterology, Barts and the London Children's Hospital, London, United Kingdom

Objectives & Study: Epidemiological studies of childhood onset Inflammatory Bowel Disease (IBD) are limited. Large cohort studies generally relate to specific population groups 1. Obesity and the proposed relationship to IBD has been described in American children 2. We cumulated data from a 10 year cohort of newly diagnosed paediatric IBD attending the Royal London Hospital. Our primary objective was to describe the prevalence of obesity and analyse contributory characteristics specific to the referral population.

Methods: Paediatric IBD diagnoses over a 10 year period made on or before a patient’s 18th birthday were included. Data was obtained via hospital electronic records, infloflex database or healthcare notes. BMI measurements were calculated using the standard formula and RCPCH UK BMI centile charts were used to stratify children into weight categories.

Results: Over the 10 year sample period there were 400 IBD diagnoses; 60% male, 40% female. 244 (61%) were Crohn’s disease (CD), 127 (32%) were ulcerative colitis (UC) and 29 (7%) were indeterminate colitis. Age range at diagnosis was 1.6-18 years, median 13.2 years, mean 12.4 years, mode 15 years. Number of diagnoses each year increased over the study duration (p<0.01).

Ethnicity - White Caucasian 57%, Bangladeshi 13% (reflecting immediate local population) Asian/Pakistani 15%, African/Caribbean 8%, European 5% and 3% mixed or unstated.

From n= 400 accurate height and weight data within 1 month of diagnosis was available on 249 patients, 73% of patients had normal BMI, 6% obese and 4% as overweight. 3% of CD patients were obese compared to 11% with UC (p<0.05).

Follow up data at 1 year was present in 65% (77% normal, 9% overweight and 8% obese). Only 24% had 5 year data mostly due to discontinued height documentation after transition to adolescent clinic (79% normal, 11% overweight and 8% obese).

Conclusion: Over 10 years diagnostic yield of IBD diagnoses has increased with time. This supports a rise in IBD prevalence suggested by other published data. BMI results suggest a correlation between obesity and newly diagnosed UC prior to any treatment bias. This differs to the EPIC study in adults and warrants further investigation.


Disclosure of Interest: None Declared
Gastroenterology
Inflammatory Bowel Disease
PO-G-0187

CARDIOVASCULAR RISK IN INFLAMMATORY BOWEL DISEASE (IBD) IN CHILDREN A SINGLE CENTRE STUDY
Paulina Krawiec 1,*, Elżbieta Pac-Kożuchowska 1, Agnieszka Pawłowska-Kamieniak 1, Katarzyna Kominek 1, Agnieszka Mroczkowska-Juchkiewicz 1
1Department of Paediatrics, Medical University of Lublin, Lublin, Poland

Objectives & Study: Atherosclerosis is a complex multifactorial disease involving the interplay of genetic, inflammatory and environmental factors. Recent reports have discussed a problem of development an early, accelerated atherosclerosis in patients with IBD. The aim of the study was to assess selected risk factors of atherosclerosis in children with IBD.

Methods: The study group consisted of 30 children, between ages 5 -17.5 years, hospitalized at the Department of Paediatrics, Medical University of Lublin with a diagnosis of the first exacerbation either Crohn’s disease (16) or ulcerative colitis (14). Control group included 20 sex- and age-matched healthy children. Blood serum samples were analyzed for total cholesterol (TC), triglycerides (TG), low-density lipoproteins (LDL), high-density lipoproteins (HDL), lipoprotein (a) Lp(a), interleukin 6 (IL-6), high sensitivity CRP (hs-CRP), and oxidized LDL (ox-LDL) concentration. Statistical analysis was carried out by Statistica 8 software, p<0,05 was considered as statistically significant.

Results: In the study group the mean values of lipids profile parameters were as follows, TC: 131.41±25.60 mg/dl, TG: 86.10±32.65 mg/dl, LDL 76.77±20.53 mg/dl, HDL 45.06±13.63 mg/dl. There were no significant differences in lipids profile parameters among study group and healthy controls. In children with IBD the mean IL-6 level (8.996 pg/ml) was significantly higher than in controls (3.502 pg/ml). The mean hs-CRP concentration was also significantly higher in children with IBD than in controls (7.648 and 1.290 µg/ml respectively). In the study group mean ox-LDL concentration (144.837 ng/ml) was lower than in control group (162.352 ng/ml), however it was non-significant (p=0.406). The mean Lp(a) serum level was higher in patients with IBD (19.418 mg/dl) than in controls (10.970 mg/dl) but it was also non-significant (p=0.313).

Conclusion: Elevated IL-6 and hs-CRP level are well-established inflammatory markers, which correlate with IBD exacerbation. Efforts should be intensified to evaluate lipids profile and markers of early atherosclerosis in all patients with IBD. Further long-term studies are needed to fully determine risk of cardiovascular and thrombotic complications in IBD.

Disclosure of Interest: None Declared
Objectives & Study: Inflammatory bowel disease (IBD) is understood to result from the interaction of genetic, immunological and environmental factors. There has been a marked increase in the incidence of IBD over the last 25 years, suggesting environmental factors are important. A previous study found a higher incidence of Coeliac disease in the least deprived socioeconomic groups[1]. The objective of this study was to investigate the relationship between IBD and socioeconomic position.

Methods: Bristol Children’s Hospital is the single regional centre where all children with suspected IBD from the South-west of England are referred. Data was collected prospectively on all children diagnosed between May 2004-March 2013. Socioeconomic status was determined by quintile rank of Index of multiple deprivation score (IMD-10 score) based on postcode at diagnosis. This has been shown to provide a nationally consistent measure of how deprived an area is. Population data was obtained from the 2011 Census. Data was analysed using Pearson Chi Squared test. Children with a postcode outside of the City of Bristol were excluded from the analysis.

Results: 384 children aged 0-17 years were diagnosed with IBD over the study period of which 50 had a postcode of residence within the City of Bristol. The incidence of IBS was higher in the three lower socioeconomic classes compared to the two highest socio-economic classes. However, the difference in incidence between the socio-economic classes was not statistically significant.

<table>
<thead>
<tr>
<th>Number of IBD Patients</th>
<th>Exposed population</th>
<th>Cumulative incidence per 100,000</th>
<th>Incidence per 100,000 per year</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 Most deprived</td>
<td>18</td>
<td>23374</td>
<td>77.01</td>
</tr>
<tr>
<td>2 Below average</td>
<td>15</td>
<td>22458</td>
<td>66.79</td>
</tr>
<tr>
<td>3 Average</td>
<td>9</td>
<td>10372</td>
<td>86.77</td>
</tr>
<tr>
<td>4 Above Average</td>
<td>5</td>
<td>13642</td>
<td>36.65</td>
</tr>
<tr>
<td>5 Least deprived</td>
<td>3</td>
<td>7202</td>
<td>41.66</td>
</tr>
<tr>
<td>Total</td>
<td>50</td>
<td>77048</td>
<td>64.89</td>
</tr>
</tbody>
</table>

p =0.204

Conclusion: Our data suggests a higher incidence of diagnosed IBD in children from lower socioeconomic classes which may favour an environmental aetiology. However this did not reach statistical significance, possibly due to small numbers. A larger study is warranted.


Disclosure of Interest: None Declared
Gastroenterology

Inflammatory Bowel Disease

PO-G-0189

FAECAL CALPROTECTIN IS A COST-EFFECTIVE TOOL THAT REDUCES NEED FOR
PAEDIATRIC COLONOSCOPY

Conor Henessey 1,* , Mary Hamzawi 1 , Siobhan Kiernan 1 , Billy Bourke 1,2 , Anne-Marie Broderick 1,2 ,
Seamus Hussey 1,2 , S Quinn 1

1National Centre for Paediatric Gastroenterology, Our Lady's Children Hospital, Crumlin, Dublin, Ireland, 2National Children's Research Centre, Crumlin and School of Medicine and Medical Science, University College Dublin, Dublin, Ireland

Objectives & Study: Ireland has a single national centre for paediatric gastroenterology. Faecal calprotectin was recently made available in our institution. Our aim was to assess the clinical performance and cost-benefit of faecal calprotectin (FC) in reducing diagnostic endoscopic procedures in symptomatic children with potential or confirmed inflammatory bowel disease (IBD).

Methods: Charts, computerised records and endoscopy results of all patients who had FC testing between Oct 2012 and August 2013 were retrospectively reviewed. New patients with a high clinical likelihood of IBD do not get routine FC testing and were not included in the analysis. FC values < 50µg/g were considered normal; 51 to 200µg/g - indeterminate and > 200µg/g –likely to have active GI inflammation.

Results: 133 patients had a FC test; of these, 57 (42.8 %) had FC > 200 (Group A), 76 had FC < 200 (Group B). The results are summarised in Table 1 below. 25/57 patients in group A had colonoscopy (43.8%); 11 were newly diagnosed with IBD; 4 of 6 patients with pre-existing IBD had a change in phenotype or treatment regimen following endoscopy findings. Two patients in group A had normal colonoscopy despite high FC. Of the rest in the same group, one patient was diagnosed as proctitis while three had gastritis. 32/57 patients in group A had no colonoscopy performed, 24 of these were known to have IBD and five were found to have bacterial or viral GI infection. 10 out of 76 patients in Group B had colonoscopy performed (13.1%), mostly due to persistent symptoms of diarrhoea and/or abdominal pain. None of these had macro- or microscopic abnormalities. Using estimated costs of FC (~€75 per test) and colonoscopy (€1000/test), the calculated net cost saving in the year examined was ~€60,300.

Table 1: The analysis of the FC and the endoscopy results

<table>
<thead>
<tr>
<th>Faecal Calprotectin (µg/g)</th>
<th>Total n=133</th>
<th>Colonoscopy n=35</th>
<th>No Colonoscopy n=98</th>
<th>Known IBD n=33</th>
<th>NEW IBD n=11</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;50</td>
<td>48</td>
<td>6</td>
<td>42</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>50-200</td>
<td>28</td>
<td>4</td>
<td>24</td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>&lt;200 in total</td>
<td>76</td>
<td>10</td>
<td>66</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>&gt;200</td>
<td>57</td>
<td>25</td>
<td>32</td>
<td>29</td>
<td>11</td>
</tr>
</tbody>
</table>

Conclusion: Faecal calprotectin is a valuable, cost-effective screening test for excluding significant intestinal inflammatory disease and avoiding colonoscopy in children with non-organic gastrointestinal symptoms that mimic IBD

Disclosure of Interest: None Declared
INFLUENZA VACCINATION COVERAGE IN INFLAMMATORY BOWEL DISEASE CHILDREN

Aleksandra Banaszkiewicz 1*, Beata Klincewicz 2, Izabella Lazowska-Przeorek 1, Paulina Kąkol 3, Aleksandra Mytyk 1, Urszula Grzybowska-Chlebowczyk 4, Anna Kofla 5, Andrzej Radzikowski 1

1Dept. of Paediatric Gastroenterology and Nutrition, The Medical University Of Warsaw, Warsaw, Poland, 2Dept. of Paediatric Gastroenterology and Metabolic Diseases, Poznan University of Medical Sciences, Poznan, Poland, 3Student Research Association, The Medical University Of Warsaw, Warsaw, Poland 4Gastroenterology Division, Dept. of Paediatrics, Medical University of Silesia, Katowice, Poland, 5Dept. of Paediatrics, Gastroenterology and Nutrition, Medical University of Wroclaw, Wroclaw, Poland

Objectives & Study: Inflammatory bowel disease (IBD) patients may be at risk for any infections, including influenza, due to an underlying disease, malnutrition, surgery, or immunosuppressive therapy. Therefore, protecting this group against infections seems to be of particular importance. The aim of the study was to describe influenza vaccination status among pediatric patients with IBD.

Methods: This prospective study was conducted in four University-affiliated hospitals for children in Poland (cities of Warsaw, Wroclaw, Katowice and Poznan) between April and June 2013. Parents of children with IBD diagnosed according to Porto criteria were asked to fill in one-page questionnaire that consisted of two parts. The first part consisted of a few questions regarding age, sex, diagnosis and current treatment. In the second part of the questionnaire, a list of potential arguments pro and against vaccination was given to parents, and they were asked to state which of these arguments applied in their case. Control group consisted of parents of healthy children.

Results: 242 IBD patients and 142 controls were enrolled to the study. Of IBD patients 7.8% received an influenza vaccine compared to 18.3% of controls (p=0.0013). There was no difference in vaccination rate between Crohn’s and ulcerative colitis patients (p=0.812). Children with IBD had less than two times chance to be vaccinated against influenza compared to controls (OR=2.6 CI95 1.4-4.9). There was no statistically significant differences in time from IBD diagnosis, disease activity and drugs between vaccinated and non-vaccinated IBD children. The most common reasons pro vaccinations were as follows: fear of influenza complications (89.47% of IBD patients and 80.77% of controls, OR=2.02 95CI 0.3-11.8) and belief in influenza vaccine efficacy (94.74% of IBD patients and 88.46% of controls, OR=2.35, 95CI 0.2-24.5; p=0.6999). 56% of IBD patients gave the fear of vaccine side effects as a major reason for not being vaccinated compared to 40% of controls (OR=1.87 95CI 1.19-2.95).

Conclusion: In conclusion, the data of our study demonstrate an alarmingly poor influenza vaccination status in the majority of children with IBD in Poland.

Disclosure of Interest: None Declared
Objectives & Study: Serological testing is commonly performed to characterize inflammatory bowel disease (IBD) using antibodies against both microbial- and autoantigens. Our aim was to evaluate anti-exocrine pancreatic autoantibodies (PAB) and anti-proteinase-3 antineutrophil cytoplasmic antibodies (cANCA) as further diagnostic markers of IBD.

Methods: We retrospectively analyzed the antibody profiles of patients who underwent antibody testing at our pediatric IBD clinic. Patients were phenotyped according to their imaging and endoscopic results using the Paris Classification at diagnosis. Additionally, the use of TNFα-therapy in the course of disease was assessed as one marker of disease severity.

Results: Antibody profiles from 43 pediatric IBD patients were included. Of those, 27 had Crohn’s Disease (CD) (median age at diagnosis 11.5 y, 17 male), and 16 suffered from Ulcerative Colitis (UC) (median age at diagnosis 11.3 y, 8 male). 19/43 (44.2%) patients received anti-TNFα treatment during follow-up in our clinic. Sixteen (59.3%) CD-patients were ASCA IgA and IgG positive. Positivity did not correlate with disease location. Only 3/15 (20.0%) UC-patients were either ASCA IgA or IgG positive. PAB-positivity was found in 9/13 (69.2%) CD-patients who were tested for PAB. In contrast, none of 11 UC-patients tested for PAB was positive. PAB was detectable in 3 CD-patients who were negative for ASCA. 10/16 (62.5%) UC- and 6/27 (22.2%) CD-patients had perinuclear staining of anti-neutrophil cytoplasmatic antibodies (pANCA) by indirect immunofluorescence (IIF). All pANCA positive CD-patients had colonic disease. Four patients (9.5 %, 3 male) were positive for cANCA determined by IIF as well as proteinase 3-ANCA-ELISA. None presented with any features of vasculitis. Two were diagnosed with CD and two with UC. The latter were classified E2 and E3 at initial diagnosis and stayed S0 during follow-up. None was treated with anti-TNFα (median time of follow up 2.1 y, range 1.6-3.3 y).

Conclusion: Our analysis supports the assumption that PAB-testing is of additional value for distinguishing patients with Crohn’s Disease from those with Ulcerative Colitis. Regarding cANCA we can neither confirm its specificity for UC nor a correlation with extensive disease.

Disclosure of Interest: None Declared
**COMPARISON OF THREE TESTS FOR FAECAL CALPROTECTIN IN A LARGE PAEDIATRIC POPULATION**

Christine Prell 1, Dorothea Nagel 2, Folke Freudenberg 1, Andrea Schwarzer 1, Sibylle Koletzko 1,*

1Dr. von Haunersches Kinderspital, University of Munich, Munich, Germany, 2Institute of Laboratory Medicine, University of Munich, Munich, Germany

**Objectives & Study:** Fecal calprotectin (FC) is used as a sensitive, non-invasive marker for gastrointestinal mucosal inflammation. We compared the performance of three different assays in a large cohort of symptomatic pediatric patients.

**Methods:** We retrospectively included 304 symptomatic patients (163 male, aged 2 to 20 years) with active inflammatory bowel disease (IBD/A, n=130), IBD in clinical remission (IBD/R, n=62), other intestinal disease (n=45), and controls without identified intestinal disease (n=67). Calprotectin was measured in homogenized fecal samples with 3 tests (A: EliA Calprotectin, Phadia AB, Sweden, B: PhiCal, Calpro AS, Norway; C: EK-Cal, Bühlmann Laboratories, Switzerland). Concordance between tests was calculated using Kendall’s τ coefficient.

**Results:** IBD/A and controls were correctly classified in 97.7%/82.1% (A), 97.7%/85.1% (B), and 98.4%/62.7% (C) (n.s.). There was a tendency to higher values of test C compared to tests A and B with a lower specificity. The concordance between two tests was 0.835 for test A and B, 0.782 for test A and C, and 0.765 for test B and C, respectively.

**Conclusion:** All three tests are highly sensitive for detecting mucosal inflammation in children, but major differences exist between specificity and absolute values. It is highly advisable to use the test of the same manufacturer for follow up and to monitor for disease activity.

**Disclosure of Interest:** C. Prell: None Declared, D. Nagel: None Declared, F. Freudenberg: None Declared, A. Schwarzer: None Declared, S. Koletzko Industry of: The study was financially supported by Phadia GmbH, part of Thermo Fisher Scientific, Freiburg, Germany.
FORMATION OF ANTIBODIES AGAINST INFliximAB IN PAEDIATRIC CROHN’S DISEASE
Joerg Jahnel 1,*, Minja Koren 1, Tatjana Stojakovic 2, Hubert Scharnagl 2, Wolfgang Erwa 2, Karl-Martin Hoffmann 1, Andrea Deutschmann 1, Almuthe Christine Hauer 1
1Department of Paediatrics, 2Clinical Institute of Medical and Chemical Laboratory Diagnostics, Medical University Graz, Graz, Austria

Objectives & Study: TNF-α-blockers such as infliximab (IFX; Remicade®) are a therapeutic option in complicated Crohn’s disease (CD). In some cases regardless of a good primary response to IFX a loss of response (LOR) to IFX can be observed. This might be due to formation of antibodies to IFX (ATI). The aim of our pilot study was to measure unbound ATI in the serum of adolescents with CD under IFX therapy with or without LOR.

Methods: We included adolescents with histologically proven CD who were receiving IFX due to disease severity at our university hospital. As control served one patient who was still IFX naïve. As a part of routine laboratory tests serum samples for ATI measurements were taken at least once, and sometimes at several time points, independent of disease activity and always just before IFX administration. Unbound ATI concentrations in serum were determined using an ELISA kit (Immundiagnostik, Bensheim, D); an extinction above 0.1 was defined as demonstrating the existence of ATI. Results were compared with clinical data (such as disease activity scores, current medication) and laboratory values.

Results: The study population consisted of 9 patients aged 12 to 18 years (female:male=7:2). 1 to 5 measurements per patient were performed, resulting in 20 measurements in total. 3 of 9 patients exhibited LOR to IFX, 5 were in remission under IFX, and one patient was IFX naïve. ATI were detected in 5 patients, including the 3 with LOR; extinction values were between 0.14 and 2.9. No disease activity was observed in the other 2 ATI-positive patients. All repeated measurements confirmed the existence of ATI. All 4 ATI-negative patients, including the ATI naïve patient, were clinically in remission.

Conclusion: Patients under IFX therapy can develop ATI detectable by a commercially available ELISA kit. In our small pilot study ATI were detected in all patients with LOR to IFX; however, some patients without LOR had ATI in serum. Unbound ATI therefore do not automatically indicate a LOR to IFX. Further studies now under way, using newly available ELISA techniques that can measure both unbound ATI and IFX-bound ATI, may give more specific results.

Disclosure of Interest: None Declared
PREVALENCE OF PAEDIATRIC-ONSET INFLAMMATORY BOWEL DISEASE: A SYSTEMATIC REVIEW

Fiona L Cameron 1,*, Paul Henderson 2, David C Wilson 1, 2
1Child Life and Health, University of Edinburgh, Edinburgh, United Kingdom, 2Paediatric Gastroenterology, Royal Hospital for Sick Children, Edinburgh, United Kingdom

Objectives & Study: Previous systematic reviews have shown the incidence of adult-onset inflammatory bowel disease (IBD) and paediatric-onset IBD (PIBD) are increasing worldwide, particularly in developed countries, however, little is known about PIBD prevalence. The determination of prevalence is crucial to inform effective service provision and delivery, and may provide clues to the aetiopathogenesis of IBD. We aimed to assess the available evidence on worldwide prevalence of PIBD, assess geographic distribution and analyse trends using systematic review.

Methods: A literature search was performed using MEDLINE (1950-2012), Medline in progress, Cochrane database and EMBASE (1980-2012) to identify relevant population-based studies. Studies were included that reported distinct paediatric prevalence data on total Inflammatory Bowel Disease (IBD), Crohn’s disease (CD), Ulcerative colitis (UC), Inflammatory Bowel Disease Unclassified (IBDU), or any combination of these. Abstracts in all languages were considered, but only included if full text was available. Data was extracted on the source of the prevalence data, age ranges, country of origin, diagnostic criteria and methodology.

Results: 4190 references were found and reviewed; 27 studies which presented data on the prevalence of PIBD and/or CD and/or UC from 11 countries were included. No prevalence data were presented on paediatric IBDU. The prevalence of PIBD ranged from 6.0-30.0 per 100,000, while CD ranged from 0.5-85.3 per 100,000 and UC from 3.0-90.1 per 100,000. Only two studies provided trend analysis over time, showing an increasing PIBD prevalence during a 5 and 10-year period respectively. There was a preponderance of reports from developed countries: 8 from North America, 10 from Europe, 5 from the Middle East, 2 from Asia, 1 from Africa, and 1 from Australasia. Prevalence rates were highest in North America and lowest in Africa and Asia. Most studies (74%) were retrospective, used a variety of sources including national registries, insurance databases, retrospective case note review and physician survey. No true population-based studies were reported. Age ranges and diagnostic criteria used varied widely.

Conclusion: PIBD prevalence was highest in North America and Europe with little data from developing nations. There were insufficient data to analyse trends over time although it is likely that, given the rising global incidence, a parallel rise in prevalence would be evident. Data reported were heterogeneous in terms of diagnosis of disease, method of case accrual and age ranges making interpretation of prevalence challenging. Well-designed studies with clear diagnostic criteria and age ranges will confirm if the increasing worldwide prevalence of adult IBD is mirrored in PIBD; such data could be used to drive future funding for enhanced clinical service provision and research.

Disclosure of Interest: None Declared
PO-G-0195

PANETH CELL METAPLASIA IN CHILDREN WITH NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE

Naomi Simmonds 1, Mark Alan Furman 2,*, Evi Karanika 2, Alan Phillips 2, Alan Bates 3

1 Tissue Sciences, St Thomas’s Hospital, 2 Centre for Paediatric Gastroenterology, Royal Free London Nhs Foundation Trust, London, United Kingdom, 3 Department of Pathology, Ucl & Royal Free Hospital, London, United Kingdom

Objectives & Study: Paneth cell metaplasia (PCM) is well described in adults but little is known about its occurrence in a paediatric population. The aim of this study is to establish the normal distribution of Paneth cells in the colon, to characterize PCM in children and to determine its prevalence in new cases of idiopathic inflammatory bowel disease (IBD).

Methods: We retrospectively reviewed colonic mucosal biopsy series from 28 new diagnoses of IBD – Crohn’s disease (CD) and ulcerative colitis (UC) and a further 14 children with IBD-like symptoms whose colonic biopsies and investigations were normal. Paneth cells were counted at 6 anatomical sites in the colon in each case; at the same sites acute and chronic inflammation were assessed and the presence or absence of crypt architectural distortion and eosinophilia was documented.

Results: In all 3 groups there was a gradient of decreasing Paneth cell numbers from caecum to rectum. Paneth cells were not seen in the distal colon in the control group, but were present in 11 of 13 patients with UC and 14 of 15 with CD. Only patients with IBD showed more than 10 Paneth cells per 10 well-oriented crypts at any site. There was a statistically significant increase in Paneth cells in the caecum, ascending, transverse and descending colon in UC and in the ascending, transverse and descending colon and caecum in CD compared with controls. There was no significant difference between UC and CD. Overall, there was no correlation between PCM and acute or chronic inflammation, crypt distortion or eosinophilia.

Conclusion: Paneth cells are found in the proximal but not the distal colon in otherwise normal paediatric colonic series. A high proportion of UC and CD patients show increased Paneth cell numbers due to metaplasia. This is present early in the disease and does not correlate with other histological features of chronicity.


Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0196

**BIOLOGICAL THERAPY AND MUCOSAL HEALING IN A PAEDIATRIC COHORT AFFECTED BY CROHNS DISEASE**

Federica Nuti 1,*, Giovanni Di Nardo 1, Fortunata Civitelli 1, Silvia Bloise 1, Anna Di Ilìlio 1, Marina Aloi 1, Franca Viola 1, Salvatore Cucchiara 1

1Department of Paediatrics, Sapienza University Rome, Paediatric Gastroenterology and Hepatology Unit, Rome, Italy

**Objectives & Study:** Efforts have been made to optimize the use of available therapies to improve Crohn's disease (CD) patients' (pts) outcome, but up to now no therapy changed the natural history of the disease. Mucosal healing (MH) appears as a therapeutic goal able to predict a sustained remission. Therapy with anti-TNFα antibodies, Infliximab (IFX) and Adalimumab (ADA), have been proven effective in achieving MH with a potent and rapid effect. Few studies evaluating MH as a therapeutic goal in pediatric CD are available. Primary aim: assess the efficacy of IFX and ADA in obtaining MH in a pediatric CD cohort. Secondary aims: evaluate response in pts with early (<1 year) or late (>1 year) disease and in pts undergoing combination therapy with biologics + immunomodulators (IM) or biologics alone. Finally we evaluated further clinical outcome of pts a year after the second endoscopy.

**Methods:** Pediatric CD pts starting IFX or ADA from January 2009 were enrolled. All pts were naïve to biological therapies. Pts' characteristics collected at baseline are: age at diagnosis, indication for therapy, age at enrollment, disease duration, concomitant medications. An endoscopy was performed before starting biologics and after 9 to 12 months to evaluate MH. Clinical and endoscopic disease activity were assessed by Pediatric Crohn’s Disease Activity Index (PCDAI) and Simple Endoscopic Score (SES CD) at time 0 (T0) and at the time of endoscopic follow-up (FU). Appropriate induction and maintenance therapeutic schemes were applied.

**Results:** Thirty-seven pts (25 IFX and 12 ADA) were enrolled, 23 males. At enrollment mean age was 12.3±3.4 years and mean disease duration was 13 ±16 months. Eighteen pts were in the early disease group. Mean ± SD values of PCDAI and SES CD at T0 and FU are 31±18 and 9.6±11, and 15.4±8 and 5.6±7 respectively; both values were significantly reduced at FU (p=0.0001). No statistical difference in obtaining MH between the early and late disease group was found, but a numerical trend towards a better outcome in the first group was observed. Considering MH + partial MH a statistically significant difference in favor of combination therapy was found. A year from second endoscopy all of the pts that had obtained a complete MH and 70% of those that had achieved a partial MH were still in clinical remission. No pt that achieved complete MH necessitated a steroid course during the further follow-up.

**Conclusion:** In our cohort biological therapy appears capable to induce MH, possibly more effectively if introduced earlier in the course of the disease and if in combination with IM. Furthermore MH appears to favor a better disease course. Larger studies will highlight the effect of MH on the long-term disease evolution.

**Disclosure of Interest:** None Declared
ASSESSMENT OF TRANSITION PROGRAM TO ADULT CARE IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE (IBD)

César Sánchez Sánchez 1,*, Marina García Morín 1, Mar Tolín Hernani 1, Jimena Pérez Moreno 1, Ignacio Marín 2, Guillermo Alvarez Calatayud 1, Luis Menchén 2, José Luis Morales Pérez 1

1Paediatric Gastroenterology Unit, 2Gastroenterology Unit, H.G.U. Gregorio Márañón, Madrid, Spain

Objectives & Study: The transition from pediatric to adult care for patients with inflammatory bowel disease (IBD) should be an ongoing process, individualized, and planned ahead. The development of common strategies enhances the patient autonomy.

Aims: To assess the satisfaction of patients with IBD of a new transition program elaborated in a tertiary hospital.

Methods: The new transition program was started in 2008. This program includes a joint meeting between both patients and family for transition planning; a schedule of visits and different communication strategies. It also offers consultations shared between pediatric and adult gastroenterologists during the two years before to the transition. All patients who received that program, underwent telephone interviews with quantitative satisfaction scales questionnaires.

Results: From 2004 to 2011, 15 patients (60% men), made the transition program. 60% (N=9) were Ulcerative Colitis, 33% Crohn's Disease and 13% (N=2) were Indeterminate Colitis. Median follow-up was 6 years (range 1.5-14 years) and median transition age was 17 years (range 16-18.5 years). There were only 2 patients who were transferred in an active phase of the disease. 73% (N=11) reported having received enough information and 73% felt adequately prepared to the transition. 8 patients (53%) and 12 families reported some problems: 45% lack of confidence in the new adult doctor, 22% fear of contact with other adults and the overcrowded consults. All patients who completed the new program expressed a degree of satisfaction "very good". The best factor valued was shared consultations between pediatric and adult gastroenterologist. Both units (pediatric and adult) were assessed positively in 95% of cases.

Conclusion: Development of a care transition program is a beneficial process, with a good rating by patients and families. The incorporation of visits with both physicians involved in the transition challenge facilitates the process and it is well considered by patients.

Disclosure of Interest: None Declared
Objectives & Study: Background. Ursodeoxycholic acid (UDCA) is the only treatment available for CFLD and has been in clinical use since more than two decades without relevant adverse events. However, there are no definitive data on the effects on survival and need for transplantation and recently concerns have been expressed on the safety of long-term UDCA administration, based on data coming from adult patients with primary sclerosing cholangitis, treated with high doses of UDCA.

Aim. To evaluate changes induced in serum bile acids (BA) composition by long-term administration of UDCA in CFLD patients.

Methods: We selected 20 patients with CFLD (13 with cirrhosis and 7 with less severe disease) on UDCA therapy (20 mg/kg/day) since at least 5 years. Blood samples were obtained in fasting conditions and after 2 hours from the morning dose of UDCA taken with breakfast. Serum BA concentrations were measured by state of the art GC-MS analysis.

Results: Data are expressed as median (IQR). Age was 16.6 yrs (12.5-24.8) and duration of UDCA therapy 8.3 yrs (6.3-15.4). During its chronic administration, UDCA became the predominant BA (3.17 μmol/l (1.25-5.56)) and accounted for more than 50% of total BA. Among the primary BA, chenodeoxycholic acid (CDCA) concentrations were 1.86 μmol/l (1.00-4.70) while cholic acid (CA) 0.40 μmol/l (0.24-2.70). With regard to secondary BA, only trace amounts of both LCA and deoxycholic acid (DCA) were found (< 0.05 μmol/l). When serum bile acid concentrations were evaluated after 2 hours from the administration of UDCA, serum concentrations of both UDCA and CDCA increased significantly, up to 5.71 μmol/l (3.26-7.11) for UDCA and up to 3.20 μmol/l (1.69-6.15) for CDCA (p< 0.01 vs fasting sample for both bile acids). No changes were observed in serum LCA concentrations.

Conclusion: During its chronic administration to CFLD patients, UDCA become the predominant BA in serum, mainly at the expenses of CA. The increase in serum concentrations of CDCA following UDCA administration indicates the well known epimerization of UDCA into its β-epimer. Our data do not suggest relevant biotransformation of UDCA into the more toxic LCA during long-term administration of UDCA and therefore do not support the hypothesis that the metabolic fate of UDCA may have a negative impact on the outcome of liver disease.

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0199

**CLINICAL EFFECT OF SEBELIPASE ALFA ON SURVIVAL AND GROWTH IN INFANTS WITH LYSOSOMAL ACID LIPASE DEFICIENCY (WOLMAN DISEASE)**

V Valayannopoulos 1,*, D Plantaz 2, R Varma 3, S Eckert 4, R Tripuraneni 4, Kim-Hanh Le Quan Sang 1, A Brassier 1, J Arnoux 1, F White 5, C Breen 5, A G Quinn 4, S A Jones 5

1Hôpital Necker-Enfants Malades, Paris, 2Hopital Couple Enfant CHU Grenoble, Grenoble, France, 3Evelina Children’s Hospital, London, United Kingdom, 4Synageva BioPharma Corp., Lexington, United States, 5Univ. of Manchester, Manchester, United Kingdom

**Objectives & Study:** Lysosomal Acid Lipase Deficiency (LAL D) presenting in infants, also known as Wolman Disease, is characterized by feeding intolerance and hepatosplenomegaly followed by a rapid clinical decline with growth failure, cytopenias, liver failure and death within the first year of life. There are currently no effective therapies.

**Methods:** A global phase 2/3 trial (LAL-CL03) was initiated to assess the safety and efficacy of sebelipase alfa (SA) in LAL deficient infants.

**Results:** In this ongoing open-label study, 6 subjects have been enrolled and receive weekly infusions of SA. The median age at first infusion is 2.8 months, range 1.1 to 5.8. As of October 1, 2013, three subjects have met the primary endpoint of survival at 12 months of age. Two additional subjects are older than 6 months of age and continue therapy. One patient with multi-organ failure at study entry, consistent with the natural history of LAL D in infants, died at 2.9 months of age after receiving 1 dose of SA. The death was deemed unrelated to SA and was thought to be disease related. The 5 subjects who continue on treatment with weekly infusions of 3 mg/kg SA have all demonstrated an encouraging response after 20 wks of therapy with improved weight gain, resolution of vomiting and diarrhea, and reductions in hepatosplenomegaly. Improvements in disease activity markers were also noted: reductions in median ALT (-50%, range -83% to +156%), and AST (-63%, range -35% to +66%) and increases in hemoglobin (median +13%, range +5% to +18%). Majority of the SAEs were unrelated and included hospitalizations for empirical treatment with antibiotics due to fever in infants with central IV lines. One SAE was deemed related to SA: an infusion reaction of malaise with tachycardia and fever which resulted in an overnight hospitalization. The majority of the infusion related reactions were febrile episodes with or without tachycardia or vomiting. To date, three subjects tested positive to anti-SA antibodies and all three continue to tolerate weekly infusions of SA at 3 mg/kg without significant infusion related reactions or change in clinical response to SA.

**Conclusion:** Analysis to date suggests that SA may provide a significant survival benefit in LAL D infants.

**Objectives & Study:** Patients with Lysosomal Acid Lipase Deficiency (LAL D) present with dyslipidemia, elevated transaminases and hepatomegaly which can progress to cirrhosis and early death. To evaluate the long-term clinical effects and safety profile of every other week dosing of sebelipase alfa (SA), 8 patients have been followed for a minimum of 78 weeks as part of a phase 1/2 study and its long-term extension trial.

**Methods:** In the extension trial patients received 4 once-weekly infusions of SA before transitioning to every-other-week infusions (1 or 3 mg/kg). Serum transaminases and lipids were followed. MRI of the liver was performed at baseline of the extension study, 10-12 weeks, 24 weeks and 52 weeks.

**Results:** For the n=7 patients with treatment data available at week 78 of the extension study, SA produced mean percent decreases for ALT and AST from the initial pretreatment baseline of 55% and 32%, respectively (p=0.031 for both comparisons). SA resulted in mean percent decreases from the pretreatment baseline to week 78 of the extension study for LDL-C of 52% (p=0.031), total cholesterol of 36% (p=0.031), triglycerides of 40% (p=0.063), as well as a mean increase in HDL of 37% (p=0.063). The mean percentage reduction (+/- SD) from baseline of the extension study in hepatic fat fraction was 55% (+/- 35%) at week 52. More than 250 infusions have been administered and no new significant safety findings have emerged over time with long term dosing. The majority of adverse events were mild and unrelated to SA. One patient with a moderate (Grade 2) allergic type infusion-related reaction paused treatment, underwent further testing and has now restarted therapy. No sebelipase alfa related serious adverse events have been reported. No anti-drug antibodies have been detected to date in this study.

**Conclusion:** These results suggest that long term every-other-week dosing with SA normalizes serum transaminases, improves the abnormal serum lipid profile, and decreases liver fat fraction in LAL D patients. Currently a phase 3 randomized placebo-controlled, double-blind clinical trial is underway to further assess the safety and efficacy of sebelipase in children and adults (ARISE study).

MANIFESTATION AND DISEASE COURSE IN 25 CHILDREN WITH MDR3 DEFECT CAUSING PFIC3

Stephanie B. Schatz 1,*, Patrick Gerner 2, Daniel Wenning 3, Stefan Gehring 4, Stefan Arens 5, Dirk Bretschneider 6, Dirk Grothues 7, Ralf Kubitz 8, Ulrich Baumann 1

1Pädiatrische Gastroenterologie und Hepatologie, Medizinische Hochschule Hannover, Hannover, Germany, 2Gastroenterologie/Lebertransplantation, Universitätskinderklinik Essen, Essen, Germany, 3Kinderheilkunde I, Gastroenterologie, Universitätsklinikum Heidelberg, Heidelberg, Germany, 4Zentrum für Kinder- und Jugendmedizin, Gastroenterologie / Hepatologie / Lebertransplantation, Universitätsklinik Mainz, Mainz, Germany, 5Kindergastroenterologie, Klinikum Kassel, Kassel, 6Klinik St. Marienstift, Magdeburg, Germany, 7Kinder- und Jugendmedizin, Hepatologie und Lebertransplantation, Universitätsklinikum Regensburg, Regensburg, Germany, 8Klinik für Gastroenterologie, Hepatologie und Infektiologie, Universitätsklinikum Düsseldorf, Düsseldorf, Germany

Objectives & Study: Progressive familial intrahepatic cholestasis (PFIC) type 3 is caused by a genetic defect of the ABCB4 gene encoding the multidrug-resistant-3-protein (MDR3). To date, only small case series exist and the clinical course is not well described 1,2. The aim of this multicenter project was to gather information on onset and progression of this rare disease.

Methods: Data of 25 children (11 males, 18 families) with homozygous or compound heterozygous mutations of the MDR3 gene were retrospectively collected: age at manifestation, symptoms, laboratory parameters, and clinical course.

Results: Detailed data for the first years of life were available in 22/25 patients. Symptoms and median age at first report were: 22/22 patients pruritus (1.0 y), 13/22 jaundice (2.9 y), 20/22 splenomegaly (1.2 y), 18/22 hepatomegaly (0.7 y), 4/22 gallstones (7.4 y). Diagnosis followed symptoms after 2.0 y in 22 children. Laboratory values (median 0.8 y) showed elevated liver enzymes (median ALT 147 U/l, GGT 203 U/l) in 21 children, in 8 bilirubin was elevated (median 20 μmol/l). 23 patients were treated with ursodesoxycholic acid. 14/25 patients (56%) received liver transplantation (6.9 y). Previous misdiagnoses included biliary atresia (3 Kasai operations), Alagille syndrome, and PFIC1.

Conclusion: The severe and early manifestation leads to the necessity of liver transplantation in more than 50% of patients, frequently in the first decade of life. 5 patients were misdiagnosed before diagnosis of PFIC3.

References:
1 Jaquemin et al., Gastroenterology 2001
2 Colombo et al., JPGN 2011

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0202

**EPICARDIAL ADIPOSE TISSUE, LEFT VENTRICULAR STRUCTURE AND FUNCTION IN OBESE CHILDREN AND ADOLESCENTS WITH NONALCOHOLIC FATTY LIVER DISEASE**

Lucia Pacifico 1,*, Stefano Bascetta 1, Sara Romaggioli 1, Michele Di Martino 2, Antonio De Merulis 1, Valeria Tromba 1, Claudio Chiesa 3

1Paediatrics, 2Radiological Sciences, Sapienza University ff Rome, Rome, Italy, 3Institute of Translational Pharmacology, National Research Council, Rome, Italy

**Objectives & Study:** Novel data indicate that nonalcoholic fatty liver disease (NAFLD) may increase the risk for cardiac abnormalities. Epicardial fat (EF) is a metabolically active ectopic fat depot with possible paracrine or mechanical effects on myocardial function. The aims of the current study were to assess EF thickness, left ventricular (LV) structure and function, and metabolic profile in children and adolescents with NAFLD, and to determine the interrelations between EF and metabolic disorders as well as cardiac alterations.

**Methods:** We performed a complete echocardiographic study including tissue Doppler imaging, magnetic resonance imaging (MRI) for measurement of hepatic fat fraction (HFF) and visceral abdominal fat (VAT), along with lipid profile, insulin sensitivity, and high-sensitivity C-reactive protein in 150 obese children, 70 with (HFF ≥ 5%) and 80 without NAFLD. A small subgroup of the children with NAFLD also underwent liver biopsy. Whole-body insulin sensitivity index (WBISI), insulinogenic index (IGI), and disposition index (DI) were obtained from oral glucose tolerance test. EF was measured during end-systole at the point on the free wall of the right ventricle along with the midline of the ultrasound beam.

**Results:** Compared to children without liver involvement, those with NAFLD had greater EF thickness, but only mild changes in cardiac geometry such as higher interventricular septal thickness at end diastole and systole. Significant differences in parameters of LV diastolic and systolic function, such as increased isovolumetric relaxation time, increased early mitral velocity/early diastolic tissue velocity ratio (E-to-e’ ratio), and reduced systolic tissue velocity (s’), were observed in children with NAFLD compared to obese subjects without NAFLD. Among children with biopsy-proven NAFLD, those with definite-NASH had worse LV dysfunction than those without NASH. However, EF thickness was similar between those with and without NASH. In the entire population of obese children, EF correlated with BMI-SD score, VAT, HFF, insulin sensitivity (WBISI and IGI), as well as with E-to-e’ ratio and s’ tissue velocity, after adjustment for age, gender, and pubertal status. In multiple regression analysis, however, liver fat was the only statistically significant variable associated with increased E-to-e’ ratio.

**Conclusion:** Our findings demonstrate that obese children with NAFLD have increased EF as well as features of early LV diastolic and systolic dysfunction.

**Disclosure of Interest:** None Declared
ULTRASTRUCTURAL FEATURES IN PATIENTS WITH FAVOURABLE AND FATAL COURSE OF ALPHA-1-ANTITRYPSIN DEFICIENCY

Agnieszka Bakula 1,*, Elzbieta Czarnowska 2, Joanna Bierla 2, Justyna Oleksiak 2, Piotr Socha 1
1Gastroenterology, Hepatology and Nutritional Disturbances, 2Pathology, The Children's Memorial Health Institute, Warsaw, Poland

Objectives & Study: α-1-antitrypsin deficiency (α-1-ATD) has variable prognosis ranging from hepatitis to liver failure but still the mechanisms of hepatocellular injury remain not clear. Studies performed over the last several years have demonstrated the importance of autophagy in disposal of mutant, aggregated α-1-antitrypsin and protection from liver disease*. Furthermore, mitochondria injury is implicated in activation of autophagic signaling. Thus, the aim of the study was to determine distinctive features of hepatocytes ultrastructure (mitochondria abnormalities and autophagy in particular) in children with variable course of α-1-ATD.

Methods: We reviewed 19 liver tissue samples obtained from homozygous patients (PiZZ), divided into 2 groups: with unfavorable prognosis (I group, N=7): alive with liver failure (2), dead in course of cirrhosis (1) or after liver transplantation (Ltx-4), and with good prognosis - no evidence of liver cirrhosis (II group, N=12). The age of biopsy sampling was 0.8(0.3–2.3)y in the I group vs. 0.3(0.2–0.4)- in II group [median (Q1-Q3)]. In I group the patients were observed until 18th year of age, LTx or death 13.8(10.3-16.3)y, while the follow up in II group was 14.7(10-17.7). Liver biopsy samples were investigated using confocal and electron microscopy, and morphometric methods. The parameters of liver function before biopsy were assessed as well. For comparison of the two groups Mann-Whitney test was used. Correlations were tested by Spearman rank test.

Results: Electron microscopical investigations revealed markedly dilated RER (rough ER), larger long mitochondria in patients with poor prognosis compared to II group [cross sectional area 1.1(1.0-1.1)µm2 vs. 0.70(0.6-0.8)] [median(Q1-Q3)]. There was a high difference in incidence of hepatocytes with long mitochondria [42(34-58)% vs. 10(8-12)], mitophagy [4.0(2.4-4.4)% vs. 17.2(16.4-18.9)] and autophagy [12(5.2-14.1)% vs. 15.2(13.3-19.9)] as well. The accumulation of mutant α1-antitrypsin in hepatocytes was more advanced in I group [41.2(30.7-72.3)% vs. 12.8(10.4-15.9)].

Conclusion: A marked increase in hepatocytes mitophagy and autophagy in the group with good prognosis may suggest its role in more efficient degradation α-1-antitrypsin protein and appears to be a significant feature of favourable prognosis in children with α-1-ATD.

References:

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0204

**PREDICTION OF VARICEAL BLEEDING IN YOUNG CHILDREN WITH BILIARY ATRESIA USING BLOOD TEST INDICES**

Simon C. Ling 1,2,*, Ashraf Alsahafi 1,2, Scott Nightingale 3, Juan Cristobal Gana 4, Binita Kamath 2,5, Vicky L Ng 2,5

1The Hospital for Sick Children, Toronto, Canada, 2Department of Paediatrics, University of Toronto, Toronto, Canada, 3John Hunter Children’s Hospital, Newcastle, Australia, 4Pontificia Universidad Catolica de Chile, Santiago, Chile, 5Hospital for Sick Children, Toronto, Canada

**Objectives & Study:** Studies of therapies to prevent variceal bleeding in children with biliary atresia (BA) would be facilitated by availability of a non-invasive test to identify infants at high risk of future bleeding. We aimed to measure the accuracy of early blood test indices to predict variceal bleeding in children with BA before 2 years of age, including platelet count, AST/ALT ratio (AAR), AST:platelet ratio index (APRI), and conjugated bilirubin (CBR).

**Methods:** Children presenting with BA to two institutions over 20 years were identified from databases. Children were excluded if they did not undergo Kasai portoenterostomy (KP). Data were obtained by chart review, including bloodwork values at time of KP, at 3, 6 and 9 months after KP, and 6 months before a variceal bleed.

**Results:** Of 151 children identified, 94 were included in the analysis after exclusions for no KP and unavailable data. 34 were female, mean±SD age at KP 74±24 days, associated malformations in 23%, cirrhosis at time of KP in 30%. Variceal bleeding occurred in 18 children (19%), 11 of which occurred before 2 years of age (mean±SD 0.9±0.4y) (“bleeders”). Only one bleeder had polysplenia. Mean platelet count of bleeders at 0, 3, 6, and 9 months post KP was not significantly different from non-bleeders (bleeders 501, 388, 203, 189 x10^9/l vs. non-bleeders 469, 267, 212, 216 x10^9/l). Each bleeder’s platelet count 6 months prior to bleed was above the age-appropriate mean value for non-bleeders and within its 95% CI. Mean AAR showed variation with age among bleeders (2.3, 1.5, 0.6, 1.8 at 0, 3, 6, 9 months post-KP), was more stable in non-bleeders (1.7, 1.4, 1.4, 1.4), but did not differ significantly between groups. No significant differences were identified in mean APRI and CBR values between bleeders and non-bleeders at each time point. A non-significant trend was identified towards higher CBR in bleeders 6-9 months post KP.

**Conclusion:** In this retrospective cohort of children with BA, early blood test indices were unable to predict variceal bleeding before 2 years of age. Platelet counts are mostly normal or high in spite of cirrhosis and portal hypertension in the first 9 months after KP. Future studies should explore the predictive ability of imaging studies or other biomarkers of portal hypertension.

**Disclosure of Interest:** None Declared
HEPATIC DYSFUNCTION AND DYSLIPIDEMIA FROM EARLY CHILDHOOD ARE COMMON IN LYSOSOMAL ACID LIPASE DEFICIENCY


1Synageva BioPharma Corp., Lexington, 2Ann & Robert H. Curie Children's Hospital of Chicago, Chicago, United States, 3Addenbrookes Hospital NHS Trust, Cambridge, United Kingdom, 4Gaslini Institute, Genoa, Italy, 5Stanford University, Stanford, United States, 6Regina Margherita Hospital, Turin, Italy, 7Univ. of Washington Children's Hospital & Regional Medical Center, Seattle, United States, 8Academic Medical Center, Amsterdam, Netherlands, 9New York-Presbyterian - Columbia, New York, United States, 101st Faculty of Medicine Charles Univ, Praha, Czech Republic, 11Hopitaux Universitaires de Geneve, Geneva, Switzerland, 12Hospital for Sick Children, Toronto, Canada, 13Birmingham Children's Hospital, Birmingham, 14Salford Royal NHS Foundation Trust, Salford, United Kingdom, 15Instytut "Pomnik-Centrum Zdrowia Dziecka" Klinika Chorob Metabolicznych, Warsaw, Poland, 16Univ of Minnesota, Minneapolis, United States, 17Hôpital Necker-Enfants Malades, Paris, France

Objectives & Study: Lysosomal Acid Lipase Deficiency (LAL D), a rare lysosomal storage disease caused by mutations in the LIPA gene, is an underappreciated cause of cirrhosis, dyslipidemia and premature atherosclerotic disease in children and adults.

Methods: Because the clinical understanding of LAL D is limited and disease manifestations resemble those seen in common disorders, delayed diagnosis is common. In order to better characterize the presentation and progression of LAL D, we conducted a multinational observational study in children and adults with this disease.

Results: 48 patients with a confirmed diagnosis of LAL D were enrolled in the study. The median age of first symptoms was 5.8 years and the median age at diagnosis was 9.5 years. The median age at which dyslipidemia or elevated transaminases was reported was 8.4 and 8.2 years, respectively. 44 of the 48 patients had an elevated ALT (median 80.5 IU/L) at the first recorded assessment, and almost all remained abnormal during their follow-up period (3 to 24 months). The median highest reported total cholesterol, LDL and triglycerides were 316 mg/dL, 239 mg/dL, and 219 mg/dL respectively and the median lowest HDL was 26.5 mg/dL. Six of the 48 patients underwent liver transplant: 4 patients were under 18 years of age and 2 patients were over 40 years of age, both of whom had developed end-stage liver disease rather precipitously.

Conclusion: This study confirms that signs and symptoms of LAL D usually develop in childhood, although the diagnosis is often delayed because of non-specific presentation. Despite management with restriction of dietary fat or lipid lowering therapy, the disease progressed. End-stage hepatic complications may develop rapidly, and further study of prognostic factors of rapid disease progression is warranted.

Declared, J. Sykut-Cegielska: None Declared, C. Whitley: None Declared, V. Valayannopoulos: None Declared
**Hepatology**

PO-H-0206

REPRODUCIBILITY OF FIBROSCAN® AND ACOUSTIC RADIATION FORCE IMPULS (ARFI) IN EVALUATION OF HEPATIC FIBROSIS IN CHILDREN WITH Cystic Fibrosis

Aude Fischer 1,*, Eric Frison 2, Sophie Missonier 3, Victor de Ledinghen 4, Paul Perez 2, Jean-francois Chateil 3, Michael Fayon 5, Thierry Lamireau 1

1Paediatric Hepatology unit and Cystic Fibrosis center, CHU Bordeaux, Bordeaux, France, 2ISPED, University of Bordeaux, Bordeaux, France, 3Paediatric Radiology, 4Hepatology unit, 5Paediatric Cystic Fibrosis center, CHU Bordeaux, Bordeaux, France

**Objectives & Study:** FibroScan® and ARFI are two non-invasive methods for measuring hepatic fibrosis which are currently used but non-validated in pediatrics. The aim of this study was to evaluate their reproducibility in cystic fibrosis-related liver disease.

**Methods:** A measurement of hepatic elasticity was performed using FibroScan® and ARFI in 56 CF-children during the annual work-up at the cystic fibrosis clinic. For each procedure (41 FibroScan® and 46 ARFI), 3 series of 10 measurements were performed by 2 different operators. S1, S2 or M probes were used for FibroScan® procedure, as recommended by the manufacturer. Interobserver and intraobserver agreement were analysed using intraclass correlation coefficient (ICC).

**Results:** Both procedure were feasible in all children.

For FibroScan®, median value of elasticity was 4.3kPa (2.5-11.5). The overall intra-observer agreement ICC was 0.91 (95%CI 0.83 to 0.95) and inter-observer agreement ICC was 0.91 (95%CI 0.84 to 0.95).

For ARFI, median value of velocity was 1.11 m/s (0.88-1.52). The overall intra-observer agreement ICC was 0.83 (95%CI 0.72 to 0.90) and inter-observer agreement ICC was 0.67 (95%CI 0.48 to 0.80).

Considering a limit of acceptable change between 2 measurements of 20%, a discrepancy was observed in 17% of cases for FibroScan® and none for ARFI. Patients with discrepancy were younger (7 vs 11 years, p<0.05).

**Conclusion:** FibroScan® and ARFI are both reproducible non-invasive methods for assessing liver fibrosis in children with cystic fibrosis.

**Disclosure of Interest:** None Declared
**ASSOCIATION OF TRIGLYCERIDE-TO-HDL CHOLESTEROL RATIO WITH CAROTID ARTERY INTIMA-MEDIA THICKNESS, INSULIN RESISTANCE AND NONALCOHOLIC FATTY LIVER DISEASE IN CAUCASIAN YOUNG CHILDREN**

Lucia Pacifico 1,*, Enea Bonci 2, Gianmarco Andreoli 1, Sara Romaggioli 1, Stefano Bascetta 1, Rossella Di Miscio 3, Concetta Valentina Lombardo 3, Claudio Chiesa 4
1Paediatrics, 2Experimental Medicine, 3Radiological Sciences, Sapienza University Of Rome, Rome, Italy, 4Institute of Translational Pharmacology, National Research Council, Rome, Italy

**Objectives & Study:** The triglyceride (TG)/high-density lipoprotein-cholesterol (HDL-C) ratio has been reported as useful marker of atherogenic lipid abnormalities, insulin resistance, and cardiovascular disease. However, very few data are still available on the role of the TG/HDL-C ratio as potential marker of early vascular damage in obese children. The aim of the present study was to evaluate in a large sample of children the association of TG/HDL-C ratio with early signs of morphological vascular changes and cardiometabolic risk factors including nonalcoholic fatty liver disease (NAFLD).

**Methods:** The study population, including 548 children (median age, 10.10 years) of whom 157 were normal-weight, 118 overweight, and 273 obese, had anthropometric, laboratory, liver and carotid ultrasonography (carotid artery intima-media thickness-cIMT) data collected. Subjects were stratified into tertiles of TG/HDL-C. NAFLD was diagnosed by the ultrasonographic evidence of liver steatosis, and the presence of persistently elevated alanine aminotransferase.

**Results:** There was a progressive increase in BMI, BMI-SD score, waist circumference (WC), blood pressure (BP), liver enzymes, glucose, insulin, homeostasis model assessment of insulin resistance, high-sensitivity C-reactive protein (HSCRP), and cIMT values across TG/HDL-C tertiles. Children with high TG/HDL-C ratio (top tertile) showed an increased risk of obesity, elevated BP, insulin resistance, high HSCRP, NAFLD, and increased cIMT, after adjustment for age, gender, and pubertal status. After additional adjustment for BMI-SD score, insulin resistance, NAFLD, and increased cIMT remained significantly associated with high TG/HDL-C ratio. When WC (instead of BMI-SD score) was included in the model, results did not change. In a stepwise multivariate logistic analysis, increased cIMT was predicted by high TG/HDL-C ratio [OR, 1.81 (95% CI, 1.08-3.04); P<0.05], elevated BP [5.13 (1.03-15.08); P<0.05], insulin resistance [2.16 (95% C,1.30-3.39); P<0.01], and NAFLD [2.70 (95% C,1.62-4.56); P<0.01].

**Conclusion:** TG/HDL-C ratio may help to identify children at high risk for structural vascular changes and metabolic derangement.

**Disclosure of Interest:** None Declared
**Hepatology**

PO-H-0208

**NON-ALCOHOLIC FATTY LIVER DISEASE AND CARDIOVASCULAR RISK IN OBESE CHILDREN**

Bart Koot 1,*, Eric De Groot 2, Olga van der Baan-Slootweg 3, Peter Jansen 4, Marc Benninga 1

1Dep of Paediatric Gastroenterology, Academic Medical Centre, Amsterdam, Netherlands, 2Department of Cardiology and Cardio-Thoracic Surgery, Academic Medical Centre, Amsterdam, Netherlands, 3Childhood Obesity Centre, Heideheuvel, Hilversum, Netherlands, 4Dep. of Hepatology, Academic Medical Centre, Amsterdam, Netherlands

**Objectives & Study:** NAFLD has been established as a risk factor for cardiovascular disease in adults, but whether NAFLD is also related to early atherosclerotic changes at pediatric age is not well established. We therefore investigated carotid arterial wall and lumen dimensions, as well as arterial stiffness in obese children with and without NAFLD.

**Methods:** In a cross-sectional study 79 severely obese children (non-diabetes, non-smoking) were evaluated for NAFLD using MR spectroscopy. Carotid intima-media thickness (CIMT), arterial wall stiffness and arterial luminal diameter were measured using ultrasonography. The relation between degree of liver steatosis and carotid arterial changes was evaluated using multivariate linear regression analyses including conventional cardiovascular risk factors.

**Results:** CIMT and arterial wall stiffness were not different between those with and without liver steatosis and were not related to liver steatosis in regression analysis. Carotid arterial luminal diameter was increased in those with steatosis (6.31 versus 5.94 mm; \( p=0.026 \)). Carotid arterial luminal diameter, together with age, was positively correlated with liver steatosis independent of conventional cardiovascular risk factors. Arterial luminal diameter increased 0.02 mm (95% CI 0.01-0.04) for every 5% increase in liver steatosis (\( p=0.013 \)).

**Conclusion:** Liver steatosis is related to an increased carotid arterial luminal diameter, but not to CIMT and arterial stiffness increase in obese children. The increased luminal diameter could be due to vascular remodeling as a response to wall shear stress or due to NAFLD specific vascular changes.

**Disclosure of Interest:** None Declared
SERUM TOTAL AND SPECIFIC IMMUNOGLOBULIN (IG) A ARE INCREASED IN POST LIVER TRANSPLANT FOOD ALLERGY

Ruth De Bruyne 1,*, Natalie De Ruyck 2, Stephanie Van Biervliet 1, Saskia Vande Velde 1, Myriam Van Winckel 1, Philippe Gevaert 2, Melissa Dullaers 3
1Department of Paediatric Gastroenterology, 2Upper Airways Research Lab, Department of Otorhinolaryngology, 3Laboratory of Immunoregulation and Mucosal Immunity, Pulmonary Department, Ghent University Hospital, Ghent, Belgium

Objectives & Study: Post transplant food allergy (PTFA) is found in 28% of our pediatric liver transplant (LT) patients. The pathogenesis remains incompletely understood but IgE seems implicated in the immunopathology. Since no data are available on serum Ig levels other than IgE in PTFA, we compared serum Ig levels between pediatric LT patients (n=49) with (n=15) and without (n=34) PTFA, renal transplant (RT) patients (n=26), FA children (n=20), children with chronic parenchymal liver disease (n=31) and healthy controls (n=83). None of the RT patients has FA. LT and RT patients were treated with a similar immunosuppression protocol.

Methods: Serum Ig levels were collected from patient records. Data were analysed in SPSS. Z-scores were calculated for each Ig value to correct for age-dependent reference ranges. Serum IgA1 and IgA2 levels were measured by ELISA (Southern Biotech®) in 25 LT patients of whom 13 with PTFA, 12 FA patients and 12 healthy controls. In the same group, specific IgA Unicap against a mix of egg, milk, fish, wheat, peanut and soybean antigens (fx5 caps, Phadia®) was performed. Kruskall-Wallis test was used to compare serum Ig levels between groups. Subsequently, Mann-Whitney U test was used to compare subgroups mutually. Because of multiple testing a p-value <0,005 was considered statistically significant.

Results: Serum Ig levels in chronic liver disease patients were not statistically different from healthy controls. No significant difference in distribution of IgM was found across groups. As expected, IgE was higher in FA compared to controls (p<0.0001), LT (p<0.001), RT (p<0.0001) patients and in PTFA versus non-FA LT patients (p<0.0001). IgG was elevated in LT compared to controls (p=0.003) and RT patients (p=0.001) and in PTFA versus non-FA LT patients (p<0.0001). IgA was raised in both FA and LT patients compared to controls (p=0.001; p<0.0001) and RT patients (p=0.001; p<0.0001). IgA was also significantly higher in PTFA compared to non-FA LT patients (p<0.0001). No significant difference in EBV viral load was found between these two groups. 1 patient in the PTFA group was diagnosed with PTLD and treated successfully with rituximab. The ratio of IgA1/total IgA (and IgA2/total IgA) was not different between groups. Specific IgA against the mix of 5 common food antigens was elevated in PTFA versus non-food allergic LT patients (p=0.0453).

Conclusion: We first report that besides serum IgE, also serum IgA and IgG are increased in PTFA. Specific IgA against common food antigens is higher in PTFA patients. Since the ratio of IgA1 (and IgA2) on total IgA remains unaltered, this supports the hypothesis that the rise of serum IgA is not the result of backleak of intestinal IgA.

Disclosure of Interest: None Declared
Objectives & Study:
Hepatitis E is an emerging disease in developed countries. Some infections are asymptomatic, especially in children. Chronic infection is possible in immunocompromised patients and in liver transplants, hepatitis E infection can simulate rejection. In this particular case treatments are different. This underlines the necessity of diagnosing hepatitis E infection in transplanted patients. We studied the prevalence of Hepatitis E Virus (HEV) in the paediatric population of liver transplants because paediatric data in France is poor.

Methods: In this retrospective study, carried out in Lyon, France, between the 1st January 2010 and the 31st May 2013, we studied hepatitis E serology (IgM & IgG anti HEV) and HEV PCR in 96 liver transplanted children (84 isolated livers & 12 combined livers & kidneys).

Results: Eight patients (8.3%, 62.5% girls, mean age 12.3 years) were HEV seropositive. The mean age post transplantation was of 10 years (range 2-21.8 years) and biliary atresia was the first indication for transplantation. Seven of the eight were children liver transplants. There was no difference between the epidemiological and clinical data of these patients and the rest of the population especially concerning the immunosuppression (7/8 tacrolimus, 50% double immunosuppression). There was no HEV chronic hepatitis but 1/8 had chronic cytolysis (EBV and adenovirus infection). For all the tested patients (4/8) it was a post transplant seroconversion. There was no significant difference between the age groups in this study (0% <5 years, 12.5% 5-10 years, 4% 10-15 years, 9.1% 15-20 years & 12.5% >20 years).

Conclusion: In France, HEV seroprevalence for liver and combined liver and kidney transplant in paediatrics is low (8.3%) like in other Europeans studies.

Disclosure of Interest: None Declared
HEALTH-RELATED QUALITY OF LIFE IN ADOLESCENTS AND YOUNG ADULTS WITH CHRONIC VIRAL HEPATITIS

Francesco Nunziata 1,*, Antonietta Giannattasio 2, Maria Tufano 1, Milena Lombardi 1, Fabiola Di Dato 1, Valentina Minicucci 2, Raffaele Iorio 1

1Department of Translational Medical Science, University Federico II, Naples, Italy,  2Medicine and Health Science Department, University of Molise, Campobasso, Italy

Objectives & Study: It has been reported that the quality of life (QoL) of children with chronic viral hepatitis (CVH) is deteriorated during interferon treatment, although QoL returned to baseline after stopping therapy. Poor data are available on the impact of chronic hepatitis C (CHC) and B (CHB) on QoL of treatment-naïve children or after a long time after stopping treatment. The aim of this study was to assess the Health-Related Quality of Life (HRQoL) of treatment-naïve or previously treated adolescents and young adults with CVH, and to analyze differences between patients with CHC and CHB.

Methods: HRQoL was prospectively investigated in patients with CVH and age and sex matched healthy controls. The generic self-reported SF-36v2 Health Survey was applied to measure it. This instrument includes 8 scales: physical functioning (PF), role physical (RP), bodily pain (BP), general health (GH), vitality (VT), social functioning (SF), role-motional (RE) and mental health (MH). The 8 scale scores are then aggregated into physical and mental component summary (PCS and MCS) scores. Socioeconomic status and school education data were also collected. Patients with psychological comorbidity were excluded.

Results: Sixty-two patients (33 males; mean age 23.2±5.6 years) with CVH (25 subjects with CHC and 27 with CHB) and 60 healthy controls (27 males; mean age 21.5±4.3 years; p>.05) were enrolled. In the group of subjects with CVH, 17 (49%) patients with CHC and 9 (33%) patients with CHB had previously received antiviral therapy (p>.05). Number of actually viremic patients did not differ between the two groups. Only one patient with CHC had cirrhosis. The Physical scores did not significantly differ between patients with CVH and controls. As well, the two groups did not differ for socioeconomic status and school education. Mental scores (VT, RM and total MCS) were surprisingly significantly better in patients than in controls (p<.05). When CHC and CHB patients were separately analyzed, we found that CHC subjects scored significantly worse for all mental scores (VT, SF, RE, MH, and MCS), and for GH, while no difference was found for the other physical scores. Age was inversely related with both physical and mental scores. In the subgroups analysis, we found that viral factors had no impact on HRQoL level.

Conclusion: Despite being a mild disease in children, early HCV-infected patients had significantly poorer health status than CHB subjects and healthy controls. The most impaired area were those of cognitive, behavioral, and emotional functioning. Host and environmental factors, rather than viral factors, seem to affect HRQoL level.

Disclosure of Interest: None Declared
**Objective & Study:** Autoimmune pancreatitis (AIP) in children is an increasingly recognized diagnosis over the last few years. Diagnostic radiological, histological and serological criteria are adult derived with some limited application in children. To identify the features of children with AIP in our centre and describe the disease progression.

**Methods:** Clinical, biochemical, histological and radiological data were reviewed in children diagnosed with AIP from 2006 to 2013.

**Results:** Six (5 F) patients with AIP were identified. A combination of abdominal pain, raised serum amylase with autoimmune markers, bile duct and pancreatic radiological involvement with histological features guided us to the diagnosis. Hereditary causes were excluded. Median age at presentation was 11.5 years (range, 9.5–13.5). All patients presented with abdominal pain. Jaundice and pruritus was also present in 3. Ulcerative colitis was diagnosed in 2. No other organ involvement was reported. Median serum amylase, lipase, triglycerides and total bilirubin were 400 IU/L, 245 IU/L, 1.4mmol/L and 45mmol/L, respectively. Antinuclear antibodies were positive in 2 and raised immunoglobulin G subclass-4 (IgG4) (2.8 g/L [nv, 0.23-1.1]) in 2 with normal total IgG (11g/L [nv, 5.4-16.1]) levels. Ultrasound Scan (USS) and Magnetic Resonance Cholangiopancreatography (MRCP) were performed in all with evidence of chronic pancreatitis. MRCP showed pancreatic atrophy (2), pancreatic head enlargement (5), pancreatic duct irregularity (3) and common bile duct dilatation (4).

Endoscopic Retrograde Cholangio-Pancreatography was performed in 4 and 3 required stent insertion for biliary obstruction. Three patients underwent uneventful Endoscopic Ultrasound ampullary (2) and Computed Tomography pancreatic (1) biopsies with evident inflammation but limited number of IgG4+ve cells. Five were treated with corticosteroids; azathioprine was added in 1 as a steroid-sparing agent due to steroid induced diabetes. One patient who presented in 2006 underwent hepaticojejunostomy for biliary obstruction due to pancreatic head enlargement and AIP was diagnosed retrospectively. Clinical and serological remission (median amylase 48 IU/L, bilirubin 4mmol/L, IgG4 0.83 g/L) were achieved with significant radiological improvement in all and sustained after a median follow-up time of 23 months.

**Conclusion:** AIP is an evolving condition in children but diagnostic criteria still need to be established. They should include implementation of IgG4 serology, radiological imaging and lately histology, as prompt diagnosis is essential for effective immunosuppressive treatment.

**Disclosure of Interest:** None Declared
OBJECTIVES & STUDY: Liver transplantation (LTx) is a successful treatment option in end-stage liver disease. Shortage of donor organs limits the efforts to increase the number of LTx worldwide. Living related LTx (LR-LTx) could be a viable, alternative life saving procedure for infants with end-stage liver disease. Our aim was to review the value of LR-LTx in children who are followed up in our centre in Budapest.

METHODS: Medical documentation of 125 Hungarian children was reviewed who underwent LTx before the age of 18 years.

RESULTS: Of the 125 children with LTx, 69 (55%) were LR-LTx, and 56 (45%) patients had cadaveric grafts transplanted. Of the 69 LR-LTx, 67 were transplanted in 8 different foreign centres, and 2 were done in Hungary. Two patients (2.9%) died from the group who were transplanted in foreign centres, while one patient died from the 2 who were transplanted in Hungary. We had one child with primary hyperoxaluria who successfully received a kidney from her mother and a liver segment from her father. Three infants received liver segment grafts from their grandmothers, one from his aunt and one from her step-grandmother. From the remaining 63 donations 33 segments came from mothers and 30 from fathers. While only 3 of the 69 LR-LTx (4.3%) children died, we unfortunately lost 14 of the 56 children with cadaveric grafts (25%). All together we lost 17 of the 125 (13.6%) children with LTx during follow-up (mean 8.2 y). The mortality ratio after LTx performed in foreign centres is 7.3% (17/237 children), and 26.3% (10/38 children) in Hungarian centres.

CONCLUSION: In our centre, paediatric LR-LTx is performed more often than cadaveric transplantation. Importantly, LR-LTx yielded better outcomes, and became the treatment of choice in infants with end-stage liver disease.

DISCLOSURE OF INTEREST: None Declared
**Hepatology**

PO-H-0214

**IS NONALCOHOLIC FATTY LIVER DISEASE ASSOCIATED WITH GASTROESOPHAGEAL REFLUX SYMPTOMS IN CHILDREN AND ADOLESCENTS?**

Lucia Pacifico 1,*, Stefano Bascetta 1, Sara Romaggioli 1, Valeria Tromba 1, Sara Giansanti 1, Alessia Gallozzi 1, Claudio Chiesa 2

1Paediatrics, Sapienza University of Rome, Rome, Italy, 2Institute of Translational Pharmacology, National Council Research, Rome, Italy

**Objectives & Study:** In recent studies, nonalcoholic fatty liver disease (NAFLD) has been found to be associated with a high prevalence of symptoms of gastroesophageal reflux disease (GERD) in adults. Evidence has emerged suggesting a link between metabolic syndrome, especially obesity and visceral fat accumulation, and the onset of GERD. NAFLD has never been investigated in children as possible risk factor for GERD. Aims of this study were to assess the prevalence of GERD symptoms in children and adolescents with NAFLD, and to determine whether ectopic fat depots, including liver fat and abdominal visceral (VAT) and subcutaneous (SAT) fat, are linked to GERD.

**Methods:** This observational study included 108 Caucasian overweight/obese children and adolescents aged 6-16 years. Fifty-four patients met the criteria for diagnosis of NAFLD [i.e. hepatic fat fraction (HFF) ≥ 5% on magnetic resonance imaging (MRI)]. All enrolled subjects underwent a detailed clinical history, a complete physical examination, laboratory tests, and phenotyping of abdominal and liver fat by MRI. GERD was evaluated using the Pediatric GERD Symptom and Quality of Life Questionnaire (PGDQ) (1).

**Results:** There were no significant differences in age, gender, pubertal status, and BMI-SD score between the two groups. By definition, HFF values were significantly different between the two groups. Children with NAFLD had a higher waist circumference (WC), and VAT than those without liver involvement. Reflux symptoms were significantly more frequent in NAFLD patients than in subjects without NAFLD (61.0% vs 31.5%; P< 0.01) and GERD symptom score resulted significantly higher [mean, 3.4 (SD, 2.6) vs 1.9 (1.4); P< 0.01]. GERD symptom score was not correlated to age, BMI-SD score, WC, and SAT. GERD symptom score was positively associated with VAT (r= 0.193; P< 0.05) and HFF (r= 0.262; P< 0.001).

**Conclusion:** Our preliminary results indicate that NAFLD is a risk factor for GERD in children and adolescents, and that the risk of GERD symptoms rises progressively with the increase in both visceral and liver fat.


**Disclosure of Interest:** None Declared
EVALUATION OF NEONATAL CHOLESTASIS IN INFANTS BORN PRE-TERM
Suzanne Davison, Emanuela Manea, Venkatesh Karthik, Sanjay Rajwal, Naved Alizai, Helen Woodley, Teresa Humphrey, Patricia McClean
1Children's Liver Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, 2Department of Radiology, Leeds Teaching Hospitals NHS trust, Leeds, United Kingdom

Objectives & Study: Investigation of cholestasis in pre-term infants can be challenging. Although mostly due to prematurity, parenteral nutrition (PN) and sepsis, other causes requiring urgent management must be identified, including biliary atresia (BA). We devised a structured proforma to record a summary of infants discussed with our Supra-Regional Referral Unit, in order to formalise documentation of history and advice given and to ensure need for transfer was carefully considered. Aim: (1) To evaluate the proforma by determining frequency of admission and final diagnosis. (2) To describe the evaluation and characteristics of pre-term infants with BA.

Methods: All infants with neonatal cholestasis referred between 01/01/2010 and 31/03/2013 whose course was documented by proforma and/or were admitted.

Results: Of 287 infants, 129 were preterm (median gestation 29 weeks (23-36)). Age at referral was median 48 days (7-156). Excluding 15 in our Neonatal Unit, decision to admit was made in 41/114 (36%) pre-term compared to 114/158 (72%) term infants (p<0.0001). Pre-term infants admitted were more likely to have a history of no PN (66% v 8% p<0.0001) and pale stools (61% v 14% p<0.0001) than those not admitted. BA was diagnosed in 8/129 (6%) preterm compared to 41/158 (26%) term infants (p<0.0001). Preterm infants with BA were born at 27-36 (median 32) weeks gestation, referred at median age 32 (9-84) days and admitted after a median of 1 (0-13) days. One died aged 14 weeks from chronic lung disease. In the remaining 7 US showed typical features of BA, and 3 also had BASM syndrome. BA was confirmed intra-operatively, and surgery was performed at median age 41 days (24-51). Six (86%) cleared jaundice, one remained cholestatic and died awaiting transplant. Of 33 admitted who did not have BA, median age at referral was 49 (8-135) days and duration of admission was median 2 days (0-8). All underwent US, which in 32 was not suggestive of BA. One with US features of BA underwent liver biopsy which excluded BA, and one with poorly distended GB on US and abnormal HIDA underwent cholangiogram to exclude BA. Sensitivity and specificity of US for BA in preterm infants were 100% and 97%. 16/33 had additional diagnoses: Cystic fibrosis (3) endocrine disorder (5) CMV infection (2) alpha-1-antitrypsin deficiency (1) Donohoe syndrome (1) PFIC (1) portosystemic shunt (2) and portal cavernoma (2). Of 73 not admitted, none were subsequently diagnosed with BA.

Conclusion: Identification and timely transfer of pre-term babies with BA was facilitated by a structured proforma. Those with BA were referred earlier than those without, were admitted promptly and had a good outcome. Imaging by US in pre-term infants for assessment of BA has good sensitivity and specificity, and facilitates short admission and the avoidance of more invasive procedures.

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0216

**EARLY PREDICTORS OF HEPATIC INJURY AFTER SUICIDE ATTEMPTS WITH ACETAMINOPHEN IN 11-15 YEAR-OLD CHILDREN**

Rikke Lindgaard Hedeland 1,*, Vibeke Brix Christensen 2, Marianne Hørby Jørgensen 2, Grete Teilmann 1, Amne Iskandar 1, Jesper Andersen 1

1Paediatric Department, Nordsjællands Hospital, Hillerød, Denmark, 2Paediatric Department, Rigshospitalet, Copenhagen, Denmark

**Objectives & Study:** To explore the following in a pediatric population with acetaminophen overdose due to suicide attempt: 1) the prevalence of episodes of pre- and in-hospital vomiting and the relationship between the total number of vomiting episodes and hepatic injury. 2) the relevance of early initiation of N-acetylcysteine (NAC) treatment to hepatic injury. 3) the presence/absence of illness prior to the suicide attempt and hepatic injury.

**Methods:** A retrospective case study based on the medical records of 107 children aged 11 to 15 years old who were admitted to a single center due to suicide attempt. The statistical significance for intergroup differences was assessed using logistic regression for binary outcomes. ANOVA analysis/linear regression was used to quantify the strength of the relationship between continuous outcomes and categorical explanatory variables.

**Results:** There was a highly significant relationship between the number of pre-hospital vomiting episodes and relevant biochemical parameters (e.g., maximum aspartate aminotransferase \( p=0.0001 \) and maximum INR \( p=0.019 \)). A similar but less significant relationship was observed between the number of in-hospital vomiting episodes and these parameters. The latency time before initiation of the NAC treatment was significantly related to relevant biochemical parameters (e.g., maximum glutathione \( p=0.0001 \) and maximum INR \( p=0.001 \)). Children suffering from illness prior to their suicide attempt had greater changes in their e.g., maximum alanine aminotransferase (p=0.01) and INR (p=0.01) levels than children without illness prior to their suicide attempt.

**Conclusion:** Children at increased risk of developing hepatotoxicity can be identified at an early stage of admission. Our results show that increased numbers of pre-and in-hospital vomiting episodes, increased latency time before NAC treatment initiation, and prior illness in a pediatric population with acetaminophen-based suicide attempts are important early clinical predictors of hepatotoxicity.

**Disclosure of Interest:** None Declared
CHILDRENS COLOUR TRAIL TEST AND PEDSQL COGNITIVE FUNCTIONING SCALE CAN DETECT IMPAIRED COGNITIVE FUNCTIONING IN CHILDREN AFTER LIVER TRANSPLANTATION

Imeke Goldschmidt 1,*, Rolf van Dick 2, Sonja Bockisch 1, Eva Doreen Pfister 1, Ulrich Baumann 1

1Paediatric Hepatology and Gastroenterology, Hannover Medical Schol, Hannover, Germany
2Institute of Psychology, Frankfurt University, Frankfurt, Germany

Objectives & Study: Cognitive functioning can be impaired in liver-transplanted children by the effects of long-standing chronic illness and by morbidity and side-effects of therapy after liver transplantation (LTx). Impairment of cognitive functioning impacts on successful rehabilitation and future development. Screening tools for cognitive functioning may identify children at risk early.

Aim: To test the feasibility and examine the results of PedsQL™ Cognitive Functioning Scale (PedsQL™ CFS) and Childrens’ Colour Trail Test (CCTT) for screening of cognitive functioning in children after LTx.

Methods: 149 children (76f, median age 10.5 (2.1-18.3) years; 5 (0.1-17) years after LTx) underwent testing with either PedsQL™ CFS (child self-report age 5-18, parent proxy-report for age 2-18) and/or CCTT1&2 (patients age 8-16). Published normative data was used to interpret CCTT1&2. Results were compared using paired or unpaired t-test as appropriate. Correlation between test results and clinical parameters was made using Pearson’s rho.

Results: Testing proved feasible and easy to apply, with response rates of 98%. Liver transplanted children showed lower performance in CCTT1&2 than healthy children, with CCTT1/2 T-scores of 37.9 (19-65)/42 (19-60) respectively. CCTT2 performance was rated above average/average/below average/impaired in 9.8%/35.4%/19.5%/35.2% respectively. Impairment was classified as mild/mild to moderate/moderate/moderate to severe/severe in 12.2%/8.5%/6.1%/6.1%/2.4%. Compared to normative data, this distribution is significantly shifted towards impairment. Older age at testing and older age at transplantation were associated with better performance in CCTT1 but not CCTT2 (r=0.25, p=0.02 and r=0.35, p<0.01). Results for the PedsQL™ CFS showed reduced cognitive functioning both in the patients’ self-report (mean 65.9, range 8-100) and in the parent proxy-report (mean 64.5, range 4-100, published data from healthy samples: means 82/90 respectively (Varni 2010)). Higher age at transplantation was associated with higher PedsQL™ scores (parents r=0.19/p=0.03, patients r=0.25/p<0.01). Longer time since transplantation was associated with poorer proxy-report score (r=-0.19, p=0.02). Patient PedsQL™ scores correlated well with performance scores in CCTT2 (r=0.3, p=0.02). No differences in test performances were found based on type of immunosuppression (Tacrolimus vs Cyclosporin).

Conclusion: PedsQL™ Cognitive Functioning Scale and CCTT1&2 show rates of impaired cognitive functioning in children after LTx that are comparable with published data (Gilmour 2009). These easily applicable tests might be useful to identify children that benefit from more extensive neuropsychological testing and support.

Gilmour S Am J Transplant 2009

Disclosure of Interest: I. Goldschmidt: None Declared, R. van Dick: None Declared, S. Bockisch: None Declared, E. D. Pfister: None Declared, U. Baumann Grant / Research Support for: Astellas Pharma supports this study with a grant covering costs for CCTT administration
**Hepatology**

PO-H-0218

**THE RISK OF ATHEROSCLEROSIS IN CHILDREN WITH ALAGILLE SYNDROME**

Dorota Gliwicz-Miedzinska 1,*, Aldona Wierzbicka 2, Maciej Dądalski 1, Piotr Socha 1, Joanna Pawłowska 1, Irena Jankowska 1

1Gastroenterology, Hepatology and Nutritional Disturbances, 2Biochemistry and Experimental Medicine, Children’s Memorial Health Institute, Warsaw, Poland

**Objectives & Study:** Alagille syndrome (AGS) is a rare multiorgan disease inherited in an autosomal dominant pattern, with cholestasis being one of the most distinct features. Hypercholesterolemia with other lipid abnormalities is a well known accompanying problem in this group of patients and it’s often discussed in literature. The mechanisms underlying the observed lipid disorders and the risk of atherosclerosis in AGS have yet to be evaluated.

**The aim** of this study was to evaluate the risk of atherosclerosis in patients with AGS

**Methods:** A detailed examination of the lipid profile was performed in 44 patients with AGS and liver involvement treated in our department. The following parameters were estimated: total cholesterol (TC), triglycerides (TG), LDL, VLDL and HDL cholesterol, lecithin-cholesterol acyltransferase (LCAT), apolipoprotein AI (ApoAI) and B (ApoB), lipoprotein(a) [Lp(a)] and lipoprotein X. The results were compared with age-matched control group. Statistical analysis was performed using the Mann-Whitney test.

**Results:** The analysis revealed increased concentration of total cholesterol and LDL cholesterol in the examined group. The concentrations of VLDL cholesterol, triglycerides, apolipoprotein B and lipoprotein(a), though within normal range, were significantly higher in the examined group as compared to the age-matched control group (Table 1). Lipoprotein X was not revealed in blood of the examined patients.

Table 1. Lipid profile in patients with AGS with reference to normal range and to results of control group.

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Reference range (unit)</th>
<th>AGS median (Q1-Q3)</th>
<th>Control group median (Q1-Q3)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>LCAT</td>
<td>50-250 (nmol/ml/h)</td>
<td>99,85 (50,5-134,6)</td>
<td>126,4 (117,3-140,8)</td>
<td>0,00038</td>
</tr>
<tr>
<td>TC</td>
<td>≤190 (mg/dl)</td>
<td>224,5 (177-256,5)</td>
<td>179 (159-190)</td>
<td>0,00001</td>
</tr>
<tr>
<td>TG</td>
<td>50-150 (mg/dl)</td>
<td>99,5 (77-125)</td>
<td>67 (53-81)</td>
<td>0,00000</td>
</tr>
<tr>
<td>LDL-C</td>
<td>96-130 (mg/dl)</td>
<td>155 (111-191)</td>
<td>117 (99-136)</td>
<td>0,00004</td>
</tr>
<tr>
<td>VLDL-C</td>
<td>5-20 (mg/dl)</td>
<td>20 (14-22,5)</td>
<td>12 (10-15)</td>
<td>0,00000</td>
</tr>
<tr>
<td>HDL-C</td>
<td>40-80 (mg/dl)</td>
<td>44 (36,5-52)</td>
<td>45 (41-50)</td>
<td>0,3371</td>
</tr>
<tr>
<td>ApoAI</td>
<td>1-2 (g/l)</td>
<td>1,4 (0,9-1,5)</td>
<td>1,45 (1,38-1,5)</td>
<td>0,1036</td>
</tr>
<tr>
<td>ApoB</td>
<td>0,5-1,5 (g/l)</td>
<td>1,17 (0,8-1,4)</td>
<td>0,85 (0,74-1)</td>
<td>0,00015</td>
</tr>
<tr>
<td>Lp(a)</td>
<td>0-30 (mg/dl)</td>
<td>16 (9,5-26,5)</td>
<td>11 (8-16)</td>
<td>0,01244</td>
</tr>
</tbody>
</table>

**Conclusion:** The increased concentrations of total cholesterol and LDL cholesterol as well as the observed tendency to increased concentration of VLDL cholesterol, triglycerides, apolipoprotein B and lipoprotein(a) in the examined group, indicate the possibility of a higher risk of atherosclerosis in AGS patients compared to the general population. However, as the revealed abnormalities are moderate with reference to normal range, the risk seems to be quite low.

**Disclosure of Interest:** None Declared
HEPATOBILIARY RISK FACTORS FOR CLINICAL OUTCOME OF KAWASAKI DISEASE IN CHILDREN

Daeyong Yi 1, HyeRan Yang 1,*

1Paediatrics, Seoul National University Bundang Hospital, Seongnam, Korea, Republic Of Korea

**Objectives & Study:** Kawasaki disease (KD) is an acute febrile vasculitis that causes coronary artery abnormality (CAA) as a complication. In some patients, an association has been noted between elevated liver enzymes or an abnormal gallbladder (GB) and hepatobiliary involvement in KD. In this study, we aimed to evaluate clinical, laboratory, and ultrasonographic (USG) risk factors of hepatobiliary involvement for the intravenous immunoglobulin (IVIG) resistance and the development of CAA in children with KD.

**Methods:** From March 2004 through January 2013, clinical features, laboratory data, echocardiographic findings, and USG findings were retrospectively reviewed regarding the response to IVIG treatment and coronary artery complications in 67 children with KD. Acute acalculous cholecystitis (AAC) was diagnosed based on USG criteria.

**Results:** Among all factors, only the prothrombin time international normalized ratio was significantly different between the IVIG-response and IVIG-resistance groups (\(p=0.024\)). CAA was statistically more frequent in the AAC group (n=24) than in the non-AAC group (n=43) (23.3% vs. 58.3%, \(p=0.019\)). Among the laboratory factors, segmented neutrophil percentage, total bilirubin level, and C-reactive protein were significant in children with CAA (\(p=0.014, p=0.009, \text{ and } p=0.010\)). Abnormal GB findings on USG were significantly more frequent in children with CAA than in those without CAA (\(p=0.007; \text{OR}=4.620; 95\% \text{ confidence interval [CI]}: 1.574–13.558\)). GB distension on USG was the only significant risk factor for CAA (\(p=0.001; \text{OR}=7.288; 95\% \text{ CI}: 2.243–23.681\)) by using multiple logistic regression analysis.

**Conclusion:** For children in the acute phase of KD, USG findings of the GB, especially GB distension, may be an important risk factor for CAA as a complication.

**Disclosure of Interest:** None Declared
TRANSIENT ELASTOGRAPHY IN AUTOSOMAL RECESSIVE POLYCYSTIC KIDNEY DISEASE

Dorota Wicher 1, Irena Jankowska 1, Joanna Cielecka-Kuszyk 2, Jakub Kmiotek 1, Wojciech Jańczyk 1, Jacek Rubik 3, Piotr Socha 1

1Department of Gastroenterology, Hepatology and Nutritional Disturbances, 2Department of Pathology, 3Department of Nephrology, Kidney Transplantation and Arterial Hypertension, The Children's Memorial Health Institute, Warsaw, Poland

Objectives & Study: Autosomal recessive polycystic kidney disease (ARPKD) belongs to a group of congenital hepatorenal fibrocystic syndromes and is a significant cause of renal- and liver-related morbidity and mortality in children. Liver involvement (congenital hepatic fibrosis, CHF) is invariably present in all ARPKD patients. Liver fibrosis in CHF is a progressive and time-dependent process, so clinical symptoms (abnormal liver echogenicity, splenomegaly) may not be detectable during early childhood. Our goal was to evaluate predictive value of transient elastography (FibroScan®, FS) in detection of liver fibrosis.

Methods: We examined 21 pediatric patients (13 girls and 8 boys) with ARPKD (diagnosis based on clinical criteria proposed by Zerres et al.) between May and November 2013. Patient’s age ranged from 5 to 17.5 (median: 11.9) y. Laboratory findings, results of abdominal ultrasound examination, upper gastrointestinal endoscopy and FS were analysed. Control group consisted of 20 healthy children, 5 girls and 15 boys, age 4.3 – 17 (median: 9). Informed and written consent was obtained from parents before the children’s inclusion in the study.

Results: All children in control group have FS results within normal limits (median: 4.25 kPa; range 2.8 - 5.6 kPa). In ARPKD group median FS result was 22 kPa (range 3.6 - 75 kPa). ARPKD group was divided into two subgroups: ARPKD patients with normal FS (n=5; FS: 3.6-6.8 kPa) and abnormal FS (n=16; FS: 10.3-75 kPa). In subgroup with normal FS no patient had portal hypertension, splenomegaly or hypersplenism. In the subgroup with abnormal FS, portal hypertension was found in 64% (9/14 patients, 2 patients without endoscopy), splenomegaly in 75% (12 / 16 patients) and hypersplenism in 69% (11 / 16 patients). 8 patients with portal hypertension underwent at least one endoscopic variceal ligation (2 patients required this procedure 5 times). All patients (n=7) with liver fibrosis confirmed by liver biopsy had abnormal FS.

Conclusion: FS is a good, non-invasive method for detection of liver fibrosis in children with ARPKD. In patients with abnormal FS results upper gastrointestinal endoscopy should be performed due to suspicion of portal hypertension. Molecular verification of ARPKD diagnosis (especially in patients from subgroup with FS) should be performed.

Disclosure of Interest: None Declared
PSYCHOLOGICAL ISSUES IN CHILDREN WITH PFIC AFTER PARTIAL EXTERNAL BILIARY DIVERSION

Irena Jankowska1*, Piotr Czubkowski1, Piotr Kalicinski2, Hor Ismail2, Joanna Pawłowska1

1Gastroenterology, Hepatology and Eating Disorders, 2Paediatric Surgery and Organ Transplantation, The Children’s Memorial Health Institute, Warsaw, Poland

Objectives & Study: Partial external biliary diversion (PEBD) is considered to be the best treatment for children with progressive familial intrahepatic cholestasis (PFIC). Alternatively, ileal bypass (IB), is performed in cases of psychological intolerance, complications of stoma or technical problems for PEBD surgery. Although children, especially teenagers, psychologically suffer very often from the presence of biliary stoma, worldwide there is no published data about successful conversion from PEBD to IB due to psychical intolerance of stoma.

Methods: In our retrospective review, IB was performed in 7 adolescent patients with PFIC (5 girls, 2 boys, mean age 17.46 +/- 1.93 years) after successful PEBD performed at the age of 2-14 y (mean age 5.65 +/- 3.98y). IB was performed 8-15 years after PEBD (mean 12.07 +/- 2.57y). In all cases conversion was performed due to stoma-related psychological issues. Genetic confirmation of PFIC-2 was present in 5 cases. Patients before the decision to close down the stoma were carefully examined clinically and psychologically with the quality of life assessment. Mean follow-up after IB was 3.43 +/- 2.91y (from 6 months to 9 years).

Results: All children before closing a stoma were free from pruritus and had normal liver function as well as normal result of liver biopsy but with poor quality of life. Seven days after IB in 5 children increase in bile acids and appearance of pruritus was observed. All patients received UDCA. Within 1 month pruritus disappeared. After 6 months full normalization of bile acids was observed in all children. All pts had very good quality of life

Conclusion: 1. In teenage patients with PFIC after successful PEBD in childhood, the conversion to IB seems to be a promising alternative for stoma and is not associated with any long-term negative effects.
2. In some patients after IB in the early period after procedure it was necessary to commence UDCA due to the pruritus and increase of bile acids.

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0222

**Fecal Bile Acid Profiles in Healthy School-Age Children and Effects of Probiotic Supplements**

Yuichiro Yamashiro¹, Chongxin Wang¹, Satoru Nagata², Hirokazu Tsuji³, Takashi Asahara³, Takuya Takahashi³, Koji Nomoto³, Akina Muto⁴, Hajime Takei⁴, Hiroshi Nittono⁴

¹Probiotics Research Laboratory, Juntendo University Graduate School of Medicine, Tokyo, Japan, ²Pediatrics, Tokyo Women’s Medical University, Tokyo, Japan, ³Yakult Central Institute for Microbiological Research, Tokyo, Japan, ⁴Junshin Clinic Bile Acid Institute, Tokyo, Japan

**Objectives & Study:** Secondary bile acids, deoxycholic acid; DCA and lithocholic acid; LCA, are produced by 7 alpha-dehydroxylation bacteria from the two primary bile acids, cholic acid; CA and chenodeoxycholic acid; CDCA in the large bowel. DCA and LCA are associated with toxic and metabolic effects and are predominant in the feces. This study aimed to investigate the fecal bile acid patterns and the amounts in school age children, and to define the effects of probiotic supplements on the composition of the fecal bile acids.

**Methods:** Twenty three children, consisting of 12 boys and 11 girls with ages 5-12 years, was recruited. Fecal samples were taken at each child’s home under instruction of collection. The sample collection was scheduled for before, and after 1, 3 and 6 months after daily ingestion of probiotic and 6 months after discontinuance of taking it. Fecal bile acid profiles were analyzed by using GC-MS. The content of the probiotic given to the children was Lactobacillus casei Shirotta (LcS) fermented milk.

**Results:** Total fecal bile acid concentration of healthy school age children was approximately 8.2±5.7μmol/g, and the concentration of primary bile acids were CA:1.0±1.6μmol/g and CDCA: 0.8±1.3μmol/g. After 6 months of the probiotic supplement, 1) total fecal bile acid concentration increased significantly. 2) LCA, one of the secondary bile acids, its constituent ratio in the fecal total bile acid decreased and DCA tended to decrease but not significant. After 6 months of discontinuance of the supplement, the total bile acid and the secondary bile acids tended to return to the values of before the supplement.

**Conclusion:** Probiotic bacteria may influence the production of secondary bile acids, however, further investigation are clearly needed.

LIVER STIFFNESS MEASUREMENT AND CONTROLLED ATTENUATION PARAMETER FOR ASSESSMENT OF FIBROSIS AND STEATOSIS IN CHILDREN WITH AUTOIMMUNE HEPATITIS

Jakub Kmiotek 1,*, Małgorzata Woźniak 1, Łukasz Obrycki 2, Joanna Pawłowska 1, Joanna Cielecka-Kuszyk 3, Piotr Socha 1

1Department of Gastroenterology, Hepatology and Feeding Disorders, Children’s Memorial Health Institute, Warsaw, Poland, 2Medical University, 3Department of Pathology, Children’s Memorial Health Institute, Warsaw, Poland

Objectives & Study: There is a strong demand to apply non-invasive methods to diagnose liver fibrosis in children with liver pathology. Liver stiffness measurement (LSM) by FibroScan®(FS) was shown to be a valuable method in detection of liver fibrosis in adults with various chronic liver diseases such as HBV, HCV and non-alcoholic fatty liver disease. The new Controlled Attenuation Parameter (CAP) available on FS additionally gives a possibility to assess the degree of liver steatosis. We aimed at evaluating LSM and CAP in children with autoimmune hepatitis (AIH) compared to healthy controls and their relationship with parameters describing liver pathology- liver biopsy (LB), liver function tests and other selected parameters.

Methods: We investigated 43 children (12 boys); with AIH aged 15,3 (5.4-18)y [median (lower-upper quartile)] with liver biopsy available prior to LSM (in 9 pts. LB was done 3-mth earlier and in 7 pts. -12-mth earlier) and 18 healthy controls aged 12.0 (6.7-15.2)y. Patients with AIH were on steroid and/or azathioprine therapy. Inflammation and fibrosis were assessed by Batts and Ludwig histopathological score. Correlations were tested by Spearman rank test.

Results: AIH patients presented with normal INR, bilirubin and normal or slightly elevated ALT [20 (11-52)U/l]. They had increased LSM compared to controls [5.6 (4.3-12.1) vs. 4.2 (3.6-4.5)] but the difference in CAP did not reach statistical significance. LSM correlated significantly with the degree of inflammation (R=0.51) and degree of liver fibrosis (R=0.71) when compared to 16 recent liver biopsies and the correlation improved when compared to the most recent 9 liver biopsies (R=0.55 for inflammation and R=0.83 for fibrosis). In the whole group of AIH patients there was also a significant correlation with ALT (R=0.64), GGTP (R=0.71), dir bilirubin (R= 0.66). Liver fat content expressed by CAP was not correlated to the studied parameters. APRI, which is regarded to be a good non-invasive indicator of liver fibrosis correlated significantly (in pts with LB) with the degree of fibrosis (R=0.56).

Conclusion: Transient elastography is easily applicable to children with AIH. LSM is strongly correlated to the degree of fibrosis on liver biopsy and also correlates significantly with liver function tests and inflammation. LSM is superior to APRI in assessment of liver fibrosis.

Disclosure of Interest: None Declared
CIRRHOSIS COMPLICATIONS AFTER DEVELOPMENT OF ASCITES IN CHILDREN WITH BILIARY ATRESIA

Renata Rostirola Guedes 1,*, Sandra Maria Gonçalves Vieira 1, Carlos Oscar Kieling 2, Carolina Roos Mariano Rocha 1
1Universidade Federal do Rio Grande do Sul, Porto Alegre/ RS, Brazil, 2Hospital de Clínicas de Porto Alegre, Porto Alegre/ RS, Brazil

Objectives & Study: The development of ascites in cirrhotic adults is a sign of poor prognosis, whereas 50% go death in a mean period of three and a half years after its first episode. This is probably related to the occurrence of several complications. So far, there are few studies in the pediatric population about this issue. The aim of this study is to assess the incidence of cirrhosis complications after the first episode of ascites in children with cirrhosis due biliary atresia.

Methods: Forty-four patients younger than 12 years old from a tertiary center in Southern Brazil, were included in a historic cohort after their first episode of ascites grade II between the period of March 2000 - November 2013. Cirrhosis complications were defined as the occurrence of - dilutional hyponatremia (DH), refractory ascites (RA), spontaneous bacterial peritonitis (SBP), hepatic encephalopathy (HE) and gastrointestinal bleeding (GB). The period of follow up was 12 months from the first episode of ascites. The cumulative incidence of each complication was calculated using the method of Kaplan-Meier and patients were censored by the time of loss of native liver, defined as patient death or liver transplantation. DH was defined as serum sodium <130mEq/L and RA following the International Ascites Club diagnostic criteria. Diagnosis of SBP was based on ascitic fluid polymorphonuclear count greater than 250 cell/mm³ and absence of data suggesting secondary peritonitis. HE was diagnosed based on electroencephalographic findings. Episodes of GB not related to portal hypertension were not considered in the analysis.

Results: Of all 44 patients, 34 (77.2%) developed DH, 9 (20.4%) RA and 11 (25%) GB during the study period. SBP occurred in 13 of 42 patients (30.9%) and HE in 17 of 33 (51.5%). The cumulative incidence of each complication at the end of follow up was: DH – 83.6%, RA – 26.4%, GB – 53%, SBP – 36.9% and HE – 59.7%.

Conclusion: The development of ascites in cirrhotic children with biliary atresia is associated with a high incidence of complications. The most frequent complication in this cohort was dilutional hyponatremia. These results underscore the high incidence of cirrhosis complications in these patients such as occurs in adult cirrhotic population.

Disclosure of Interest: None Declared
**Objectives & Study:** Identifying the underlying cause of acute liver failure (ALF) is essential to institute disease-specific medical treatment and to evaluate indication for liver transplantation (LTX). Aetiology differs according to age and geographical location. No report in Italian children has been published so far in this setting. We aimed to determine aetiology, outcome and prognostic indicators in Italian children with ALF.

**Methods:** We retrospectively reviewed all cases of ALF referred to our Hospital in the last 16 years. ALF was defined by acute onset of liver disease with high transaminases, INR ≥ 2.0 regardless of hepatic encephalopathy (HE) and no evidence of an underlying chronic liver disease. Treatment included supportive medical therapy or liver transplantation when required. Based on the outcome we defined 2 groups: G1= survivors with supportive management; G2= transplanted or deceased before LTX. Demographic features, the presence of hepatic encephalopathy (HE) and liver function on admission were compared in the two groups. Prognostic indicators were assessed by multivariate analysis.

**Results:** we identified 55 children with ALF (median age 2.6 years, range 0.69-7.41 y; M/F=31/24; 38 children, 11 infants and 6 neonates). Aetiology was autoimmune hepatitis in 10 patients (18.2%, AIH-1 in 4 and AIH-2 in 6), metabolic disorders in 9 (16.3%), paracetamol overdose in 6 (11.0%), mushroom poisoning in 3 (5.4%), viral infection in 1 (1.8%) and unknown in 26 (47.2%); 25/55 recovered with supportive management (45.5%, G1); 28/55 underwent LTX, 2 (3.6%) died on the waiting list and 2 died after transplant (54.5%,G2). Overall the survival rate was 92.7%. Children who died or required LTX had severe HE (83.3% in G2 vs 32% in G1), higher INR (4.5 vs 3.3), higher bilirubin (18.8 vs 4.2 mg/dl), higher ammonia (174 vs 125 µmol/l) and lower alanine aminotransferase (1609 IU/L vs 4570 IU/L) on admission (p<0.05). On multivariate analysis the significant independent predictors of failure of conservative therapy were the presence of severe HE (grade 3-4 vs 2-3) and bilirubin ≥12 mg/dl (p<0.05).

**Conclusion:** AIH is the most common recognizable cause of ALF in our cohort of children. Patients who had severe HE and high bilirubin on admission were more likely to require LTX, as previously described. The overall outcome of children with ALF was excellent as compared to previous series and it was not different from that of children with end-stage chronic liver disease managed at our centre.

**Disclosure of Interest:** None Declared
CHILDREN WITH ESOPHAGEAL VARICES, THREE YEARS OF FOLLOW UP

Juan Cristóbal Gana 1*, Tassos Grammatikopoulos 2, Yael Mozer-Glassberg 3, Jason Yap 4, Veronique Morinville 5, Yaron Avitzur 6, Sofia Verdaguer 7, Luis Villarroel 8, Simon C Ling 8

1Gastroenterology, Hepatology and Nutrition Unit, Division of Paediatrics, Pontificia Universidad Católica de Chile, Santiago, Chile, 2King’s College Hospital, London, United Kingdom, 3Schneider Children’s Medical Centre, Petach Tikva, Israel, 4University of Alberta, Edmonton, Canada, 5Montreal Children’s Hospital, Montreal, Canada, 6Hospital for Sick Children, Toronto, Canada, 7Escuela de Medicina, Pontificia Universidad Católica de Chile, Santiago, Chile, 8Pontificia Universidad Católica de Chile, Santiago, Chile

Objectives & Study: Background: There is little published data on the outcomes of children with endoscopically-proven varices. We aimed to describe 3-year outcomes in a group of children with esophageal varices characterized at endoscopy at multiple centres.

Methods: 3-year follow-up data was collected on children previously identified to have esophageal varices during our previous multicentre study of non-invasive diagnosis of varices (1). Data collected included details of subsequent endoscopies and outcomes including bleeding episodes, transplant and death. We explored potential predictors of bleeding, including platelet count and our previously described clinical prediction rule (CPR) (1).

Results: 53 patients were included in this follow-up study. 5 patients had portal vein thrombosis, 21 biliary atresia, 9 autoimmune hepatitis, 4 PSC, 2 Alagille syndrome, 2 PFIC and 10 other cirrhotic conditions. At baseline 36% had grade 1 varices by the Paquet classification, 32% grade 2, 25% grade 3 and 2% grade 4 varices. Of 24 children (55%) who were re-scoped during the follow-up period, 42% had the same grade of varices, 21% had increased grade by one, 4% had increased grade by two, 25% had decreased grade by one, and 4% had decreased grade by two. Treatment to prevent bleeding was provided to 11 children (8 beta-blockers, 2 banding, 1 combined). Four patients (8%) had bleeding episodes, 1 with initially grade 2 varices and 3 with initially grade 3 varices (one of whom still had grade 3 varices when re-scoped). Platelet counts were 49, 95 and 72 x10^9/l in the bleeders, compared to a mean (SD) of 95 (50) x10^9/l in non-bleeders. The CPR was not available in one bleeder, and calculated as 129 and 93 in the other two. CPR mean (SD) in non-bleeders was 103 (19). 2 patients (4%) died due to massive esophageal bleeding and sepsis. 1 patient underwent portosystemic shunt surgery and 7 patients (13%) underwent liver transplant.

Conclusion: In this cohort of children with varices, the incidence of variceal bleeding was low (8%) during a 3-year follow-up period, however 4% died due this complication. Variceal grade progresses slowly in a minority of patients.


This work was partially supported by Fondecyt Grant; Proyect number: 11121146

Disclosure of Interest: None Declared
Hepatology
PO-H-0227

DIAGNOSTIC VALUE OF THE 13C METHACETIN BREATH TEST IN CHILDREN WITH AUTOIMMUNE HEPATITIS

Karolina Piwczynska 1,*, Marek Woynarowski 2, Maciej Dądalski 2, Małgorzata Woźniak 2
1 Department of Gastroenterology, Hepatology and Feeding Disorders, 2 Department of Gastroenterology, Hepatology and Feeding Disorders, Children's Memorial Health Institute, Warsaw, Poland

Objectives & Study: The results (grade of inflammation and fibrosis) of liver biopsy remain the most trustworthy prognostic test in Autoimmune Hepatitis (AIH). Methacetin is metabolised to acetaminophen and CO₂ in the liver with first pass effect and ¹³C labelled methacetin breath test can possibly be used as a liver function test in children AIH. The aim of the study was to assess diagnostic value of ¹³C labelled metacetin breath test in AIH children as liver disease progression test.

Methods: 51 AIH patients received orally 75 mg of ¹³C labelled methacetin and had ¹³CO₂ excretion measured every 10 minutes within the first hour and every 20 minutes within the second hour of the test. Measurements of excreted isotope were presented as the rate of the total dose per hour (D/H) and cumulative dose (CD). For each subject the time from methactin administration to peak isotope excretion (TTP) was calculated. Children had routine liver biopsy taken within 6 months of ¹³C methacetin breath test. Liver biopsies were scored according to Batts and Ludwig classification and patients were classified according to grading and staging as follows:
- no or minimal inflammatory activity (grading 0-1) and well visible inflammatory activity (grading 2-4);
- no or minimal fibrosis (staging 0-1) and well visible fibrosis (staging 2-4).

Receiver operating characteristics (ROC) analysis was used to calculate the optimal cut off point for TTP, D/H and CD as well as their specificity and sensitivity for differentiation of children with minimal or present injury in liver biopsy (AccuROC, Canada).

Results: 20 children (40%) were in group G0-1 and 31 (60%) in group G2-4. The groups did not differ according to sex or age distribution. ROC analysis showed that D/H 40-60 minutes and CD 80-120 minutes had weak ability to differentiate inflammatory activity (groups G0-1 and G2-4) - AUC: 0,6-0,7. 10 children (20%) were in group S0-1 and 41 (80%) to group S2-4. The groups did not differ according to sex or age distribution. ROC analysis showed that D/H 10-20 minutes and CD between minutes 10 and 60 had moderate differentiation power (AUC: 0,7-0,8) while D/H 30 minute and CD at minutes 80 and 100 had worse fibrosis differentiation ability (AUC: 0,6-0,7). The TTP optimal cut off point =30 had the best power for differentiation of children from groups S0-1 and S2-4 (AUC-0,8) with sensitivity (95% CI) = 0,58 (0,42 to 0,73) and specificity (95% CI) = 0,9 (0,55 to 0,99).

Conclusion: None of ¹³C methacetin breath tests parameters could differentiate AIH patients with minimal or absent inflammatory activity from those with marked inflammatory activity in the liver tissue. ¹³C methacetin breath test allowed to discriminate AIH patients with different staging in liver tissue, thus repeated ¹³C methacetin breath test in individual patient can be used to track the progression of liver fibrosis in the course of AIH.

Disclosure of Interest: None Declared
**Objectives & Study:** Elastography is a novel non-invasive method that involves applying local mechanical compression on soft tissue using focused ultrasonography (US) and acquiring strain images that show tissue responses. Several studies have found elastography measurements to show strong correlations with the stage of liver fibrosis (1). Our goal was to assess the performance of shear-wave elastography (SWE) in the staging of liver fibrosis in children with various etiologies of liver disease.

**Methods:** The study involved measuring SWE values in the right lobe of the liver in a 76 children with chronic liver disease and in 50 healthy children with normal physical examinations, transaminase levels, prothrombin time and without any change in liver echo structure on a baseline gray-scale US. In the first group, SWE values were compared with liver biopsy results, evaluated semiquantitatively, according to the Brunt scoring system (F0: portal fibrosis, F1: perisinusoidal or portal/periportal fibrosis, F2: both perisinusoidal and portal/periportal fibrosis, F3: bridging fibrosis and F4: cirrhosis). Performance of SWE in estimating liver fibrosis in children was determined based on a receiver-operating characteristics (ROC) analysis.

**Results:** The mean elasticity values of the control group and F0 group were not statistically significantly different (p=0.106). The mean elasticity values of the F1, F2, F3, and F4 groups were higher than that of the control group [F0(n=17)=9.9±6.14kPa, F1(n=14)=18.5±10.0kPa, F2(n=18)=18.2±10.33kPa, F3(n=12)=20.2±5.79kPa, F4(n=15)=25.3±6.51kPa, control(n=50)=7.41±4.2kPa] (all p<0.001). Based on kPa values, the area under the ROC curve was 95.2% (95% CI = 92.1-99.5%) with a sensitivity for diagnosing liver fibrosis of 91.5%, a specificity of 94.0%, a positive predictive value of 93.1%, and a negative predictive value of 92.6%. Mean SWE values for patients with non-alcoholic steatohepatitis were higher than those in the remainder of the study group (Table).

<table>
<thead>
<tr>
<th>Elastography (kPa)</th>
<th>n</th>
<th>Mean range</th>
<th>Standard deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>NASH</strong></td>
<td>18</td>
<td>23.54</td>
<td>11.77</td>
</tr>
<tr>
<td><strong>Other patients</strong></td>
<td>58</td>
<td>16.49</td>
<td>7.97</td>
</tr>
<tr>
<td>Elastography (m/s)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>NASH</strong></td>
<td>18</td>
<td>2.68</td>
<td>0.72</td>
</tr>
<tr>
<td><strong>Other patients</strong></td>
<td>58</td>
<td>2.28</td>
<td>0.54</td>
</tr>
</tbody>
</table>

**Conclusion:** Although liver fibrosis can be detected using SWE, differentiation of fibrosis stages could not be achieved. The presence of steatosis significantly increased the mean liver stiffness values on elastography and so care should be taken when assessing children with non-alcoholic steatohepatitis.


**Disclosure of Interest:** None Declared
A PROSPECTIVE STUDY OF 1000 PERCUTANEOUS LIVER BIOPSIES IN CHILDREN

Suzanne Davison 1, Venkatesh Karthik 1, Sanjay Rajwal 1,*, Peter Sewell 1, Patricia McClean 1

1Children’s Liver Unit, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom

Objectives & Study: Percutaneous liver biopsy is a well established procedure to permit histological assessment for diagnosis and monitoring. A wide range of techniques are available, including differing needle types (suction and cutting), method of ultrasound (US) assistance (guided or localised) and patient preparation. There are no established guidelines for indications for antibiotics or threshold for blood product support. The aim of this study was to evaluate the complications, risk factors and histological adequacy of 1000 liver biopsies in a single centre.

Methods: Since June 2000, biopsy procedures have been performed according to a standard protocol, with platelets > 70x10^9/l or prothrombin time > 3 seconds prolonged being supported, antibiotics on induction and after 6 hours for those on immunosuppression, and all being guided or site localised by US. Needle type was according to the preference of the operator. A proforma captured the biopsy procedure data. Electronic theatre records were used to assess completeness of data collection.

Results: Of 1000 biopsies, 618 were native liver and 382 transplant (LT) recipients. Age at biopsy was < 3 months in 87, 3-12 months in 144 and > 12 months in 769. Operator was hepatologist in 712, radiologist in 245, surgeon in 5, and not recorded in 38. Biopsy needle was Temno in 804, Jamshidi in 136, both in 12, other in 5 and 43 not recorded. Fragmentation or inadequate tissue was seen in 44/804 (5%) Temno and 33/136 (24%) Jamshidi (p<0.001). This difference was apparent on interim analysis of 500 biopsies, (33/136 (24%) v 18/364 (5%) p<0.001)) after which time Jamshidi was no longer used. Significant haemodynamic or cardiorespiratory complications post biopsy occurred in 10/1000 (1%). Two with low platelets pre-biopsy (28 and 62) had received support. Major bleeding requiring emergency embolisation occurred in 2. Other complications were AV fistula (1), blood loss requiring transfusion (4) haemothorax (1) and pneumothorax (1) (both resolved without drainage). One infant had increased ventilatory requirements. There was no increased risk in LT recipients (p=0.6), in localised v guided biopsy (p=0.68)or according to needle type Temno v Jamshidi (p=0.2). Evidence of sepsis occurred in 9/1000 (0.9%). Seven were LT recipients, of which one had bile leak, and 8/9 received peri-biopsy antibiotics. Risk of sepsis was higher in LT recipients (p=0.014). Minor complications occurred in an additional 11/1000: 5 had pain at site or shoulder tip and 6 an asymptomatic drop in Hb of > 1g/dl. Two infants had respiratory complications at induction of anaesthesia.

Conclusion: Liver biopsy complication rate was 1.9% of which bleeding or pneumothorax accounted for 1%. Sepsis occurred predominantly in LT recipients despite prophylactic antibiotics. There was no mortality. The audit identified the superior biopsy sample obtained with Temno rather than Jamshidi needle.

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0230

**FISH-OIL BASED INTRAVENOUS LIPID EMULSION AS A RESCUE IN SEPTIC INFANTS WITH INTESTINAL FAILURE AND WITH OR AT RISK OF DEVELOPING LIVER DISEASE**

Huey Miin Lee 1, Ann Hickey 2, Helen Callaby 3, Marie O'Meara 3, Lucy Thompson 3, Jonathan Hind 1,*

1Paediatric Hepatology, 2Paediatrics, 3Pharmacy, King's College Hospital, London, United Kingdom

**Objectives & Study:** In infants with intestinal failure, it is known that episodes of sepsis can be accompanied by a significant deterioration in liver function. We hypothesised that an intravenous lipid emulsion (ILE) comprised solely of fish oil, such as Omegaven®, may protect the liver in these infants during episodes of sepsis. Our aim is to describe our single centre experience with Omegaven® as a rescue therapy in septic infants with intestinal failure and with or at risk of developing liver disease.

**Methods:** A mixed source ILE containing both omega-3 and omega-6 fatty acids (SMOFlipid®) was used as first-line in infants at high risk of IFALD or severe liver disease. When these infants developed sepsis, Omegaven® was used as the sole ILE for up to 14 days. A retrospective review of their case notes was conducted.

**Results:** 10 infants had Omegaven® treatment during a 2-year period (August 2011-August 2013). Of the 10 patients, 2 had gastroschisis, 5 had necrotising enterocolitis (NEC), 2 patients had congenital infection with conjugated hyperbilirubinaemia, and 1 had conjugated jaundice associated with maternal liver failure. 2 patients were late transfers at 4-5 months of age from other hospitals with severe and progressive IFALD. Both subsequently died. Median age at start of Omegaven® was 38 days (range 2-189). 5 patients did not complete the full 2-week course of Omegaven®, 1 patient had 3 courses of Omegaven® treatment due to recurrent episodes of sepsis. 9 patients had conjugated hyperbilirubinaemia with total bilirubin levels above 80µmol/l at commencement of Omegaven®. Out of these 9 patients, 5 had conjugated bilirubin levels above 100µmol/l when Omegaven® was started. In the other patients, clinical assessment of the severity of sepsis led to the decision to commence Omegaven® prophylactically to ameliorate potential liver damage. During their episodes of sepsis, bilirubin and CRP rose as expected in all patients. Transaminases were deranged in all. Those with established liver disease did not demonstrate the marked rise in bilirubin that would normally be anticipated. In those that were treated prophylactically, the liver function did not show marked deterioration despite the severity of sepsis. 7 patients showed improvement in bilirubin levels during treatment and this was maintained in the long term in 6.

**Image:**

![Image of bilirubin levels over time](image-url)
**Conclusion:** Use of Omegaven® as a short term rescue ILE in septic infants with intestinal failure and with or at risk of developing liver disease appears safe. The expected deterioration in liver function associated with sepsis was not seen in this series.

**Disclosure of Interest:** None Declared
**Hepatology**

PO-H-0231

**MOLECULAR CHARACTERISTIC OF PATIENTS WITH ACUTE LIVER FAILURE DUE TO WILSON’S DISEASE – SINGLE CENTER EXPERIENCE**

Diana Kamińska¹, Hartmut Schmidt², Maciej Dądalski¹, Krystyna Becherka³, Natalia Mucha³, Wojciech Jańczyk¹, Piotr Socha¹

¹Gastroenterology, Hepatology and Feeding disorders, Children’s Memorial Health Institute, Warsaw, Poland, ²University Hospital, Munster, Germany, ³Medical University, Warsaw, Poland

**Objectives & Study:** Wilson’s disease (WD) may have a variable course and may present with hepatitis, chronic cirrhosis or acute/fulminant liver failure (ALF). The direct relationship of the type of ATP7B mutation and clinical presentation was not established, still some mutations were regarded to be associated with a milder clinical presentation including p.H1069Q mutation. The aim of the study was to evaluate p.H1069Q mutation distribution in patients with acute liver due to WD vs. patients with WD of other clinical presentation.

**Methods:** From the database of 121 patients with Wilson disease we analyzed data in a subgroup of 82 patients with confirmed Wilson’s disease and molecular mutations available and in a subgroup of 13 patients with WD and acute liver failure (defined as INR>2.0 or INR >1.5 and encephalopathy), treated in a single referral center for Poland.

**Results:** In 82 patients with non-acute disease presentation the most frequent mutation was H.1069Q found in 93 out of 164 alleles (57%). 32 children were homozygous for this mutation (39%). Other 13 patients fulfilled criteria of ALF. p.H1069Q mutation was found in all children (two homozygous-15%- in sum 15 alleles out of 26 (58%). No significant difference was found in p.H1069Q distribution between both groups as well as in frequency of p.H1069Q homozygous patients. All ALF patients were listed for liver transplantation, 12 patients underwent liver transplantation, two patients died.

**Conclusion:** p. H1069Q mutation is predominant in Polish children with Wilson’s disease and and can be associated with acute liver failure in this group of patients.

**Disclosure of Interest:** None Declared
USEFULNESS OF DIAGNOSTIC SCORING SYSTEMS FOR SERONEGATIVE AUTOIMMUNE HEPATITIS IN CHILDREN

Dinesh Rawat 1,* Sanjeev Kumar 1, Vikrant Sood 1, Rajiv Khanna 1, Seema Alam 1

1Paediatric Hepatology, Institute of Liver & Biliary Sciences, New Delhi, India

Objectives & Study: Diagnosis of seronegative autoimmune hepatitis (AIH) poses challenge due to inadequacies of diagnostic criteria and lack of gold standard diagnostic tests. We aim to assess the utility of simplified AIH criteria in comparison to the revised criteria proposed in 1999 by International Autoimmune Hepatitis Group (IAIHG) score for diagnosis of seronegative AIH.

Methods: Case records of patients who presented to a single centre between Jan 2011-June 2013 were analysed and data collected for clinical features & laboratory tests including IgG levels, autoimmune markers, viral serology, liver biopsy, imaging and endoscopy findings. Diagnosis of seronegative AIH was based on high IgG, typical liver histology (interface hepatitis, portal based lymphoplasmacytic infiltrates & pseudorosettes), response to steroids and exclusion of other etiologies in the absence of non organ specific autoantibodies.

Results: 27 children (16 boys) with median age 11.5 yrs (range 3.3-18 yrs) were included while 23 children with other etiologies for chronic liver disease taken as controls. 12/27 (44%) children categorized as seronegative AIH. Acute hepatitis like presentation was more common in seronegative AIH (50% vs 7%, p=0.04; OR 2.18) Autoimmune hemolysis was the commonest extrahepatic autoimmune disorder (22%) while celiac disease was seen in 18%. All seronegative children were diagnosed as probable AIH based on revised IAIHG criteria with score≥ 10 (sensitivity 100%, specificity 82%, NPV 100%) but only 58% were diagnosed by simplified AIH criteria with score≥ 6 (sensitivity 58%, specificity 91%, NPV 80%). Amongst seropositive AIH children, only 73% were correctly diagnosed as probable or definite AIH by simplified criteria.

Conclusion: Revised IAIHG score is helpful in diagnosis of seronegative autoimmune hepatitis while simplified AIH score has limited utility and requires further modification. Patients should be carefully screened for presence of autoimmune disorders, especially autoimmune hemolysis and celiac disease.

Disclosure of Interest: None Declared
Factors with Impact on the Incidence of Cholestasis in Preterm Newborns Receiving Parenteral Nutrition

Mihaela Gheonea¹, Elena Coleta¹,*, Mirela Sirbu¹

¹University of Medicine and Pharmacy of Craiova, Craiova, Romania

Objectives & Study: Parenteral nutrition-associated cholestasis (PNAC) is one of the most common complication of parenteral nutrition in preterm infants. We performed a study to evaluate factors with impact on incidence and clinical manifestations of PNAC in this group of patients in a tertiary intensive care unit for newborns.

Methods: The design used was a retrospective case-control study on preterm infants with cholestasis (N=21) and control subjects (N=58) who received parenteral nutrition for more than 14 days. Clinical features and medical management were examined, including PNAC time to debutue, duration, the degree of PNAC and hepatic injury.

Results: Regression analysis showed that preterm infants with PNAC had longer duration of parenteral nutrition, longer duration of ventilation, longer duration of fasting, lower birth weights, higher cumulated amino acid and lipid emulsion intake, and later breast feeding beginning than controls. Best independent predictors of PNAC identified were duration of fasting (OR=0.78; 95%CI: 0.59-0.83; p=0.028), oxygen therapy (OR 1.01; 95%CI: 0.92-1.09; p=0.001), and duration of parenteral nutrition (OR=0.11; 95%CI: 1.02-1.21; p=0.007). The prognosis of PNAC was good.

Conclusion: Multiple factors are associated with PNAC. Our data identify early enteral nutrition and short duration of parenteral nutrition as the main factors for lowering the incidence of PNAC.

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0234

**PREVALENCE AND OUTCOME OF ABNORMAL LIVER FUNCTION TESTS IN CHILDREN ON PROPHYLACTIC TREATMENT FOR TUBERCULOSIS INFECTION**

Sara Leeb 1,*, Charlotte Buxbaum 1, Björn Fischler 1

1Dept. of Paediatrics, Karolinska University Hospital, CLINTEC, Karolinska Institutet, 14186 Stockholm, Sweden

**Objectives & Study:**
To investigate the prevalence and outcome of elevated transaminases in a population based setting of children undergoing prophylactic treatment for Tuberculosis (TB) infection.

**Methods:**
All children (0-18 years) who were started on TB prophylactic treatment 2009-2011 living in a geographically defined area in Stockholm, Sweden were included. The patients were diagnosed in immigrant screening or contact investigation through Tuberculin skin test and/or Interferon-Gamma Release Assay. Signs and symptoms of active TB disease were negated. At baseline and at 1,2,4,6 and 9 months, blood tests were performed, including ALT and AST. Data on background factors, treatment regimen (Isoniazid 5-10 mg/kg/day for 6-9 months, or Rifampicin 10-15 mg/kg/day combined with Isoniazid 5-10 mg/kg/day for 3 months, or Rifampicin 10-15 mg/kg/day alone for 4 months), ALT and AST levels and clinical side effects were retrospectively collected. If elevation of transaminases developed, the management of this was recorded. Comparison of data was performed between the group of patients who developed elevated transaminases (Group A) and those who did not (Group B). Statistical analysis by Fisher and Chi-square test was done.

**Results:**
A total of 277 children were included, of these, 113 (41%) had elevated transaminases. 95 children (35%) had elevations <3 times the upper limit of normal range (ULN) and 16 (6%) had elevations >3 times ULN. Of these 16 patients, 7 had to stop treatment. They all medicated with Isoniazid, 5 could re-start with Rifampicin monotherapy and for 2 the duration of treatment was shortened. In the end, all patients could finish one treatment regimen and the transaminase elevations were always reversible. The highest transaminase peak occurred within the first 4 months in 81 patients (72% of those with elevated transaminases), but in 17 patients (15%) it occurred after >6 months of treatment. No one had clinical symptoms of hepatotoxicity. When comparing group A with B, there was no difference in body mass index, hepatitis B status or treatment regimen. However, in patients aged <9 years there was a higher percentage with elevated transaminases (61% compared to 41% in the whole group, p< 0,0001). Conversely, in children aged 10-14 years, elevated transaminases were significantly less common. 44% of all boys and 36 % of all girls had elevation of transaminases (p=0,041).

**Conclusion:**
1. Elevated transaminases are very common in this patient group with an onset throughout the entire treatment period. Young age and male sex seemed to indicate an increased risk.
2. The rate of elevations >3 ULN was as high as 6%, but all patients could in the end finish one regimen of TB drugs.
3. When resources allow, regular blood tests need to be performed throughout the treatment.

**Disclosure of Interest:** None Declared
**Hepatology**

PO-H-0235

**PULSE OXIMETRY IS INSUFFICIENT FOR TIMELY DIAGNOSIS OF HEPATOPULMONARY SYNDROME IN CHILDREN WITH LIVER CIRRHOSIS**

André Hoerning 1,*, Simon Raub 1, Ulrich Neudorf 2, Carsten Müntjes 2, Simone Kathemann 1, Elke Lainka 1, Florian Stehling 3, Peter Hoyer 4, Patrick Gerner 1

1Paediatric Gastroenterology and Hepatology, 2Paediatric Cardiology, 3Paediatric Pulmonology, 4Paediatric Nephrology, Gastroenterology, Endocrinology and Transplantation Medicine, University Hospital Essen, Essen, Germany

**Objectives & Study:** Hepatopulmonary syndrome (HPS) is a severe pulmonary vascular complication from liver cirrhosis or portal hypertension, wherein intrapulmonary vasodilatation (IPVD) causes hypoxemia. Here, we prospectively investigated HPS prevalence, importance of pulse oximetry for its diagnosis and the longitudinal course in cirrhotic children referred for liver transplantation.

**Methods:** Fifty-six patients with liver cirrhosis between 1-17 years old (mean 4.6±5.0 yrs) were screened for HPS using hyperemic capillary blood gas analysis (CBG) and contrast-enhanced echocardiography. Eleven patients were excluded due to conditions that can produce cardiopulmonary dysfunction, e.g. cystic fibrosis (n=5), pulmonary arterial hypertension (n=1) or intracardial shunts (n=5). HPS was classified in accordance with ERS Task Force criteria on Pulmonary-Hepatic Disorders. Patient groups were compared for biochemical and clinical characteristics.

**Results:** Eighteen children (40%) were IPVD+ and had pulse oximetry levels >98%. Two of these (11%) exhibited a moderate HPS with an elevated PΔAaO₂ >15 mmHg and PaO₂ <70 mmHg; they deceased before liver transplantation was performed. The sensitivity and specificity of CBGs to detect elevated PΔAaO₂ in IPVD+ children was 94% and 53%, respectively. HPS was associated with late hepatopportoenterostomy (p<0.04). Liver transplantation led to HPS resolution in all patients.

**Conclusion:** IPVD is frequent in children with liver cirrhosis (40%). Pulse oximetry is insufficient for timely HPS diagnosis. Pathological CBGs indicate IPVD in the majority of cases but they were imprecise in children <2 years old. For HPS evaluation in cirrhotic children contrast-enhanced echocardiography and CBG is recommended regardless of liver synthesis capacity and clinical chemistry.

**Disclosure of Interest:** None Declared
SUCCESSFUL TREATMENT OF AN AUTOCHTONOUS CHRONIC HEPATITIS E INFECTION (GENOTYPE 3) IN A POST LIVER TRANSPLANT RECIPIENT

Palaniswamy Karthikeyan 1,*, Alberto Quaglia 1, Emer Fitzpatrick 1, Anil Dhawan 1, Sanjay Bansal 1
1Paediatric Hepatology, Gastroenterology and nutrition, Kings college Hospital, London, United Kingdom

Objectives & Study: Autochtonous HEV infection can lead to chronic hepatitis in immunocompromised or immunosuppressed patients. In post liver transplant setting, it can present as persistent abnormal liver function tests with lobular hepatitis on liver biopsy. If left untreated, it can lead to end stage liver disease requiring re-transplantation.

Methods: MB, 10 yr old, had a left lateral segment liver transplant on 13/2/2009 for end stage liver disease due to MDR 3 deficiency. He was started on Tacrolimus & Prednisolone. On D7, He had a presumed ACR(biopsy not proven) and responded to steroid pulse. He had a steroid resistant rejection at D40 post-transplant needing Basiliximab and addition of Mycophenolate. Thereafter for 2 yrs he had persistent mild transaminitis. In Nov 2011, he had a liver biopsy showing portal inflammation and bile duct damage requiring steroid pulse. Since, he has had 5 biopsies which showed varying degree of lobular hepatitis +/-portal inflammation, occasionally showing features of rejection. We modified his immunosuppression but without much success(Table 1). An extended viral hepatitis work up in April 2013 showed HEV IgM, IgG & HEV RNA (Genotype 3) positivity. Retrospective analysis of stored blood sample showed that, at 157 days post liver transplant he became HEV IgM and RNA positive but HEV IgG negative(time of HEV exposure). Thereafter he has had persistent HEV viraemia along with HEV IgM and IgG positivity. Initially MMF, then sirolimus was stopped and his tacrolimus dose was reduced. Due to non-response, Ribavirin was started at 15 mg/kg in 2 divided doses for 12 wks. His liver function tests normalised within 10 days. His HEV RNA became negative after 4 wks. Even after stopping Ribavirin, he remained non viraemic with normal liver function tests but positive HEV IgM and IgG.

Results:

<table>
<thead>
<tr>
<th>Days Post OLT</th>
<th>AST/ ALT</th>
<th>Biopsy</th>
<th>Treatment</th>
<th>HEV IgM</th>
<th>HEV IgG</th>
<th>HEV RNA</th>
</tr>
</thead>
<tbody>
<tr>
<td>D157</td>
<td>85/114</td>
<td>LH+portal inflammation</td>
<td>Tac +MMF ↓</td>
<td>POS</td>
<td>NEG</td>
<td>8.58E06</td>
</tr>
<tr>
<td>D1006</td>
<td>90/120</td>
<td>Portal inflammation + bile duct damage</td>
<td>Steroid bolus</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D1392</td>
<td>236/368</td>
<td>LH + Fib</td>
<td>Sirolimus ↓</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D1419</td>
<td>472/534</td>
<td>LH+ Fib</td>
<td>Tacrolimus ↓</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>D1470</td>
<td>346/394</td>
<td>LH+ Fib</td>
<td>Sirolimus stopped</td>
<td>POS</td>
<td>POS</td>
<td>1.78E05</td>
</tr>
<tr>
<td>D1515</td>
<td>311/303</td>
<td>-</td>
<td>Tacrolimus ↓</td>
<td>POS</td>
<td>POS</td>
<td>1.41E06</td>
</tr>
<tr>
<td>D1620</td>
<td>352/352</td>
<td>LH+Fib</td>
<td>Ribavirin started</td>
<td>POS</td>
<td>POS</td>
<td>1.52E06</td>
</tr>
<tr>
<td>D1704</td>
<td>23/15</td>
<td>n/d</td>
<td>Ribavirin stopped</td>
<td>POS</td>
<td>POS</td>
<td>-</td>
</tr>
</tbody>
</table>

POS-Positive, NEG-Negative, LH- lobular Hepatitis, ACR-Acute Cellular Rejection, Fib- Fibrosis.

Conclusion: Chronic Hepatitis E virus infection should be considered in the differential diagnosis of persistant graft dysfunction in post liver transplant patients specially in presence of lobular hepatitis on liver biopsy. Early detection and treatment may help in preventing the progression of liver fibrosis and prolonging the survival of the graft.

Disclosure of Interest: None Declared
HIGH RISK BEHAVIOUR IN YOUNG PEOPLE – AN OPPORTUNITY FOR TARGETED INTERVENTION WITH HEPATITIS B VACCINATION IN THE UK

Jaswant Sira 1,*, Maxine Brown 1, Sangeeta Ambegakaor 2, Deirdre A Kelly 1

1Liver Unit, 2CAMS, Birmingham Children's Hospital, Birmingham, United Kingdom

Objectives & Study: Background: The prevalence of blood borne viruses (BBV), hepatitis B (HBV), hepatitis C (HCV) and Human Immunodeficiency Virus (HIV) in adults involved in intravenous (IV) drug use or unsafe sexual behaviour is 50-80% in the UK and accordingly, HBV vaccination is advised for these adults. The incidence of BBV infection in at risk young people <18 years in the UK is unknown.

Aim: To identify the prevalence of BBV infection and establish the need for health promotion including HBV vaccination in young people involved in at risk behaviour.

Study Population: All young people (age <18yrs) attending the Young Person’s Substance Misuse service in Birmingham.

Design: Non-randomised, quantitative study and descriptive questionnaire to ascertain risk behaviour and screen for BBV infection.

Methods: Study information provided to the young people by their key workers. Those who agreed to take part were seen by study team and informed consent obtained. Data collected included: demographics details of risk behaviour, HBV, HCV and HIV serology. Information about BBV prevention provided. Non-immune young people were offered HBV vaccination; those found to be infected referred for clinical care.

Results: 65/500 young people were recruited by their case worker; (56M; Median Age 17.5; Range13 to 18 yrs). Caucasian 66%, Afro-Caribbean 13% and Asian 9%. Refusal was either due to fear of needles or they had been tested. Risk behaviour included: 6 IV drug users; 58 cannabis users; 59 had multiple sexual partners (40 had 1 - 5 sexual partners and 19 had > 6 sexual partners). 51 had engaged in unprotected sex. 56 were negative for HBV, HCV, and HIV: 8 were HBV immune following vaccination and 1 was naturally immune. HBV vaccination was recommended to 56 non-immune young people, but was declined by most of them: The main reasons were that as vaccination was not available at the centre, the young people were reluctant for their confidential information to be disclosed to their family doctors.

Summary: The study found that no young person screened had yet been infected by BBV which may be related to the small number of IV drug users. The main risk factor for acquiring BBVs in this population was related to unprotected sex with multiple sexual partners. There was no routine provision of hepatitis B vaccination to this at risk group. Refusal by young people to accept screening for BBVs may be due to fear and inadequate counselling.

Conclusion: The prevalence of BBV infection was low in this group of young people involved in high risk behaviour, but is a major problem in older adults. There is need for better awareness and education about prevention of BBV infection in key workers and at risk young people. This is an opportunity for targeted intervention of hepatitis B vaccination in this group of young people.

Disclosure of Interest: None Declared
CLINICAL FEATURES OF PRIMARY SCLEROSING CHOLANGITIS IN CHILDREN

Nadezhda Pakhomovskaya, Alexander Potapov, Galina Volynec, Tatyana Chetkina, Natalia Evlyukhina, Maria Varichkina

1Gastroenterology and Hepatology, Scientific Centre of Children Health RAMS, Moscow, Russian Federation

Objectives & Study: Primary sclerosing cholangitis (PSC) is a chronic cholestatic liver disease characterized by inflammation and progressive bile duct fibrosis. The diagnosis is based on presence of typical abnormal bile ducts at cholangiography (MRCP), compatible biochemical findings and/or histologic features. Patients who present with clinical, biochemical and histological features compatible with PSC and normal cholangiogram, were classified as small duct PSC. This study aims to investigate the clinical characteristics and diagnostic criteria of PSC in children.

Methods: In our study were included children with PSC admitted to a gastroenterological department in a five year period (2007 to 2012). We observed 30 children with PSC, 19 male (63.3%), 11 female (36.7%), and mean age 10.5±2.5 years.

Results: At presentation 26 children (86.6%) were asymptomatic and PSC was suspected based on abnormal liver test detected during routine medical evaluation in 2 children or routine screening in 24 children with IBD; 3 children (10%) presented hepatomegaly and 1 child (3.4%) – jaundice. IBD was found in 80%: 12 ulcerative colitis and 6 Crohn’s disease. Other associated disease was overlap syndrome/autoimmune hepatitis in 2 children (6.6%). These patients had positive autoimmune markers, histologic features of AIH and obliteration of bile ducts. At the time of diagnosis, liver cirrhosis was diagnosed in 6 children (20%) and 5 children progressed to cirrhosis during the observation period. The mean of ALT and AST were 358±12.5 and 275.3±13.2 IU/L, respectively. The mean of γGT and AP were 496±42.4 and 323.3±24.5 IU/L, respectively. 20% had the normal level of AP. The level of IgG was at least 1.1 times above normal in 89.8%. The positive results for anti-neutrophil cytoplasmic antibodies, anti-nuclear antibodies and smooth muscle antibodies were 73.3%, 36.6%, and 23.3%, respectively. MRCP revealed both extrahepatic and intrahepatic, isolated intrahepatic and no biliary involvement (small duct PSC) in 12 (40%), 8 (26.7%), 10 (33.3%) children, respectively. Liver biopsy performed in 22 children (73.3%); showed histologic features of PSC in 91.7%; in 8.3% - biliary lesions and interface hepatitis. All children were treated with UDCA; 23 children also received immunosuppressants. 28 children receive maintenance therapy now. Orthotopic liver transplantation was performed in 2 children.

Conclusion: Clinical features PSC in children are characterized by aggressive and rapid progression of liver disease to liver cirrhosis. γGT is more significant marker of cholestasis than AP in children with PSC. Radiologic findings typical of PSC is absent in one-third of children, that allows to diagnose small duct PSC. Most children with PSC compared with adults have high immunological activity and the need to use immunosuppressants.

Disclosure of Interest: None Declared
PROGRESSION OF LIVER DISEASE IN PIZZ ALPHA-I-ANTITRYPSIN DEFICIENCY LARGELY PREDOMINATES IN MALE CHILDREN

Xavier Stephenne 1,*, Liza Eta 1, Francoise Smets 1, Etienne Sokal 1
1Paediatrics-Division of paediatric hepatology and gastroenterology, Cliniques St Luc et Université catholique de Louvain, 1200 Brussels, Belgium

Objectives & Study: About 10% of PIZZ infants with Alpha-I-Antitrypsin Deficiency (AATD) develop neonatal cholestasis and of these about 25%-30% develop end-stage liver disease requiring liver transplantation in the first decade of life. AATD present also with incidental finding of elevated liver function tests while few patients may present with cirrhosis at diagnosis. Sex prevalence of liver disease associated to AATD has so far not been reported in paediatric cohort.

Methods: We reviewed retrospectively data on 37 PI ZZ AATD (24 males & 13 PIZZ females) referred in our paediatric liver unit. To compare categorical variables, data were analyzed using the Fischer exact.

Results: At the time of AATD diagnosis, 23 of 37 (62%) PI ZZ patients had clinical liver disease such as neonatal cholestasis and/or cirrhosis. Neonatal cholestasis was diagnosed at presentation in 18 PiZZ patients (11 males and 7 females) while cirrhosis was diagnosed in 5 male patients and not in females. Thirteen (56%) of 23 liver affected patients developed end-stage liver disease requiring liver transplantation (LT), among which 11 were males, accounting for 46% of male patients (11/24,) and 2 were PI ZZ females (2/13, 15% of female patients) (p=0.0006 and p=0.06 respectively). Six of the 11 male transplanted patients (55%) had presented initially with neonatal cholestasis, and 5 with compensated cirrhosis. The 2 transplanted girls had presented initially with neonatal cholestasis. Of 24 patients who did not require LT, 10 (42%) presented with neonatal cholestasis (5 males & 5 females) and 14 had no history of liver disease.

Conclusion: In a tertiary pediatric liver unit, cirrhosis at presentation in PiZZ AATD is associated with male gender, and males account for 85% of the transplanted cases. Despite a recruitment bias, our finding suggests a more severe disease evolution in male children.

Disclosure of Interest: None Declared
LIVER STIFFNESS MEASUREMENT AND CONTROLLED ATTENUATION PARAMETER FOR ASSESSMENT OF FIBROSIS AND STEATOSIS IN CHILDREN WITH WILSON DISEASE

Wojciech Janczyk 1,*, Krystyna Becherka 1, Natalia Mucha 1, Maciej Dadalski 1, Dorota Wicher 1, Piotr Socha 1

1Gastroenterology, Hepatology and Eating Disorders, Children's Health Memorial Institute, Warsaw, Poland

Objectives & Study: Liver stiffness measurement (LSM) by FibroScan® (FS) has been shown to be a valuable method in detection of liver fibrosis in adults with various chronic liver diseases such as HBV, HCV and NAFLD. The Controlled Attenuation Parameter (CAP) available on FS allows simultaneous assessment of the degree of liver steatosis. We aimed at evaluating LSM and CAP in children with Wilson disease compared to healthy controls and their relationship with liver function tests.

Methods: We investigated 29 children with Wilson disease aged 13.7y (9.9-16.2) [median (Q1-Q3)] treated with penicillamine or zinc and 18 healthy controls aged 12y (6.7-15.2). All children with Wilson disease presented with increased ALT and/or hepatomegaly at the time of diagnosis. Correlations were tested by Spearman rank test.

Results: Patients with Wilson disease had normal or slightly increased transaminases ALT (45 (29-61 IU/L)). LSM did not show any differences between patients and healthy controls [4.4 (4.1-5.4) vs. 4.2 (3.6-4.4) kPa] whereas CAP was significantly higher in patients with Wilson disease [243 (208-278) vs. 187 (112-217) dB/m], p<0.05. LSM significantly correlated with total bilirubin levels (r=0.43) but not with other liver function tests and CAP was inversely correlated to INR (r=(0.49)).

Conclusion: 1. LSM and CAP are easily applicable to children with Wilson disease. 2. LSM is not significantly increased in children with Wilson disease with mild clinical symptoms, still these patients have increased CAP which corresponds to liver steatosis.

Disclosure of Interest: None Declared
**Hepatology**

PO-H-0241

**NON TRANSPLANT TREATMENT OF FAMILIAL CHOLESTASIS TYPE II**

Sharat Varma 1,* Xavier Stephonne 1, Françoise Smets 1, Raymond Redding 1, Etienne Sokal 1

1Cliniques Universitaires Saint Luc, Brussels, Belgium

**Objectives & Study:** To evaluate non-transplant treatment modalities for familial cholestasis type II (PFIC-II).

**Methods:** Analysis of our non-transplanted PFIC-II patients.

**Results:** n=11, mean age of presentation 30.8 months, males 5/11, family history of PFIC in 3/11. Presenting symptoms were pruritus and increased liver enzymes (AST/ALT) in 9/11. Bile salt exporter pump (BSEP) was present on canalicular surface in 3/9 by immuno-chemistry. Heterozygous mutations was seen in 10/11 (9/10 compound hétérozygote, 1/11 homozygous mutation). Mean bile acid level on diagnosis was 329.81µMol/l. Treatment modalities were urso-deoxycholic acid (UDCA), UDCA followed by biliary diversion (BD) and UDCA followed by 4-phenybutyrate (4-PBA).

7/11 received only UDCA with a mean duration of follow up of 93 months. Bile acid levels monitored in 6/7 and normalized in 23.25 months (mean) in 4/6. 1/6 had sustained decrease but no normalization and 1/6 showed a transient decrease. AST & ALT were increased in 4/7 before treatment and normalized at a mean of 32.3 months. Follow up biopsy was done in 4/7, fibrosis remained stable in 1/4 at F1 after 21.5 months of treatment, increased from F1 to F2 in 2/4 after 84 months and increased from F1-F4 in 205 months in 1 of 4.

3/11 received UDCA followed by BD. No intergroup variation was seen from the group who received only UDCA in genetic mutation frequency, zygosity, bile acid levels or AST, ALT levels. The age of presentation was lower – 2, 6 and 48 months. Mean duration of follow up is 153 months. The indication for BD was increasing pruritus and bile acid levels after a transient decrease with ursodeoxycholic acid. After BD, pruritus grade decreased from 4 to 1 in 2/3 and from 3 to 1 in 1/3. Mean duration of ursodeoxycholic therapy was 111.3 months and the upswing of bile acids was seen after mean of 89.6 months of therapy. After BD 2/3 have normalized bile acid levels in mean 21.5 mo (15 and 28 mo) and continue to be normal. In the 3rd after 22 months of BD the bile acid level is 40.8 (614 pre-BD) and shows sustained decreasing trend.

1/11 received ursodeoxycholic followed by 4-PBA. His presenting symptom was pruritus and increased liver enzymes. Homozygous mutation is present. Duration of UDCA therapy was 12 months and increase in pruritus from grade 2 to 4, increase in bile acids and non normalization of AST/ALT was observed. Subsequently 4-PBA therapy for 1 month produced a decrease in pruritus from grade 4 to grade 1 and bile acids decrease from 462 to 399, AST/ALT also decreased though not normalized.

**Conclusion:** Non transplant modalities in patients with heterozygote mutations have good response. Those with non-normalization of bile acid and liver enzyme levels with UDCA benefit from BD. 4-PBA shows promising result but long term evaluation is pending.

**Disclosure of Interest:** None Declared
**Hepatology**

PO-H-0242

**MMP-2, MMP-9 AND TIMP-1 SERUM LEVELS IN CHILDREN WITH DIFFERENT STAGES OF HEPATIC FIBROSIS**

Andrey Surkov 1,*, Leyla Namazova-Baranova 1, Alexandr Potapov 1, Ivan Smirnov 1, Alla Kutcherenko 1

1Scientific Centre of Children's Health under the RAMS, Moscow, Russian Federation

**Objectives & Study:** to determine the diagnostic significance of MMP-2, MMP-9 and TIMP-1 serum levels as non-invasive markers of different stages of hepatic fibrosis (NMHF) in children with chronic liver diseases.

**Methods:** 95 children with CLD with different etiology (among them: chronic viral hepatitis B and C – 17, autoimmune hepatitis – 20, Wilson’s disease – 11, primary sclerosing cholangitis – 9, glycogen storage disease – 16, cryptogenic hepatitis – 22) at the age of 2-17 years (average age – 12.5±4.3 years) were examined. All patients were performed percutaneous liver biopsy with estimation of the histological index of sclerosis by Desmet: mild fibrosis (F1) was diagnosed in 27 children, advanced fibrosis (F3) – in 35 children and liver cirrhosis (F4) in 33 children. Control group consisted of 15 healthy children without pathology of the liver. In all patients by immunoenzyme analysis were found serum levels of MMP-2, MMP-9 and TIMP-1 as NMHF. Concentration of these markers was measured in ng/ml.

**Results:** In control group the levels of NMHF were: MMP-2 – 351.5 [319.0; 373.5], MMP-9 – 150.0 [130.0; 200.0], TIMP-1 – 408.0 [284.0; 424.0]. In children with F1 stage: MMP-2 – 255.0 [219.0; 306.0], MMP-9 – 240.0 [190.0; 500.0], TIMP-1 – 492.0 [414.0; 502.0], in children with F3 stage: MMP-2 – 273.0 [219.0; 311.0], MMP-9 – 220.0 [160.0; 290.0], TIMP-1 – 498.0 [424.0; 500.0] and in children with F4 stage: MMP-2 – 321.0 [276.0; 376.0], MMP-9 – 240.0 [150.0; 290.0], TIMP-1 – 498.0 [478.0; 548.0]. Thus serum levels of MMP-2 were significantly lower in children with F1 and F3 stages of hepatic fibrosis than in control group (p=0.002 and p=0.014, respectively). Serum level of MMP-9 were significantly higher in children with F1 stage than in control group (p=0.016). Serum levels of TIMP-1 were significantly higher in children with F3 and F4 stages than in control group (p=0.025 and p=0.003, respectively). But there was no difference in MMP-2, MMP-9 and TIMP-1 levels between different stages of hepatic fibrosis.

**Conclusion:** Determination of serum levels of MMP-2, MMP-9 and TIMP-1 allows detecting hepatic fibrosis in children with CLD, but does not allow differentiating its stages.

**Disclosure of Interest:** None Declared
COMPARISON OF THE NEW WHO AND CDC, 2000 GROWTH CHARTS IN THE NUTRITIONAL ASSESSMENT OF CHILDREN ADMITTED IN A PAEDIATRIC DIGESTIVE ENDOSCOPY UNIT

Victoria Hurduc 1,*, Felicia Cora 1, Luiza Bordei 1, Mirela Iancu 1, Eugenia Buzoianu 1, Doina Plesca 1

1 Victor Gomoiu Clinical Hospital, Carol Davila University of Medicine and Pharmacy, Bucharest, Romania

Objectives & Study: The systematic assessment of nutritional status at the hospital admission is an essential part of optimal clinical care and prompt interventions. To compare the agreement of child nutritional pattern estimated by the new World Health Organization (WHO) and the Centers for Disease Control (CDC) growth charts.

Methods: This was an observational study of 232 consecutive symptomatic children (159 girls, mean age 9.9 years, range 6 months - 19 years) submitted for the first esophagogastroduodenoscopy in our pediatric endoscopy unit over the last 2 years. All patients were evaluated for z-score indexes: weight / age (W/A), stature / age (S/A), and body mass index (BMI) – for age (BMI/A), in each of the two references, to compare the differences in the prevalence of the nutritional patterns (underweight / wasting; risk to underweight, stunting, healthy / normal, overweight and obese). The following applications were used: EPI INFO 3.5.3, ANTHRO PLUS 2006, SPSS 18.0, (p<0.05 statistically significant).

Results: Despite the high agreement observed between the two criteria for the three z-score indexes: W/A, S/A, BMI/A (significant Pearson correlation, respectively 0.714, 0.960 and 0.962, with > 0.5 high correlation) there are some differences. Thus, z-score of BMI/A estimated by new WHO criteria were more rigorous than the CDC criteria for the diagnosis of undernutrition: wasting 33 (14.22%) and risk for underweight 36 (15.52%) versus underweight 59 (25.43%) and more patients were classified as presenting overnutrition, respectively: 26 (11.21%) versus 22 (9.48%). However, the prevalence of stunting was similar by each of the two references, respectively: 14 (6.03%) versus 15 (6.47%), with significant Pearson correlation (0.960).

Conclusion: The use of new WHO references has a significant advantage over CDC criteria for children’s nutritional screening at the hospital admission, because they are enables to detect a higher number of children at nutritional risk, in particular in developing countries.

Disclosure of Interest: None Declared
BARIATRIC SURGERY IN ADOLESCENT’S FACING THE "FASHION"

Dragan Kravarusic 1,*, Naftali Freud 1

1Paediatric Surgery, Schneider Children's Medical Center, Petah Tikva, Israel

Objectives & Study: Obesity has been identified as one of the most important public health concerns. Conservative weight management programs have shown only mild/modest weight loss results. There has been increasing enthusiasm for bariatric surgery for adolescent patients with morbid obesity. Because of the relatively low world-wide reported morbidity associated with laparoscopic sleeve gastrectomy - we have begun to explore this as an alternative strategy.

Methods: We have prospectively collected data from all patients undergoing bariatric surgery at our institution since the inception of our adolescent weight loss surgery program in 2011. Baseline data collected included age, gender, height, weight, body mass index, and comorbid conditions. Postoperative data collected included the length of stay, operative morbidity and percent excess weight loss - body mass index at 3-month intervals.

Results: Nine patients have undergone laparoscopic sleeve gastrectomy at our institution since May 2011. Of these, 5 were female and 4 were male. The mean age was 13.3 ± 1.8 years of age. The mean preoperative weight was 139 ± 30 kg with a body mass index of 46 ± 9 kg/m(2). There were no intra-operative complications, and the only postoperative complication has been "blood transfusion" in 1 patient. The mean length of stay was 2.2 ± 1.1 days. The mean follow-up was 6.9 ± 1.4 months. The percent excess weight loss at 3/6/12 months, postoperatively was 32%, 38%, and 40%, respectively, in those who had reached these time points.

Conclusion: Laparoscopic sleeve gastrectomy is a safe operation for adolescent patients with morbid obesity and represents an effective early treatment strategy with approximately 40% excess weight loss at 6 months of follow-up and in our opinion should be considered as an option for select group of adolescent patients.

Disclosure of Interest: None Declared
IGF-I IN INFANTS FED BREASTMILK OR DIFFERENT INFANT FORMULAE
Manja Fleddermann 1,*, Hans Demmelmaier 1, Martin Bidlingmaier 2, Philipp Grimminger 2, Maximilian Bielohuby 2, Berthold Koletzko 1
1Division of Metabolic and Nutritional Medicine, Dr. von Hauner Children’s Hospital, University of Munich, Germany, 2Endocrine Research Unit, Medizinische Klinik und Poliklinik IV, Klinikum der LMU, Munich, Germany

Objectives & Study: Insulin-like growth factor I (IGF-I) is related to growth and can be influenced by nutrition e.g. protein intake, in early infancy. This study examined the relationship of IGF-I with early growth until the age of 120 days and the influence of nutritional factors in groups of infants receiving different infant formulae or breast milk.

Methods: Healthy formula-fed infants (n=213) were randomly assigned to receive a protein-reduced infant formula with alpha-lactalbumin and LC-PUFA (IF, 67kcal, 1.3g protein/100mL) or an isocaloric standard formula without LC-PUFA (CF, 1.5g protein/100mL) for the first 120 days of life. A group of breastfed (BF) infants was studied as non-randomized reference. Biochemical variables were measured shortly after birth (subpopulation) and at 120 days of age.

Results: After birth IGF-I values were not different between the groups and correlated positively with birth weight (R=0.31, p=0.0002). Concentration of IGF-I 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. The weight gain tended to be higher in IF than in CF infants (30.2±6.3 vs. 28.3±6.5g/d; Mean±SD; p=0.06). BF infants had a weight gain of 26.7±6.4g/d. Including all infants in the analysis (IF, CF and BF), weight gain from 30 to 120 days correlated with IGF-I at 120 days (R=0.44, p<0.0001). The differences in amino acid composition between the study formulae and breast milk, respectively, induced significantly different plasma concentrations of essential amino acids (CF>IF>BF). As already described in other populations, plasma branched chain amino acids, lysine and phenylalanine were positively associated with insulin in our study (mean R=0.50, p<0.001). All essential amino acids were positively associated with IGF-I in our study independent correlation analysis (mean R=0.26, p<0.001). No correlations between IGF-I and these amino acids were found within each study group.

Conclusion: Higher weight gain and IGF-I levels in infants receiving protein-reduced IF indicate that protein concentration alone does not control IGF-I levels and growth. Rather, the overall correlation of essential amino acids and IGF-I levels suggest that certain protein components are possible key drivers. In addition, other components and the macronutrient composition of infant formula might influence IGF-I in recipient infants. The endocrine response still differs markedly between breastfed infants and infants fed current formula.

Disclosure of Interest: None Declared
**Objective & Study:** The use of probiotics has been suggested in the treatment of acute gastroenteritis (AGE) in addition to early rehydration and avoidance of dietary restrictions. The ESPGHAN Working Group (WG) on Probiotics and Prebiotics aimed to develop recommendations for the use of probiotics for the treatment of AGE in infants and children.

**Methods:** Systematic review of previously completed systematic reviews and of randomized controlled trials (RCTs) published subsequently to these reviews. The recommendations were formulated only if at least 2 RCTs that used a given probiotic (with strain specification) were available. The GRADE system, developed by the Grading of Recommendations, Assessment, Development and Evaluations Working Group, was used to grade the strength of evidence and grades of recommendations. In brief, the GRADE system offers four categories of the quality of the evidence (high; moderate; low; and very low) and two categories of the strength of recommendation (strong or weak).

**Results:** The use of the following probiotics (in alphabetical order) may be considered in the management of children with AGE in addition to rehydration therapy: *L. rhamnosus* GG (low quality of evidence; strong recommendation) and *S. boulardii* (low quality of evidence; strong recommendation). Less compelling evidence is available for *L. reuteri* DSM 17938 (very low quality of evidence; weak recommendation) and heat-inactivated *L. acidophilus* LB (very low quality of evidence; weak recommendation). The latter, although traditionally discussed with other probiotics, does not fit with the definition of probiotics. Other strains or combinations of strains have been tested, but evidence of their efficacy is weak or preliminary. The safety and clinical effects of one probiotic microorganism should not be extrapolated to other probiotic microorganisms.

**Conclusion:** The WG recommends choosing a probiotic, the efficacy of which has been confirmed in well-conducted RCTs, from a manufacturer who has a regulated quality control of factors including the composition and content of the probiotic agent.

**Disclosure of Interest:** H. Szajewska Grant / Research Support for: Arla, Biogaia, Biocodex, Danone, Dicofarm, Hipp, Nestle, Nestle Nutrition Institute, Nutricia, Mead Johnson, Merck, and Sequoia. , A. Guarino Grant / Research Support for: Biocodex and Dicofarm and in clinical trials and/or advisory boards and/or conference grant by Nutricia, Humana, Malesci and Mead Johnson., I. Hojsak Grant /
Research Support for: has participated as a clinical investigator for Biogaia and Chr Hansen, F. Indrio
Grant / Research Support for: has participated as a clinical investigator and/or consultant and/or speaker for Arla Food, Biogaia, Noos, Nestle, and Nestle Nutrition Institute., S. Kolacek Grant / Research Support for: has participated as a clinical investigator, and/or speaker for Abbott, Arla, Biogaia, Chr. Hansen, Danone, Dukat, Nestle, Nutricia, and MSD., R. Shamir Grant / Research Support for: has participated as a clinical investigator, and/or advisory board member, and/or consultant, and/or speaker for Abbott, Danone Institute International, Danone, Enzymotec, Nestle, Nestle Nutrition Institute, and Nutricia., Y. Vandenplas Industry of: is a consultant at Biocodex and United Pharmaceuticals., Z. Weizman Grant / Research Support for: has participated as a clinical investigator, and/or consultant and/or speaker for BioCodex, BioGaia, Hipp, Materna, Mead Johnson, Nestle, Nutricia, and Sensus.
PROBIOTICS DURING WEANING: A FOLLOW-UP STUDY ON EFFECTS ON BODY COMPOSITION AND METABOLIC MARKERS AT SCHOOL AGE

Frida Karlsson Videhult 1,*, Inger Öhlund 1, Olle Hernell 1, Hans Stenlund 2, Christina E West 1
1 Clinical sciences, Paediatrics, Umeå University, Umeå, Sweden, 2 Public Health and Clinical Medicine, Epidemiology and Global Health, Umeå, Sweden

Objectives & Study: An aberrant gut microbiome has been suggested to be part of the worldwide obesity epidemic, and probiotic intervention is one candidate for gut microbiome modulation. In experimental animal models, the probiotic *Lactobacillus paracasei* ssp. *paracasei* F19 (LF19) up-regulated genes involved in energy homeostasis, reduced body fat and altered the lipoprotein profile. In our previous report, feeding LF19 to infants during weaning impacted aspects of the global plasma metabolome. LF19 lowered palmitoleic acid, a monounsaturated fatty acid (MUFA) associated with hypertriglyceridemia and increased visceral adiposity. Therefore, we assessed if feeding LF19 from 4 to 13 months of age would have long-term effects on body composition, growth and metabolic markers at school age.

Methods: Of 179 randomised children 171 completed the baseline study and 120 entered the follow-up at 8-9 years of age, n=58 in the LF19 and n=62 in the placebo group. Body composition was measured using Dual Energy X-ray Absorptiometry (DEXA). Weight, height and sagittal abdominal diameter (SAD) were assessed also for accompanying parent/s. S-lipids, insulin, glucose and transaminases were determined after overnight fasting. Dietary intake was analysed following a four-day food record. Physical activity was assessed using a pedometer for seven days.

Results: In children classified as overweight/obese based on ISO-BMI 25 and 30 kg/m² as cut offs, S-insulin and HOMA-index were higher (p=0.001) whereas HDL levels were lower (p=0.022) compared with normal weight children. Further, the BMI z-score was higher at every measurement in overweight/obese children from 4 months to 8 years of age compared with normal weight children. LF19 did not affect BMI z-score, SAD, fat free mass, fat mass index, truncal fat %, android or gynoid fat % and had no long-term impact on any of the assessed metabolic markers (p>0.05).

Conclusion: This is the first study that has evaluated long-term effects of probiotic feeding in infancy on markers of body composition. This study provides further evidence that early probiotic feeding does not adversely affect growth, and extends previous findings by showing that this probiotic strain does not modulate body composition, serum glucose or lipid metabolism in a long-term perspective. The observed adverse metabolic response in overweight children underscores the need for early prevention strategies.

Disclosure of Interest: F. Karlsson Videhult: None Declared, I. Öhlund: None Declared, O. Hernell Grant / Research Support for: Grant support from Semper AB Sweden and ARLA Foods AB Denmark, Consultant for: Member of the Advisory Board of Semper AB Sweden, H. Stenlund: None Declared, C. West Grant / Research Support for: Grant support from ARLA Foods AB Denmark, Speakers bureau of: ARLA Foods AB Denmark
The Effect of Probiotics in Abdominal-Pain Related Functional Gastrointestinal Disorders in Childhood – A Systematic Literature Review

Zvi Weizman¹, Viki Blumin¹, Jaber Abu-Abed¹, Mauricio Binszto⁴¹
¹Paediatric Gastroenterology, Soroka University Medical Center, Beer-Sheva, Israel

Objectives & Study: Functional gastrointestinal disorders are common but without a proven effective therapy. Our aim was to examine whether probiotics are effective in the management of childhood abdominal-pain related functional gastrointestinal disorders, according to the Rome III criteria, using a systematic literature review.

Methods: Data for this analysis were identified using a computer-assisted search of the English literature using the online databases MEDLINE, PubMed, EMBASE and the Cochrane Library. Trial quality and risk of bias were assessed according to the Cochrane Handbook for systematic Reviews of Interventions. The extreme diversity of probiotic supplements did not allow for the performance of a meta-analysis.

Results: Six of the 102 initially identified studies were selected. Results are presented in the following table.

<table>
<thead>
<tr>
<th>Study</th>
<th>Dg.</th>
<th>Agent</th>
<th>Suppl. (wks)</th>
<th>n</th>
<th>Age (yrs)</th>
<th>Pain relief</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bausserman 2005</td>
<td>IBS</td>
<td>L-GG</td>
<td>6</td>
<td>50</td>
<td>6-20</td>
<td>No</td>
</tr>
<tr>
<td>Gawronska 2007</td>
<td>IBS, FAP, FD</td>
<td>L-GG</td>
<td>4</td>
<td>104</td>
<td>6-16</td>
<td>IBS - Yes  FAP - No FD - No</td>
</tr>
<tr>
<td>Francavilla 2010</td>
<td>IBS, FAP</td>
<td>L-GG</td>
<td>8</td>
<td>136</td>
<td>5-14</td>
<td>IBS – Yes FAP - No</td>
</tr>
<tr>
<td>Romano 2010</td>
<td>FAP</td>
<td>L.reuteri</td>
<td>4</td>
<td>52</td>
<td>6-16</td>
<td>Yes</td>
</tr>
<tr>
<td>Guandalini 2010</td>
<td>IBS</td>
<td>VSL#3 (8 strains)</td>
<td>6x2</td>
<td>59</td>
<td>5-18</td>
<td>Yes</td>
</tr>
<tr>
<td>Weizman 2013</td>
<td>FAP</td>
<td>L.reuteri</td>
<td>4</td>
<td>93</td>
<td>6-15</td>
<td>Yes</td>
</tr>
</tbody>
</table>


Conclusion: Probiotics may serve as a therapeutic aid in selected childhood abdominal-pain related functional disorders, mainly FAP and IBS.

Disclosure of Interest: None Declared
SERUM ANGIOGENIC GROWTH FACTORS IN CHILDREN WITH ACTIVE INFLAMMATORY BOWEL DISEASES TREATED WITH EXCLUSIVE ENTERAL NUTRITION THERAPY

Andrzej Wedrychowicz 1,*, Przemyslaw Tomasik 2, Kinga Kowalska-Duplaga 1, Stanislaw Pieczarkowski 1, Lukasz Cichy 1, Krzysztof Fyderek 1

1Dept. of Paediatrics, Gastroenterology and Nutrition, 2Dept. of Clinical Biochemistry, Jagiellonian University Medical College, Krakow, Poland

Objectives & Study: Exclusive enteral nutrition (EEN) is effective method of treatment in inflammatory bowel diseases (IBD) in children. The postulated mechanism of action of the treatment is connected with its anti-inflammatory activity. Angiogenic growth factors as transforming growth factor beta 1 (TGF-beta 1) and transforming growth factor beta 2 (TGF-beta 2) play an important role in the early stage of inflammation, stimulating the angiogenesis and healing processes during the inflammation. Tumor necrosis factor-alpha (TNF-alpha) is one of the main pro-inflammatory mediators in the pathogenesis of IBD, both Crohn’s disease (CD) and ulcerative colitis (UC). The objective of our study was to assess the influence of the EEN alone or combined with the immunosuppressive treatment with steroids and thiopurins on serum TGF-beta 1, TGF-beta 2 and TNF-alpha concentrations in children with active IBD.

Methods: Thirty children with active CD (14 boys, 16 girls, mean age: 14.5 yrs, range: 8.5 – 18 yrs), 22 with active UC (12 boys, 10 girls, mean age: 10.7 yrs, range: 6 -17 yrs) and 16 healthy controls were enrolled into the study. Patients were treated with EEN carrying 130% of daily requirements, through naso-gastric tube, 24 hour a day for 6 weeks using semi-elemental, fibre-free diet. Serum TGF-beta 1, TGF-beta 2 and TNF-alpha concentrations were assessed at the baseline and after 2 and 4 weeks of EEN using enzyme-linked immunosorbent assay (R and D Systems, USA). Statistical analysis was performed with Statistica 7.0 software (StatSoft, USA) using Mann-Whitney U test, Wilcoxon signed rank test and Spearman’s correlation rank test. P<0.05 was considered statistically significant.

Results: We found increased serum TGF-beta 2 and TNF-alpha and decreased TGF-beta 1 concentrations at baseline in CD group compared to UC and control group (p<0.05). During EEN we observed an increase of serum TGF-beta 1 and TGF-beta 2 and simultaneous decrease of TNF-alpha in CD group (p<0.05). In UC group, both TGF-beta 1 and TNF-alpha, which were increased at baseline, decreased during EEN (p<0.05), while TGF-beta 2 was comparable to controls during whole the study. We did not find statistically significant differences of TGF-beta 1 and 2 concentrations between CD and UC subgroups treated with EEN alone and combined (EEN and immunosuppressants) therapy. We found better improvement of nutritional status of the patients and faster induction of remission (p<0.05) in CD and UC subgroups with combined therapy when compared to EEN alone treatment.

Conclusion: EEN stimulate production of TGF-beta 1 and 2 and decrease of TNF-alpha in CD children. Immunosuppressive therapy used as additional treatment with EEN resulted in faster induction of remission of the disease but not in enhancing stimulation of angiogenic growth factors.

Disclosure of Interest: None Declared
SN-2 PALMITATE REDUCES CRYING AND SOAPED FATTY ACIDS EXCRETION IN CHINESE INFANTS FED FORMULA ENRICHED WITH PREBIOTICS: A DOUBLE-BLIND RANDOMIZED CLINICAL TRIAL

Fabiana Bar-Yoseph 1,*, Yael Lifshitz 1, Tzafra Cohen 1, Paterice Malard 2, Zailing Li 3, Hong Cui 4, Aimin Zhang 5, Huimin Yang 6, Jing Wu 7, Chundi Xu 7

1Enzymotec, Migdal HaEmeq, Israel, 2Biostime, Guangzhou, 3The Third Ward, Peking University Third Hospital, Beijing, China, 4Paediatric Ward, The Friendship Hospital Affiliated to Capital Medical University, Beijing, China, 5Department of Paediatrics, The People's Hospital of Hunan Province, Changsha, China, 6Department of Child Health, West China Second University Hospital of Sichuan University, Chengdu, China, 7Department of Paediatrics, Ruijin Hospital Affiliated to Shanghai Jiaotong University School of Medicine, Shanghai, China

Objectives & Study: Palmitic acid (PA) constitutes 17-25% of human milk fatty acids (FA), and is mainly (~70%) esterified to the triglycerides middle position (SN-2 palmitate), position from which PA is better absorbed. SN-2 palmitate formulas were shown to enhance fat and calcium absorption, reduce stool hardness and promote beneficial bacteria gut colonization. On the other hand, prebiotics, such as GOS, were shown to benefit digestion, reduce stool hardness and reduce crying. The aim of the trial was to study for the first time the effect of SN-2 palmitate on top of prebiotics in Chinese term infants.

Methods: One hundred seventy one Chinese term infants were included in a 24 weeks multi-center study within 14 days from birth: 114 were formula-fed and 57 were breastfed and served as a reference group. Formula-fed infants were randomly assigned to receive either formula with SN-2 palmitate (INFAT®, Advanced Lipids), (n=57), or a Control formula with regular vegetable oils (n=57). Both formulas (Biostime, China) contained 2.5% GOS and differed only in the ratio of PA at sn-2 position (43% vs. 13%). Stool FA were measured at 6 weeks postnatal and parents filled 3 days reports on infant's feeding, stool characteristics and crying at 6, 12 and 24 weeks postnatal.

Results: There were no significant differences in anthropometrics at randomization and by the end of the study at 24 weeks postnatal. At 6 weeks postnatal, the mean stool soaped FA of the infants in the SN-2 palmitate group was significantly lower than that of the infants in the Control group (15.9% vs 12.0% of stool dry weight, p<0.05). Further, the pattern of crying in mean of crying duration and percentage of crying infants was statistically different between the control formula and the SN-2 palmitate formula groups during afternoon (10.9 vs 0%, p<0.05) and evening hours (41.1 vs 23.2%, p<0.05), and the latter was similar to breastfed infants (p>0.1).

Conclusion: SN-2 palmitate formula consumption results in benefits to the infant in mean of fat absorption and crying. Importantly, those effects were observed although both formulas contained prebiotics. Comparable to breastfeeding, the formula with SN-2 palmitate reduces soaped FA excretion and affects infant crying patterns during the first weeks of life. Thereby SN-2 palmitate fat ingredient improves the well-being of formula-fed infants and their parents.

Objectives & Study: The prevalence of obesity is increasing worldwide and in Israel. To meet this challenge our study tests a new educational approach through a controlled school-based trial to achieve an improvement in eating habits and reduced obesity in Grades 2-3. Intervention included 5 joint parent-children classroom activities on nutritional topics and 5 educational workshops for parents only. Alfred Adler’s concepts were the guiding principles.

Methods: A cluster randomized controlled trial allocated 4 elementary schools (3 2nd grade classes each) to intervention or control groups. This allocation was switched with the next cohort of children. Recruitment was in first grade, randomization at the beginning of second grade, evaluation of results at the end of second grade and the beginning of third grade.

Results: Of 743 children in 23 2nd grade classes, parents provided informed consent for 508 (68%), and for the third grade follow-up 432 (58%). At the end of the trial the intervention group showed significant improvement in nutrition knowledge in comparison with the control group (p=0.005). Sources of knowledge cited by the children were parents, media, school, and self-acquired knowledge. At the end of the 2nd grade the children in the intervention group based more answers on their personal knowledge than children in the control group (p=0.007). The results regarding behavioral changes were assessed by interview and observation of their ten o’clock snacks. The observations showed that the percentage of children who brought vegetables, water, and healthy spreads on sandwiches increased in the intervention group and the percentage of children who brought sweet and snacks to the ten o’clock snack declined relative to the control group at the end of 2nd grade but did not persist to the 3rd grade. The interviews indicated a greater consumption of fruits and vegetables (p=0.009), and a reduction in consumption of snacks and sweets (p=0.038) in the intervention group. The intervention was associated with a significantly more varied diet (p=0.032). Children who were overweight or obese at baseline, the intervention group showed a lower daily increase in BMI up to the end of the 2nd grade (p=0.048) and during the summer (p=0.013). We found a significant interaction between BMI percentile at baseline (overweight vs not), the trial groups, and the times of measurements (end 2nd and 3rd grades) for BMI (p<0.0001), weight (p<0.0001) and height (p=0.005).

Conclusion: There were encouraging changes in eating habits. The anthropometric measurements changed more in Children who were overweight or obese at baseline. To maintain changes over longer periods, refreshing these nutrition themes annually in school using the model is required.

Disclosure of Interest: None Declared
PLASMA FATTY ACID COMPOSITION IN INFANTS WITH COW'S MILK ALLERGY RECEIVING FREE AMINO ACID FORMULA WITH LC-PUFAS OR EXTENSIVELY HYDROLYSED SOY PROTEIN COMPARED WITH HEALTHY BREAST-FED INFANTS

Karina Vieira Barros 1,*, Marisa Silva Laranjeira 2, Neusa Wandalsen 2, Susana Passeti 2, Roberta Oliveira 2, Regina Munekata 2, Elizabeth Miles 3, Paul Noakes 3, Vera Silveira 4, Philip Calder 3
1Departamento de Fisiologia, Universidade Federal De São Paulo, São Paulo, Brazil, 2Departamento de Pediatria, Faculdade de Medicina do ABC, Santo André, Brazil, 3Human Development and Health Academic Unit, University of Southampton, Southampton, United Kingdom, 4Departamento de Ciências Biológicas, Universidade Federal De São Paulo, Diadema, Brazil

Objectives & Study: Considering the influence of breast milk composition in metabolic imprinting and in atopic diseases development, the aim of this study was to compare the fatty acid (FA) composition of plasma phospholipids in infants with cow's milk allergy (CMA) fed with amino acids based formula with LC-PUFAs (AAF) or extensively hydrolysed soy protein (HSF) with that of healthy infants who were exclusively breast-fed for 6 months (BF).

Methods: Fifty-four infants with CMA were allocated to one of 2 groups: AAF (n= 28) or HSF (n = 26). After 4 months and in the absence of clinical symptoms, blood samples were collected to verify the FA composition of plasma phospholipids using a gas chromatography. Thirteen healthy BF infants were used as a comparator group. Individual FA are expressed as percentage of total FA.

Results: The mean ages (months) were 9.4 ± 0.5 (AAF), 13.0 ± 1.0 (HSF) and 14.5 ± 1.8 (BF). Analysing saturated FA, we found higher myristic acid (14:0) in the BF group (0.37 ± 0.02) compared to the AAF (0.21 ± 0.01) and HSF (0.25 ± 0.01) groups (p= 0.01). No difference was found in monounsaturated and trans FA. In relation to n-6 FA, lower concentrations of total n-6 and arachidonic acid (ARA) were found in the HSF group (36.1 ± 0.4 and 8.33 ± 0.47, respectively) when compared to the AAF (38.6 ± 0.59 and 11.2 ± 0.39) and BF (39.9 ± 0.51 and 10.17 ± 0.67) groups (p=0.03 and 0.007, respectively). A lower percentage of alpha-linolenic acid (18:3n-3) was found in BF (0.05 ± 0.07) compared to AAF (0.20 ± 0.01) and HSF (0.23 ± 0.01 groups. However, surprisingly the amount of eicosapentaenoic acid (EPA) (20:5n-3), docosahexaenoic acid (DHA) (22:6n-3) and total n-3 in BF were not different from the HSF group, perhaps reflecting good activity of desaturase enzymes in BF group. Infants from AAF group had significantly higher DHA (3.69 ± 0.25) and total n-3 (4.7 ± 0.28) compared to the HSF and BF groups, likely due to the DHA supplementation of the formula.

Conclusion: There are significant differences in plasma FA among the BF, HSF and AAF groups, confirming that dietary composition may influence the plasma FA composition in infants. These findings may relate to future disease risk.

Disclosure of Interest: None Declared
A NOVEL INFANT FORMULA, COMBINING SCGOS/LCFOS WITH A SPECIFIC FERMENTED INFANT FORMULA, SHOWS LOWER INCIDENCE OF COLIC IN INFANTS AT 4 WEEKS OF AGE COMPARED TO CONTROL FORMULAS

Yvan Vandenplas 1,*, Hetty Bouritius 2, Thomas Ludwig 2, Frederic Huet 3, Jonathan Hourihane 4
1Department of Paediatrics, UZ Brussels, Free University of Brussels, Brussels, Belgium, 2Nutricia Research, Utrecht, Netherlands, 3Pédiatrie, Hôpital d’Enfants, Dijon, France, 4Paediatrics and Child Health, University College Cork, Cork, Ireland

Objectives & Study: Infant formulas (IFs) that contain short-chain galacto-oligosaccharides and long-chain fructo-oligosaccharides scGOS/lcFOS, ratio 9:1, or the fermented IF Lactofidus™ (LF), have been shown to have distinct benefits in supporting a healthy digestive system during infancy. In this randomized, controlled, double-blind, multicenter intervention study, the effects of combining LF with scGOS/lcFOS, 0.8g/100ml, ratio 9:1, on gastrointestinal tolerance, and crying (secondary outcome parameters) were explored.

Methods: After parent’s own decision to discontinue breast feeding, 432 healthy, term infants aged 0-28 days were randomized to receive one of four different IFs until 17 weeks of age: IF with scGOS/lcFOS and 50% LF (LF50+), IF with scGOS/lcFOS and 15% LF (LF15+), and as controls IF with 50% LF only (LF50), or IF with scGOS/lcFOS only (IF+). Percentages of LF relate to the ratio of fermented infant formula mixed with non-fermented formula during production. After the baseline visit, visits were scheduled at the infants’ age of 4, 8, 13, and 17 weeks. Before each of these visits, standardized 7-day diaries with daily entries on gastrointestinal tolerance, and duration and frequency of crying were completed by the parents. 292 infants with valid diary data at 4 weeks of age were available for analysis of gastrointestinal tolerance and crying. Colic was defined by at least 3 hours of crying per day, on at least 3 days within one week.

Results: Based on low mean gastrointestinal symptom scores, we conclude that the newly-developed IFs with a combination of scGOS/lcFOS and LF were well tolerated, during the first 4 months after birth. The incidence of colic was highest (16.1% of 292 infants) at the 4 week visit (10.6% of 284 infants at 8 weeks, and 2.2% of 272 infants at 13 weeks, respectively). The overall incidence of colic was in line with data reported from population based studies (i.e. 20.5% in a population based study [1]). However, the incidence of colic was significantly lower with LF50+ (8% of 75 infants) compared to IF+ (20% of 75 infants) (P=0.034; chi-square test), and LF50 (20% of 70 infants)(P=0.036) at the 4 week visit. There was no significant difference at this visit in the incidence of colic between either LF15+ (16.7% of 72 infants) and LF50+ or IF+, or any of the four IFs on the consecutive visits, nor on the cumulative incidence of colic over the whole study period.

Conclusion: The IF with the combination of scGOS/lcFOS with 50% Lactofidus™ was well tolerated, and this combination displayed a 60% lower incidence of colic in infants specifically at 4 weeks of age compared to control IFs.

References: 1) Iacono et al., Dig Liver Dis 2005, 37(6):432-438

THE ROLE REVERSAL METHOD FOR TREATMENT OF FOOD REFUSAL ASSOCIATED WITH INFANTILE FEEDING DISORDERS
Idit Segal 1,*, Anat Tirosh 2, Tali Sinai 2, Sari Alony 2, Anat Levi 1, Lia Korenfeld 1, Tsili Zangen 1, Avi Mizrachi 1, Mona Boaz 3, Arie Levine 1

1Paediatric Gastroenterology, Wolfson Medical Center, Holon, Israel, 2School of Nutritional Sciences, Rehovot, Israel, 3Epidemiology Unit, Wolfson Medical Center, Holon, Israel

Objectives & Study: Backgrounds: Infantile feeding disorders (IFD) are common causes of food refusal and failure to thrive, and are frequently encountered by primary care physicians and specialists. We have previously published the Wolfson Criteria for IFD, which have eased the approach to diagnosis of IFD. Along with and complementary to the Wolfson Criteria, we have also developed the Role Reversal treatment method for IFD, which has been briefly described previously.

Aims: To prospectively validate the Role Reversal treatment method on a cohort of infants diagnosed with IFD, and for the first time present a detailed description of this method.

Methods: Methods: Parents of infants and children diagnosed with IFD were invited to participate in the study, which was designed as a questionnaire comprised of 6 categories of questions recording patient and parents behaviors, attitudes and perceptions, which was completed at initiation and at the end of treatment. Full response was defined as improved normative feeding, cessation of abnormal parental feeding and improved or normal growth patterns. A partial response was defined as success with 2/3 categories.

Results: Results: We enrolled 38 patients, 32 patients completed the study. Improved feeding occurred in 78%, full recovery was documented in 53% of infants by 6 months, and partial response in another 25%. All forms of pathological feeding improved significantly (mechanistic, nocturnal, persecutory, forced feeding and distraction).

Conclusion: Conclusion: The Role Reversal treatment method is a simple and effective approach to treatment of food refusal associated with IFD.

Disclosure of Interest: None Declared
FERMENTATION PATTERN OF INFANT FORMULAS CONTAINING DIFFERENT PREBIOTICS

Jon Vanderhoof 1,*, Paul Ferguson 1, Colin Rudolph 1, Paul V Strong 1, Rosemary Pauley-Hunter 2, Laurel Prestridge 2

1Medical Affairs, Mead Johnson Nutrition, Evansville, United States, 2Boys Town National Research Hospital, Boys Town, United States

Objectives & Study: Prebiotics are thought to play a role in the development of intestinal flora which may impact the developing immune system. When exposed to unabsorbed food, such as carbohydrates, intestinal bacteria produce hydrogen, which is exhaled in the breath. An increase in breath hydrogen may signify an increase in hydrogen-producing bacteria. Our objective was to determine if cow’s milk-based infant formulas containing either galacto-oligosaccharides (GOS) or the combination of GOS and polydextrose (PDX) altered breath hydrogen. We hypothesized PDX/GOS would produce greater sustained release of hydrogen compared to GOS alone, which undergoes a more rapid and complete digestion. Given the diversity of oligosaccharides present in human milk, we proposed that PDX/GOS would produce a pattern of breath hydrogen excretion that more closely resembled that of a breastfed infant.

Methods: In this blinded, crossover, pilot study, infants (n=12) consumed infant formula containing either 4 g/L GOS or 4 g/L of GOS and PDX (1:1 ratio). To ensure standardized diets prior to testing, all infants were given the same, non-prebiotic formula for 7 days prior to testing. On the testing day, no formula was administered 4 hours prior to baseline breath measures. Fifteen minutes after the baseline measure was obtained, infants were randomly assigned to receive one of the two prebiotic formulas. Breath hydrogen was measured after the feeding. Four hours after the last measurement, infants were given 1 ounce of the assigned formula and additional breath samples were obtained. Infants continued to consume the non-prebiotic formula for 7 days until they returned for a repeat visit in which they were crossed over to the other prebiotic formula. The data were analyzed by repeated measures ANOVA and p<0.05 was considered significant. Ten breastfed infants were added as a reference group but not included in the statistical analysis.

Results: Breath hydrogen was higher in the PDX/GOS group vs. GOS only (Mean ± S.E.; 25.35 ± 2.87 ppm vs. 13.69 ± 2.87 ppm; p=0.0001). The pattern of breath hydrogen in the PDX/GOS group closely followed that of the breast-fed group.

Conclusion: Greater sustained hydrogen production was observed in infants fed formula with PDX/GOS vs. formula with GOS alone and could reflect a change in beneficial, hydrogen-producing bacteria such as bifidobacteria, which are commonly present in larger numbers in the stools of breastfed infants. The pattern of breath hydrogen in the PDX/GOS group followed that of breastfed infants, suggesting a mix of prebiotics may more closely resemble the diversity of oligosaccharides present in human milk.


437
FALTERING WEIGHT GAIN NORMALIZES WITH AN EXTENSIVELY HYDROLYZED RICE PROTEIN FORMULA IN THE TREATMENT OF COW’S MILK PROTEIN ALLERGY IN INFANTS


1Paediatrics, UZ BRUSSEL, Brussels, Belgium

Objectives & Study: Guidelines recommend the use of extensively hydrolyzed cow’s milk protein formulas for infants with cow’s milk protein allergy (CMPA). Recently, extensively hydrolyzed rice protein infant formulas (eHRF) have become an available option.

Methods: A prospective clinical study was performed to evaluate the tolerance of a new eHRF (Novarice). Forty infants (mean age 3.4 months, range 1–6 months) with CMPA proven with a food challenge were enrolled. Clinical tolerance of the eHRF was assessed and the symptoms were followed throughout the study by the evaluation of the Symptom-Based-Score (SBS) at each time point. Patients were followed for six months for growth as well as tolerance.

Results: All infants tolerated the eHRF. 36 patients were fed with the study formula for 6 months (3 dropped out because of taste and 1 was lost to follow-up). The mean (± SD) SBS before the challenge was 8.6 ± 5.6 (n:38). At inclusion (= positive challenge) the SBS increased to 13.5 ± 5.2 (p<0.001). The SBS decreased significantly as of the 1st month intervention to 3.5 ± 2.3 (p<0.001), and further to 2.4 ± 1.9 (p<0.001) and 1.5 ± 2.0 (p<0.001) after 3 and 6 months, respectively. In particular, the percentage of infants having normal stools increased from 5.3% to 52.6% (p<0.0001, McNemar’s test) as of the 1st month. The regurgitation score decreased by 75% over one month (from 2.4 ± 2.2 to 0.6 ± 0.9, p<0.0001) and this decrease persists at day 90 and day 180.

During the intervention period, the evolution of the weight-for-age, weight-for-height and BMI z-scores was positive: from -0.7 to -0.1 (weight) and -0.7 to 0 (weight-for-height, and BMI)(Table1).

Table 1: Evolution (inclusion - 6 months) of the z-score for weight, length, weight for height and BMI

<table>
<thead>
<tr>
<th></th>
<th>Weight for age</th>
<th>Length for age</th>
<th>Weight for height</th>
<th>BMI</th>
</tr>
</thead>
<tbody>
<tr>
<td>At inclusion</td>
<td>-0.7 (1.0)</td>
<td>-0.1 (1.0)</td>
<td>-0.7 (0.9)</td>
<td>-0.7 (0.9)</td>
</tr>
<tr>
<td>At 1 month</td>
<td>-0.5 (0.9)</td>
<td>-0.1 (1.1)</td>
<td>-0.5 (0.8)</td>
<td>-0.6 (0.8)</td>
</tr>
<tr>
<td>At 3 months</td>
<td>-0.3 (1.0)</td>
<td>-0.1 (1.1)</td>
<td>-0.3 (0.9)</td>
<td>-0.4 (0.9)</td>
</tr>
<tr>
<td>At 6 months</td>
<td>-0.1 (0.9)</td>
<td>-0.1 (1.1)</td>
<td>0 (0.8)</td>
<td>0 (0.8)</td>
</tr>
<tr>
<td>P (incl-6moths)</td>
<td>&lt;0.001</td>
<td>NS</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

p: student t-test

Conclusion: In infants with CMPA, feeding with this eHRF allows a significant growth as of the 1st month and a normalization of the weight-for-age, weight-for-height and BMI z-score within 6 months as well as a good acceptance promoting compliance to the pediatricians’ recommendation.

Disclosure of Interest: Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals, E. De Greef: None Declared, B. Hauser: None Declared
LOW DOSE VERSUS REGULAR DOSE OF BIFIDOBACTERIUM LACTIS IN A STARTER INFANT FORMULA: EFFECTS ON EARLY-LIFE PROTECTION, IMMUNE AND GUT MATURATION, MICROBIOTA, AND GROWTH IN C-SECTION DELIVERED BABIES

L Baglatzi 1, S. Gavrili 1, K. Stamouli 1, S. Zachaki 1, L. Favre 2, N. de Groot 3, D. Egli 3, S. Pecquet 4, L. Philippe 5, S Emady-Azar 5, S Lamberti 5, J. Benyacoub 2, C. Costalos 1.*

1Alexandra Hospital, Athens, Greece, 2Nestlé Research Center, Lausanne, Switzerland, 3Nestlé Nutrition, Vevey, Switzerland, 4Clinical Department Unit, Nestlé Nutrition, Vevey, Switzerland, 5Clinical Department Unit, Nestlé, Lausanne, Switzerland

Objectives & Study: Due to the immaturity of their immune system, neonates represent a population particularly vulnerable to infections. While breast feeding delivers beneficial post-natal immunomodulatory factors, supplementation of infant formula (IF) with probiotics is currently used to compensate this gap in formula fed babies. This is aligned with recent demonstration that breast milk (BM) naturally contains bacteria. However, bacterial counts are about 1000 times lower in BM than in current IF with probiotics. The aim of the present study was to assess whether immune-related beneficial effects of starter IF containing regular dose of probiotics could be maintained with a lower dose of probiotics, closer to the counts found in BM.

Methods: This trial was designed as exploratory, prospective, double-blind, single center (Alexandra General Hospital, Athens, Greece) clinical trial with 2 randomized parallel groups of infants receiving starter IF containing either low (10^4 CFU/gr of powder) or regular (10^7 CFU/gr of powder) dose of the probiotic Bifidobacterium lactis CNCM I-3446 from birth to 6 months of age (n=77 infants/group). From 6 to 12 months of age, infants were prescribed a follow-up formula without probiotic. In addition, a breastfed reference group (n=47) was followed from birth to 12 months of age. Inclusion criteria for all infants consisted of being born at full term by C-section and, for randomized groups, not being breast fed for more than 14 days. Protection against diarrhea as primary outcome (incidence, total episode counts, duration), immune and gut maturation, immune responsiveness (responses to Polio, Diphtheria, B. pertussis, Tetanus, H. influenza B vaccinations) and growth were followed over 12 months.

Results: On the basis of ITT statistical analyses, no consistent significant difference was observed between the low and regular probiotic dose groups for primary and secondary outcomes. None of the probiotic dose groups either showed consistent significant difference with the breast fed reference.

Conclusion: The present study supports the concept that feeding IF containing low dose of the probiotic B. lactis may be sufficient to promote development of early life immunity comparable to the one provided by IF containing regular dose probiotics. In absence of breast milk, low dose probiotic formula could be an adequate alternative feeding.

Nutrition
Clinical Trials
PO-N-0258
HIGH-SENSITIVITY C-REACTIVE PROTEIN AND OBESITY: CHARACTERIZATION IN PAEDIATRIC AGE
Sandra Silva 1,*, Henedina Antunes 1, 2
1 Paediatric Gastroenterology, Hepatology and Nutrition Unit, Braga Hospital, 2 Life and Health Sciences Research Institute (ICVS), School of Health Sciences, University of Minho, Braga, Portugal; ICVS/3B’s, PT Government Associate Laboratory, Braga/Guimarães, Portugal., University of Minho, Braga, Portugal

Objectives & Study: The chronic raised levels of inflammatory markers may be the mechanism that connects the elevated adiposity, as in obesity, to its co-morbidities, as insulin resistance, type 2 diabetes mellitus and cardiovascular disease, as atherosclerosis. The high-sensitivity C-reactive protein (HS-CRP) is the most stable inflammatory marker and is also an independent and predictive cardiovascular risk marker.

Objective: Study the association between HS-CRP and the anthropometric and metabolic profile of the overweight/obese children followed in a Nutrition unit at a tertiary hospital.

Methods: From a population of 1211 children, the last first consultations that had the HS-CRP result (n=106, between 2 February 2011 and 11 March 2013) collected, as the protocol, a blood sample, anthropometric data and realized an abdominal ultrasound. The exclusion criteria was HS-CRP >10mg/L because indicates an acute inflammation (n=3). The exercise was classified as rare (only scholar), moderate (scholar + um extra activity) and intense (scholar + one or more extra activities).

Results: The 103 children were aged between 3 and 17 years old (median of 10 years); 53.4% were female. The HS-CRP levels were elevated in 28.2%. It was found a positive correlation between the HS-CRP levels and the Body Mass Index (BMI) percentile (p=0.021); the Waist-to-Height Ratio (WtHR) (p=0.009); the glycosylated hemoglobin (HbA1c) (p=0.047) and the HOMA-IR (Homeostasis Model Assessment for Insulin Resistance) (p=0.006). It was also found an inverse association between HS-CRP and the exercise (p=0.047). It wasn’t found statistically significant differences between HS-CRP and the total cholesterol (p=0.245) or LDL cholesterol (p=0.473). We found 29 children with raised HS-CRP; 11 with raised LDL cholesterol; 25 with raised HS-CRP but normal LDL cholesterol; 7 with normal HS-CRP but raised LDL cholesterol.

Conclusion: The high levels of HS-CRP in this risk population demonstrate that the inflammation and the consequent cardiovascular risk may be present and independently from other factors, as cholesterol, even in the pediatric age. It was found statistically significant differences with the increase of BMI, WtHR, insulin resistance and HbA1c. The increased frequency of physical exercise was found to be a protective factor. The use of HS-CRP in clinical practice increase predictive value to the traditional factors in the cardiovascular risk prevention, even in pediatrics.

Disclosure of Interest: None Declared
**Objectives & Study:** Nutrition during early life is crucial for optimal health and cognitive skills. Sialic acid (Sia) is one of the candidates in human milk which may improve cognitive abilities, but its role has not been unambiguously demonstrated to date. The aim of this study was to evaluate the long term effects of sialic acid, free or conjugated, on learning and memory in rats.

**Methods:** Rat milk naturally contains Sia, which peaks at postnatal day (PND9) and then drops to a minimum by PND15. In order to bypass this peak of Sia, a cohort of foster mothers (PND16 and beyond) was used to raise the experimental pups from PND3 to weaning. Thus, pups received less Sia during early developmental than normal rats. A group of these pups received an oral supplementation of Sia to mimic the amount of rat milk, another group received the same molar amount of Sia given as 6'-sialyllactose (6'-SL), and the third group (control) received vehicle. After weaning, all animals were fed standard chow until the end of the procedure. Learning and memory capabilities were evaluated at age 1 year by widely published tests, i.e. Y maze and novel object recognition (NOR), as well as by a spatial paradigm using the new technology Intellicage. In vivo long-term potentiation (LTP) in the hippocampus was also performed at age 1 year.

**Results:** Rats receiving Sia or 6' SL during lactation performed significantly better in the tests. They were able to identify the novel arm in the Y-maze and the new object in the NOR, while control rats were not able to differentiate between novel and familiar objects or amongst the maze arms. In a place learning paradigm performed in the Intellicage, the number of mistakes made by the control rats was significantly higher than those of groups exposed to Sia during lactation. Moreover, the increase in LTP was significantly higher and more persistent in Sia and 6' SL animals when compared to controls, demonstrating the physiological basis of the observed behavioral improvement.

**Conclusion:** Sialic acid and a sialylated milk oligosaccharide administered during lactation enhanced memory and potentiated hippocampus function in rats. These effects lasted to adulthood, although exposure to these compounds ended at weaning.

**Disclosure of Interest:** None Declared
**Nutrition**

**Nutrition and Metabolism, Mechanisms**

PO-N-0260

**MINIMAL ENTERAL FEEDING WITH AMNIOTIC FLUID IN PRETERM PIGS**

Mette Viberg Østergaard 1*, Rene Liang Shen 1, Ann Cathrine F. Støy 2, Stine Brandt Bering 1, Per Torp Sangild 1

1Department of Nutrition, Exercise and Sports, University of Copenhagen, Frederiksberg C, Denmark, 2National Veterinary Institute, Technical University of Denmark, Frederiksberg, Denmark

**Objectives & Study:** The optimal diet and feeding strategy after preterm birth is unknown, especially if breastfeeding is scarce or absent. Amniotic fluid (AF), colostrum, and milk exert a continuum of beneficial effects on the developing intestine in the perinatal period via growth promoting and immunomodulatory factors. We hypothesized that small enteral feeds with AF, as an adjunct to parenteral nutrition during the first days after preterm birth, improve gut functions.

**Methods:** Preterm pigs (105–106 d of gestation, term 115–117 d) were delivered by cesarean section and fed parenteral nutrition with nil per os (NPO, n = 14) or AF (AF, n = 13) given as small enteral feeds advancing from 24 to 72 ml/kg/d over the first five days after delivery. An enteral galactose challenge test was performed on d4. After an enteral challenge with infant formula and a lactulose-mannitol bolus on d5, blood samples were collected to evaluate gut hormones and citrulline in plasma, and intestinal permeability, respectively. The pigs were then euthanized for tissue collection.

**Results:** The incidence of NEC (AF 8%, NPO 14%) and diarrhea (AF 23%, NPO 7%) were low and did not differ between groups. Body weight gain was higher in AF vs. NPO pigs (64 ± 3 vs. 23 ± 3 g, P < 0.001). The relative weights of the stomach (mean across groups 6.8±0.2 g/kg), small intestine (24.2±0.8 g/kg), and colon (9.4±0.6 g/kg) did not differ between groups, and there was no effect of AF on intestinal mucosa percentage, villus height, and crypt depth. Likewise, galactose uptake capacity (670±79 µM), plasma cortisol (55.0±7.6 ng/ml), citrulline (64.5±4.5 µM), and glucagon-like peptide 2 levels (55.0±3.7 pM) did not differ between groups, whereas gastric inhibitory polypeptide was higher in NPO vs. AF pigs (112 ± 20 vs. 58 ± 11 pM, P <0.05).

**Conclusion:** Small enteral feeds with AF during five days of parenteral nutrition were well tolerated in preterm pigs. AF stimulated body weight gain, but had limited effects on gastrointestinal growth, structure, and function. Further studies are required to evaluate how minimal enteral AF feeding improves weight gain and any effects on later intestinal adaptation following transition to full enteral milk feeding.

**Disclosure of Interest:** None Declared
HUMAN DONOR MILK AND BOVINE COLOSTRUM IMPROVES BODY GROWTH AND GUT HEALTH RELATIVE TO INFANT FORMULA IN PRETERM PIGS

Stine Ostenfeldt Petersen 1, Mette Viberg Østergaard 1, Lena Martin 2, Stine Brandt Bering 1, Per Torp Sangild 1,*

1Clinical and Experimental Nutrition, NEXS, University of Copenhagen, Frederiksberg C, Denmark,
2Institute of Animal Nutrition, Freie Universität, Berlin, Germany

Objectives & Study: Mother’s milk is the optimal diet for preterm infants but supply is often limited following preterm delivery. Infant formula (IF) and human donor milk (DM) are therefore used as alternatives, although both diets are not efficient in preventing gut dysfunction and necrotizing enterocolitis (NEC), relative to mother’s own milk. Both DM and bovine colostrum (BC) exert NEC-preventive effects within the first week after birth in preterm pigs (Jensen et al. 2013). In this study, we hypothesized that DM and BC would also improve growth and NEC resistance beyond the immediate postnatal period.

Methods: For ten days after birth, caesarean-delivered preterm pigs were fed slowly increasing doses (3–15 mL/kg/3 h) of three iso-energetic diets: preterm IF (n = 14), BC (n = 18), or DM (n = 15). Clinical condition, NEC lesions, mucosa proportion, and body and organ weights were recorded on day 10.

Results: NEC incidence was lowest in the DM pigs (40%), relative to BC (67%) and IF pigs (79%, p < 0.05 compared with DM). Mucosal weight in the proximal and middle intestine was elevated in BC pigs, relative to DM and IF pigs (both p < 0.05). Throughout the study, diarrhoea severity score was lower in BC pigs, relative to IF pigs (p < 0.01), and after day 6, BC diarrhoea score was also lower than in DM pigs (p < 0.001). Correspondingly, weight gain was higher in BC pigs (30 g/day), relative to both DM and IF pigs (-3 g/day, p < 0.01) and IF pigs (-12 g/day, p < 0.01), and food passage time on day 8 was longer (19 h vs. 7 and 3 h, respectively, both p < 0.05).

Conclusion: Slowly advancing volumes of DM and BC prevented NEC, diarrhoea, and poor clinical condition within the first week after birth. During the second week after birth, only BC had beneficial effects on weight gain, diarrhoea outcome, and mucosal weight, relative to IF. All three diets were associated with significant NEC lesions on day 10. Both BC and DM may be alternatives to IF during the critical neonatal period of preterm infants, but piglet model studies suggest that the length and volume of feedings must be carefully optimized to avoid negative effects.


Disclosure of Interest: None Declared
GROWTH IN EXCLUSIVELY BREASTFED INFANTS: A CONTROLLED METABOLIC STUDY USING FOR THE FIRST TIME NON-INVASIVE STABLE ISOTOPE METHODOLOGY

Marine Frasquet-Darrieux¹,²,³, Marie-Agnès Gaud¹,²,³, Patricia Christin³,⁴, Arnaud De Luca¹,²,³,⁷, Clair-Yves Boquien⁵,⁶, Catherine Millet⁷, Manon Herviou¹,², Dominique Darmaun⁵,⁶, Illa Tea⁶,⁸, Pierre Ingrand¹,², Richard J Robins⁶,⁸, Régis Hankard⁹,¹⁰

¹Inserm CIC0802, ²University of Poitiers, ³Paediatrics, CHU, Poitiers, France, ⁴Maternity, CH, Chatellerault, ⁵INRA, UMR 1280, IMAD, CRNH Ouest, ⁶University of Nantes, Nantes, France, ⁷Nuclear Medicine laboratory, CHU, Poitiers, France, ⁸CEISAM, CNRS, UMR 6230, Nantes, ⁹Inserm U1069, ¹⁰University of Tours, Tours, France

Objectives & Study: Infants born to obese mothers and fully breastfed gain less weight than infants born to lean mothers during the first month of postnatal life. Whether protein metabolism in children differs between obese and lean mothers regarding isotopic fractionation remains unknown. This prospective controlled study aimed at comparing isotopic composition in exclusively breastfed infants born from obese (OBE) and non-obese (NOBE) mothers at 1 month.

Methods: OBE mothers were matched for age (±5 years), parity, ethnic origin, and educational level with NOBE mothers. Infant protein metabolism was estimated from ¹⁵N natural enrichment in hair and milk using isotope ratio mass spectrometry.

Results: Of 165 mothers included between Feb. 2010 and Sept. 2012, 100 were followed up at 1 month. We did not observe any difference between groups at birth or at 1 month of age regarding weight, height, head circumference. Infants exclusively breastfed born to obese mothers gained 90 g less than control infants but the difference did not reach statistical significance. Natural ¹⁵N enrichment in milk was higher in the OBE group (6.4 [6.1-6.7] vs. 5.9 [5.6-6.2] ‰, p=0.006) but both ¹⁵N in hair protein and the difference between hair and milk ¹⁵N (an index of protein synthesis) were identical in both groups.

Conclusion: Our study is the first to assess protein metabolism in fully breastfed infants using a non-invasive methodology taking advantage of stable isotopes at natural enrichment levels in infant hair combined with an analysis of the ¹⁵N content in breast milk. The absence of difference between groups may be due to same growth rate. New studies in more contrasted nutritional situations are warranted.

Disclosure of Interest: None Declared
COWS MILK AND RICE FERMENTED WITH LACTOBACILLUS PARACASEI CBA L74 PREVENT GASTROINTESTINAL AND RESPIRATORY TRACT INFECTIONS IN YOUNG CHILDREN: A PROSPECTIVE RANDOMIZED STUDY

Rita Nocerino, Lorella Paparo, Ylenia Maddalena, Simona Caprio, Antonio Amoroso, Vincenza Pezzella, Rosita Aitoro, Linda Cosenza, Andrea Budelli, Francesca Fasano, Tommaso Cozzolino, Carmen Di Scala, Roberto Berni Canani

Objectives & Study: Gastrointestinal and respiratory tract infections are major causes of morbidity in childhood. Fermented foods have been proposed for prevention of infectious diseases. The purpose of this study was to evaluate the efficacy of new fermented foods in reducing common winter infectious diseases in children.

Methods: A prospective randomized, double-blind, placebo-controlled study was conducted in healthy children (12-48 months of age) attending educational program (either at nursery or primary school) during the winter season. They were supplemented daily for 3 months with a novel dietary product deriving from cow’s milk (Group A) or rice fermentation (Group B) with the Heinz proprietary strain Lactobacillis paracasei CBA L74 (International Depository Accession Number LMG P-24778) or placebo (Group C). 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: 405 children were evaluated, 377 children (193 male; mean age 32.5 months, 95% CI 31.4-33.5) completed the study: 137 in Group A, 118 in Group B and 122 in Group C. Demographic and anthropometric characteristics were similar among groups. The interventions were well accepted by the children. No adverse events were observed. During the study period 242 out of the 377 enrolled children experienced at least one infectious episode: 50.4% in Group A, 64.4% in Group B and 79.5% in Group C (p<0.05). URTI were observed in 48.2% of subjects in Group A, 58.5% in Group B and 31.1% in Group C, with a significant difference between the Group A vs Group C (p<0.001). AGE were recorded in 13.1% of subjects in Group A, 19.5% in Group B and 31.1% in Group C, with a significant difference between the Group A vs Group C (p<0.001) and vs Group B (p<0.05). After 3 months of intervention we observed a significant increase of α- and β-defensins, LL-37 and secretory IgA levels in Group A and B compared to Group C (p<0.05).

Conclusion: Dietary supplementation with cow’s milk or rice fermented with Lactobacillus paracasei CBA L74 efficiently prevents common infectious diseases in schooled children through a positive stimulation of innate and acquired immunity.

METABOLIC SYNDROME IN OBESE CHILDREN AND ADOLESCENTS: BETWEEN HEPATIC STEATOSIS AND CARDIOVASCULAR RISK

Irene Rutigliano 1,*, Roberta Vinci 2, Monica Mancini 1, Donatella De Giovanni 1, Mariangela Guglielmi 1, Annarita Centola 2, Massimo Pettoello-Mantovani 1, Angelo Campanozzi 1

1Paediatrics, 2Radiology, University of Foggia, Foggia, Italy

Objectives & Study:
The prevalence of MS is rising among obese children and adolescents. No consensus has been already reached for diagnosis of MS in childhood. AIM OF THE STUDY: 1) To evaluate the prevalence of MS in a large population of obese children and adolescents; 2) To assess the relationship between MS and HS and the possible role of HS in defining the syndrome.

Methods: The study population consisted of 803 obese children (395 girls and 408 boys, mean age 9.43±2.5 yrs), whose mean BMI z-score was 2.23±0.53. Collected data included: age, gender, medical history and a complete medical examination. Biological evaluation included serum triglycerides, total cholesterol, cLDL and cHDL, glucose, insulin, HOMA index and transaminases. We defined MS using 2 different definitions: Criteria of Weiss et al. (MSWEISS), modified Criteria of American Heart Association (MSAHA). The diagnosis and severity of HS was based on Ultrasonographic Steatosis Score (USS). All patients received an ultrasonography to measure the intima-media thickness of carotids (cIMT).

Results: The prevalence of MS was 13.07% (105 pts) according to MSAHA, 4.36% (35 pts) according to MSWEISS. The prevalence of HS was 40.9% in patients with MSAHA vs 18.5% in group without MSAHA (p<0.0001), 37% in children with MSWEISS vs 20.7% in patients without MSWEISS (p=0.020). Spearman’s correlation between USS and the number of criteria for MS presented by each patient was significant (rho=0.282, p<0.0001 for MSAHA, rho=0.261 p<0.0001 for MSWEISS). Mean cIMT and cIMT z-score were not statistically different between patients with MS and without MS, according to either definition. Instead, when HS was included as additional criterion for the diagnosis of MS, mean cIMT and cIMT z-score were statistically different between the two groups (Table). In multiple stepwise linear regression analysis, cIMT z-score was better predicted by using USS and MSAHA cluster (adjusted R² 2.6%, p<0.0001), than using only MSAHA cluster (adjusted R² 1.7%, p<0.0001).

<table>
<thead>
<tr>
<th></th>
<th>cIMT mm</th>
<th>cIMT z-score</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>AHA definition + HS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group with MSAHA</td>
<td>0.51±0.08</td>
<td>2.8±1.8</td>
</tr>
<tr>
<td>Group without MSAHA</td>
<td>0.48±0.07</td>
<td>2.2±1.6</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>&lt;0.0001</td>
<td>0.001</td>
</tr>
<tr>
<td><strong>WEISS definition + HS</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Group with MSWEISS</td>
<td>0.51±0.07</td>
<td>2.9±0.16</td>
</tr>
<tr>
<td>Group without MSWEISS</td>
<td>0.48±0.07</td>
<td>2.2±1.6</td>
</tr>
<tr>
<td><strong>P value</strong></td>
<td>0.001</td>
<td>0.001</td>
</tr>
</tbody>
</table>

Conclusion:
HS should be used as additional criterion in MS diagnosis to better recognize children at higher risk for cardiovascular morbidity and mortality in adulthood.

Disclosure of Interest: None Declared
FORMULA WITH HIGH LEVEL OF BIOACTIVE PROTEINS AND LACTOSE STIMULATES GUT FUNCTION IN PRETERM PIGLETS
Yanqi Li 1,*, Thomas Thymann 1, Dereck Chatterton 1, Anne Kvistgaard 2, Per Sangild 1
1University of Copenhagen, Frederiksberg, Denmark, 2Arla Foods Ingredients Group P/S, Aarhus, Denmark

Objectives & Study: Relative to intact milk diets such as colostrum and milk, formula feeding is associated with compromised intestinal maturation and a higher incidence of necrotizing enterocolitis (NEC) in preterm neonates. This may be explained by the use of whey protein concentrates (WPC) with reduced levels of bioactive proteins or use of maltodextrin rather than lactose as the carbohydrates source. We investigated the effects of two WPCs with high (WPC H) or low level (WPC L) of bioactive proteins on intestinal health in preterm pigs. WPC H had higher levels of native lactoferrin (5 times), IgG (3 times) and IGF-I (3 times) than values in WPC L. Formula predominantly based on lactose (relative to maltodextrin) protects against NEC in preterm pigs. Therefore, each WPC was included into formulas based on either lactose or maltodextrin to test the interaction between the nature of the protein and carbohydrate fractions.

Methods: Sixty-one caesarean-delivered preterm pigs were distributed into four groups and given parenteral nutrition and one of four formulas: lactose-dominant formulas (75% lactose+25% maltodextrin) containing WPC H (L/H, n=15) or WPC L (L/L, n=15), or maltodextrin-dominant formulas (75% maltodextrin+25% lactose) containing WPC H (M/H, n=15) or WPC L (M/L, n=16). The four formulas were isoenergetic and had similar macronutrient concentrations. A series of gut structural and functional indices, including mucosal lesions, were evaluated on day 5.

Results: Birth weight, daily weight gain, the weights of lung, heart, liver, kidney, spleen, stomach, colon and intestine, relative to body weight, and NEC incidence (51% NEC across the groups) were all similar among the four groups. Pigs fed WPC H containing formulas (L/H and M/H) had an increased proportion of mucosa (P < 0.05) and increased villus height (P = 0.09) in the proximal intestine, relative to the ones fed formula containing WPC L (L/L and M/L), respectively. Only in the lactose-dominant formula, did WPC H (L/H) stimulate galactose and lactose absorptive capacity and lactase activity, relative to WPC L (L/L, P < 0.05).

Conclusion: WPCs with different levels of bioactive proteins differ in their effects on gut structure and function in formula-fed preterm pigs. The effects interact with the composition of the carbohydrate fraction, with the beneficial effect of WPC H formula disappearing when the main carbohydrate source in formula is maltodextrin and not lactose. While formulas based almost 100% on lactose are known to be protective against NEC in preterm pigs, we now show that 25 and 75% lactose formulas fail to protect against NEC. Optimization of the levels of bioactive proteins in WPC, together with the composition of the carbohydrate source in formulas, is important to enhance both the nutritional contents as well as the gut protective effects in highly sensitive preterm neonates.

Disclosure of Interest: Y. Li Conflict with: This author was employed at Arla Foods Ingredients Group P/S as an industrial PhD when this study was performed., T. Thymann: None Declared, D. Chatterton: None Declared, A. Kvistgaard Employee of: Arla Foods Ingredients Group P/S, P. Sangild: None Declared
MINIMAL ENTERAL NUTRITION INDUCES DIET-DEPENDENT EFFECTS ON GUT MATURATION AND NEC SENSITIVITY IN PRETERM PIGS

Rene Liang Shen 1,*, Mette Viberg Østergaard 1, Ann Cathrine Findal Støy 2, Pingping Jiang 1, Bolette Hartmann 3, Jens Juul Holst 3, Douglas Guy Burrin 4, Per Torp Sangild 5

1Dept. of Nutrition, Exercise and Sports, University of Copenhagen, Frederiksberg, Denmark, 2National Veterinary Institute, Technical University of Denmark, 3Dept. of Biomedical Sciences, University of Copenhagen, Copenhagen, Denmark, 4USDA/ARS Children's Nutrition Research Center, Baylor College of Medicine, Houston, Texas, United States, 5Dept. of Nutrition, Exercise and Sports, University of Copenhagen, Copenhagen, Denmark

Objectives & Study: The optimal way to feed newborn preterm infants, when breast-feeding is impossible, is not clear. We hypothesized that feeding small volumes of enteral nutrition just after preterm birth stimulates gut maturation and that the response to infant formula differs from that of a highly bioactive milk diet, such as bovine colostrum.

Methods: Pigs fed total parenteral nutrition (TPN, n=14) for five days after preterm birth were compared with pigs fed slowly advancing volumes (16-64 ml/kg/d) of preterm formula (IF, n=15) or bovine colostrum (BC, n=13), as supplement to PN. The three groups received the same amount of calories (74-110 kcal/kg/d) and fluids (96-144 mL/kg/d). After a meal test on day 5, blood samples were collected to measure gut hormones, urine was sampled to measure intestinal permeability (lactulose-mannitol test), and internal organs were collected and weighed.

Results: On day 5, diarrhea and NEC incidences were markedly increased in the IF group (93 and 60%, respectively), compared with the BC (15 and 0%) and TPN (7 and 15%) groups. At necropsy, the IF pigs also had higher gastric residual volume than the other two groups (26±3 vs. 17±1 ml/kg, pooled values for BC and TPN, p<0.05). The TPN group showed higher weight gain (31±6 g/kg/d) than the other groups (14±2, p<0.05). Intestinal permeability was markedly reduced in the BC group (0.02±0.00) relative to the other two groups (0.11±0.03, p<0.05). Intestinal mass was reduced in the TPN group, compared with the other groups (22±1 vs. 27±1 g/kg, p<0.05). Plasma citrulline (a marker of functional enterocyte mass) was reduced in the IF group (38±3 µM) relative to the other groups (65±5 µM). Plasma levels of glucagon-like peptide 2 (GLP-2) following the meal test, were reduced in the TPN pigs (60±6 vs. 101±7 pmol/L, p<0.05) while levels of gastric inhibitory polypeptide (GIP) were highest in the BC group (139±13 vs. 87±8 pmol/L in the other groups, p<0.05).

Conclusion: The effect of minimal enteral nutrition on the immature gut is highly diet-dependent. Minimal enteral feeding with infant formula increases the risk of NEC compared with TPN, bovine colostrum more effectively promotes gut growth and function and protects against NEC.

Disclosure of Interest: R. Shen: None Declared, M. Østergaard: None Declared, A. C. Støy: None Declared, P. Jiang: None Declared, B. Hartmann: None Declared, J. Holst: None Declared, D. Burrin: None Declared, P. Sangild Conflict with: University of Copenhagen (Inventor: Per T. Sangild) has filed a patent application regarding the use of bovine colostrum for pediatric patients
GROWTH OF INTESTINAL BACTERIA ON MILK SACCHARIDES

Vojtech Rada 1,*, Sarka Musilova 2, Gabriela Kunova 3, Eva Vlkova 2, Jiri Nevoral 4

1Microbiology, Nutrition and Dietetics, Czech University of Agriculture Prague, Czech Republic,
2Microbiology, Nutrition and Dietetics, Czech University of Life Science Prague, Czech Republic,
3Milcom a.s., 4Department of Paediatrics, Charles University in Prague, Prague, Czech Republic

Objectives & Study: For healthy infants, which were vaginally delivered are fully breastfed, the dominant component of the intestinal microflora are bifidobacteria. However, infants born by caesarean section possess clostridia as a dominant intestinal bacterial group (Vlkova et al., 2005). The aim of the present study was to determine whether bifidobacteria, clostridia nad lactobacilli are able to grow on different carbon sources originated from milk.

Methods: Human milk oligosaccharides (HMOs) were isolated from breast milk and purified using gel chromatography and thin layer chromatography. Bifidobacteria, clostridia and lactobacilli isolated from infant faeces were tested for the ability to grow on HMOs, lactose, cow milk (CM) and human milk (HM). Susceptibility of bacteria to lysozyme was tested using lyso-plate method (Rada et al., 2010). Lysozyme content in milk was determine using lyso-plate method and by ELISA test.

Results: All bacteria grew on lactose and in CM. Bifidobacteria of human origin mostly grew in HM and on HMOs. In contrast, clostridia, lactobacilli and bifidobacteria of animal origin were not able to grow in HM. Resistance to lysozyme and the ability to utilize human milk oligosaccharides (HMOs) were identified as the most important factors affecting the growth of intestinal bacteria in human milk. Bifidobacteria were more resistant to lysozyme compared to other bacteria. Lysozyme content ranged from 2 to 130 mg/L in HM. No lysozyme was detected in CM.

Conclusion: The ability to grow in HM and to utilize HMOs seem to be important properties of bifidobacteria which are able to colonize infant intestinal tract. Bifidobacterium bifidum seems to be the most perspective probiotic species for infants.


Disclosure of Interest: None Declared
Objective & Study: Emerging research suggests that modulation of intestinal bacterial populations can result in demonstrable changes in brain development, neurotransmitter systems and expression of anxiety-like behaviors in rodents. These observations have been largely limited to fairly extreme physiological perturbations such as germ-free environments or extensive antibiotic treatment regimens. Consumption of dietary prebiotics has been shown to alter the bacterial population in the gut, however little research has explored their ability alone to impact the brain. This study assessed the impact of consuming dietary prebiotics polydextrose (PDX) and galactooligosaccharide (GOS) during normal early postnatal development on cognition, social- and anxiety-related behaviors in rodents.

Methods: Weaning male C57BL/6J mice, Sprague-Dawley and Long Evans rats (N=12 each) were fed control or prebiotic diet (7 g/kg and 15 g/kg PDX-GOS for rat and mouse, respectively) from postnatal day (pd) 21 throughout the behavioral testing at pd 50. Memory was assessed using the time-dependent version of novel object recognition. Social behavior was evaluated using the social interaction test and anxiety was assessed using the marble burying test.

Results: Mice fed the prebiotic diet buried fewer marbles (P<0.05) and prebiotic fed SD rats displayed more positive social interactions (P<0.01) than the control groups. The novel object recognition test revealed that prebiotic fed LE rats had a significantly higher recognition index than rats fed control diet (P<0.05). Body weights, water consumption and food intake did not differ between the PDX-GOS diet and control diet-treated animals. Preliminary results indicate that alteration of the gut microbiota may partially explain the effects observed here.

Conclusion: The present results demonstrate that adding prebiotics to the diet of rodents early in life positively influences behavior and cognitive functions later in life. Further assessments of gut microbiota, metabolome, and neurochemical profiles are necessary to identify possible mechanisms behind these effects.

Dietary supplementation with 2’fucosyllactose (2FL) increases the expression of key brain molecular factors involved in neuronal signalling pathways in rats

Enrique Vazquez 1, Alejandro Barranco 1, Maria Ramirez 1,*, Esther Martinez-Lara 2, Rachael Buck 3, Pedro Prieto 3, Ricardo Rueda 1
1Discovery R&D, Abbott Laboratories, Granada, Spain, 2Biochemistry, University of Jaen, Jaen, Spain, 3Discovery R&D, Abbott Laboratories, Columbus, OH, United States

Objectives & Study: Several health benefits, including cognitive development have been ascribed to breast milk and its unique repertoire of human milk oligosaccharides (HMOs). Learning and memory are mainly mediated by functional and structural modifications at synapses between neurons. Protein synaptic density protein (PSD)-95, calcium calmodulin kinase II (CaMKII) and brain-derived neurotrophic factor (BDNF) are involved in the neuronal signaling pathways that regulate synaptic plasticity, and therefore memory storage expression mechanisms.

Aim: To study if dietary supplementation with 2’FL—the most abundant HMO—is able to modulate the expression of specific brain markers with key roles in the neuronal signaling pathways

Methods: Method: Young adult Sprague Dawley rats were fed AIN93M diet control or AIN93M supplemented with 2’FL (350 mg/kg BW) for five weeks. Rats were then sacrificed and their brains were studied to determine the expression of PSD-95, CaMKII and BDNF in the hippocampus, striatum and frontal cortex. Qualitative expression of PSD-95 and CaMKII was done by histologic studies after staining with specific antibodies, and quantitative expression was done by western blot. BDNF levels were measured by ELISA in the same brain areas.

Results: Results: Rats fed 2’-FL showed a significant increase in the expression of neuronal markers PSD-95 (hippocampus and cortex), CaMKII (hippocampus), and BDNF (striatum and hippocampus).

Conclusion: Conclusion: Our results demonstrate that 2’-FL diet supplementation for 5 weeks produces an increased expression of markers related to brain functionality and synaptic plasticity mechanisms. Feeding 2’-FL may confer cognitive advantages derived from an increased expression of molecules recognized as brain markers which, in turn, may lead to improved synaptic plasticity and improved learning and memory functions.

Disclosure of Interest: None Declared
**Nutrition**

**Nutrition and Metabolism, Mechanisms**

PO-N-0270

**DISTURBED INTESTINAL NITROGEN HOMEOSTASIS IN A MOUSE MODEL OF HIGH FAT DIET-INDUCED OBESITY AND DIABETES: ROLE OF THE MICROBIOTA?**

TTH. Do 1, 2, A. J. Waligora-Dupriet 3, 7, P. Hindlet 1, 4, N. Kapel 3, 5, N. Neveux 6, 7, V. Mignon 8, C. Deloménie 9, R. Farinotti 1, B. Fève 2, 4, 10, M. Buyse 1, 2, 4, 10


**Objectives & Study:** We have recently reported that mice fed a high fat diet (HFD) during 4 weeks exhibited a decrease in nitrogen excretion suggesting an intestinal adaptation. Two hypotheses could be questioned: either a modification in nitrogen absorption through oligopeptides and free amino acids and/or a modification in the production of fecal nitrogen mainly dependent on cell desquamation or gut microbiota.

**Methods:** Six-week-old male C57Bl6/J mice were fed for 6 weeks with *ad libitum* access to standard laboratory chow (SC, 2820 kcal/kg of food, 3% fat) or a high-fat diet (HFD, 5320 kcal/kg, 36% fat). Glucose tolerance test, fecal nitrogen, portal amino acid analysis, intestinal permeability and transit time were assessed. Real-time PCR was used to quantify fecal bacteria populations.

**Results:** Upon HFD, overweight and diabetic mice exhibited an increase concentration of free amino acids in the portal vein (+60%). Modification of amino-acid absorption was associated with a selective increase in the expression of 2 AA transporters (*Slc6a20a, Slc36a1*), an increase intestinal permeability (+80%) and a delayed transit time (+40%). Besides, HFD mice had a 2.2-fold decrease in fecal DNA resulting from a reduction in nitrogen catabolism from cell desquamation and/or in the intestinal microbiota. A dramatic quantitative and qualitative changes in gut microbiota was observed with a 2.5-fold reduction in total fecal bacteria (3.9.10^{11} versus 9.7.10^{11} in feces of HFD and SC mice, respectively) and an almost extinction of the *Lactobacillus-Leuconostoc-Pediococcus* group in HFD mice (0.15% in feces in HFD mice versus 15.8% in control, *p* < 0.001) compensated by the emergence of the *Bifidobacterium* group and to a lesser extent of *Clostridium cluster XI* and *C. leptum* groups.

**Conclusion:** Taken together, these results indicate that during induction of diabetes and obesity, both an increase in amino acid absorption and a decrease in production of fecal nitrogen may occur, and could be involved in the disturbed metabolic profile. Whether the observed gut microbiota modifications are beneficial or detrimental for the HFD-associated metabolic complications remain an open issue.

**Disclosure of Interest:** None Declared
CHILDREN'S DEVELOPMENT NEGATIVELY AFFECTED BY PRENATAL EXPOSURE TO ORGANOCHLORINE PESTICIDES (MIREX)

Mary Carmen Baltazar1, 2, Francisco Jose Torres-Espinola2, Angela Muñoz-Machicao2, Cristina Martínez-Zaldívar2, Juan de Dios Luna3, Francisco Cruz4, Maria Fatima Olea6, Nicolas Olea6, Miguel Pérez-García4, Cristina Campoy2, 7,*

1Environmental Health, National Institute of Public Health, Cuernavaca, Mexico, 2EURISTIKOS Excellence Centre For Paediatric Research, University of Granada, Granada, Spain, 3Department of Bioestatistics, University of Granada, Granada, Spain, 4Department of Clinical Psychology, Evaluation & Personality, University of Granada, Granada, Spain, 5Department of Nutrition and Bromatology, University of Granada, Granada, Spain, 6Department of Radiology and Physics Medicine, University of Granada, Granada, Spain, 7Department of Paediatrics, University of Granada, Granada, Spain

Objectives & Study: The Mirex is considered to be one of the most stable and persistent pesticides, with a half life of up to 10 years. The main route of human exposure to mirex is through food, particularly meat and fish.

We aim to evaluate the long-term neurodevelopment effects of intrauterine exposure to mirex in children participants in the NUHEAL Spanish cohort.

Methods: 154 Spanish pregnant women were randomized to receive daily 500 mg docosahexaenoic acid (DHA)+150 mg eicosapentaenoic acid (EPA), 400 µg 5-Methyltetrahydrofolate (5-MTHF), both or placebo from 20 weeks up to the delivery. Blood samples were obtained from 96 mothers-baby pairs at delivery. Mirex was determined using HPLC, GC/ECD and GC/MS and was expressed in ng/g of lipids. The offspring were followed-up and revised at 7.5 and 9.5 years old, using the NUTRIMENTHE Neuropsychological Battery. ANOVA, Bonferroni test, multiple lineal regression and quantile regression were done using STATA 12.

Results: There were no significant differences on the mirex concentrations between groups neither on the long-term neurological outcomes depending on the prenatal supplementation. At 9.5 years, those children whose mothers had high Mirex concentrations in plasma showed long-term negative effects in verbal comprehension (language) (Token test B = -0.061, p=0.001, IC= -0.097 a -0.026) and in viso-perceptual integration (perception) (HVOT test B = -0.051, p= 0.03, IC= -0.097 a -0.005).

Conclusion: From the OC analysed, Mirex concentrations during pregnancy seems to have a major negative long-term effect on verbal comprehension and perception integration in children at 9.5 years.

**This work was partially supported by the NUTRIMENTHE EU Project, Grant agreement nº: 212652 and by the Spanish Ministry of Health (FIS 02/1314, FIS G03/176) and European Union (QLK4-CT-2002-00603-EDEN and NoE CASCADE-2003-506319)

Disclosure of Interest: None Declared
OBESITY AND GESTATIONAL DIABETES MELLITUS CAUSE SIMILAR ALTERATIONS IN PLACENTAL PHOSPHOLIPID SPECIES

Olaf Uhl 1,* , Hans Demmelmaier 1 , María Teresa Segura 2 , Cristina Campoy 2, 3, Berthold Koletzko 1

1Div. Metabolic and Nutritional Medicine, Dr. von Hauner Children’s Hospital, LMU Munich, Munich, Germany, 2Department of Paediatrics, 3Excellence Centre for Paediatric Research, University of Granada, Granada, Spain

Objectives & Study: Maternal obesity and gestational diabetes mellitus (GDM) are risk factors for development of metabolic syndrome of the offspring. GDM does not only affect maternal and fetal glycaemia, but also affects amino acid and lipid metabolism.

We investigated placental glycerophospholipid (GPL) species in obese (BMI ≥ 30 kg/m², n=17), GDM (BMI 18-24.9 kg/m², n=15) and healthy pregnant women (BMI 18-24.9 kg/m², n=31).

Methods: Samples were obtained from the participants of the observational PREOBE study, which enrolled pregnant women during week 20 of gestation. Aliquots of frozen placenta were analyzed by high performance liquid chromatography coupled to triple quadrupole mass spectrometry for levels of phosphatidylcholines (PC), phosphatidylethanolamines (PE), and phosphatidylserines (PS). Mann-Whitney-U tests were performed to investigate differences between groups. Spearman rank correlation was performed to determine the relation between GPL species and the placenta weight. Significance was accepted at p <0.05.

Results: Mann-Whitney-U test identified 3 GPL species to be significantly different between obese and controls. In the group of GDM 4 GPLs were significantly different from controls. In GDM and obese, 2 species containing dihomo-gamma-linolenic acid were found with smaller percentages compared to the controls. Besides the significantly decreased species, all GPL species containing dihomo-gamma-linolenic acid tended towards lower levels in GDM and obese.

However, significantly increased percentages of PE(16:0/22:6) and PE(18:0/20:4) were only found in GDM. Manhattan-plot showed that the placental lipid profiles of GDM patients and of obese woman deviate in a similar way from controls.

Significant correlations between placental weight and GPL percentages were found for 2 PC, 1 PS and 4 PE species. Three out of the four PE species with significant positive correlations contained arachidonic acid (PE(16:0/20:4), PE(18:0/20:4) and PE(18:1/20:4)).

Conclusion: Non-obese GDM and non-diabetic obesity in pregnancy are associated with similar subtle but potentially relevant changes of placental GPL composition. We speculate that the placenta lipid profile may be affected by the maternal blood level of insulin and related factors and fetal availability of dihomo-gamma-linolenic acid might be an early programming factor of insulin resistance.

A relation of GPL species containing arachidonic acid to growth factors modulating placental weight is conceivable, as are changes in the total GPL pattern due to changes in placental tissue cellularity, reflecting GPL composition differences between cells.

**This study was granted by Junta de Andalucía: Excellence Projects (P06-CTS-02341) and Abbott Laboratories-General Foundation University of Granada (Contract agreement: 3346).**

Disclosure of Interest: None Declared
**Nutrition**

**Nutrition and Metabolism, Mechanisms**

PO-N-0273

**PRE-WEANING CONSUMPTION OF SCGOS/LCFOS DURABLY IMPRINTS THE INTESTINAL MICROBIOTA IN RATS**

Fanny Morel¹,²,³, Raish Oozeer²,* Anthony Pagniez¹, Annemarie Oosting², Jan Knol²,⁴, Dominique Darmaun¹, Catherine Michel¹,³

¹Université de Nantes, Nantes, France, ²Danone Nutricia Research, Utrecht, Netherlands, ³INRA, Nantes, France, ⁴Wageningen University, Wageningen, Netherlands

**Objectives & Study:** Increasing evidence indicates that nutrition in early life has sustained effects on adult health. Identifying mechanisms underlying this nutritional imprinting may enable new disease prevention strategies. Intestinal microbiota could be a key player in this since i) it affects metabolic homeostasis of its host, ii) its postnatal implement can be modulated by nutrition, iii) its initial set-up is thought to have a sustained impact on microbiota composition throughout life. Our objective was to determine whether preweaning modification of intestinal microbiota could have long-lasting effects in rats.

**Methods:** Suckling rat pups were supplemented with short chain fructo-oligosaccharides (scFOS), galactooligosaccharides/long chain fructo-oligosaccharides mix (scGOS/lcFOS, 9/1), acidic oligosaccharides (AOS), amoxicillin or control solution from postnatal day 5 to 15 then were weaned to standard chow until day 130. We characterized caecocolonic microbiota at day 15 and 130 using qPCR, pyrosequencing and metabolites analyses.

**Results:** At day 14-15, all the treatments did affect the microbiota. Amoxicillin had a higher impact without being very specific. All oligosaccharides decreased Firmicutes counts whereas bifidobacteria were specifically increased in scFOS and scGOS/lcFOS rats. At day 130, solely the scGOS/lcFOS preweaning treatment exerted a sustained effect as reflected by an increased bacterial richness, decreased counts of *Roseburia intestinalis* cluster and *Erysipelotrichaceae*. The sustained bacterial composition changes are associated, as well as, with a decrease of butyrate kinase genes.

**Conclusion:** We concluded that scGOS/lcFOS provided before weaning exerted a mild imprinting impact on intestinal microbiota. Such finding suggest that pioneer bacterial colonizers may be involved in the control of the adult microbiota structure and sustain the idea that intestinal microbiota may act as a long lasting relay of neonatal nutrition and thus contribute to nutritional programming.

**Nutrition**

**Nutrition and Metabolism, Mechanisms**

PO-N-0274

**RAPID WEIGHT GAIN DURING COMPLEMENTARY FEEDING PERIOD AND OVERWEIGHT RISK**

Mireia Morera 1, Gerardo Rodríguez 2*, Mª Jesús Cabero 3, Pilar Samper 2, Mª Luisa Alvarez 2, Laura Monje 3, Anna Miralles 2, Lino Alvarez 2, Montse Rivero 1, Miguel García-Fuentes 3, Luis Moreno 2

1Scientific Unit, Laboratorios Ordesa, Sant Boi de Llobregat, Spain, 2Paediatric Department, University of Zaragoza, Zaragoza, Spain, 3Paediatric Department, University of Cantabria, Santander, Spain

**Objectives & Study:** The importance of complementary feeding period on infant growth and later overweight development has not been already established. We aimed to describe feeding patterns, anthropometric characteristics and overweight prevalence of infants with rapid weight gain (RWGI) during this period.

**Methods:** Longitudinal study involving 195 healthy infants (108 males), enrolled at 6 months of age and followed-up until 18 months, as part of a larger study in Northern Spain. 24-h food recall questionnaires were used to assess food intake (breastfeeding, formula, cereals, fruits, yogurt, vegetables and meat or fish porridge (VMFP)) at 6, 9 and 12 months of age. Weight and length were measured and Z-scores (ZS) were calculated from WHO references until 18 months. Rapid weight gain was defined as a change in weight from 6 to 12 months >0.67 ZS and overweight when body mass index (BMI) >1.0 ZS.

**Results:** At 6 months, RWGI (n=52) had smaller weight (p<0.004) and BMI (p<0.015) than their counterparts (n=143). RWGI consumed more food (p<0.005), cereals (p<0.007), fruits (p<0.017) and VMFP (p<0.039) during complementary feeding period. In RWGI at 12 months of age, the likelihood of breastfeeding was lower (RR:0.32; IC95%:0.12-0.86) and their weight (p<0.002), BMI (p<0.004) and risk of being overweight were higher (36.5% vs. 21%; p<0.039) (RR:2.17; IC95%:1.68-2.80) than in non-RWGI. These anthropometric differences persisted up to 24 months of age. There were no significant differences in social or parental characteristics or birth anthropometry between both groups.

**Conclusion:** Rapid weight gain after complementary feeding introduction is associated with a lower rate of breastfeeding maintenance, higher amounts of food intake and greater risk of overweight up to 24 months of age.

**Disclosure of Interest:** None Declared
COMBINED EFFECT OF LIPID MIXTURE WITH FISH OIL AND PURE FISH OIL ON LIVER FUNCTION IN CHILDREN ON LONG-TERM PARENTERAL NUTRITION

Mikolaj Danko 1, Aleksandra Zyla 1, Katarzyna Popinska 1, Marta Sibilska 1, Katarzyna Olszewska 1, Joanna Friedman-Gruszczynska 1, Janusz Ksiazyk 1.

1Dept. Pediatrics, Nutrition and Metabolic Disorders, The Children's Memorial Health Institute, Warsaw, Poland

Objectives & Study: The main complications of long-time parenteral nutrition include intestinal failure associated liver disease (IFALD). Influence of combination of two lipid emulsion with increased dose of fish oil on liver function in patients with abnormal liver tests was the aim of the study.

Methods: Twenty six paediatric patients, age 1 – 200 months (median 18 months) on long term parenteral nutrition (> 1 month), with elevated liver enzymes activity or/and bilirubin serum levels were included to the study. All were nourished parentally and only 7 patients were also fed by enteral route. The main indication for parenteral nutrition was short bowel syndrome (18 patients), total aganglionosis (3 patients), intestinal pseudoobstruction syndrome (2 patients), megacystis-microcolon-intestinal hypoperistalsis syndrome (Berdon syndrome – 2 patients) and sodium diarrhea (1 patient). In each patient a combination of 2 lipid emulsions in parenteral admixture – 20% mixture of soybean, olive, fish oil and MCT oil with 10 % pure fish oil - were used. The dose of fish oil from both emulsions was over 0.8 g/kg/day (median; range 0.54 – 1,3). Total non-protein intake was 83 kcal/kg/d (median; range 45 – 140). Majority of the patients were given mixture of soybean, olive and fish oil with MCT oil before the study. Laboratory tests were performed at least after 28 days of therapy (median: 124 days; range: 28 – 377 days). Analysed parameters were: total bilirubin (TB), conjugated bilirubin (CB), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT), platelet count and International Normalized Ratio (INR). Patients’ weight was monitored. The results were statistically analysed by the Wilcoxon test.

Results: The duration of therapy with combination of lipid emulsions was from 28 to 250 days, median 124 days. Initial median TB median was 2.45 mg/dl and dropped to 0.87 (p< 0.006). Median CB also decreased from 2.15 mg/dl to 0.48 mg/dl (p=0.007). Median activity of AST decreased from 156 IU to 64 IU (p<0.002), ALT from 130 IU to 70 IU (p=0.003) IU. GGT from 116 IU to 64 IU (p<0.004). Significant changes in platelet count and INR were not observed. The median body weight increased significantly from 7.12 to 11.2 kg (p<0.001). Infants’ median body weight increased from 3.75 to 5.4 kg. Five patients didn’t respond to the therapy – their bilirubin level increased or remained elevated. The median time of parenteral nutrition before the study was longer in non-responders group: 78 vs 7 months. Among these patients in only one case the indication for parenteral nutrition was short bowel syndrome.

Conclusion: Enrichment of lipid mixture containing fish oil with pure fish oil is beneficial for resolution of IFALD, particularly in patients with short bowel syndrome requiring long-term parenteral nutrition.

Disclosure of Interest: None Declared
MONTMORILLONITE TO REDUCE PROTEIN INTESTINAL ABSORPTION: AN IDEA FOR MORE TASTY LOW PROTEIN DIET

Sara Quaglia 1, Luigina De Leo 1, Sara Mazzucco 2, Fabiana Ziberna 1, Serena Vatta 1, Gianni Biolo 2, Tarcisio Not 1, 2,*

1Institute for Maternal Child Health, IRCCS “Burlo Garofolo”, 2University of Trieste, Trieste, Italy

Objectives & Study: Montmorillonite (MONT) is a phyllosilicate layered mineral and, for its physicochemical properties, it is able to immobilize proteins and others molecules (e.g. gas, toxins). MONT is already used for therapeutic purposes (e.g. irritable bowel syndrome), in pharmaceutical formulations and in food preparation. The aim of this study is to understand if MONT could be useful to entrap alimentary proteins and to reduce their intestinal absorption.

Methods: We performed in vitro and in vivo experiments.

In vitro: MONT and whey protein at 4 different ratio w/w (1:1, 1:2, 1:5, 1:15) were dissolved in acetate buffer 0.1M pH 5 as well as a control sample without MONT. Samples were incubated at room temperature for 1, 10, 30, 60 minutes and then centrifuged at 10000g. The supernatants were analyzed by LOWRY method. The amount of immobilized protein was calculated compared to the protein control sample and the differences in protein concentration were analyzed using t Test.

In vivo: 25 healthy volunteers were enrolled (12M, 13 F, 25-30 years). Fasting from morning, they drank a solution of MONT and whey protein at different ratio. Volunteers were divided into 4 groups: 10 subjects consumed 15g of protein alone; 5 subjects swallowed MONT-protein ratio 1:3 (5g + 15g); 5 consumed MONT-protein ratio 1:5 (3g + 15g); 5 ingested MONT-Protein ratio 1:15 (1g + 15g). Each subject was provided of a peripheral intravenous catheter used to drop off 3 ml blood samples before solution ingestion and after 30, 60, 90, 120 minutes. Samples were centrifuged and freezed at -80°C. Plasma samples were analyzed by mass spectrometry to measure plasma leucine concentration that is considered the specific marker for protein intestinal absorption. Concentrations were compared in the different study groups and analyzed with a non parametric test. The study was approved by independent ethical committee (IEC 05/2013).

Results: The in vitro assay showed a significant decrease of protein in solutions with MONT at ratio (MONT-Protein) of 1:1, 1:2, 1:5 (p< 0,01; p< 0,01; p< 0,05 respectively) at each time point.

In in vivo experiments the MONT (MONT-Protein 1:3, MONT-Protein 1:5 and MONT-protein 1:15) reduced the plasma leucine concentration of 32% (p<0,05), 30% (P<0,05) and 10% (p>0,05) respectively after 120 minutes.

Conclusion: MONT leads to a decrease in the intestinal absorption of whey protein. More studies could be performed to verify the safety in a prolonged use and to evaluate its contribution in the formulation of more tasty diet for those subjects suffering from impaired renal function or metabolic diseases (e.g. Urea cycle disorder) who need low protein consumption.

Disclosure of Interest: None Declared
TRANSIENT RENAL TUBULAR ACIDOSIS AS A CAUSE OF FAILURE TO THRIVE IN CHILDREN
Erick Toro 1,*, Roberto Cervantes 1, Jaime Ramirez 1, Chiharu Murata 1, Ericka Montijo 1, Flora Zarate 1, Jose Cadena 1, Monserrat Cazares 1, Martha Lopez 1
1Gastroenterology, INP, Mexico, Mexico

Objectives & Study: Failure to thrive is a challenge in daily pediatric practice, the differential diagnosis is broad and includes metabolic disease like renal tubular acidosis (RTA). RTA is a clinical syndrome characterized by hyperchloremic metabolic acidosis. The clinical pictures includes stunting, anorexia and gastroesophageal reflux. Its considered a rare disease however in our hospital we faced with this condition very often, as a cause of failure to thrive. The aim of this study was to describe the way we do the diagnose of RTA and analyze the z score of height and weight with treatment over 9 months in the group of patients evaluated.

Methods: We reviewed the records of 104 patients with the diagnosis of RTA in our hospital from 2009 to 2013. We analyze serum bicarbonate, urinary pH, total CO2, serum and urinary electrolytes, initial dose of bicarbonate. For the analysis of growth we review the initial Z scores for height and weight and in 9th month of follow up.

Results: The demographic and characteristics of RTA diagnosis are describe in Table No. 1. The initial z scores for weight was -2.62 and for height was -2.57, at 9 months the Z scores for weight and height was -1.99 and -2.096 respectively, both with a statistically significant difference (p <0.0001).

Conclusion: Transient renal tubular acidosis is a unexplored cause of failure to thrive, we demonstrate the recovery in both weight and height in these patients with appropriate treatment. This study may result in a prospective study and even a clinical trial that evaluates the efficacy and safety of the treatment in children with failure to thrive.

Disclosure of Interest: None Declared
OUTCOME OF LONG TERM PARENTERAL NUTRITION IN CHILDREN WITH CONGENITAL ENTEROPATHIES AND OTHER DISEASES CAUSING INTESTINAL FAILURE (IF)

Francesca Barbieri 1,*, Meta Starc 1

1Università Degli Studi di Trieste, Trieste, Italy

Objectives & Study: This study aims to analyse the outcome of long term parenteral nutrition (PN) in children with early onset intestinal failure due to different causes: chronic enteropathies (CE: structural enteropathies, syndromic congenital diarrhoea, autoimmune enteropathy), short bowel syndrome (SBS) and motility disorders (MD).

Methods: Clinical notes of children affected by intestinal failure causing long term (more than 2 years) PN dependant IF and followed at our gastroenterology department between 1999 and 2012 were retrospectively evaluated. We analysed the duration of PN, the weaning from PN and the referral for intestinal transplantation (ITx), the number of hospital admissions, the occurrence of catheter-related sepsis and deep venous thrombosis, the occurrence of hydroelectrolytic disorders, cholestatic liver disease and osteoporosis and the total number of central venous catheter (CVC) utilized. A comparison between the 3 groups was made with multivariate analysis (Kruskal Wallis).

Results: 22 children were evaluated (8 with SBS, 8 with MD, 6 with CE). The median duration of PN was 91.4 months (33.5-192.6). The number of hospital admissions was similar in the 3 groups (average 5.37 in 1000 days on PN, SD 3.32). The occurrence of catheter related sepsis and thrombosis was similar in the 3 groups (respectively 2.23, SD 2.71 and 0.44, SD 0.68 in 1000 days on PN). The average number of catheter replacement was 2.55, SD 1.30, in 1000 days on PN. The number of catheter replacement was significantly lower in CE (1.6 SD 0.52). The occurrence of hydroelectrolytic disorders was significatively higher in motility disorders (3.30 in 1000 days on PN, vs average of 1.64 SD 1.83). 12 patients developed the IF-related liver disease (2/6 with CE, 4/8 with MD, 2/8 with SBS). 11 patients developed osteoporosis (5/6 with CE, 2/8 with SBS and 4/8 with MD) with significantly higher incidence in patients starting PN before 1998. 8 children were weaned from PN (5 SBS, 1 CE, 2 MD) after a median of 31 months on PN. Other 4 patients (1 CE, 2 SBS, 1 MD) underwent succesfully intestinal transplantation after a median period of 12.6 years on PN.

Conclusion: The current study shows that some outcomes of long term PN depends on the cause of intestinal failure rather than on PN alone. Catheter related complications are less frequent in CE (lower catheter replacement number). The occurrence of hydroelectrolytic disorders is higher in motility disorders. Liver disease develops in all diseases, independently from duration of PN. Differently, the development of osteoporosis is related to the duration of PN. Weaning from PN is more frequent in patients with SBS. ITx is a good long-term solution when life-threatening complications develop.

Disclosure of Interest: None Declared
**Objective & Study:** Optimal nutrition and care is crucial to stimulate growth and development of preterm infants. Relative to term neonates, growth deficits may be caused by low nutrient intake in combination with possible organ dysfunctions, infections and metabolic disturbances. We hypothesized that preterm neonates show diminished growth and organ development during the first 4 weeks after birth, despite being delivered the same way and provided identical diet and rearing conditions as piglets born at full term.

**Methods:** Pigs were delivered by caesarean section at preterm (106 d, n=12) or term gestation (118 d, n=22). For the first 4 postnatal days pigs from both groups were reared in incubators and fed isoenergetic diets (74-110 kcal/kg/d) of parenteral nutrition (PN), with or without supplemental minimal enteral nutrition (MEN, 0-64 ml/kg/d bovine colostrum). This was followed by individual rearing in open cages and feeding with bovine milk-based formula until day 26 (64-200 ml/kg/d). In-feed antibiotics were provided temporarily to all these immune-compromised pigs to prevent sepsis and infections. Growth was recorded daily and organ weights were recorded on day 26.

**Results:** Preterm pigs showed severe signs of prematurity, including hypothermia, respiratory distress and delayed motor skill development for the first 5 days of life. The time to first eye lid opening and first stand and walk was markedly increased in preterm vs. term pigs (all P<0.001). Likewise, the average number of days with diarrhea was higher in preterm vs. term pigs (+100%, P<0.001) indicating a dysfunctional digestive system. Preterm pigs had a slower growth rate (2 and 6 g/kg/d) on d 0-5, compared to that of the term pigs that grew 32 and 19 g/kg/d in the PN and MEN groups, respectively (P <0.05). Growth deficits in the preterms remained until d 26 (20-22 vs. 31-34 g/kg/d). Relative to their body weight, preterm pigs had lower weight of the colon, liver and spleen on d 26, compared with term pigs (-32, -10 and -74% respectively, all P<0.05), while lungs, kidneys and brain were increased by 11, 14 and 23%, respectively (all P<0.001).

**Conclusion:** Preterm neonatal piglets are severely growth-restricted in the postnatal period, even when provided the same diet and rearing environment as term neonates. Specific reductions in internal organ growth and function in preterm neonates may inhibit digestive and metabolic capacity in the postnatal period. Minimal enteral nutrition relative to total parenteral nutrition during the first days after birth does not affect later growth rates. The immature, immune-compromised preterm pig may be a highly sensitive model to test effects of diet and rearing conditions on organ development in weak newborn infants.

**Disclosure of Interest:** None Declared
ANALYSIS OF FOOD ADVERTISING FOR CHILDREN IN SPANISH TELEVISION: WHERE ARE WE GOING?

Daniel Campos 1, Juanjo Hernández-Torres 2, Mariano Comino 1, Victoria Macías 1, Juan Carlos López-Robles 1, Cristina Campoy 1, 3, *

1EURISTIKOS Excellence Centre for Paediatric Research, University of Granada, Granada, Spain, 2San Rafael University Hospital, 3Department of Paediatrics, University of Granada, Granada, Spain

Objectives & Study: Nowadays 28.3% of Spanish children, younger than 12 years old, are overweight or obese; television (TV) food advertising has an important role on this problem. In 2011, new European and Spanish general public health laws were designed to control food advertising. The aims of this study were to measure children's exposure to healthy and unhealthy food advertisements in thematic channels for children (TC) and Generalist Channels (GC) in Spain during 2013 and the nature of broadcast in children’s peak time slots.

Methods: Following the studies of Spanish TV Marketing in 2007, we recorded TV programs from the 2 channels most watched by children, and 2 channels addressed to all ages, between April and May 2013, 2 week days and 2 weekend days, from 6:00 to 22:00. We classified food advertisements as core (nutrient dense, low in energy), noncore, (high content of undesirable nutrients or energy), or others (supermarkets and special foods). We also analyzed if advertisements were shown in children’s peak time slots (7:00-8:59 and 15:30-22:00 on weekdays, and 7:30-10:29 and 15:30-22:00 on weekend days) or children’s nonpeak time slots (9:00-15:29 on weekdays and 10:30-15:29 on weekend days).

Results: A total of 1263 foods advertisements were recorded (579 TC/684 GC). Non-core food advertisements were the most shown (54.9%) in the regular full day TV programming (57.3% of TC and 52.2% of GC); their appearance in TV resulted lower when compared with the percentage observed six years ago (66.6%). Core food advertisements were displayed with higher frequency, 47.2%, in TC in comparison with 23.7% shown on GC in 2013 and 36% in TC in 2007. Broadcast of non-core food advertisements in children’s peak time slots had a ratio slightly higher in TC in 2013 (5.63 adv/h/c) than in TC during 2007 (5 adv/h/c), and also above that of GC 2013 (4.3 adv/h/c).

Conclusion: Broadcast of unhealthy TV food advertising is lower today than six years ago in TC. However, children’s exposure to television advertising of unhealthy foods is worrying in Spain, and there is still more exposure to unhealthy food TV commercials. Therefore, there is evidence that, by the moment, Spanish laws on food advertising control are still insufficient to avoid unhealthy food advertising in TV and consequently facilitate an early prevention of obesity and other non communicable diseases.

**This work was partially supported by the NUTRIMENTHE EU Project, Grant agreement n°: 212652.

Disclosure of Interest: None Declared
FOOD INTAKE IN OBESE CHILDREN AND ADOLESCENTS AT HIGHER RISK OF METABOLIC SYNDROME
Irene Rutigliano 1,*, Nicola d’Altilia 1, Ilaria Pizzolorusso 1, Filippo Di Ninno 1, Roberta Merla 1, Angelo Guida 1, Massimo Pettoello-Mantovani 1, Angelo Campanozzi 1
1Paediatrics, University of Foggia, Foggia, Italy

Objectives & Study: The world wide epidemic of childhood obesity is followed by increasing prevalence of Metabolic Syndrome (MS) in pediatric population. Visceral adiposity is well described in MS cluster and waist circumference has been shown to be a marker of upper body fat accumulation in children: in particular waist circumference to height ratio (WHtR) represents a simple tool for detecting visceral adiposity. A cut-off value of 0.62 has been reported to better identify children at higher risk of MS. AIM OF THE STUDY: To identify the role of nutrition in pathophysiology of MS.

Methods: The study population was made by 397 children (mean age 9.4±2.3 yrs, median 9.5), 196 males and 201 females, whose BMI z-score was 2.2±0.5. Collected data included: age, gender, medical history and complete medical examination. For each patient we measured WC and calculated WHtR (WC (cm)/Height (cm)). The diagnosis of MS was made according to modified Criteria of American Hearth Association. Dietary habits were assessed by a trained dietician, using a one week alimentary diary. A computerized database (Winfood) was used to calculate food energy and nutrient intakes.

Results: We divided our population in two groups: group A obese children with WHtR ≥0.62 (193 pts, mean age 9.4±2.4 yrs), group B obese children with WHtR<0.62 (204 pts, mean age 9.5±2.3 yrs; p=0.741). Total energy Intake was 1843±459 kcal/day in group A and 1723.6±402 Kcal/day in group B (p=0.008). No difference was recorded between intake (%) of proteins, carbohydrates and fats between the groups (group A: 14.8±3.2%, 45.7±5.6%, 39.3±5.7%; Group B: 15±3.3%, 45±5.8%, 39.5±5.9%). Group A presented a caloric intake by snacks and other commercial foods greater then Group B (442±265.2 kcal/day vs 383±209.8 kcal/day; p=0.014). In group A the prevalence rate of MS was 19.7%, in group B 4.4% (p<0.001).

Conclusion: Obese children with WHtR≥0.62 usually eat larger quantities of snacks and commercial foods. It’s well known the role of this kind of foods, generally rich in trans fatty acids, in the genesis of cardiovascular disease. A correct nutritional education is required to reduce cardiovascular risk.

Disclosure of Interest: None Declared
Objectives & Study: Parenteral nutrition-associated liver disease (PNALD) is a major complication for patients who require long-term parenteral nutrition. Treatment options for PNALD are limited and its pathogenesis is poorly understood. Tribbles homolog 3 (TRB3) is a pseudokinase that modulates many signal transduction cascades and may be involved in the pathogenesis of PNALD. The aim of this study was to examine the role of TRB3 in palmitate-induced endoplasmic reticulum (ER) stress, in the human liver cell line L02.

Methods: L02 cells were treated with palmitate, and its effect on cell viability, mitochondrial membrane potential, apoptosis and TRB3 expression were assessed. The role of TRB3 was also studied using transient overexpression of TRB3 in L02 cells, as well as its interaction with Akt signaling.

Results: We found that palmitate-induced ER stress and apoptosis in L02 cells. Palmitate-associated ER stress was accompanied by a significant induction of TRB3 expression at the mRNA and protein level. Overexpression of TRB3 potentiated the deleterious effects of palmitate, which was associated with decreased levels of phospho-Akt.

Conclusion: TRB3 is an important mediator of palmitate-induced apoptosis in human liver cells, suggesting that it is a potential target for the treatment of PNALD.

Disclosure of Interest: None Declared
RELATIONSHIP BETWEEN EYE COORDINATION DEVELOPMENT AND CHILDREN FITNESS AT 10 YEARS

Christelle Gillet de Ruyver 1, Cristina Martínez-Zaldívar 1, Francisco Jose Torres-Espinola 1, Daniel Campos 1, Miguel Martín-Matillas 2, 3, Miguel Pérez-García 4, Cristina Campoy 1, 5,*

1EURISTIKOS Excellence Centre for Paediatric Research, University of Granada, Granada, Spain, 2Department of Physical Education and Sport, School of Physical Activity and Sport Sciences, University of Granada, Granada, Spain, 3PROFITH “Promoting Fitness and Health through Physical Activity” Research Group, 4EURISTIKOS Excellence Centre For Paediatric Research. Department of Clinical Psychology, Evaluation & Personality, University of Granada, Granada, Spain, 5Department of Paediatrics, University of Granada, Granada, Spain

Objectives & Study: Visuomotor coordination (VC) gives us information through the eye which is transmitted to the muscles groups to perform a movement, thereby merging with motion perception, and having great importance for the quality of its execution. Its development involves a period of discovery of experiences from birth to around the age of 16; generally, the development involves important muscles’ nervous control above all the edges ones. The relationship between the VC and the correct testing Physical Condition (PC) seems obvious; there are only few studies that link them. The present study explores the relationship between VC and PC in children at 10 years, taken into account all potential confounder factors that may have influence on them.

Methods: 55 children participants in the NUHEAL Project were included in this analysis. VC was explored using the Grooved Pegboard test at 7.5 and 9 years and PC was assessed using the ALPHA-fitness battery at 10 years. SPSS v.20 was used for the analysis.

Results: Agility (A) and flexibility (F) conditions resulted lower in boys than in girls (A: P=0.048; F right leg: P=0.016, F left leg: P=0.009, respectively). However, boys scored higher than girls at 9 years in VC with the dominant hand (33.87±6,02 vs 30.85±7,31, P=0.032). A significant relationship between VC with legs (r: 0.314, P=0.021) and hands (right hand: r: 0.32, P=0.018; left hand: r: 0.312, P=0.022) strength was shown, and also with the agility test (r: 0.34, P=0.012). Children born to smoking mothers showed significant higher runtime solving the VC test. A significant correlation was also shown between parents’ educational level and child cardiorespiratory endurance (P=0.006).

Conclusion: Cigarette smoking during pregnancy has adverse long-term effects on children neurodevelopment. Children born to parents with university studies did better on the cardiorespiratory endurance test. Children showing better VC development were better developed in strength and agility.

**This work was supported by the NUTRIMENTHE EU Project, Grant agreement nº: 212652.

Disclosure of Interest: None Declared
MEASUREMENT OF ADVANCED GLYcation END-PRODUCTS (AGE) WITH SKIN AUTO-FLUORESCENCE IN THE NEWBORN

Aurélie Gallineau 1, Adélaïde Dousseau 2, Christophe Elleau 3, Vincent Rigalleau 4, Thierry Lamireau 5.*
1Maternity Hospital, 2Methodology Unit, 3Neonatal Unit, 4Department of Nutrition, 5Paediatric Gastroenterology and Nutrition, CHU Bordeaux, Bordeaux, France

Objectives & Study: Advanced glycation end-products (AGE) accumulate in the tissues with the age and are considered as long-term metabolic memory. Normal values have been published in adults and in children above the age of 18 months. AGE are increased by smoking and chronic disease as diabetes, chronic renal failure, and liver cirrhosis. The aim of this study was to establish normal values of AGE in the newborn.

Methods: AGE was measured with skin auto-fluorescence (AGE Reader*) in one hundred couple of term neonates and mother on the second day after delivery. Several measurements were performed on the arm and on the leg, and reproducibility of AGE measurement was assessed with the intra-classe correlation coefficient (ICC).

Results: Mean AGE was 1.9 ± 0.3 UA in mothers, and 1.37 ± 0.31 UA in neonates. Newborn AGE was positively correlated (r=0.20) with mother AGE (p<0.01). Body mass index and smoking in the mother, and sex and bilirubin in the newborn did not influence AGE in the newborn. ICC was 0.45 [0.28-0.59] when AGE was measured on the arm and 0.16 [0.02-0.33] on the leg.

Conclusion: AGE measured with skin auto-fluorescence in the term neonate is positively correlated to AGE of the mother. Reproducibility of AGE measurement was better when measured on the arm as compared to the leg.

Disclosure of Interest: None Declared
Objectives & Study: Alkylglycerols (AKGs) are ether-linked glycerols mainly derived from shark liver oil, and they include such substances as batyl alcohol, chimyl alcohol and selachyl alcohol. AKGs are also synthesized in normal human, and women need to make more AKGs during lactation to meet the requirement of infant development. This study is to explore the AKGs contents and their variations in the breast milk samples of Chinese breastfeeding women. In our earlier study, we’ve found that some AKG compounds can modulate immune responses in vitro by boosting the proliferation and maturation of murine lymphocytes.

Methods: Milk samples from 10 Chinese breastfeeding women on lactation week (LW) 1, 2, 3, 4, 8, 12, 16, 20 and 24 were collected. Samples were extracted with 12 volumes of a mixture of chloroform-methanol mixture (2:1 v/v). The solvents were then evaporated from the lipid extract and the residue was dried under a stream of nitrogen. The lipid fraction was saponified in 10ml 1M KOH in methanol at 80 for 3 h. The non-saponifiable material was extracted into 8ml petroleum ether, and repeated three times. The organic phase was washed by water until the PH reached 7, and was evaporated under reduced pressure. The non-saponifiable material was then converted to their substituted derivatives by silanization, and submitted to GC-MS.

Results: The concentration of batyl alcohol in breast-milk decreased gradually from 17.31ppm down to 11.14ppm during LW1-24, while chimyl alcohol decreased gradually from 14.95ppm down to 9.68ppm. The selachyl alcohol concentration fluctuates between 4.64ppm and 3.86ppm during LW1-24. It was found the AKGs contents in Chinese breastfeeding women were lower than those in Western women based on previous literature. However, no detectable level of AKGs was found in some infant formula samples.

Conclusion: AKGs exist in the breast-milk of Chinese breastfeeding women. The level seems to diminish during the course of lactation, and it will be necessary to analyze the AKGs level in larger population. The biological role and function of AKGs in infant immune development deserve to be further explored.

Disclosure of Interest: L. Qian Grant / Research Support for: This work was supported by Meadjohnson nutrition, Y. Zhong Employee of: Zhong Yan is the employee of Mead Johnson Nutrition, E. van Tol Employee of: Eric van Tol is the employee of Mead Johnson Nutrition, W. Cai: None Declared
FORMULA FEEDING INFLUENCES TASTE SENSITIVITY AND FOOD PREFERENCES IN CHILDREN WITH COW MILK ALLERGY

Andrea Smarrazzo 1, Rita Nocerino 1, Roberto Berni Canani 1, Ludovica Leone 1, Anna Coruzzo 1, Rossella Negri 1, Luigi Greco 1

1Department of Translational Medical Science-Paediatric Section and European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy

Objectives & Study: Early flavor experiences can modulate innate feeding behaviour influencing food acceptance. We hypothesized that in children with cow’s milk allergy (CMA) the use of hypoallergenic formulas or soy formula could modulate bitter taste perception. Sensitivity to bitterness is mostly controlled by the two main haplotypes of TAS2R38 receptor (PAV-taster, AVI- non taster) that mediate the responsivity to the sulphur compound 6-propyl-2-thiouracil (PROP). Effects of early exposure to different flavour experiences on innate taste sensitivity was comparatively evaluated in patients with CMA and in healthy breast-fed subjects.

Methods: Bitter perception was assessed by PROP sensitivity in children aged from 1 to 6 years who received for at least 6 months: soy or hypoallergenic formulas (Group 1); breast milk (Group 2). Allelic variations in the bitter taste receptor TAS2R38 were determined on genomic DNA collected from saliva.

Results: In Group 1, 46 subjects (30 male; mean age 3 years ± 20 months) were evaluated. They received an average of 26 months a diet therapy with soy- (n=10) or hydrolyzed rice- (n= 12) or extensively hydrolyzed casein- (n=18) or amino acid-based formula (n=6). In Group 2 we evaluated 57 healthy children who received breast milk for a median period of 8 months (29 male; mean age 4 years ± 21 months). The “non taster” hyposensitive phenotype was more frequent in Group 1 (47.8% vs 29.6%, p<0.05), although there was not statistically significant differences in the TAS2R38 genotypes. The effect was formula-type-related, with a higher effect associated to the use of amino acid-based formula.

Conclusion: Our data suggest that feeding during infancy influences the innate taste sensitivity phenotype. The type of formula used for CMA treatment affects taste sensitivity. Children fed with amino acid-based formula are more frequently bitter insensitive than those fed with other formulas.

Disclosure of Interest: None Declared
ENERGY INTAKE IN THE FIRST TWO YEARS OF LIFE ON BODY WEIGHT AT 24 MONTHS

Gerd Schütze 1, Martina Weber 1, Dariusz Gruszfeld 2, Anna Stolarczyk 2, Annick Xhonneux 3, Veronica Luque 4, Natalia Ferre 5, Berthold Koletzko 1, Veit Grote 1,* and European Childhood Obesity Project

1Dr. von Hauner Children’s Hospital, Univ. of Munich Medical Centre, Munich, Germany, 2Department of Gastroenterology, Children’s Memorial Health Institute, Warsaw, Poland, 3CHC St Vincent, Liège-Rocourt, Belgium, 4Universitat Rovira i Virgili, Reus, 5Universitat Rovira i Virgili, Tarragona, Spain

Objectives & Study: Rapid weight gain in the first two years of life has been shown to be a risk factor for overweight in later childhood. In this context the role of energy intake in infants is not well investigated. The objective of this study was to analyze the influence of energy intake in the first 24 months on body weight at 24 months.

Methods: Eight-hundred fifty-two, term and formula-fed infants of a multicenter prospective European study were analyzed. Energy intake was determined by three day weighed food records at the age of 3, 6, 12 and 24 months. Weight and length were measured at the same time. Weight was expressed as weight-for-length z-score (WFL) based on the 2006 World Health Organization growth standards. Statistical analysis was carried out using linear regression and life course plots. Furthermore, we categorized children into quartiles of energy intake at 3 months (high energy intake: 4th quartile; low energy intake: 1st quartile) and into overweight and normal weight children (overweight: z score WFL at 24 months > 1.65; normal weight: WFL ≤ 1.65).

Results: Energy intake at 3 months of age was significantly affected by country, gender, gestational age, number of meals per day and time of introduction of solid foods. The effect of energy intake on WFL at 24 months decreased from three to 24 months of age, with the strongest effect at 3 months of age. Each 100 kcal per day increase in energy intake at 3 months was associated with an increase in weight-for-length z-score at 24 months of 0.12 (0.05, 0.19, p = 0.001). In children with high energy intake at 3 months WFL at 24 months was 0.28 (0.09, 0.48; p < 0.001) higher than in children with low energy intake. Accordingly, overweight children at 24 months consumed at the age of 3 months 35 (95% CI 4, 66; p=0.027) calories per day more than normal-weight children after adjustment for WFL at 3 months.

Conclusion: Energy intake in early infancy has a stronger impact on early weight gain than at later time points. In formula-fed infants energy intake at the age of 3 months significantly influences body weight at 24 months of age.

Disclosure of Interest: None Declared
REGISTRATION OF CHILDREN WITH INTESTINAL FAILURE IN THE NETHERLANDS

Esther Neelis 1, Merit Tabbers 2, Gerard Damen 3, Hankje Escher 4, Edmond Rings 4,*

1Paediatrics, Beatrix Children's Hospital, University Medical Center, Groningen, Netherlands, 2Paediatrics, Emma Children's Hospital Academic Medical Center, Amsterdam, Netherlands, 3Paediatrics, Radboud University Medical Center, Nijmegen, Netherlands, 4Paediatrics, Erasmus MC-Sophia Children's Hospital, Rotterdam, Netherlands

Objectives & Study: Intestinal failure is characterised by inadequate absorption of food to maintain function and integrity of the body. Causes of intestinal failure are classified as anatomical (short bowel syndrome) or functional (motility disorder or enteropathy). Children with intestinal failure are dependent on parenteral nutrition (PN) to survive, which can be provided at home (HPN). When HPN fails, due to for example parenteral nutrition-associated liver disease or loss of vascular access, intestinal transplantation (ITx) is indicated. Both therapies, however, are associated with frequent complications and cause substantial morbidity and mortality. To date, no exact information on children with intestinal failure on HPN or after ITx in the Netherlands is available.

Methods: Therefore, the Dutch working group for Intestinal Failure developed the web-based Dutch Registry of Intestinal Failure and Intestinal Transplantation (DRIFT), in order to monitor individual patients and facilitate multidisciplinary treatment between HPN centers and the ITx center. Demographic and clinical data of all children were registered on January 1, 2013.

Results: HPN is provided by the three tertiary HPN centres for children, located in Amsterdam, Nijmegen and Rotterdam. In total, 37 children (23 boys and 14 girls) with intestinal failure were receiving HPN on January 1, 2013, resulting in a point prevalence of 9.56/million. Underlying diseases were motility disorder (n = 17, 46%), short bowel syndrome (n = 14, 38%) or enteropathy (n = 6, 16%). PN had been started within the age of 1 year in 28 children. The median age of the other 9 children was 5.17 years (range 2.42 - 11.97). The median duration on PN was 3.05 years (range 0.35 - 11.97). The median duration on PN for motility disorder was 3.82 (range 0.35 - 11.97), for short bowel syndrome 2.62 (range 0.36 - 9.46) and for enteropathy 3.04 years (range 1.55 - 8.88). Since 2001, 5 children (4 boys and 1 girl) have had ITx in the Netherlands. Three children received an isolated small bowel transplant and 2 children a combined intestinal, colon, pancreas and liver transplant. The underlying diseases were enteropathy (n = 3), short bowel syndrome (n = 1) and motility disorder (n = 1). On January 1, 2013, 4 children (80%) were alive after ITx. Two children (40%) had explantation of the transplant because of rejection and were again dependent on HPN.

Conclusion: This nationwide registry (DRIFT) revealed an up-to-date prevalence and registration of children with intestinal failure on HPN and after ITx in the Netherlands, thereby supporting multidisciplinary care and decision-making.

Disclosure of Interest: None Declared
A META-ANALYSIS ON SAFETY OF SOY-BASED INFANT FORMULA IN CHILDREN

Yvan Vandenplas 1,*, Pedro Gutierrez Castrellon 2, Pedro Alarcon 3

1Paediatrics, UZ BRUSSEL, Brussels, Belgium, 2Instituto Nacional de Perinatologia, Hospital General “Dr. Manuel Gea Gonzalez”, Facultad de Medicina, Universidad La Salle, Mexico, 3National Institute of Child Health, Lima, Peru

Objectives & Study: To conduct a systematic review and meta-analysis with all available evidence related to the safety of soy-based infant formulas (SBIFs) in children in order to evaluate their effect on bone development, immunity, cognitive development, reproductive and endocrine functions, and growth.

Methods: Databases searched included: PubMed (up to July 2013); Embase (up to May 2013), LILACS (up to May 2011), ARTEMISA (up to December 2012), Cochrane controlled trials register, Bandolier and DARE using Cochrane methodology. Our review included cross-sectional, case-control, cohort studies or clinical trials performed in children up to 18 years of age; in which a SBIF was used in at least one arm, compared with other types of infant formula and which measured any safety parameters.

Results: Children fed SBIFs showed comparable patterns of anthropometric growth when compared to children fed cow’s milk-based formulas (CMBIF) or human milk (HM). Higher levels of phytates and aluminum in SBIFs did not show any negative impact on serum levels of hemoglobin, proteins, zinc, calcium or bone mineralization when compared to children fed either CMBIFs or HM. Also, we did not find statistically significant evidence of a negative effect of SBIFs on reproductive, endocrine, immune and cognition measurements of SBIF (Fig 1).

Image:

Conclusion: Our evidence-based analysis showed that modern SBIFs are safe for children. In fact, our evaluation showed that children fed SBIFs exhibited growth, immune, reproductive, endocrine and bone developments similar to those children fed either CMBIFs or HM.
Disclosure of Interest: Y. Vandenplas Consultant for: Biocodex and United Pharmaceuticals, P. Gutierrez Castrellon: None Declared, P. Alarcon: None Declared
Nutrition
Observational and Epidemiological Studies
PO-N-0290

TOLERANCE IN A PAEDIATRIC POPULATION TO A FORMULA FOR CHRONIC KIDNEY DISEASE DESIGNED FOR ADULT PATIENTS

Ana Moráis 1,*, Héctor Ruiz 1, Rosa A Lama 1, Ángel Alonso 2, Carlota Fernández 2, Laura Espinosa 2
1Paediatric Nutrition Unit, 2Paediatric Nephrology, Hospital Universitario La Paz, Madrid, Spain

Objectives & Study: There is currently no specific nutritional supplement available designed for children with chronic renal failure, apart from diets designed for infants. The aim of this study was to analyse clinical tolerance and safety in children of a formula designed for adult patients with chronic kidney disease.

Methods: Children with chronic kidney disease under conservative treatment and sent for nutritional counseling were studied. Inclusion criteria were: metabolic stability, controlled blood pressure and absence of intercurrent disease in the previous 30 days. Monthly nutritional assessment and control of digestive tolerance was performed during 3 consecutive months. Z-score for weight, height and body mass index (BMI), Waterlow index (WI) for weight and phosphorus and potassium levels were assessed, as well as the presence of vomiting related to formula intake.

Results: 40 children (23 male) were included. Mean age 5.8±3.98 years (1.16-16.0 years). The specific formula accounted for 28±15.4% of the energy intake. Formula administration was interrupted in 4 patients: 3 (7%) due to daily vomiting and 1 due to difficulties for drinking the whole recommended amount. No changes in phosphorus or potassium levels were observed.

-Initial assessment (mean and range): z-weight -1.3 (-1.82, -0.7); z-height -1.0 (-1.95, +0.08); WI 87% (78-96). Percentage of energy requirements satisfied by oral intake before supplementation: 88% (72.6-109.32).

-Final assessment: z-weight -1.0 (-1.7, -0.6); WI 91.3% (76-100). Percentage of energy requirements satisfied by oral intake (diet+supplement): 95% (80-109%).

Conclusion: - The formula was well tolerated by most patients, even by the youngest ones (<2 years).
- It was possible to use the formula as a supplement in children with chronic kidney disease under 6 years of age, without increasing phosphorus and potassium levels.

Disclosure of Interest: None Declared
ADOLESCENTS AND CAFFEINE CONTAINING BEVERAGES: TO TAKE OR NOT TO TAKE ENERGY DRINKS?
Rosa Lapolla 1,*, Barbara Santangelo 1, Nicola D’Altilia 1, Roberta Merla 1, Filippo Di Ninno 1, Ilaria Pizzolorusso 1, Massimo Pettoello-Mantovani 1, Angelo Campanozzi 1
1Paediatrics, University of Foggia, Italy, Foggia, Italy

Objectives & Study: Energy Drinks (EDs) are beverages marketed to improve energy, weight loss, attention, athletic performance, and concentration. Caffeine is the main active ingredient in EDs; many of them contain 70 to 80 mg of caffeine for a 33 cl serving. Heavy caffeine consumption, such as drinking EDs, has been associated with serious consequences such as seizures, mania, stroke, and sudden death. Adolescent’s and child’s caffeine consumption should not exceed 100 mg/day and 2.5 mg/kg/day, respectively. The daily caffeine’s intake should take account of all sources of this substance (coffee, tea, soft and energy drinks).

OBJECTIVE: 1) To investigate the extent of energy drink consumption in adolescents; 2) to understand the reasons why teens’ consumption is widespread; 3) to estimate the amount of daily caffeine taken from coffee and beverages containing caffeine (including EDs).

Methods: A self-report questionnaire related to EDs’ consumption has been developed and then proposed to 1232 students aged 12-19 years old (mean age 14.8 ± 3.8). The data have been collected and then analyzed.

Results: According to our surveys, EDs are consumed by 378/1232 (30.7%) of subjects; among them 27/378 (7.1%) drink these beverages 1 time/day at least, 122/378 (32.3%) 1-2 times/week and 179/378 (47.3%) 1-2 times/month. Most of them, 341/378 (90.2%) admit to consume EDs for the flavour, 147/378 (38.9%) find them refreshing, 68/378 (18%) and 39/378 (10.3%) declare to achieve an improvement in sports performance and intellectual activity, respectively. 270/378 (71.4%) of participants declare to consume these beverages when outside, 106/378 (28%) at meals, 74/378 (19.6%) in front of TV/PC, only 39/378 (10.3%) at school and 38/378 (10%) during or after physical exercise. We have also evaluated the amount (in mg) of caffeine (from coffee and caffeinated beverages) taken daily. Among consumers of caffeine (891/1232 – 72.3%), 495/891 (55.5%) consume less than the daily maximum level allowed, 265/891 (29.7%) consume between 100 and 200 mg/day of caffeine and 131/891 (14.7%) exceed the maximum dose, consuming daily more than 200 mg and up to 300 mg/day.

Conclusion: Our data show that, among a pediatric population consuming caffeine, 396/891 of subjects (44.4%) exceeded the maximum recommended dose. Pediatricians should be aware of the possible effects of EDs and screen for their consumption to educate children and their families to decrease or eliminate the inappropriate use of these beverages.

- Committee on nutrition and council on sports medicine and fitness. Clinical Report- Sport drinks and energy drinks for children and adolescents: are they appropriate? Pediatrics 2011; 127(6): 1182-9

Disclosure of Interest: None Declared
MATERNAL AND NEONATAL VITAMIN B12 DEFICIENCY DETECTED BY EXPANDED NEWBORN SCREENING

Juliana Serrano-Nieto 1, Raquel Yahyaoui Macías 2, Javier Blasco Alonso 1, Inmaculada Rueda Fernandez 2, Victor Manuel Navas López 1, Francisco Girón 1, Carlos Sierra Salinas 1

1Paediatric Gastroenterology, Hepatology and Nutrition, 2Clinical Laboratory, Hospital Materno Infantil Carlos Haya, Málaga, Spain

Objectives & Study: Vitamin B12 deficiency in newborns and infants can result in anemia, failure to thrive and neurological impairment. We describe the diagnosis, treatment and follow up of newborn cobalamin deficiency cases secondary to maternal deficient status during pregnancy, detected by the implementation of expanded newborn screening program.

Methods: Amino acid and acylcarnitine levels were determined from single dried blood-spot samples using tandem mass spectrometry (MS/MS). Between April 1, 2010 and October 31, 2013, a total of 137320 newborns were screened. A new sample was requested if there was an increase in propionyl carnitine -C3- (> 3.97 µmol/L) and/or propionyl carnitine/Acetylcarnitine ratio -C3/C2- (>0.2). All cases with persistently high levels and their mothers underwent further laboratory testing. Complete blood count test (CBC), plasma vitamin B12, serum homocysteine (tHcy), folate, plasma acylcarnitines and urinary organic acids, including methylmalonic acid (MMA) were determined in the newborns. CBC, vitamin B12, tHcy, folate and intrinsic factor and parietal cell antibodies were evaluated in the mothers. Vitamin B12 level < 211 pg/ml (= 156 pmol/L) and/or tHcy > 10 µmol/L and or urinary MMA > 11 mmol/mol creatinine were considered as cobalamin deficiency.

Results: Of 36 newborns with persistent increased C3 levels or C3/C2 ratio identified by MS/MS, 25 had vitamin B12 deficiency secondary to maternal vitamin B12 deficiency (18 /100000 newborns). Levels (given as median and interquartile range) of vitamin B12 were 289 pg/ml (157-436), tHcy 15.2 µmol/L (10.8-24.5) and urinary MMA 46 mmol/mol creat (27-89). Seventeen of the 25 were exclusively breast fed. Just one newborn was symptomatic (poor sucking and failure to thrive), presenting a quick and remarkable response to treatment. Fifteen of the 25 were treated. Several regimes were used, most of infants receiving from 8 to 12 orally doses of 1000 µg of cyanocobalamin within one to two months time. Ten of the 25 mothers had vitamin B12 supplements during pregnancy (2 µg/day), but just 3 of them continued during breast feeding. None of the mothers were vegetarian and just one of them had previously known risk factors (bariatric surgery). Pernicious anemia, unrecognized condition before the study protocol, was diagnosed in nine mothers.

Conclusion: Although it is not a primary target of newborn screening programs, the identification of newborn and maternal cobalamin deficiency could be an additional advantage. The limited sample size does not allow generalization, but the high frequency of B12 deficiency among our population leads us to hypothesize that evaluation of vitamin B12 status and/or supplementation during pregnancy should be considered.

Disclosure of Interest: None Declared
Nutrition
Observational and Epidemiological Studies
PO-N-0293

RELATIVE COST-EFFECTIVENESS OF AN EXTENSIVELY HYDROLYZED CASEIN FORMULA PLUS THE PROBIOTIC LACTOBACILLUS RHAMNOSUS GG IN THE MANAGEMENT OF INFANTS WITH COW'S MILK ALLERGY IN ITALY
Julian F Guest 1, 2,*, Monica Panca 1
1Catalyst Health Economics Consultants, Northwood, 2King's College, London, United Kingdom

Objectives & Study: To estimate the cost-effectiveness of using an extensively hydrolyzed casein formula plus the probiotic Lactobacillus rhamnosus GG (eHCF plus LGG) as a first-line management for cow's milk allergy (CMA) compared with eHCF, soy-based formulae, hydrolysed rice formulae or amino acid formulae (AAF) in Italy, from the perspective of the National Health Service (SSN) and from parents.

Methods: A decision model was constructed depicting the management of infants with CMA who are managed first-line with each formula over a period of 18 months. The model was populated with data from a previously published clinical trial [1] and estimates of healthcare resource use derived from interviews with Italian paediatricians. The model estimated the probability of infants acquiring tolerance to CMA by 18 months and the cost of (1) healthcare resource use funded by the SSN and (2) formulae paid by parents over 18 months from the start of feeding with a formula at 2012/2013 prices. The model also estimated the relative cost-effectiveness of each of the formulae.

Results: The probability of acquiring tolerance to cow's milk by 18 months was higher among infants fed eHCF plus LGG compared to those fed eHCF, soy, rice or AAF (Table 1). Similarly, the 18-months SSN cost of managing these infants was lower among those fed eHCF plus LGG as was the cost incurred by parents for formulae (Table 1). Sensitivity analyses showed the model to be robust to plausible changes in the model’s inputs.

Table 1: Cost and outcomes over 18 months associated with feeding CMA infants with eHCF plus LGG, eHCF, soy, rice or AAF.

<table>
<thead>
<tr>
<th>Formula</th>
<th>IgE-mediated CMA</th>
<th>Non-IgE-mediated CMA</th>
<th>18-months SSN cost per infant</th>
<th>18-months parental cost for formulae per infant</th>
</tr>
</thead>
<tbody>
<tr>
<td>eHCF plus LGG</td>
<td>0.66</td>
<td>0.94</td>
<td>€224</td>
<td>€2,178</td>
</tr>
<tr>
<td>eHCF</td>
<td>0.36</td>
<td>0.73</td>
<td>€251</td>
<td>€2,643</td>
</tr>
<tr>
<td>Soy</td>
<td>0.19</td>
<td>0.42</td>
<td>€261</td>
<td>€2,223</td>
</tr>
<tr>
<td>Rice</td>
<td>0.12</td>
<td>0.66</td>
<td>€267</td>
<td>€2,353</td>
</tr>
<tr>
<td>AAF</td>
<td>0.00</td>
<td>0.43</td>
<td>€272</td>
<td>€4,745</td>
</tr>
</tbody>
</table>

Conclusion: First-line management of newly-diagnosed infants with CMA with eHCF plus LGG instead of the other formulae improves outcome and affords a cost-effective use of publicly funded resources and is cost-effective from parents’ perspective. Hence, eHCF plus LGG is the preferred first-line formula in newly-diagnosed infants compared to the other dietetic choices.


Disclosure of Interest: J. Guest Grant / Research Support for: Mead Johnson Nutrition, M. Panca Grant / Research Support for: Mead Johnson Nutrition
**Nutrition**

**Observational and Epidemiological Studies**

PO-N-0294

**COST AND OUTCOME OF THE BELGIAN PAEDIATRIC PATIENTS COHORT REQUIRING HOME PARENTERAL NUTRITION**

Isabelle Scheers^1^, Ilse Hoffmann^2^, Patrick Schlesser^3^, Els Van de Vijver^4^, Myriam Van Winckel^5^, Dominique Hermans^6^

^1^Paediatric Gastroenterology, Hepatology and Nutrition, Cliniques Universitaires St-Luc / Université Catholique De Louvain, Brussels, Belgium, ^2^Paediatric Gastroenterology Unit, University Hospitals Leuven, Katholieke Universiteit Leuven, Leuven, Belgium, ^3^Paediatric Unit, Clinique De l’Esperance, Liege, ^4^Paediatric Gastroenterology Unit, University Hospital Antwerp, Antwerp, Belgium, ^5^Paediatric Gastroenterology Unit, University Hospital Ghent, Ghent, Belgium, ^6^Paediatric Unit, Cliniques Universitaires St-Luc, Brussels, Belgium

**Objectives & Study:** The Belgian convention for pediatric home parenteral nutrition (HPN) was created 3 years ago between five specialized centers and the national health insurance system. The primary aims of this convention was to financially support the costs of the multidisciplinary medical team and the training of parents and home caregivers regarding catheter care. The aims of this study were to report the costs related to this program and review the complication rates including eventual patient mortality.

**Methods:** Data were retrospectively collected from medical records of 39 pediatric patients requiring long-term total or partial HPN between September 2009-2012. All children received cyclical HPN and parents underwent regular training for adequate catheter care. Catheters were locked with either physiologic water or diluted heparin. The assessed outcome parameters included the number of catheter infections, mechanic dysfunction or thrombosis. Furthermore metabolic and hepatic complications and eventual mortality were recorded.

**Results:** 39 children were included in the study. The patients age ranged between 6 mo and 17 yrs (mean 6.7 yrs, median 3.8 yrs), with a sex ratio of 1.4 (M/F). HPN was administrated for nutritional management in following disorders: 23/39 (59%) presented short bowel syndrome (related to laparoschisis in 3 cases, intestinal atresia in 9, enterocolitis in 9 and extensive Hirschsprung disease in 2), 6/39 (15%) intestinal motility disorders and 10/39 (26%) for enteropathy. The mean number of catheter infections per 1000 catheter days was 1.2 and the mean number of catheter changes per 1000 catheter days was 1.2. Their were no hepatic or metabolic complications or mortality recorded during the study period. Fourteen children could be weaned from HPN during the follow-up period. The mean total cost of the program per year represented 80,895 euros.

**Conclusion:** The prevalence of HPN in Belgium is low compared to other European countries. The number of recorded catheter infections in our cohort was 1.2 infections/1000 catheter days, which stands in the lower part of the reported pediatric series published in the literature (ranges between 0.8 and 9.9/1000 catheter-days). and this without the use of antibiotic or chemical locks. The cost for the Belgian government is limited. These parameters indicate the benefit of a targeted aid program towards a reduced number of multidisciplinary caregivers programs operating in chosen expert-centers.

**Disclosure of Interest:** None Declared
Nutrition

Observational and Epidemiological Studies

PO-N-0295

NUTRITIONAL ASSESSMENT IN PAEDIATRIC IBD, ONE YEAR FOLLOW UP STUDY

Corina Hartman 1, 2,*, Dana Reznik 3, Keren Davidson 3, Luba Marderfeld 3, Noa Shitrit 3, Neta Biran 3, Yoram Rosenbach 1, Ari Silbermintz 1, Noam Zevit 1, Rivka Shapiro 1, 2, Yael Mozer- Glazberg 1, Firas Rinawi 1, Hava Flysheker 1, Raanan Shamir 1, 2

1Institute of Gastroenterology, Nutrition and Liver diseases, Schneider Children's Medical Center of Israel, Petah Tikva, Israel, 2Sackler School of Medicine, Tel Aviv University, Tel Aviv, Israel, 3Dietetic Service, Schneider Children's Medical Center of Israel, Petah Tikva, Israel

Objectives & Study: Assessment of nutritional status in a cohort of children with inflammatory bowel disease (IBD) during a one year follow up.

Methods: Children with Crohn’s disease (CD) or Ulcerative colitis (UC) underwent thoroughly nutritional assessment including anthropometry and dietary assessment at enrolment and after 6 and 12 months. Resting energy expenditure (REE) was also assessed. Disease activity using PCDAI or PUCAI was assessed at each visit. Statistical association tests analysed relationships between anthropometry variables and disease activity during follow up.

Results: This prospective study included 90 patients, 58/90 with CD, 32 with UC, mean age 14.3±3.7 years, 35 female. According to PCDAI/PUCAI score, 42% were in remission and 68% had moderate to severe disease activity at study entry. At 6 and 12 months 37% and 55% of participants were in remission, respectively. Immunosupressive or biologic agents were prescribed to 60% of patients at the first visit, 68% and 62% at the 6 and 12 months visits, respectively. Mean dietary intake was 78±26% of RDA for the all group and did not differ significantly between patients in remission or patients with active disease. Enteral formula supplements were taken by 31% of children at the first visit, but only by 20% and 18 at the 6 and 12 months visits. At the first study visit, SDS weight, height and body mass index (BMI) visit were -0.54±1.47, -0.46±1.0 and -0.28±1.17 respectively and were not significantly different when compared to 6 and 12 months visits. Mean SFT and MUAC percentiles were 46.1±32.7 and 42.7±31.6 at the first visit and not significantly different between first, 6 and 12 months visits. REE was measured in 26 children with CD. Average values for measured and calculated REE were not statistically different. However, for each patient, the differences between measured and calculated REE were up to 30-40% up or downward. There were no correlations between REE and disease activity or anthropometry at any of the 3 study visits.

Conclusion: This group of paediatric patients with IBD had relatively preserved good nutritional status during the study period. Disease activity was not correlated with anthropometric indices. Measuring REE in individuals with IBD can show up to 30-40% differences and is a better guide for nutrition planning.

Disclosure of Interest: None Declared
SHOULD PREBIOTIC SUPPLEMENTATION BE USED FOR THE PREVENTION OF ACUTE INFECTIOUS DISEASES IN HEALTHY INFANTS AND CHILDREN?

Szimonetta Lohner 1,*, Daniela Küllenberg 2, Gerd Antes 2, Tamás Decsi 1, Joerg J Meerpohl 2
1Department of Paediatrics, University of Pécs, Pécs, Hungary, 2German Cochrane Centre, Department of Medical Biometry and Medical Informatics, University Medical Center Freiburg, Freiburg, Germany

Objectives & Study: To systematically review published data on the role of prebiotics in decreasing the incidence of acute infectious diseases in the pediatric age group.

Methods: The Ovid MEDLINE, Scopus, Web of Science and the Cochrane Library CENTRAL databases were searched for randomized controlled trials investigating the effects of prebiotic supplementation on the incidence of acute respiratory, gastrointestinal or urinary infections in infants and children aged 0 to 18 years. We used pre-defined inclusion/exclusion criteria and applied standard procedures for data extraction, assessment of heterogeneity and risk of bias; meta-analyses were conducted where appropriate.

Results: Five randomized controlled trials investigating 0 to 24 months old infants were included into this review. The pooled estimate for number of infection episodes requiring antibiotic therapy based on three studies revealed significant decrease in the prebiotic as compared to the placebo group (rate ratio [RR]: 0.68; 95% confidence interval [CI]: 0.61-0.77). In one study investigating incidence of any infection as outcome, infants consuming formula supplemented with prebiotics had significantly fewer episodes of any type of infection during the supplementation-observation period as compared to those infants supplemented with placebo (RR: 0.47, 95% CI: 0.32 – 0.68).

No statistically significant differences were found in the incidences of fever episodes, gastrointestinal tract infections and diarrhea, upper respiratory tract infections, otitis media, lower respiratory tract infections or urinary tract infections between the prebiotic supplemented and placebo groups. However, eligible count data from at least three RCTs were available only for the incidence of diarrhea episodes, the other incidences were reported in one or two RCTs, respectively.

Conclusion: 1. Available studies indicate that prebiotics may be effective in decreasing the rate of overall infections and the incidence of bacterial infections in 0 to 24 months old infants. 2. Further studies are required in the 3 to 18 years old age group to answer the question whether prebiotics can be considered for the prevention of acute infectious diseases in older children.

Disclosure of Interest: None Declared
Objectives & Study: We conducted for the fourth year a systematic nutritional assessment survey in hospitalized children. This cross-sectional survey involved five countries using our web-based tool: e-Pinut (www.epinut.fr).

Methods: All children admitted the same week were measured, weighed and their diagnoses (ICD-10) were recorded. Children below the 3rd centile of BMI for age and sex had full diagnostic procedure (clinical and growth charts examinations) according to the 2012 guidelines of the French Society of Paediatrics.

Results: One hundred and thirty-one wards from 62 centres participated in this survey. We analysed 4735 observations, totalizing 1829 patients (52% boys, median age: 3.4 years). Weight for height <-2SD (acute protein energy malnutrition) was found in 14% of the whole population: 50% in Congo (DRC), 24% in Colombia (Co), 13% in Belgium (Be), 12% in France (F) and 8% in Tunisia (Tu). Height for age <-2SD was present in 14% of the children (DRC: 33%, Co: 25%, Be: 16%, F: 11%, Tu: 15%). Children with chronic diseases accounted for 41.3% of children and had a higher rate of protein energy malnutrition (15.9% vs. 12.0%, p=0.01). Protein energy malnutrition was more frequent in gastroenterology (18%), psychiatry (17%), cardiology (16%) and neurology (16%). Mid Upper Arm Circumference (MUAC) was measured in 1446 patients and was significantly lower in children with protein energy malnutrition (-1.6±2.5SD vs. 0±3SD, p<10^-14). Negative likelihood ratio for MUAC was 0.5. Eight percent of children were obese. Seventy-eight percent of the participating centres claimed to use e-Pinut as a tool to develop the awareness of malnutrition within their staff. Fourteen centres claimed having a written procedure for systematic nutritional assessment.

Conclusion: For the fourth consecutive year, a growing number of paediatric wards joined the Paediatric Nutrition Week. For the first time, ICD-10 diagnoses were available for most of the children, ranking gastroenterology on the top of the diseases leading to protein energy malnutrition. MUAC may offer a simple and reliable index of PEM. Next step for 2014 is to widen the initiative as a European awareness nutrition week.

Disclosure of Interest: A. De Luca Grant / Research Support for: Research support from Nutricia, Advanced Medical Nutrition-France, M. Frasquet-Darrieux: None Declared, H. Piloquet: None Declared, V. Colomb: None Declared, M. Fischbach: None Declared, D. Guimber: None Declared, N. Peretti: None Declared, R. Hankard: None Declared
**Nutrition**

*Observational and Epidemiological Studies*

PO-N-0298

**MOTIVATIONS OF MOTHERS GIVING THEIR MILK TO HUMAN MILK BANK**

Hanane Kadi¹, Delphine Lamireau¹, Thierry Lamireau²,*

¹Lactarium, ²Paediatric Gastroenterology and Nutrition, CHU Bordeaux, Bordeaux, France

**Objectives & Study:** Human milk, which is essential for feeding premature neonates, can be obtained via human milk banks. The aim of this study was to assess the motivations of human milk donors.

**Methods:** A questionnaire was proposed by collectors to 214 nursing mothers who were giving milk to a human milk bank. Mothers were aged of 31.4 ± 4.6 years and attended secondary school (85%). Infants, aged of 4.7 months (15 days-25 months), were exclusively breast-feed (88%). Mothers have been given their milk for 3.7 ± 3 months.

**Results:** Main mother’s motivations for giving their milk were: too much milk (30.3%), help babies (27%), will to make donation (25.2%), help premature babies (24.7%). The father was favorable (97.7%). Mothers have been informed of the possibility of making a gift to human milk bank during pregnancy (23.4%) or after delivery (67.3%), by midwives (58%), collectors (15%), acquaintances (8%), internet (6%), brochures (5.6%), or family (5.1%). Mothers found that blood collection for serology was not annoying (92.5%), process of milk donation was very easy (72%) or easy (23.8%) and rarely constraining (3.7%). The majority of mothers (92.5%) declared to be willing to give their milk in case of a future baby.

**Conclusion:** Human milk donation is found to be an easy procedure for the majority of mothers, who are willing to give again in case of a future baby. Information of the population about human milk donation is warranted to allow collection of enough human milk for feeding premature babies.

**Disclosure of Interest:** None Declared
CLINICAL AND VIDEOFLUOROSCOPIC CHARACTERISTICS OF ACUTE DYSPHAGIA IN CHILDREN POST TRAUMATIC BRAIN INJURY
Sergio Pinillos 1,*, Raquel García 1, Silvia Meavilla 1, Alejandra Gutiérrez 1, Natalia Egea 1, Ricard Alcarfaz 2, Vicente Varea 1
1Paediatric Gastroenterology, Hepatology and Nutrition, 2Paediatric Radiology, Hospital Sant Joan de Deu, Barcelona, Spain

Objectives & Study: Traumatic brain injury (TBI) is the most common acquired cause of neurological disability in childhood. Improving medical management has increased survival. Oropharyngeal Dysphagia is common in these patients. The aim is describe clinical and videofluoroscopic characteristics of acute dysphagia in this group of children.

Methods: Retrospective study of children admitted with severe TBI (Glasgow less than 9) from January 2009 to April 2012 in a tertiary hospital (trauma center). Clinical and videofluoroscopic characteristics income and evolution have been collected.

Results: 16 patients, mean age 14 years and 6 months. 9 males. Mean admission Glasgow 7. Drainage of intracranial injury was needed in focal parenchymal lesions in 9. Average 10 days of mechanical ventilation. Average day stay in PICU 21. Average days on nasogastric tube 42. Initial videofluoroscopy (conditions: medical stability, ability to maintain upright position and to follow simple commands), mean day 34: altered (penetration - aspiration airway and pharyngeal residue) in 81% (n = 13, severe = 3, moderate = 6, mild = 7); for solids, liquids or both and in oral phase, pharyngeal phase or both. Initial oral-motor impaired exploration in 12 patients: hypomotility jaw, labial and lingual, oral and pharyngeal residue. Thickeners were required initially in 9 patients, and adapted diet in 13. Oral-motor rehabilitation program in 12. Average hospital stay 56 days. Normalized early videofluoroscopy in 12 and oral-motor alterations were normal in 14 patients after 12 weeks of income.

Conclusion: Incidence of Oropharyngeal Dysphagia in children with severe TBI is high (90%), mostly mild or moderate. Progression is parallel to the neurological outcome, with an early resolution in most cases. Dysphagia is often for solids and liquids, and both efficacy and safety are affected. Management requires an adaptation of diet for solids and liquids and oral-motor rehabilitation.

Disclosure of Interest: None Declared
**Nutrition**

*Observational and Epidemiological Studies*

PO-N-0300

**THE RELATIONSHIP BETWEEN AEROBIC CAPACITY, ACTIVITY ENERGY EXPENDITURE AND BODY COMPOSITION IN OVERWEIGHT AND OBESE CHILDREN**

Huijuan Ruan 1,*, Xuelin Zhao 1, Qingya Tang 1

1Department of Clinical Nutrition, Xinhua Hospital, School of Medicine, Shanghai Jiao Tong University, Shanghai, China

**Objectives & Study:** The aims of this study were to assess the association between (i) aerobic capacity and body composition; and (ii) body composition and activity energy expenditure (AEE) in overweight/obese children aged 9-10 years.

**Methods:** Overweight and obesity were defined according to the World Health Organization (WHO 2007) classification. Body composition were estimated using bioelectrical impedance analysis (BIA). The variables analyzed were body weight, body mass index (BMI), fat-free mass (FFM), fat-free mass index (FFMI) and percentage of body fat (FAT%). Activity energy expenditure (AEE) and aerobic capacity (peak oxygen uptake \( VO_2 \) peak) and oxygen pulse were assessed during a 10-minute cycle ergometer test (50W, 60r/min) by indirect calorimetry. The expired air was measured and analyzed continuously using an automated metabolic system, and the heart rate was monitored and recorded throughout the test.

**Results:** 28 overweight and obese children (age: 9-10 y, BMI: 20.03-24.37 kg/m²) were evaluated. The \( VO_2 \) peak of the boys (n=22) and girls (n=6) were 23.80±4.33 ml/kg/min and 24.12±4.81 ml/kg/min, respectively. Oxygen pulse and FFMI (kg/m²) were correlated (F=0.395, p=0.041), even after controlling for gender and age (F=0.448, p=0.025). The measured AEE/body weight of the boys and girls were 0.11±0.02 kcal/kg/min, and 0.10±0.02 kcal/kg/min, respectively. Measured AEE/body weight was negatively correlated with FAT% (F=-0.587, p=0.003) and positively correlated with \( VO_2 \) peak (F=0.885, P<0.001). However, no statistically significant association was found between AEE/body weight and FFM (F=-0.168, p=0.434).

**Conclusion:** The hypothesis that obesity reduces activity energy expenditure in children is supported. Children with more lean body mass tend to have better aerobic capacity. Aerobic exercise has been shown to prevent weight gain and improve fitness. However, further studies need to be implemented to explore exercise intensity and duration in overweight and obese children, and to formulate recommendations regarding the suitable plan of exercise for obesity.

**Disclosure of Interest:** None Declared
WHATS THE REASONABLE NUTRITION INTERVENTION IN HOSPITALIZED CHILDREN: COMPARED STAMP SCORE AT ADMISSION WITH DISCHARGE

Li Hong 1,*  
Yi Feng 1  
1Clinical Nutrition, Shanghai Children's Medical Center, Shanghai, China

Objectives & Study: To evaluate the impact of reasonable nutritional intervention on clinical outcomes in hospitalized pediatrics.

Methods: In this retrospective cohort study, totally 2930 hospitalized patients (age from 1 month to 18 years) were recruited from March 2013 to June 2013 in Shanghai Children’s Medical Center. Data were collected on the STAMP Score (Screening Tool for Assessment of Malnutrition in Pediatric, STAMP) at admission and discharge, application of parenteral nutrition (PN) and/or enteral nutrition (EN), nosocomial infection, hospital length of stay (LOS), ICU stay and hospitalization expenses. The application of PN and/or EN ordered by Nutrition Support Team (NST) was defined into “nutrition therapy”.

Results: The patients were classified in different groups according to the STAMP score and nutrition therapy: STAMP score≥ 4 (high nutrition risk) at admission without nutrition therapy defined into ‘underfeeding’(n=628), STAMP score<4 (low nutrition risk) at admission with nutrition therapy defined into ‘overfeeding’(n=129), underfeeding and overfeeding defined into ‘unreasonable nutrition intervention group’(n=757 totally); STAMP score≥ 4 (high nutrition risk) at admission with nutrition therapy (n=157), plus STAMP score<4 (low nutrition risk) at admission without nutrition therapy (n=2016) defined into ‘reasonable nutrition intervention group’ (n=2173 totally). The nosocomial infection rate was significantly higher in the unreasonable group than that in the reasonable group; LOS and ICU stay were longer. When discharge, there were 13.6% patients still in ‘high nutrition risk’ (STAMP Score≥ 4) in unreasonable group, higher than that in reasonable group (table 1).

<table>
<thead>
<tr>
<th></th>
<th>reasonable</th>
<th>unreasonable</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient number</td>
<td>2173(74.2%)</td>
<td>757(25.8%)</td>
<td></td>
</tr>
<tr>
<td>LOS</td>
<td>10.23±7.85</td>
<td>11.90±8.54</td>
<td>0.000</td>
</tr>
<tr>
<td>Hospitalized cost(RMB)</td>
<td>21568.82±25692.84</td>
<td>24157.99±27218.19</td>
<td>0.079</td>
</tr>
<tr>
<td>ICU stay</td>
<td>5.68±6.27</td>
<td>6.35±6.10</td>
<td>0.014</td>
</tr>
<tr>
<td>Nosocomial infection</td>
<td>30(1.4%)</td>
<td>26(3.4%)</td>
<td>0.000</td>
</tr>
<tr>
<td>High nutrition risk</td>
<td>39(1.8%)</td>
<td>103(13.6%)</td>
<td>0.000</td>
</tr>
</tbody>
</table>

|                          |  |
|--------------------------|  |
| STAMP≥4 at discharge     |  |

Conclusion: Reasonable nutrition intervention connected with optimal clinical outcomes. However, we should pay attention to that patients in unreasonable (overfeeding or underfeeding) nutrition intervention, because it linked to poor clinical outcomes.

Disclosure of Interest: L. Hong Grant / Research Support for: AFINS, Y. Feng Grant / Research Support for: AFINS
**Nutrition**

**Observational and Epidemiological Studies**

PO-N-0302

**LIVER DAMAGE IN PAEDIATRIC PATIENTS WITH EATING DISORDERS**

Silvia Ghione 1,* Silvia Scardigli 2, Elena Brunori 2, Sandra Maestro 2, Silvano Bertelloni 2, Giuseppe Maggiore 1

1 Department of Clinical and Experimental Medicine University of Pisa, Pisa, Italy
2 IRCCS Stella Maris, University Hospital Santa Chiara, Pisa, Italy

**Objectives & Study:** To investigate: a) the prevalence of evidence of liver damage in pediatric patients with eating disorders (ED); b) risk factors and specific ED diagnoses associated with increased liver enzymes.

**Methods:** A retrospective analysis was performed with review of medical records (age, sex, type eating disorder, hepatic parameters (AST, ALT, γGT), serum electrolytes, abdominal ultrasound, echocardiography and electrocardiography) of 57 paediatric patients admitted to our tertiary centre from December 1998 to October 2008. Diagnosis of ED was made according to the DSM-IV: anorexia nervosa (Restricting Type ANR or Binge Eating/Purging Type ANBE), bulimia nervosa (Purging or Non-purging Type) and eating disorder not otherwise specified (EDNOS). Abnormal aminotransferase serum activity was considered when AST and (or) ALT values were > 2 x the upper limit of normal (N).

**Results:** The majority of patients was girls (55/57, 96%: mean age at admission was 13.5 ± 2.0 years) and BMI 15.9±2.5 kg/m². Forty-two patients (78%) had ANR and twelve (22%) bulimia nervosa or EDNOS. For three patients, the specific diagnosis was missed. Seven patients (12%) presented AST and/or ALT activity > 2 x N) at admission. Comparing patients with (group 1= 7) or without (group 2, n=50) abnormal liver enzymes, the former group had lower BMI [kg/m²]: 14.4 ± 1.8 (SD -3.8±2.2) vs 16.2±2.6 (SD -2.3±1.4); p < 0.05] and showed more ultrasound abnormalities (i.e. liver hyperechogenicity and abdominal fluid) (60 % vs 15%, p <0.05, respectively) then the latter. The two groups don’t differ in term of age at onset of the disease (years 13.1± 2.4 vs 13.6±2.0, p= ns) and age at hospital admission (14.9±2.2 vs 14.8±1.8, p=ns). Hypertransaminasemia was present among AN patients (precisely ANR: 16.7%), while no patients with EDNOS or bulimia nervosa showed increasing of liver enzymes.

**Conclusion:** To our knowledge, this is the first study that evaluated liver function in a large sample of exclusive paediatric patients with ED. Albeit hepatic involvement in ED is not well characterized in its pathophysiology, risk factors and incidence, our data indicate that it is a main finding in young girls with severe ANR, suggesting to perform routine analyses of transaminases in medical evaluation on adolescents with AN.

**Disclosure of Interest:** None Declared
MATERNAL BODY MASS INDEX AND FOOD INTAKE IN SCHOOL-AGED CHILDREN - RESULTS OF THE GINIPLUS AND LISAPLUS STUDIES

Zhengcun Pei 1,2,*, Claudia Flexeder 1, Elaine Fuertes 1,3, Marie Standl 1, Anette Buyken 4, Dietrich Berdel 5, Andrea von Berg 5, Beate Schaaf 6, Sibylle Koletzko 7, Joachim Heinrich 1 on behalf of the GINIplus and LISAplus Study Group

1Helmholtz Zentrum München, 2Ludwig-Maximilians-University, Munich, Germany, 3University of British Columbia, Vancouver, Canada, 4University of Bonn, Bonn, 5Marien-Hospital, Wesel, Germany, 6Medical Practice for Paediatrics, Bad Honnef, Germany, 7Dr. von Hauner Children’s Hospital, Munich, Germany

Objective & Study: Maternal body mass index (BMI) is a strong predictor of child BMI. Whether maternal BMI correlates with child food intake is unclear. Using data from two German population based birth cohorts, GINIplus and LISAplus, we investigated the associations between maternal BMI and the intake of eleven food groups in school-aged children.

Methods: Energy and food intake from 3230 participants were derived from parent-completed food frequency questionnaires administered to children 10 years old. Seventy-nine food items were clustered into 11 food groups according to the Codex General Standard for Food Additives’ food category system. Food intakes were categorized into three levels (low, medium, high) using group- and sex-specific tertile cut-offs. Maternal BMI was calculated based on weight and height provided by questionnaires. Maternal overweight was defined as having a BMI ≥ 25 kg/m². Linear regression models assessed associations between total energy intake and maternal BMI. Multinomial regression models assessed associations between child food intake with maternal BMI and maternal overweight. Models were adjusted for study region, maternal education, age, sex, pubertal status, energy intake, and BMIs of the child and father.

Results: Overweight was observed in 28.2% of the mothers. For every one-unit increase in maternal BMI, total energy intake in children increased by 9.2 kcal [3.7; 14.7]. However, this effect was not significant after adjustments (4.2 kcal [-1.9; 10.3]). Step-by-step adjustments revealed that the only consistent associations between maternal BMI/being overweight and child food intake were for meat and eggs. Median intake of meat products was 97g per day (33rd and 66th percentile [75; 122]), which corresponds to a median percent energy (%En) of 12.0% [9.7; 14.7]. Median egg intake was 18 g per day ([12; 24], %En = 1.4% [1.0; 1.9]). For every one-unit increase in maternal BMI, the rate of high meat intake in children increased by 1.04 (adjusted rate ratio [95%CI] = 1.04 [1.01; 1.06]). For children whose mothers were overweight, the ratios of medium and high meat intake compared to low intake increased by 1.37 [1.13; 1.66] and 1.53 [1.26; 1.84], respectively. The rates of medium and high egg intake increased by 1.28 [1.06; 1.54] and 1.34 [1.10; 1.62], respectively.

Conclusion: Our results suggest that maternal BMI and maternal overweight are important correlates of a child’s intake of energy, meat and eggs.

Disclosure of Interest: None Declared
IMPACT OF FAT COMPOSITION IN PARENTERAL NUTRITION ON FREQUENCY AND SEVERITY OF CHOLESTATIC LIVER DISEASE IN PRETERM INFANTS: A POPULATION BASED STUDY

Jonas Teng 1,* , Henrik Arnell 1, Kajsa Bohlin 1, Antal Nemeth 1, Björn Fischler 1
1Department of Paediatrics, Karolinska University Hospital, CLINTEC, Karolinska Institutet, Stockholm, Sweden

Objectives & Study: Parenteral nutrition associated liver disease (PNALD) in neonatal intensive care units (NICUs) is common. A relationship to the parenteral lipid emulsion (LE) used has been established. In 2009, all NICUs in Stockholm county replaced the soy oil based LE (Intralipid®) with the mainly olive oil containing (Clinoleic®).

In a population based retrospective study the impact of this nutritional change on cholestasis was studied.

Methods: All preterm infants with a gestational age (GA) <30 weeks in Stockholm County were identified in two populations, born in March 2006 - February 2008 (SOY population) and January 2010 - December 2011 (OLIVE population), respectively. Cholestasis was defined as conjugated serum bilirubin ≥ 30 µmol/L, exceeding 20% of the total, on at least two occasions. Two GA-matched controls were randomized from the corresponding population. Logistic regression analysis on cases and controls using the stepwise forward method was performed to identify independent risk factors for cholestasis.

Results: The two populations were comparable regarding mean birth weight and mean gestational age with small and non-significant differences.

In the SOY population 14.8% (37/250) were cholestatic compared to 12.7% (34/268) in the OLIVE population (p=0.525). Mean duration of cholestasis was 63.2 days in the SOY population and 59.8 days in the OLIVE population (p=0.76). Mean peak conjugated bilirubin was 130.1 µmol/L in the SOY population and 126.6 µmol/L in the OLIVE population (p=0.89). When the cholestatic cases in each population were compared, several significant differences were observed. In the OLIVE population they had significantly lower GA, longer duration of parenteral nutrition, the rate of necrotizing enterocolitis (NEC) was higher whereas fewer were small for gestational age (SGA). Logistic regression analysis on cases and controls identified NEC and duration of parenteral nutrition as highly significant risk factors for cholestasis (all p≤0.01). Belonging to the SOY population was also identified as an independent risk factor for developing cholestasis (p=0.016).

Conclusion: 1. The rate of cholestasis in a population based cohort of preterm infants <30 weeks is as high as 1 out of 7.
2. Neither incidence nor severity of cholestasis differed significantly between the two time periods.
3. However, in a multivariate analysis including a large number of variables, the time period with soy LE was identified as an independent risk factor for cholestasis. This could indicate an impact of the type of LE used.

Disclosure of Interest: J. Teng: None Declared, H. Arnell Conflict with: Consulting services for Baxter and Fresenius-Kabi, K. Bohlin: None Declared, A. Nemeth: None Declared, B. Fischler: None Declared
Objectives & Study: Hepatic fibrosis is one of major complications affecting prognosis of children treated with long-term parenteral nutrition (PN). Liver biopsy is the accepted standard for diagnosing fibrosis but it is an invasive technique with potentially serious complications. Transient elastography (Fibroscan®) is a non-invasive, reproducible method for the assessment of fibrosis that has been recently validated in children. The aim of the present study was to examine the evolution of liver stiffness using Fibroscan® and associated factors in children on home PN.

Methods: Thirty-four patients aged 6 months to 16 years on home PN for 6 to 192 months were included in this prospective multicenter study. At least, 2 liver stiffness measurements using transient elastography were realized every 6 to 30 months. Clinical and biological data were collected at the time (+/- 1 month) of measurement.

Results: Liver stiffness decreased during follow-up in 21 patients (from 7.0 +/- 2.7 kPa to 5.3 +/- 2.4 kPa, p<0.05). Liver stiffness evolution positively correlated to serum alkaline phosphatases (p=0.04) and negatively to haemoglobin blood levels (p=0.05). Elevated alkaline phosphatases and presence of gastrostomy at T0 were significantly associated to increase liver stiffness at follow-up. Controversially, prematurity and liver stiffness >6.1 kPa at T0 were significantly associated to a decrease in liver stiffness at follow-up. Age of onset, duration of PN and short bowel syndrome did not influence evolution of liver stiffness. At T0, fibrosis >6.1 kPa -defining liver fibrosis- was present in only 11 patients (significant fibrosis >7.5 kPa in 7 patients), 8 of them being born prematurely. No patient had cirrhosis. Patients with fibrosis at T0 improved significantly during follow-up (9.0 +/- 1.6 kPa versus 6.8 +/- 2.6 kPa, p<0.05).

Conclusion: Liver stiffness is slightly altered in children treated with home parenteral nutrition even prolonged, and improved usually with time even if PN is continued. Since few clinical and biological data were associated with evolution of stiffness we suggest to routinely monitor liver stiffness in children on long-term PN every year.

Disclosure of Interest: None Declared
USE OF ATM NASAL BRIDLE TO SECURE NASAL FEEDING TUBES IN CHILDREN
Susan Bunn 1,*, Hanaa Marzouk 1, Sarah Cunningham 1, David Derry 1
1Paediatric Gastroenterology, Great North Children's Hospital, Newcastle upon Tyne, United Kingdom

Objectives & Study:
The ATM Bridle™ was developed to secure nasal feeding tubes in confused / agitated adults to prevent inadvertent removal. It has clear application in paediatrics where children, due to young age or neurodisability, frequently remove nasal feeding tubes.

Aim:
To review the early experience in one paediatric centre of the use of ATM Bridle™ to secure nasal feeding tubes.

Methods:

Results:
10 children (8 boys) had 16 nasal bridles inserted for 3 nasogastric tubes (NG) and 13 nasojejunal tubes (NJ). The median age of first nasal bridle insertion was 9.5 months (range 2-169). NG / NJ placement and bridle insertion was performed under GA with endoscopy in 11 (NG=1, NJ=10), with xray screening in 2 (NJ=2) and on ward in 3 (NG=2, NJ=1). 6/10 children had history of frequent NG / NJ removals prior to bridle insertion.

Sizes of feeding tube & nasal bridle were 8 French in 15 and 6 French in 1. Underlying conditions were ex-preterm 2, cardiac surgery 3, neurodisability 2, renal disease 2, food allergy 3, GI dismotility 1. Indications for tube feeding included vomiting in 10 (100%), faltering growth in 9 (90%) and low intake due to feed aversion in 4 (40%).

The median length of time single NG/NJ & bridle in situ was 32 days (range 5 – 144). Three children required more than 1 bridle due to i) long term NJ requirement - NJ & bridle electively changed 4 times each after ~90 days; ii) NJ tube pulled out despite bridle after 5 days due to clip not completely closed – NJ & bridle replaced; iii) NJ blocked after 45 days - NJ & bridle replaced.

Presently 4 still have a NJ & bridle, one is awaiting fundoplication & gastrostomy; one is awaiting PEG with trans-gastrostomy jejunal extension insertion. Of the 6 remaining children who no longer need the bridle, 1/6 have been transitioned from NJ to NG, 2/6 have a PEG, 2/6 (food allergy with feed aversion & severe transient gastroparesis) are now orally fed and 1/6 is on total parenteral nutrition for severe gut dysmotility & attempts at jejunal feeding have been aborted.

There have been no significant complications. One child (as above) removed his NJ despite bridle after 5 days & required repassage. One family requested bridle removal after 56 days as felt nasal tape uncomfortable & child would not now pull out a NG tube secured without bridle.

Conclusion:
The ATM Bridle™ has proven safe & effective in securing short – medium term nasal feeding tubes in children aged from 2 – 169 months. It has proved especially useful in securing of NJ feeding tubes allowing longer term NJ feeding. Experience of insertion and confidence in its effectiveness has seen an increase in applications, most markedly in cardiac & renal conditions where NJ feeding is required for growth but vomiting will often resolve with management of underlying disease.

Disclosure of Interest: None Declared
ASSOCIATION BETWEEN WOMEN’S NUTRITION DURING PREGNANCY AND THE BODY COMPOSITION OF THE OFFSPRING UNTIL 18 MONTHS

Liliana Ladino 1,2,* , Rosario Moreno-Torres 1, Dani Campos 1, Mary-Carmen Baltazar 1,3, Cristina Campoy 1,4 and the PREOBE Research Group

1EURISTIKOS Excellence Centre for Paediatric Research, University of Granada, Granada, Spain,
2Institute of Research in Nutrition, Genetics and Metabolism, El Bosque University, Bogotá, Colombia,
3National Institute of Public Health, Cuernavaca, Mexico, 4Department of Paediatrics, University of Granada, Granada, Spain

Objectives & Study: Evidence shows that maternal nutrition is related to the body composition of the offspring and the potential risk on developing obesity and chronic diseases in adulthood. We aimed to evaluate the associations of nutrition during the third trimester of pregnancy of women with normal weight, overweight, obesity and gestational diabetes, with the evolution of the triceps skinfold thickness (TST), subscapular skinfold thickness (SST) and mid-arm circumference (MAC) between 3 and 18 months of life of the offspring.

Methods: The dietary assessment was performed with 7-day food diary at 34 weeks gestation; macronutrients intake and the percentage of total energy value (%TEV) was analysed using the DIAL program, and as normal intake was considered the DRIs of the Food and Nutrition Board. Anthropometric measurements were obtained according to the WHO standards and Anthro program, at 3, 6, 12 and 18 months of life in the offspring. Multiple linear regression models were used for data analysis. Dependent variables were the ratio of the expected evolution of the TST, SST and MAC, and independent variables were the %TEV of the intake of macronutrients.

Results: Eighty-six mothers and their children were evaluated. We found that a maternal intake during third trimester of pregnancy high in %TEV protein (R= 0.762, b= 0.299, p= 0.000) and high in %TEV carbohydrates (R= 0.761, b= -0.096, p= 0.000) was associated to a less decrease of the offspring TST during the first 18 months of life. In the same way, a maternal intake high in %TEV protein (R= 0.251, b= -0.079, p= 0.001) and high in %TEV carbohydrates (R= 0.234, b= -0.024, p= 0.002) were also related to a less decrease in the offspring SST during the first 12 months of life. Finally, a maternal intake high in %TEV protein (R= 0.307, b= 0.073, p= 0.000) and high in %TEV carbohydrates (R= 0.296, b= 0.022, p= 0.001) was associated to an increased MAC at 18 months of age in their offspring, after confounder adjustment for BMI before and during pregnancy and other confounder factors. The maternal lipids intake does not show association with the evolution of TST, SST and MAC at any moment of the examination.

Conclusion: The minor decrease in TST and SST is associated to the increment of maternal intake in proteins and carbohydrates during the third trimester of pregnancy, but not with mother’s lipid intake before and during pregnancy. These results support the Early Nutrition Programming hypothesis, about how intrauterine exposure to large amounts of glucose and high maternal protein intake during pregnancy could cause changes in the fetus and increase the risk to develop obesity in later stages of life.

*This study was granted by Spanish Ministry of Innovation and Science, Excellence Projects (P06-CTS-02341).

Disclosure of Interest: None Declared
Nutrition
Observational and Epidemiological Studies
PO-N-0308

CLINICAL CHARACTERISTICS OF PATIENTS WITH FEEDING DISORDERS
Aleksandra Rekosz 1, 2, Malgorzata Matuszczyk 1, Ewa Winnicka-Makulec 1, Piotr Socha 1, Anna Rybak 1,*
1Gastroenterology, Hepatology and Feeding Disorders, Children’s Memorial Health Institute, 2Medical University of Warsaw, Warsaw, Poland

Objectives & Study: Feeding disorders (FD), described as food refusal, picky eating or inability to eat, are one of the most common problems, affecting up to 40% of normally developing children and 80% of neurological patients. Some of them require hospitalization and a multidisciplinary care provided by a specially qualified team consisting of pediatrician, nutritionist, psychologist and speech therapist. The aim of the study was to describe the clinical characteristic of patients with severe FD with respect to the underlying disease based on multidisciplinary team’s experience in our hospital, which is a referral center in Poland. Detailed results are presented for patients with behavioral issues, as it is the most common cause of FD.

Methods: Patients with FD (n=356) who were hospitalised between September 2009 and May 2013 were enrolled into the study. Based on the underlying disease, patients were classified into 7 groups: behavioral, neurological, anatomical, gastrological, metabolic, cardio-pulmonary and mixed. The retrospective analysis was made based on age, nutritional status (at admission to the hospital), birth history, presence of gastroesophageal reflux disease (GERD), feeding practices and used therapy.

Results: Complete data were obtained for a total of 284 patients. The count of patients in each of the 7 groups was as follows: 42% behavioral (n=119), 32% neurological (n=91), 8% gastrological (n=24), 5% metabolic (n=15), 3% cardiopulmonary (n=8), 7% anatomical (n=19), 3% mixed (n=8). Groups did not differ with respect to malnutrition. Among children with behavioral issues, 13% had a history of prematurity and 29% were born through caesarian section; 10% were diagnosed with GERD; 78% of the children were 3 years old or younger (mean age= 36 months); 40% of patients were undernourished (BMI <3pc) at the day of admission, 54% of the patients had their BMI between 3-85pc, whereas 56% of them (n=37) had BMI between 3-15pc; 97% of the patients were fed orally, 3% (n=4) were fed both orally and through the nasogastric tube.

Conclusion: Our results show that the most common cause of FD are behavioral problems, which are manifested mostly as picky or fussy eating. The age of patients corresponds with the theory for a neophobic period to start at the age of 1-2 years. The rate of undernourished children is very alarming: 40% were undernourished and 31% were at risk of undernutrition. This indicates that FD are not diagnosed on time and patients are admitted to hospital too late. This also shows the need for improving the diagnostic and therapeutic approach by creating feeding teams in pediatric units.

Disclosure of Interest: None Declared
Nutrition
Observational and Epidemiological Studies
PO-N-0309

COMPARISON OF SURVIVAL TIME OF CENTRAL VENOUS CATHETERS USED TO ADMINISTER PARENTERAL NUTRITION IN HOSPITAL AND AT HOME

Corina Hartman 1,*, Anna Hughes 2, Debra Knapp 2, Donna Forbes-Penfold 3, Jutta Koeglmeier 2, Susan Hill 4

1Gastroenterology, Great Ormond Street Hospital for Children, 2Great Ormond Street Hospital, London, United Kingdom, 3Gastroenterology, Great Ormond Street Hospital, London, United Kingdom, 4Gastroenterology, Great Ormond Street Hospital for Children, London, United Kingdom

Objectives & Study: To compare survival time of central venous catheters (CVC) used for parenteral nutrition (PN) in children when hospitalised and after discharge home. Care at home was by parents who underwent a formal 2-week catheter care and use training programme prior to discharge. Children were given a single lumen catheter that was either a tunnelled, cuffed CVC or a peripherally inserted central line (PICC).

Methods:
Information was obtained from the clinical records of children on treatment with long-term/home PN attending a specialist intestinal rehabilitation clinic on catheter survival time and dates of catheter replacement. Data obtained when the patients were originally treated as in-patients was compared with data following discharge home. Age, sex and underlying diagnosis were recorded.

Results: A total of 56 patients (31 male, 25 female, aged 1.2-19.2 years) were reviewed. Underlying diagnoses were short bowel syndrome (SBS) in 21, enteropathy in 21 and intestinal dysmotility/pseudobstruction in 14. The total number of days reviewed was 96580, median 1117 days (range 175-6540)/patient. Children were hospitalised for a total of 12126 (median 170, range 30-1320) days and required 134 (median 2, range 1-6) catheters i.e. 13 catheters/1000 patient days. When patients were discharged home they were treated for 84454 (median 945, range 141-6474) days. 159 (median 2, range 1-6) catheters were used, i.e. 1.6 catheters/1000 days. Catheter survival time was increased 8-fold when patients were at home.

Conclusion: In children with severe intestinal failure and long-term dependence on PN there was an 8-fold increase in central venous catheter survival time when patients were discharged home from a specialist hospital ward with catheter care administered by formally trained parents. This finding reinforces the practice of sending patients with severe long-term IF home at the earliest opportunity with parents managing the PN infusions. The lower risk of complications requiring catheter change should be associated with achieving maximal intestinal function. Gradual reduction of PN infusion aiming to reduce and stop treatment may be more successful at home.

Disclosure of Interest: None Declared
DIETARY HABITS INFLUENCE ON PUFA COMPOSITION OF BREAST MILK - A COMPARATIVE STUDY ON THE COMPOSITION BETWEEN THE LOCAL WOMEN OF LOWER AND MODERATE SEAFOOD CONSUMPTION IN JAPAN

Yuichiro Yamashiro 1,*, Kyoko Kamiya 2, Masashi Kamiya 2, Hiroshige Ishii 3, Tsuneyo Yamada 3, Yohei Kitamura 4, Takashi Shimizu 4, Satoru Nagata 5

1 Probiotics Research Laboratory, Juntendo University Graduate School Of Medicine, Tokyo, Japan, 2 Kamiya Maternal & Children’s Clinic, Okinawa, 3 Ishii Daiichi Ob. Gy. Clinic, Shizuoka, 4 Morinaga Milk Industry Co., LTD. Nutritional Science Institute, 5 Paediatrics, Tokyo Women's Medical University, Tokyo, Japan

Objectives & Study: Human milk is specially designed for the needs of the human infant. Its nutritional advantages have been noted to be especially important for brain growth, for which docosahexaenoic acid (DHA, 22:6n-3), a n-3 polyunsaturated fatty acid (PUFA) plays a critical role. Recent studies found that breast milk DHA is significantly associated with lower risk of development of obesity and metabolic syndrome. We tested the hypothesis that a local dietary habits would influence PUFA composition of milk of women from two different regions, because only dietary lipid intake reflects in the concentration of the milk among macro nutrients.

Methods: Analysis of PUFA concentration were performed in breast milk providing by 51 lactating healthy women who gave a normal full-term baby birth one month before and a half of them lived in either region of lower or moderate seafood consumption.

Results: Concentrations of n-3 PUFAs of DHA and eicosapentaenoic acid (EPA, 20:5n-3) were significantly lower in breast milk of women in the region of lower seafood consumption, however α-Linolenic acid (ALA, 18:3n-3) and n-6 PUFA, arachidonic acid (AA, 20:4n-6) were not different between the groups. DHA/ AA was higher in breast milk of women in the region of moderate seafood consumption.

Conclusion: Local dietary habits of seafood consumption strongly influence PUFA composition of breast milk. Therefore, strategies such as diet and even supplement of DHA to pregnant and lactating women living in the region of low seafood consumption should be considered to bring benefit of breast feeding for the infants and also for the women.

Disclosure of Interest: None Declared
FEEDING HABITS OF INFANTS AND TODDLERS IN BELGIUM

Koen Huysentruyt 1,*, Annemie Van de Sompel 2, Dorothée Laire 3, Tom Van Avondt 3, Jean De Schepper 1, Yvan Vandenplas 1

1Paediatrics, UZ BRUSSEL, Brussels, Belgium, 2Paediatrics, University Hospital Antwerp, Antwerp, Belgium, 3Ipsos Healthcare, Ipsos, Market Research Agency, Ghent, Belgium

Objectives & Study: To assess the micro- and macronutrient intake of Belgian infants and toddlers and to compare this intake to our national and international recommended dietary intake (RDI).

Methods: 500 mothers completed a diary in which they registered all foods, drinks and supplements consumed by their child (6 - 36 months) during a period of 4 days. Participants were stratified for age of the child, region (North/South), occupation and day of the week for diary completion. Average daily intake per child was calculated for each nutrient. In case of breastfeeding, the estimated amount of mother milk was based on the average daily amount in the corresponding age category.

Results: Our population consisted of 97 (19.4%) 6-12 month-old, 204 (40.8%) 13-24 month-old and 199 (39.8%) 25-36 month-old children. Median daily (Q1; Q3) energy-intake was 93.7 kCal/kg/d (78.0; 114.3) for the whole population, with a strong trend (p=0.05) for a higher intake in girls than in boys (respectively 95 vs 92 kCal/kg/d). The youngest children had a significantly (p=0.04) higher median intake (105.8 kCal/kg/d) than the 1-2 year-olds (98.0 kCal/kg/d) and the oldest children (86.8 kCal/kg/d; p<0.01). Mean (SD) protein intake was between 200 and 300% of the national RDI: 3.3 (1.2) mg/kg/d for the youngest children and 3.5 (1.1) and 3.2 (1.0) mg/kg/d for respectively the 1-2 and the 2-3 year-olds. The mean fat intake was slightly under the norm (30 % of total E-intake for all age groups for a norm of 35%), but median (Q1; Q3) omega-3 and omega-6 intakes were 50% lower than the RDA in children under one year old (respectively 0.25 (0.15; 0.43) g and 1.6 (0.8; 2.7) g) and 20-40% below the RDA for one to three year old. The mean daily intake of dietary fibres (10 g/d) was far below the recommended 15 g/d. Median (Q1; Q3) copper and zinc intake was according to the norms in all age categories. Median (Q1;Q3) iron intake was 6.5 mg (4.5, 9.0) per day (Belgian norm: 3.9 - 6.2 mg/d, European norm: 6-8 mg/d). The recommended Vit. D supplementation was only given in 10% of the population, despite recent national recommendations, and the median (Q1; Q3) Vit. D-intake was especially low in 2-3 year olds (2.9 µg (1.4; 6.4)).

Conclusion: Energy and especially protein intake in Belgian infants and toddlers is very high, whilst the median daily intake of Vit. D, fibers and fatty acids is too low. Preventative intervention campaigns should focus on alerting and informing parents about the long term consequences of obesity in children.

Acknowledgments: This independent research was performed by Ipsos Healthcare Ltd, Ipsos, Market Research Agency, Ghent, Belgium supported by Nutricia BE.

**Nutrition**

*Observational and Epidemiological Studies*

PO-N-0312

**DOES PERORAL NALOXONE IMPROVE POSTOPERATIVE ENTERAL NUTRITION IN CHILDREN AFTER CARDIAC SURGERY?**

Karina Maria Steiner 1,*, Stefan Ring 1, Gerald Wendelin 1, Klaus Pfurtscheller 1, Andrea Deutschmann 1, Almuthe Christine Hauer 1, Siegfried Rödl 1, Gerfried Zobel 1, Karl Martin Hoffmann 1

1Department of Paediatrics and Adolescent Medicine, Medical University Graz, Graz, Austria

**Objectives & Study:** Opioids are frequently used in postoperative pain management. Besides analgesia opioids have potential side effects, especially gastrointestinal paralysis and constipation, which complicates postoperative nutrition. Studies in adults and one small study in pediatric intensive care patients suggest that by using naloxone per os (p.o.), an opioid antagonist with a complete first-pass metabolism in the liver, postoperative enteral nutrition can be improved. Especially in children after heart surgery, postoperative enteral nutrition remains challenging. The aim of this work was to examine the effects of naloxone p.o. on the postoperative nutrition in children after cardiac surgery.

**Methods:** We conducted a retrospective analysis of pediatric patients treated at our intensive care unit after cardiac surgery. Since 2011, patients receiving an analgesic therapy with either fentanyl or dipidolor were treated with naloxone 0.4 mg/kg/day p.o. (divided in 4 single doses). Patients treated with naloxone were compared with a historical control group (matched for age and diagnosis). Clinical outcome parameters were days until full enteral nutrition, until first stool, until extubation, until no gastric residual volume and days until discharge from the hospital. Additionally, we compared cumulative days of parenteral nutrition and cumulative kcal/kg (parenteral, oral and total), oral nutrition (ml/kg) and gastric residual volume (ml/kg). In a subanalysis we studied data of patients who received fentanyl only. After testing for normal distribution Mann-Whitney-U-Test was used (p-value < 0.05).

**Results:** 40 patients (mean age 132 days, 43 % male) were investigated. 20 children received a therapy with naloxone p.o. after cardiac surgery from 2011 to 2013. The 20 control patients were treated at the same intensive care unit after cardiac surgery from 2009 to 2013. There were no differences in gender, age, length, weight and body surface area between the groups. The morphine equivalent was significantly higher in the naloxone group (29.3 vs. 14.25 mg/kg; p = 0.009). There was no statistic difference in the outcome data between the two groups except in the number of days until extubation (8.7 days naloxone group vs. 7.0 days control group, p = 0.02). In the subanalysis of fentanyl-patients (12 patients in each group) there was no significant difference in the parameters analyzed. One naloxone patient had a repeated increase in heart rate in immediate association with the application of naloxone, which was interpreted as a pain break-through caused by naloxone.

**Conclusion:** Peroral naloxone did not improve postoperative nutrition after cardiac surgery in our patient cohort. Currently, it remains doubtful if naloxone p.o. should be recommended for children after heart surgery.

**Disclosure of Interest:** None Declared
Objectives & Study: There is lack of data about reproducibility and reliability of nutritional screening tools (NST) when they are performed by non-expert staff in pediatric patients. The objective of this study was to assess this aspects regarding three NST: Screening Tool for Risk on Nutritional status and Growth (STRONGkids), Screening Tool for the Assessment of Malnutrition in Pediatrics (STAMP) and La Paz Nutritional Screening Tool (CRINUTPAZ).

Methods: Prospective observational multi-centre study in five secondary and tertiary hospitals. During 3 weeks, all patients ≥1 month admitted to pediatric and surgical wards were tested, in the first 24 hours of admission, by two independent observers: expert (doctors or dieticians specialist in pediatric nutrition) and non-expert staff (trained nurses or pediatric residents). Length of stay (LOS) was registered in all cases. Statistics: Kappa index to evaluate the agreement between observers and ANOVA test to assessment the relation between risk scores at admission and LOS.

Results: 223 patients were included (53.4% boys). Median age 5.59±0.32 years. Agreement between expert and non-expert staff was 94.78% for STRONGkids [kappa 0.718 (p<0.001)], 92.55% for STAMP [kappa 0.741 (p<0.001)] and 91.55% for CRINUTPAZ [kappa 0.769 (p<0.001)]. Mean LOS was 4.14±0.27 days. Regardless of whether NST were applied by expert or non-expert staff, high-risk scores were significantly associated with longer LOS.

Conclusion: The agreement between expert and non-expert staff was good. These three NST were useful for detecting patients with longer LOS both in expert and non-expert hands.

Disclosure of Interest: None Declared
THE ASSOCIATION BETWEEN LEPTIN CONCENTRATIONS IN BREAST MILK AND MATERNAL CHARACTERISTICS

Nicholas Andreas 1,*, Matthew Hyde 1, James RC Parkinson 1, Suzan Jeffries 1, Ran Xiong 1, Nicola Fitz-Simon 1, Chris Gale 1, Neena Modi 1
1Neonatal Medicine, Imperial College London, London, United Kingdom

Objectives & Study: The aim of this study was to determine if there was a relationship between leptin concentration in breast milk and key maternal characteristics.

Methods: Thirty seven mothers were recruited from the post-natal ward at Chelsea and Westminster Hospital. Breast milk samples were collected 7 days post-partum and stored at -20°C. 1ml of sample was sonicated using an ultrasound probe prior to analysis. Leptin was measured using commercially available ELISA kits. Concentrations of leptin in breast milk were correlated with maternal data (age, duration of pregnancy, weight and BMI pre-pregnancy, and at time of sample collection). Linear regression was performed in SPSS 20 using log leptin concentrations.

Results: Regression analysis revealed a significant association between leptin and maternal weight (p=0.008, Figure 1), and maternal BMI (p=0.027). Regression analysis revealed a 1.2% increase in leptin concentration per kg increase in maternal weight (95% CI 0.3%, 2%) and a 3.2% increase in leptin concentration per unit increase in maternal BMI (95% CI 0.4%, 6%). No association was observed between leptin and other maternal characteristics (age, duration of pregnancy, pre-pregnancy weight and BMI).

Figure 1. Plot of maternal weight at sample collection (kg) and log leptin concentrations. Line of best fit and 95% CI are also shown.

Conclusion: These data indicate an association between foremilk leptin concentration with maternal weight and BMI, at the time of sample collection. Though the bioactivity of breast milk leptin is unknown, we speculate that this may be part of a feedback mechanism serving to regulate infant milk intake.
Disclosure of Interest: N. Andreas Grant / Research Support for: Westminster Medical School Research Trust, Conflict with: Received support from Medela to attend an educational conference, M. Hyde Conflict with: Received support from Danone International to attend an educational conference, J. Parkinson: None Declared, S. Jeffries: None Declared, R. Xiong: None Declared, N. Fitz-Simon: None Declared, C. Gale Conflict with: Received support from Pfizer Nutrition to attend an educational conference, N. Modi Grant / Research Support for: Medical Research Council, National Institute of Health Research, Westminster Children's Trust Fund, Child Growth Foundation, Action Medical Research, HCA International, Danone, Bliss, British Heart Foundation, and Department of Health, Consultant for: Ferring Pharmaceuticals, Speakers bureau of: Nestle International
Identifying Clinical, Sociological, Economic and Regional Determinants of the Duration of Maternal Breastfeeding

Frederic Huet 1,*, Aurore Tabellion 2, Francois André Allaert 3

1Pediatry Dpt, University Hospital, Dijon, France, 2Medical Dpt, Menarini Laboratory, Paris, France, 3Medical Evaluation Chair, Esc Dijon Cen Nutriment, Dijon, France

Objectives & Study: To evaluate the mean duration of exclusive maternal breastfeeding nationally and regionally in 2012 and to identify its clinical and socio-economic determinants.

Methods: Cross-sectional observational survey in everyday paediatric practice. Each doctor included in the survey the first five mothers attending consultations who wanted or had to discontinue exclusive breastfeeding of her infant. The survey comprised a clinical questionnaire completed by the doctor and a self-administered questionnaire completed by the mother. Determinants favouring a duration of maternal breastfeeding greater than the third quartile (here 4 months) were identified by logistic regression adjusted for the set of socio-economic and clinical characteristics of the mothers.

Results: 747 doctors enrolled 2773 mothers in the study who either wished or were forced to stop exclusive maternal breastfeeding. They were aged 30.6 ± 4.5 years and for 96.1% of them lived with their partners. The decision to breastfeed was made before pregnancy for 68.8% of women, during pregnancy for 25.4% and during birth or in the maternity ward for 2.6% and 2.8% of them respectively. The two main motives for mothers to begin breastfeeding were the infant’s health (95.4%) and mother/child bonding (75.4%). The mean duration of exclusive breastfeeding was 11.3 ± 7.7 weeks (median 9.6 weeks) and varied markedly among regions from 13.8 weeks in Burgundy to 9.9 weeks in Lower Normandy. The main reasons given by mothers for discontinuing were returning to work and/or leaving the infant at a day-nursery or with a nanny (45.6%), tiredness or health problems for the mother (24.6%) and lactation problems (15.8%). The principal determinants of a breastfeeding period exceeding four months were the mother enjoying breastfeeding (OR: 5.2 [2.2; 12.2]; p<0.0001), financial difficulties (OR: 2.8 [1.2; 6.3] p = 0.0142), being aged over 35 years (OR: 2.4 [1.5; 4.0] p = 0.0006), the mother’s ability to breast-feed her baby in a public place (OR: 2.2 [1.8; 2.8] p<0.0001), the mother not going out to work (OR: 2.0 [1.4; 2.8] p<0.0001), the mother being a non-smoker (OR: 1.8 [1.2; 2.8] p=0.0066). The lack of support from employers was strongly criticised with 64.1% of women judging the support not at all satisfactory and 16.0% unsatisfactory. After the consultation, 65.6% of mothers opted for mixed feeding and 34.4% for formula-feeding exclusively.

Conclusion: The survey reveals a duration of exclusive maternal breastfeeding of 11 weeks on average, which varies widely from 10 to 14 weeks by region and in the light of earlier studies attests to a lack of progress over recent years. This underscores the need to continue efforts to inform mothers about the benefits of maternal breastfeeding for infants but also to increase socio-economic measures to support breastfeeding especially in the workplace.

Disclosure of Interest: F. Huet: None Declared, A. Tabellion Employee of: Menarini, F. Allaert Grant / Research Support for: a research grant was given by Menarini
**Nutrition**

**Observational and Epidemiological Studies**

PO-N-0316

**ATOPIC DISORDERS, ASTHMA, MIGRAINE AND BMI Z-SCORE IN CHILDREN TREATED WITH LACTOBACILLUS REUTERI FOR INFANTILE COLIC: A POST HOC ANALYSIS**

Simone Ceratto 1,*, Angela De Marco 1, Roberto Calabrese 2, Francesco Savino 1

1Public Health and Paediatric Sciences Department, University of Turin, Turin, Italy “Regina Margherita” Children’s Hospital, Turin, Italy ; 2Statistics Department, Italian Ministry of Justice, Turin, Italy

**Objectives & Study:** Infantile colic could be the first sign of atopic disorders and recently some authors have suggested that probiotics may have a preventive effect on atopic disease. We performed a longitudinal five year follow up on a group of exclusively breastfed colicky infants treated with *Lactobacillus reuteri* in a randomized, double-blind, placebo-controlled trial (ClinicalTrials.gov ID NCT00893711). Our aim was to evaluate if the use of this probiotic in treating colicky infants could prevent atopic diseases (cow’s milk allergy and atopic dermatitis), asthma and migraine at five years of age and also if there was any influence on body parameters.

**Methods:** Fifty exclusively breastfed colicky infants, diagnosed according to modified Wessel’s criteria, were randomly assigned to receive either *L. reuteri* DSM 17 938 (10⁸ colony-forming units) or placebo daily. The study went on 21 days. Breastfeeding mothers were asked to avoid cow’s milk and cow’s milk products in their diets. We performed a *post hoc* follow up for long-term outcomes as cited above; we also measured height and weight in order to evaluate the BMI Z-score, based on the Center for Disease Control (CDC). Data were analyzed using Odds Ratio with 95%CI and t test.

**Results:** We evaluated 25 children treated with *L. reuteri* and 23 children of the placebo group. Two controls were lost because they went abroad. The average age of the *L. reuteri* group was 4 years and 11 months and the placebo group was 4 years and 10 months.

<table>
<thead>
<tr>
<th></th>
<th><em>L. reuteri</em> group (n = 25 children)</th>
<th>Placebo group (n = 23 children)</th>
<th>Statistical evaluation</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atopic disorders</td>
<td>2 (8%)</td>
<td>8 (34.8%)</td>
<td>Odds ratio: 0.16</td>
<td>3.71</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>95%CI (0.03-0.88)</td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td>0</td>
<td>0</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Migraine</td>
<td>0</td>
<td>1 (4.3%)</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>BMI Z-score</td>
<td>0.79 ± 1.07</td>
<td>0.68 ± 1.24</td>
<td>Δ = 0.11</td>
<td></td>
</tr>
<tr>
<td>(mean ± SD)</td>
<td></td>
<td></td>
<td>t = 0.328</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>p = 0.744</td>
<td></td>
</tr>
</tbody>
</table>

The use of *L. reuteri* in the treatment of infantile colic had a beneficial effect by significantly reducing the prevalence of atopic disorders at five years of age. Data about asthma and migraine are inconsistent, probably due to children’s young age. No significant difference was observed in BMI Z-score.

**Conclusion:** Our results provide preliminary evidence of clinical efficacy of *L. reuteri* DSM 17 938 supplementation in the first months of life on clinical outcomes at five years of age. Further larger evaluations of these outcomes are needed.

Disclosure of Interest: None Declared
OUTCOME OF COMPLICATED ACUTE MALNUTRITION IN CHILDREN TREATED ACCORDING TO WHO GUIDELINES IN RURAL BURKINA FASO
Elena Banci 1,*, Silvia Collini 2, Antonio Liguori 3, Elena Sieni 2, Cristina Brondello 1, Monica Paci 1, Paolo Lionetti 1
1Gastroenterology and Nutrition Unit, University of Florence - Meyer Children's Hospital, Florence, Italy, 2Meyer Children's Hospital, Florence, Italy, 3University of Florence - Meyer Children's Hospital, Florence, Italy

Objectives & Study: To evaluate the implementation of the World Health Organization (WHO) guidelines for the treatment of children with complicated acute malnutrition in an area with high prevalence of co-morbidities in a developing country.

Methods: This descriptive and prospective study was carried out in a rural hospital in Burkina Faso. Between 2008 and 2012, 615 children under 5 years with moderate (36.4%) and severe (63.6%) acute malnutrition associated with illness were hospitalized and treated by staff trained according to the WHO guidelines. After discharge children entered the follow up phase as outpatients until complete rehabilitation.

Results: The most frequent type of severe malnutrition was marasmus (90.3%) followed by kwashiorkor (7.9%) and mixed malnutrition (1.8%). Frequency of co-morbidity at admission was very high, being malaria the most common (59.7%) followed by diarrhoea (25.5%), pneumonia (15.3%) and intestinal parasites (11.3%). In 76.8% of cases severe malaria was present associated with severe anemia and/or neurologic manifestation. Starvation was identified as a health problem by mothers or caregivers only in a minority of children (5.5%). Children with moderate malnutrition were significantly younger than those with severe malnutrition. At discharge 27.8% of children reached -2 standard deviations of weight for height (W/H) whereas the others were discharged gaining weight before attaining the target weight because of socio-economic and epidemic reasons. Mortality rate was 11.7%. Early deaths, in the first 48 hours of hospitalization, were 56.9%, late deaths 43.1%. Lack of attendance to the outpatient phase was very high especially during the rainy season.

<table>
<thead>
<tr>
<th>Severe malnutrition</th>
<th>Marasmus</th>
<th>Kwashiorkor</th>
<th>Mixed</th>
<th>Moderate</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Attainment of goal W/H &gt; -2 SD or gradual weight gain (%)</td>
<td>79.6</td>
<td>83.9</td>
<td>85.7</td>
<td>83.1</td>
<td>81.1</td>
</tr>
<tr>
<td>No weight gain (%)</td>
<td>2.5</td>
<td>0</td>
<td>0</td>
<td>7.1</td>
<td>4.1</td>
</tr>
<tr>
<td>Death (%)</td>
<td>14.4</td>
<td>16.1</td>
<td>14.3</td>
<td>6.7</td>
<td>11.7</td>
</tr>
<tr>
<td>Self-discharged (%)</td>
<td>2.3</td>
<td>-</td>
<td>-</td>
<td>1.3</td>
<td>1.8</td>
</tr>
<tr>
<td>Referred to other hospitals (%)</td>
<td>0.3</td>
<td>-</td>
<td>-</td>
<td>0.4</td>
<td>0.3</td>
</tr>
<tr>
<td>No data available (%)</td>
<td>0.8</td>
<td>-</td>
<td>-</td>
<td>1.3</td>
<td>1</td>
</tr>
</tbody>
</table>

Table: Outcome variables according to type of malnutrition

Conclusion: Implementation of WHO guidelines for inpatient treatment of children with both severe and moderate acute malnutrition can lead to an acceptable mortality rate in developing countries also in areas with high prevalence of co-morbidity. Lack of attendance of outpatient care supports the concept of a Community-Based Therapeutic Model.

Disclosure of Interest: None Declared
Nutrition

Observational and Epidemiological Studies

PO-N-0318

ARE INFANT FEEDING PRACTICES ASSOCIATED WITH INFANT OVERWEIGHT AND OBESITY?

Rebecca J Foskey 1,*, Matthew A Sabin 2, Jennifer J Koplin 2, Shyamali Chandrika Dharmage 3, Melissa Wake 2,4,5, Katrina J Allen 2

1Monash University, 2Murdoch Childrens Research Institute, 3Centre for Mega Epidemiology, Melbourne School of Population and Global Health, Melbourne, Australia, 4Royal Children's Hospital, 5University of Melbourne, Melbourne, Australia

Objectives & Study: This study aims to determine the prevalence of overweight and obesity in a population-based cohort of Victorian children at age one year, and to determine whether infant feeding practices are associated with above-normal body mass index (BMI).

Methods: We analysed questionnaire data on infant feeding and BMI measurements of age one infants (n=3397) from the HealthNuts longitudinal cohort study. Weights and lengths (transcribed from Maternal and Child Health Nurse measurements in Victorian Health Record) were converted to centiles of BMI using sex-age-specific World Health Organization (WHO) Child Growth Standards. Prevalence of overweight and obesity were calculated using WHO cut-points. We used multiple logistic regression to determine odds ratios for above-normal BMI according to various feeding practices (duration of any breastfeeding, duration of full breastfeeding, age at introduction of solid foods) while adjusting for confounding factors.

Results: Four percent (95% confidence interval [CI] 3.5-4.8) of one-year-old infants were overweight and a further one percent were obese (95% CI 0.4-1.0). The mean duration of any breastfeeding was eight months (standard deviation [±] 4), mean duration of full breastfeeding amongst those ever breastfed was three months (±2) and mean age at introduction of solids was five months (±1). Compared with introduction of solids at six months of age, introduction at four months of age was associated with increased odds of above-normal BMI (adjusted odds ratio [aOR] 1.7, 95% CI 1.1-2.7, P<0.05) as was introduction after six months (aOR 2.6, 95% CI 1.2-5.5, P<0.05). Longer duration of any breastfeeding decreased the odds of above-normal BMI at age one in a linear fashion with lowest odds in the group breastfed the longest (aOR 0.4, 95% CI 0.2-0.6, P<0.001). Among breastfed infants, those fully breastfed the longest were at significantly decreased odds of above-normal BMI after adjustment for confounding (aOR 0.4, 95% CI 0.2-0.7, P<0.01).

Conclusion: Our study demonstrates the prevalence of overweight/obesity in a Victorian infant population. These findings add impetus to research into early life modifiable risk factors. Our data suggest that optimal infant feeding practices (introduction of solid foods at 5-6 months of age and a longer duration of breastfeeding) minimise overweight and obesity at age one. Further follow up of this study, with its detailed repeated dietary information, will further elucidate relationships between infant feeding and later outcomes.

Disclosure of Interest: None Declared
GASTROSTOMY TECHNIQUES: A SINGLE CENTER PAEDIATRIC EXPERIENCE

Kirsten Das 1,*; Marc Miserez 2; Tania Claey s 1; Marguerite Stas 3; Daniels Johannes 1; Ilse Hoffman 1
1Uz Gasthuisberg - Dep of Paediatrics, 2Uz Gasthuisberg - Dept Abdominal Surgery, 3Uz Gasthuisberg - Dep Of Oncological Surgery, Leuven, Belgium

Objectives & Study: Percutaneous endoscopic gastrostomy (PEG) is widely used for long-term enteral feeding in children. Recently laparoscopic gastrostomy (LG) had gained interest, because of reported lower complication rates and its adaptability to almost any patient. The aim of this study is to compare LG with PEG outcome and complications.

Methods: A retrospective review of all PEG and LG placements in our center between January 2009 and December 2012 was performed. Patient demographics, major comorbidity, operative time, postoperative hospital stay, and postoperative follow-up were recorded. Outcome was assessed using the Clavien-Dindo classification of surgical complications. Statistics were performed using chi square and Mann-Whitney U test. P ≤ .05 was considered significant.

Results: Of 61 gastrostomies created, 36 were PEG and 25 were LG. Patients in the LG group weighed significantly less (6.6kg vs 12.5kg). Most patients had neurological, tumoral or orofacial comorbidity. In the PEG groups median operative time was shorter (10minutes vs 55minutes, P < .05), feedings were started earlier (1day vs 2days, P < .05) and postoperative hospital stay was shorter (3days vs 6 days, P < .05). There were no intraoperative complications. The majority of adverse events were classified as grade I or II events. Procedure related events scored as grade III or higher were observed in 6 patients in LG and 8 in PEG (24% vs 22%). There was no significant difference in complications or outcome between LG and PEG.

Conclusion: Although patients in the LG group were significantly younger, complication rate and outcome was comparable to PEG. If no other contraindications are present both LG and PEG are equally good options and the decision should be made multidisciplinary and in consultation with the child’s parents.

Disclosure of Interest: None Declared
Objectives & Study: Patients with chronic pancreatitis (CP) often suffer from progressive multifactorial malnutrition caused by decreased dietary intake, malabsorption, surgical and diagnostic procedures, and recurrent infections. Pediatric studies investigating nutritional status in children with CP are not available. The aim of our research was to investigate the nutritional status of children with chronic pancreatitis and to identify factors contributing malnutrition in this group.

Methods: The prevalence of malnutrition was studied in 208 children with CP hospitalized in the Department of Gastroenterology, The Children’s Memorial Health Institute since 1988 to 2012. The severity of malnutrition was expressed by means of Cole’s ratio (LMS) by McLaren’s classification and LMS < 85% was established as cutoff value. The prevalence of malnutrition was assessed in groups of patients with various etiological factors of CP. Moreover analysis of discrimination was performed to identify factors contributing malnutrition among following ones: age of CP onset, duration of CP, number of CP exacerbations, number of ERCP performed, the grade of pancreatic damage in imaging methods, the results of 72h faecal fat quantification.

Results: In studied group 52 children with chronic pancreatitis (25%) had features of the malnutrition and amid them 38 children (18.3%) was clinically crucial undernourished (LMS < 85%). There was no significant difference in the prevalence of malnutrition among different groups of patients divided on the basis of etiological factor of CP. The further analysis showed that age of CP onset is a factor with best discrimination ability of malnourished children with CP Malnourished patients had CP onset later than well-nourished ones (10.8±3.6 years vs 8.5±4.1).

Conclusion:
1. Our study revealed that meaningful percentage of children with chronic pancreatitis had features of malnutrition.
2. Later age of CP onset contributes presence of malnutrition.

Disclosure of Interest: None Declared
GHRELIN, ADIPONECTIN, LEPTIN AND TRUE INSULIN IN HUMAN MILK FROM MOTHERS WITH GDM

Xiujing Sun 1,*, Xinting Yu 1, Ming Li 2, Danhua Wang 1
1Department of Paediatrics, 2Department of Endocrinology, Chinese Academy of Medical Sciences, Peking Union Medical College Hospital, Beijing, China

Objectives & Study: To evaluate the level of ghrelin, adiponectin, leptin and true insulin in human milk from mothers with GDM (Gestational Diabetes Mellitus) and without GDM, and to assess the effects of ghrelin, adiponectin, leptin and true insulin on infant growth.

Methods: GDM and non-GDM mothers were enrolled from Jan. 2010 to Aug. 2010. Baseline informations including maternal age, gestational age, BMI at pre-pregnancy / prenatal / 42 days postpartum / 90 days postpartum, delivery mode, family history of diabetes, 50g oral glucose tolerance test, OGTT, glycated hemoglobin and history of insulin administration during pregnancy were collected. The level of ghrelin, adiponectin, leptin and true insulin in cord blood, colostrums, human milk on 42 days postpartum and 90 days postpartum, of normal mother were tested using ELISA.

Results: In total 103 mother-infant pairs were recruited. (1). Ghrelin in human milk was significantly lower than that in cord blood. Ghrelin was lower in human milk from GDM mothers both in colostrums and 90-day mature milk. (2). Adiponectin in human milk was significantly lower than that in cord blood. Adiponectin was lower in colostrums, 90-day milk from GDM mothers. (3). Leptin level in cord blood of infants from GDM mothers was higher than that in cord blood from non-GDM mothers’ infants. True insulin in GDM mother’s milk was higher than that in non-GDM mothers. True insulin in cord blood, colostrums and 90-day mature milk from GDM mothers was higher than from non-GDM mothers. (4). In colostrums, adiponectin level was negatively with birth weight; adiponectin/leptin ratio was negatively associated with birth weight and head circumference at birth; true insulin level was negatively associated with head circumference at birth. adiponectin level in 90d mature milk was negatively associated with length in 90th day. In non-GDM group, adiponectin, leptin levels were both positively associated with birth weight; leptin level in cord blood, leptin/adiponectin ratio were positively associated with length at birth; leptin/adiponectin ratio of colostum was negatively associated with head circumference at birth. In mature milk, adiponectin level was positively associated with weight gain on 42 days and 90 days. leptin/adiponectin ratio was negatively associated with weight gain on 42 days and 90 days.

Conclusion: Women with GDM have decreased ghrelin and adiponectin levels and increased insulin levels in their breast milk. Hormone levels in breast milk were associated with maternal metabolic status. Leptin, adiponectin, and insulin in breast milk were associated with infant growth.

Disclosure of Interest: None Declared
EVALUATION OF PHYSICAL ACTIVITY WITH A CALORIC MONITOR IS USEFUL IN THE MANAGEMENT OF CHILD OVERWEIGHT AND OBESITY

Cecilia Martínez-Costa 1,*, Francisco Núñez 1, Ángeles Montal 1, Parisá Khodayar-Pardo 1
1Paediatrics, University of Valencia, Valencia, Spain

Objectives & Study: Objectives and study: The lack of physical exercise, together with other unhealthy habits, are factors that contribute to the energy imbalance responsible for the development of obesity in children. The measurement of physical activity (PA) might be helpful in the individual assessment of children with overweight and obesity in order to plan effective treatment. The use of new instruments to assess the duration and intensity of PA would help to understand the relationship between PA and obesity to make specific activity recommendations. This study aims to evaluate the time and intensity of PA, and activity-induced energy expenditure (AIEE) in children with overweight and obesity using a caloric monitor.

Methods: Materials and methods: The study was conducted in 70 schoolchildren and adolescents aged 8-16 years. Based on body mass index (BMI)-for-age z-scores according to WHO cut-offs, 43 children were categorized as obese (BMI z-score >+2 SD), 13 overweight children (BMI z-score >+1 y ≤+2 SD), and 14 controls (BMI z-score -1.99 a +1 SD). PA per day was evaluated for 3 consecutive days using a caloric monitor (SenseWear Armand® -SWA-). It was placed on the childrens’ right arm, in the middle point between the acromion and the olecranon over the triceps muscle. Average time for PA, together with its intensity, were assessed in METs (metabolic equivalent of task), using the monitor’s specific software. 3-5.9 METs was considered as moderate PA, 6-8.9 METs as intense PA, and ≥9 METs as very intense PA. The AIEE were also recorded. SPSS 17.0 software was used for statistical evaluation.

Results: Results: The BMI z-score was 2.81±0.70 for obese children; 1.61±0.27 for children with overweight; and 0.00±0.64 for controls. Average time for moderate and intense PA was significantly lower in obese children (1.90±1.31 hours) compared to controls (3.04±0.98 hours) (p<0.01) and overweight children (2.22±1.05 hours). The AIEE (kcal/day) was significantly lower in obese children (555±243) compared to controls (735±227), p<0.05; in overweight children the AIEE was 563±190, without significant differences with respect to others groups.

Conclusion: Conclusions: Obese children devoted less time to moderate and intense physical activity compared to overweight children and controls. In obese children, simple device such as SWA can prove very effective in the estimation of the energy expenditure associated to physical exercise and in establishing strategies to promote effective weight loss combined with nutritional and behavioural interventions. This study has no conflicts of interest.

Disclosure of Interest: None Declared
ENERGY DENSITY IN 8 YEARS-OLD PKU AND HEALTHY CHILDREN: AN ITALIAN STUDY
Elvira Verduci 1,*, Enrica Riva 1, Elisabetta Salvatici 1, Graziella Cefalo 1, Juri Zuvadelli 1, Alice Re Dionigi 1, Giuseppe Banderali 1, Marcello Giovannini 1
1Department of Paediatrics, University of Milan, San Paolo Hospital, Milan, Italy

Objectives & Study: WHO suggests that frequent intake of energy-dense food promotes weight gain 1. The aim of the present study was to evaluate energy density (ED) of the diet in PKU children on low-Phe diet and compare it with healthy Italian children.

Methods: Forty PKU children, on low-Phe diet, and 40 healthy controls were analyzed; children were normal-weight, according to the International Obesity Task Force, and matched for sex and age (median age 8 years). A 3 days food record was collected. ED (kcal/g) was calculated as daily energy divided by relative weight of all food and beverage (excluded drunk water) by 3-days-weighted food record. In PKU children the free protein substitutes have been included in ED calculation.

Results: Mean ED (SD) was 1.38 (0.14) in PKU and 1.45 (0.17) in healthy children, respectively (P=0.048). No differences in energy density according to sex were found in each group. On equal energy intake, PKU children showed higher consumption of vegetables (g) than healthy children (P<0.0001). Between groups no difference in fruit consumption (g) and energy-providing liquids ED was found.

Conclusion: Energy density should be considered a parameter for the global evaluation of children diet, also in PKU population.


Disclosure of Interest: None Declared
Different Nutritional Approaches for the Management of Pancreatic Insufficiency in Shwachman-Diamond Syndrome and Cystic Fibrosis

Marianna Daldoss¹, Sandra Perobelli¹, Sonia Volpi¹, Barouck Maurice Assael¹, Marco Cipolli¹
¹CF CENTRE, Azienda Ospedaliera Universitaria Integrata Verona, Verona, Italy

Objectives & Study: Cystic Fibrosis (CF) and Shwachman Diamond Syndrome (SDS) are the two most common causes of inherited exocrine pancreatic insufficiency in children. Assessment of nutritional status in children with CF is known to be clinically relevant while there is a lack of knowledge regarding this aspect in SDS. Body composition is the most reliable estimate of nutritional status and is essential in understanding the patterns of growth and development. The aim of the present investigation was to compare body composition in two groups: SDS children and CF children with mild lung disease. This may help to understand what nutritional interventions could be suitable and to identify patterns of growth, fat free mass, and body fat in SDS.

Methods: We performed an observational study of 20 SDS patients (age <18 years) and 40 age/sex matched CF patients. Anthropometric parameters such as height, weight, arm and waist circumferences, and four skinfold thicknesses were measured. Physical activity level using International Physical Activity Questionnaire, enzymes therapy and nutritional intake using 24-hour Dietary Recall were investigated. Consent and assent forms were obtained from children and parents.

Results: Among 1-5 years old subjects, BMI, height-, weight- and head circumference percentiles were not significantly different between the groups. Among 5-18 years old subjects, height and height percentiles were significantly lower in SDS compared with CF (p<0.05). Mean weight and weight percentiles were not different between the groups. The suprailiac skinfold thickness and the mean arm fat area were significantly higher in the SDS group. Percent body fat and biceps, and subscapular skinfold-thickness tended to be lower in the CF group. 77% of SDS presented waist-to-height-ratio (WHtR) above 0.5 (mean=0.54±0.069 vs 0.44±0.044 in CF). The value increased with age in SDS up to 5 years of age. The level of physical activity was significantly lower in SDS. Total energy intake tended to be slightly but not significantly higher in the CF group for all ages.

Conclusion: The different WHtR seems to suggest that individual measurements of height and weight could not be good indicators of nutritional status in SDS particularly after the first years of age. Aggressive nutritional intervention in SDS children may be useful in newborns and toddlers. In older children the nutritional intervention should probably focalise more on prevention of fat mass gain and improvement of quality of food. Conversely, in CF subjects with mild disease, lower fat stores may indicate the beginning of clinical worsening and of the need of more aggressive nutritional interventions in order to prevent weight loss.

Disclosure of Interest: None Declared
**Nutrition**

*Observational and Epidemiological Studies*

PO-N-0325

**ASSOCIATION OF VITAMIN D LEVELS WITH PHYSICAL AND SOCIOCULTURAL FACTORS AMONG SELECTED FILIPINO HIGH SCHOOL STUDENTS IN QUEZON CITY**

Hazel Valdoria Arnaldo 1,*, Randy Urtula 2, Maria Estela Ronquillo Nolasco 1

1Gastroenterology, Hepatology and Nutrition, 2Gastroenterology, Hepatology and Nutrition, Philippine Children’s Medical Center, Quezon City, Philippines

**Objectives & Study:** To determine the vitamin D status and its association with physical and sociocultural factors among Filipino high school students in selected schools in Quezon City.

**Methods:** A cross-sectional study of Filipino high school students was undertaken. Ninety-seven boys and girls, 11-18 years old, attending selected private and public secondary schools in Quezon City participated in the study. Self-administered pretested questionnaires were given to the participants under the investigator's supervision. Serum 25-hydroxyvitamin D levels were determined by electrochemiluminescence immunoassay.

**Results:** The total serum 25-hydroxyvitamin D levels of the students ranged from 19.92 nmol/L to 88.63 nmol/L with a mean of 52.43 nmol/L. There was a prevalence of hypovitaminosis D (serum 25-hydroxyvitamin D levels <50 nmol/L) of 41.2% with 20.6% having deficient (<37.5 nmol/L) and 20.6% insufficient (37.5 - <50 nmol/L) serum 25-hydroxyvitamin D levels. Low vitamin D intake (p=0.019), Body mass index Z-score outside the normal range of 0 to <1SD (p=0.012) and upper socioeconomic status (p=0.001) were significantly associated with hypovitaminosis D.

**Table 1. Independent Predictors of Hypovitaminosis D**

<table>
<thead>
<tr>
<th>Predictor</th>
<th>OR</th>
<th>95 CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Skin Color (Type IV-VI)</td>
<td>2.531</td>
<td>0.571 - 11.208</td>
<td>0.221 (NS)</td>
</tr>
<tr>
<td>Sun exposure (&lt;15 mins)</td>
<td>0.850</td>
<td>0.279 - 2.591</td>
<td>0.775 (NS)</td>
</tr>
<tr>
<td>Clothing Style</td>
<td>0.000</td>
<td>0.000</td>
<td>1.00 (NS)</td>
</tr>
<tr>
<td>Use sunscreen (Yes)</td>
<td>0.437</td>
<td>0.132 - 1.446</td>
<td>0.175 (NS)</td>
</tr>
<tr>
<td>Sex (Female)</td>
<td>1.425</td>
<td>0.382 - 5.318</td>
<td>0.598 (NS)</td>
</tr>
<tr>
<td>Socioeconomic status (USES)</td>
<td>17.285</td>
<td>3.327 - 89.810</td>
<td>0.001 (S)</td>
</tr>
<tr>
<td>BMI (0 to &lt;1 SD- No)</td>
<td>10.381</td>
<td>1.660 - 64.900</td>
<td>0.012 (S)</td>
</tr>
<tr>
<td>Drink Milk (No)</td>
<td>0.407</td>
<td>0.090 - 1.840</td>
<td>0.243 (NS)</td>
</tr>
<tr>
<td>Vitamin D intake &lt;5ug/day</td>
<td>28.768</td>
<td>1.723 - 480.207</td>
<td>0.019 (S)</td>
</tr>
</tbody>
</table>

*OR, odds ratio; CI, confidence interval

**Conclusion:** Hypovitaminosis D is highly prevalent among Filipino high school students in selected schools in Quezon City despite abundance of sunlight. Low vitamin D intake, Body mass index Z-score outside the normal range of 0 to <1SD and upper socioeconomic status were significantly associated with hypovitaminosis D. Given the characteristics of the adolescent population, appropriate interventions are needed to address the problem of poor vitamin D status in schoolchildren.

**Disclosure of Interest:** None Declared
Objectives & Study: Neonatal short bowel syndrome (SBS) is a disease with a significant morbidity and mortality. Recent data have demonstrated improved survival in children with SBS. Based on this, we retrospectively analyze treatment outcomes and to identify risk factors for mortality in neonatal SBS.

Methods: We reviewed the medical records of all inpatients and outpatients with SBS treated from January 1, 1988 to October 31, 2013 in our hospital. SBS has also been defined as the need for PN greater than 42 days or 2 mo after bowel resection of $\geq$70% or a residual small bowel length of less than 25% of that expected for gestational age. Data collected included etiology of SBS, small intestinal length, the presence of the ileo-cecal valve, colonic remnant, highest serum direct bilirubin, duration of PN use, and number of documented episodes of sepsis. Multiple logistic regression was applied to identify independent predictors of mortality in neonatal SBS.

Results: Fifty-seven patients were included. Demographic and clinical data for these patients are provided in table. Diagnoses included intestinal atresias (n=26), malrotation or volvulus (n=10), necrotizing enterocolitis (n=9), Hirschsprung disease or NID (n=6) gastrochisis (n=2), and others (n=4). Complications: 17.5% patients had PN-associated cholestasis (direct bilirubin $>2.0$ mg/dL) and 19.3% had catheter-related infections. Outcomes: All the patients were free of PN at follow-up. Fourteen patients died during the study period for an overall survival rate was 75%. Primary cause of death was: sepsis (n = 4), liver failure (n = 3), cardiopulmonary failure (n = 2), unknown (n = 4). Univariate analysis showed no significant differences between mortality and survival for the following variables: sex, prematurity, birth weight, diagnosis, presence of ileocecal valve, and residual small bowel length. Multiple logistic regression analysis confirmed that enteral intolerance (EI) and peak direct bilirubin (DB) were independently predictors of mortality (EI: OR=10.861; 95%CI, 1.576-74.844, P= 0.015; DB: OR=1.045; 95% CI, 1.011-1.080, P=0.009).

Table Characteristics of 57 patients with SBS

<table>
<thead>
<tr>
<th>Characteristic (n=57)</th>
<th>Mean (sd) or Median (range) or n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male sex</td>
<td>34(60%)</td>
</tr>
<tr>
<td>Prematurity</td>
<td>20(35%)</td>
</tr>
<tr>
<td>Admission weight-WAZ</td>
<td>-3.0(2.4)</td>
</tr>
<tr>
<td>Residual small bowel length, cm</td>
<td>68.0 (21.5)</td>
</tr>
<tr>
<td>ICV preserved (n=53)</td>
<td>27(47%)</td>
</tr>
<tr>
<td>Intact colon (n=53)</td>
<td>46(87%)</td>
</tr>
<tr>
<td>Enteral nutrition at admission, %total calories</td>
<td>21.2(13.1)</td>
</tr>
<tr>
<td>Weaned off PN at discharge (n=50)</td>
<td>44(88%)</td>
</tr>
<tr>
<td>Duration of PN, d</td>
<td>60 (33-104)</td>
</tr>
</tbody>
</table>

Conclusion: Cholestasis and enteral intolerance are the major predictors of mortality in neonatal SBS. Those patients on long-term PN therefore require careful management to identify complications early, and this is associated with improved outcome.

References: Key Words
Short bowel syndrome; neonate; outcomes

Disclosure of Interest: None Declared
SEASONAL VITAMIN D STATUS IN HOSPITALISED ITALIAN CHILDREN
Giorgia Di Fazzio 1, Alexandra Iori 1, Valentina Alberghini 1, Sergio Amarri 2,*
1Paediatrics, Azienda Ospedaliera Santa Maria Nuova – IRCCS, 42123 Reggio Emilia, Italy
2Paediatrics, Azienda Ospedaliera Santa Maria Nuova – IRCCS, Reggio Emilia, Italy

Objectives & Study: The aim of this study was to evaluate Vitamin D 25(OH)3 (D3) status during winter (W) and summer (S) in hospitalised children living at 44° north latitude, and to search correlations with age, sex, and ethnia.

Methods: We measured D3 in patients hospitalised for acute and chronic diseases in W (1/10/12-31/03/13) and S (1/04/13-30/09/13), and adopted 2 cut-off according to definitions of D3 insufficiency and deficiency by American Academy of Pediatrics and The American Endocrine Society respectively: < 30 (group A) and < 20 ng/ml (B). Severe and extreme deficiency were considered when D3 was respectively <10 (C), and < 5 ng/ml (D). Statistical analysis by chi square test was performed (PASW Statistics 18.0, SPSS, Chicago, IL) for sex, ethnia and 3 age groups: < 1 year (y) (group 1: W 37 patients; S 35 patients), 1-5 y (group 2: W 121 patients; S 102 patients) and > 5 y (group 3: W 94 patients; S 121 patients).

Results: Patient mean age was 4.7 y; 208 (42.3%) females and 272 (56.7%) males. 348 patients (72.5%) had light skin (caucasian and chinese), while 129 (26.7%) had dark skin (African and indo-pakistan). D3 levels were skewed towards low levels and the medians were 17.3 ng/ml (W) and 21.5 (S), with 25° interquartile 10.7 ng/ml (W) and 12.9 (S) and 75° interquartile 41.1 ng/ml (W) and 29.4 (S). We observed a seasonal trend with a lower prevalence of D3 deficiency in S (although not significant): A [75.5% vs 88.2% W], B [45.3% vs 60.8% W], C [14.3% vs 21.1 W] and D [2.3% vs 4.5% W].

<table>
<thead>
<tr>
<th>Vitamin D Level (ng/ml)</th>
<th>Season</th>
<th>Light skin (N°/Tot)</th>
<th>%</th>
<th>Dark skin (N°/Tot)</th>
<th>%</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt; 30 (A)</td>
<td>W</td>
<td>137/160</td>
<td>85.6</td>
<td>56/59</td>
<td>94.9</td>
<td>0.7200</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>137/188</td>
<td>72.8</td>
<td>58/70</td>
<td>82.8</td>
<td>0.6129</td>
</tr>
<tr>
<td>&lt; 20 (B)</td>
<td>W</td>
<td>91/160</td>
<td>56.8</td>
<td>42/59</td>
<td>71.1</td>
<td>0.4100</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>78/188</td>
<td>41.4</td>
<td>39/70</td>
<td>55.7</td>
<td>0.2702</td>
</tr>
<tr>
<td>&lt; 10 (C)</td>
<td>W</td>
<td>20/160</td>
<td>12.5</td>
<td>25/59</td>
<td>42.3</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>17/188</td>
<td>9.0</td>
<td>20/70</td>
<td>28.5</td>
<td>0.0017</td>
</tr>
<tr>
<td>&lt; 5 (D)</td>
<td>W</td>
<td>1/160</td>
<td>0.6</td>
<td>8/59</td>
<td>13.5</td>
<td>0.0003</td>
</tr>
<tr>
<td></td>
<td>S</td>
<td>1/188</td>
<td>0.5</td>
<td>5/70</td>
<td>7.1</td>
<td>0.0105</td>
</tr>
</tbody>
</table>

There were no statistical differences for sex and skin colour for group A and B, while a difference was found between dark and light skin patients for groups C and D (p=0.0003 in W; p 0.001 in S). Older children have higher risk of D3 insufficiency with a statistical difference between group 2 and 3 only in W (p 0.03).

Conclusion: Inpatients show a very high prevalence of sub-optimal Vitamin D status; in W almost 25% of children show levels < 10 ng/ml (in S 15%). Light and dark skin are both at risk of D3 insufficiency with significant differences when comparing the two populations for severe and extreme deficiency in both seasons. We didn’t find any significant seasonal difference both analysing total population or patients by gender, age and skin colour. These findings warrant a widespread supplementation during both W and S. Inpatients should be screened to treat appropriately D3 deficiency and prevent complications.

Disclosure of Interest: None Declared
Nutrition

Observational and Epidemiological Studies

PO-N-0328

VITAMIN STATUS OF YOUNG ATHLETES AND ITS CORRECTION

Svetlana Makarova 1,*, Lejla Namazova-Baranova 2, Tatiana Borovik 1, Sergej Polyakov 3, Irina Korneeva 3, Tamara Chumbadze 1, Vladimir Spiričev 4, Olga Vrzhesinskaya 5, Vera Kodentsova 5

1Children’s Nutrition, 2Scientific Center of Children’s Health, Russian Academy of Medical Sciences, Moscow, Russian Federation, 3Sports Medicine and Physical Therapy, Scientific Center of Children’s Health, Russian Academy of Medical Sciences, Moscow, Russian Federation, 4Research Institute of Nutrition, Russian Academy of Medical Sciences, Moscow, Russian Federation, 52 Research Institute of Nutrition, Russian Academy of Medical Sciences, Moscow, Russian Federation

Objectives & Study: Physical activity increases the body need in most vitamins (vitamins C and E, thiamin, riboflavin, vitamin B-6) and electrolytes. Thus, the supply of vitamins is very important for young athletes. The aim of the study was investigation of special vitamin-mineral drink influence on vitamin status of young swimmers.

Methods: The study was a double-blind, placebo–controlled, prospective, comparative medical supervision. 39 young athletes aged 11-17 engaged in swimming were under examination. Vitamin status assessment was performed by two methods: by calculation of dietary intake and by analytical method (determination of vitamins content in the blood serum) and was done twice – before examination and after 21 days of performing it.

Results: Analysis of the dietary intake of vitamins, according to the requirements and physical activity of young swimmers showed that in the whole the young sportsmen had a deficit of various nutrients in their diet, most frequently – of vitamins, PUFA, Calcium. The initial examination revealed low level of serum vitamin E in 31%, vitamin B2 - in 54%, beta-carotene - in 80% of young swimmers. The children were divided into 2 groups. The first group (20 athletes) received vitamin-mineral drink regularly during 21 days. 19 children received “placebo drink” without vitamin and mineral. The vitamins supplementation of young athletes has significantly improved in the first group after 21 day period of uptake of the vitamin-mineral drink. During the second examination the number of children with low vitamin provision in the first group was: vitamin E - 11%, vitamin B2 - 40%, beta-carotene - 44%; in the control group: vitamin E - 33%, vitamin B2 - 67%, beta-carotene - 50%.

Conclusion: The placebo-controlled study demonstrated the possibility of optimizing the vitamin status of young sportsmen by vitamin-mineral drink supplementation.

References:

Disclosure of Interest: None Declared
Nutrition
Observational and Epidemiological Studies
PO-N-0329

NUTRITION OF INFANTS AND YOUNG CHILDREN (1-3 YEARS) AND ITS EFFECT ON LATER HEALTH: A SYSTEMATIC REVIEW OF CURRENT RECOMMENDATIONS

Bartłomiej Zalewski 1,*, Bernadeta Patro 1, Margriet Veldhorst 2, Stefanie Kouvenhoven 2, Paula Crespo 3, Joaquim Calvo 3, Berthold Koletzko 4, Hans van Goudoever 2, Hania Szajewska 1

1Department of Paediatrics, The Medical University of Warsaw, Warsaw, Poland, 2Department of Paediatrics, VU University Medical Center Amsterdam, Amsterdam, Netherlands, 3La Fe University, Valencia, Spain, 4Div. Metabolic Diseases and Nutrition, Department of Paediatrics, Dr. v. Haunersches Kinderspital, Klinikum der Universität München, Munich, Germany

Objectives & Study: EarlyNutrition (www.project-earlynutrition.eu) is an international research project investigating the effects of early (prenatal and postnatal) nutrition on metabolic programming with special consideration of long-term outcomes.

Objective: To summarize, by performing a systematic review, current standards, recommendations, guidelines, and regulations (hereafter, referred to as documents) on the nutrition of children aged 1-3 years. Special emphasis was placed on the evaluation of long-term effects of early nutrition, such as cardiovascular disease, hypertension, overweight or obesity, metabolic syndrome, diabetes, or glucose intolerance.

Methods: MEDLINE, selected databases, and websites of relevant professional organizations were searched for documents published in English between 2008 and 2013.

Results: Forty-two documents met the inclusion criteria. The strongest and most consistent evidence for a protective, long-term effect of early nutrition was documented for breastfeeding. Other recommended actions, such as limitation of sodium and rapidly absorbed carbohydrates intake, use of a specific meal pattern, reducing the consumption of saturated fatty acids by replacing them with polyunsaturated fatty acids, and lowering the intake of trans fatty acids, also seem to have a beneficial effect on reducing the risk of obesity and/or related diseases. However, of the 42 included documents, many did not evaluate long-term outcomes of interest to us, or reported insufficient or imprecise data that did not allow conclusions to be drawn, or provided recommendations based on studies with suboptimal study designs. With regard to some outcomes, inconsistency in recommendations from different organizations was noted. Research gaps were identified.

Conclusion: The findings of this review may act as a helpful tool in planning preventive actions against important diet-related diseases. Identified research gaps form a basis for further research and guidelines improvement.

Disclosure of Interest: None Declared
MILK INTAKE IN BELGIAN TODDLERS: DOES GROWING UP MILK (GUM) HAS A PLACE?
Koen Huysentruyt 1,*, Annemie Van de Sompel 2, Dorothée Laire 3, Tom Van Avondt 3, Jean De Schepper 1, Yvan Vandenplas 1
1Paediatrics, UZ BRUSSEL, Brussels, Belgium, 2Paediatrics, University Hospital Antwerp, Antwerp, Belgium, 3Ipsos Healthcare, Ipsos, Market Research Agency, Ghent, Belgium

Objectives & Study: To study if there are any beneficial effects of GUM on macro- and micronutrient intake in a population of Belgian toddlers that was studied between January and February 2012.

Methods: 500 mothers completed a diary in which they registered all foods, drinks and supplements consumed by their child (6 - 36 months) during a period of 4 days. Participants were stratified for age of the child, region (North/South), occupation and day of the week for diary completion. Average daily intake per child was calculated for each nutrient. The relative contribution of each type of milk (milk was classified using the following subdivisions: standard formula, standard cow's milk, soy/other formula (e.g. goat milk) and GUM) in relation to the total quantity of consumed milk was calculated.

Results: Our population consisted of 204 (50.6%) 13-24 month-old and 199 (49.4%) 25-36 month-old children. Seven (1.7%) children were breastfed and were not included in our statistical analysis; 47 children did not drink milk at all. In the milk drinking population, milk consisted exclusively of standard formula in 45 (12.7%) children, 171 (48.2%) exclusively drank standard cow's milk, 61 (17.2%) exclusively GUM and 71 (20.0%) children mixed different types of milk. The proportion of GUM correlated significantly (p<0.01) with the amount of protein (ρ=-0.28) and energy (ρ=-0.15) intake, the average daily amount of iron (ρ=0.53), zinc (ρ=0.31), vitamin D (ρ=0.52) and omega-3 (ρ=-0.12; p=0.02) and omega-6 (ρ=-0.13; p=0.01) in the diet. It did however not correlate with copper or fatty acids (NS). The mean (SD) daily amount of dietary protein was significantly (p<0.01) lower in the GUM group than in the cow's milk group (respectively 35.3 g (9.2) vs 45.7g (13.1)), but not significantly (p=0.53) different than in the standard formula group (35.3 g (9.2)). Median (range) Vit D intake was significantly (p<0.01) higher in the GUM group than in the cow's milk or standard formula group (8.8 µg (0.1-205) vs respectively 2.1 µg (0.1 - 22) and 6.4 µg (0.1-31)). Median zinc and iron intake was also significantly (p<0.01) higher in the GUM vs the other two groups (respectively 6.5 mg and 9.7 mg vs 4.6 mg and 7.1 mg for standard formula and 5.3 mg and 4.7 mg for cow's milk).

Conclusion: GUM makes it easier to fulfill dietary requirements since it reduces protein intake (which is too high) and increases iron, zinc and Vit. D intake (which are too low). Therefore, the composition of GUM needs to be regulated, as it is for standard and follow-up formula.

Acknowledgments: This independent research was performed by Ipsos Healthcare Ltd, Ipsos, Market Research Agency, Ghent, Belgium supported by Nutricia BE.

**Nutrition**

**Observational and Epidemiological Studies**

PO-N-0331

**BONE MINERAL DENSITY IN CHILDREN WITH INTESTINAL FAILURE WEANED OFF PARENTERAL NUTRITION**

Katarzyna Olszewska 1,*, Elżbieta Banaś 1, Małgorzata Janusz 1, Maciej Jaworski 2, Agnieszka Różdżyńska-Świątkowska 3, Joanna Friedman-Gruszcyńska 1, Mikołaj Danko 1, Katarzyna Popińska 1, Janusz Benedykt Książyk 1

1Department of Paediatrics, Nutrition and Metabolic Disorders, 2Department of Biochemistry and Experimental Medicine, 3Anthropology Laboratory, The Children’s Memorial Health Institute, Warsaw, Poland

**Objectives & Study:** Patients with intestinal failure (IF) during and after weaning off parenteral nutrition (PN) are at high risk of nutritional deficiencies, which may lead in consequence to the metabolic bone disease. Assessment of bone health and nutritional status in paediatric intestinal failure patients weaned off PN was the aim of the study.

**Methods:** 34 patients (20 female and 14 male) with intestinal failure aged 5,07-17,9 years (median: 8,44 years) weaned off parenteral nutrition (PN) were selected for the study. The median duration of PN was 24 months. The main indication for PN was short bowel syndrome (n=33). 9 patients had large small intestine resection (remnant small intestine <40 cm). Median time period between weaning off PN and examination equalled 57 months (4,75 years). Antero-posterior (AP) spine and total body bone mineral density (BMD) were measured by DXA and results were compared to chronological age. Skeletal age was assessed by DXA. Nutrition status and growth were evaluated based on anthropometric measurements. The student’s t-test was used to analyze the data.

**Results:** Median Z-score BMD (Total body) in the research sample was -0,285. Median Z-score BMD (Spine) in whole group was -0,825. 15 patients from the whole research group had BMD Z-score (Spine) < -1 and 5 patients had Z-score BMD (Spine) < -2. Extension of resection had not influence on bone mineral density. Z-score BMD (Total body, Spine) was lower in patients with large resection but correlation was not statistically significant. Z-score BMD (Total body) correlated negatively with period of time from weaning off PN (p=0,011). Decreased BMD, defined as DXA Total Z-score < -1, was more prevalent in older patients (p=0,037). In underweight patients (SDS body mass according to chronological age) as well as in the patients with short stature (SDS height according to chronological age) bone mineral density (Z-score BMD Spine) was decreased (p=0,051; p=0,051)(NS).

**Conclusion:** Long-term parenteral nutrition history is related to the risk of impaired BMD later in life. The risk increases with the length of time from weaning off PN.

**Disclosure of Interest:** None Declared
BREASTFEEDING IN THE MEDITERRANEAN AREA: FINDINGS FROM THE MEDICEL COUNTRIES

Camilla Panico 1,*, Francesca Tucci 1, Pio Stellato 1, Andrea Smarrazzo 1, Luigi Greco 1

1Dipartimento di Scienze Traslazionali, University of Naples "Federico II", Naples, Italy

Objectives & Study: Exclusive breastfeeding until month 6 and continued over the first year of life, in tandem with the weaning process, is important for a number of reasons. It prevents a number of conditions in children maintains good nutrition, influences the immune system, and delays the occurrence of symptomatic disease (i.e. celiac disease). In the Mediterranean area, where breastfeeding had always been favored as a result of cultural and religious tradition a change has been seen in the few last decades. Firstly, in the economically developed countries (the European side) habits started to differ significantly from the WHO guidelines and later on the African side there has also been a progressive decline in the exclusive breastfeeding until month 6.

Methods: As a key task of the MEDICEL Research Network on Celiac Disease in the Mediterranean, coordinated by the research group at the Federico II University in Naples, Italy, it was decided to harmonized data on exclusive breastfeeding in the populations living in the countries participating to the MEDICEL Network. Data on exclusive breastfeeding have been revised during a working group meeting held in Tunis in April 2013.

Results: The description of data indicates that in any MEDICEL country the prevalence rates are under 50% (see figure).

Image:

Conclusion: Investments in educational programs on breastfeeding are of high priority in the Mediterranean area both in Europe and in Africa

Disclosure of Interest: None Declared
Objective & Study: Adolescence is a period of rapid growth and development. Balanced nutrition is vital for ensuring optimal outcomes. Athletes of all ages competing in sports such as judo are categorized by weight. This tries to guarantee that matches are equitable among competitors in terms of body size, strength and agility. In order to obtain the greatest physical advantage over an opponent, efforts are made to be categorized in the lowest possible body weight category. Thus, rapid weight loss prior to competition is a common behavior among athletes who practice categorical sports. The need to reduce weight rapidly leads to extreme measures such as fasting, skipping meals and variety of methods to promote dehydration. Partaking these methods poses a serious health threat and can put an athlete at risk of malnutrition. This is of particular importance in adolescent competitors. Very few studies have been published in this area. To the best of our knowledge, this is the first study that examines the prevalence and methods of rapid weight loss among Israeli adolescents on the National Judo Team.

Methods: Study Population: Fifteen adolescent male athletes aged 12-16 were recruited for this study. Each subject completed a previously validated questionnaire which was developed to examine the magnitude and the prevalence of rapid weight loss in judo athletes. Weight and height were measured using a digital scale with height rod (MS4900) and BMI was calculated from this data.

Results: Average age was 15.4±0.6 yr, weight=61.77±9.74 kg, height=169±7 cm, BMI=21.5±2.5. Initial results show that 93% of the athletes were already practicing weight loss prior to competitions and began doing so at age 13.15±1.8 yr. The average pre-competition weight loss duration was 11±8 days, and it lead to an average reduction of 1.86±1.22 kg. The greatest weight loss reported was on average 3.15±1.9 kg. The number of weight loss efforts per athlete in the past season was 3.23±1.5. The majority of the participants were skipping meals (93%), increasing their exercise (93%), training in heated rooms (72%), and 40% reported that they had tried fasting at least once. 79% of the athletes indicated that their coaches were the most influential figure in regards to the weight loss process.

Conclusion: Rapid weight loss is highly prevalent in adolescent judo competitors. The methods used by these athletes are potentially harmful and can put them at nutritional risk and possibly impair performance and development. Efforts should be made to promote the awareness of athletes, coaches and parents about the risks of rapid weight loss in order to limit this phenomenon.

Disclosure of Interest: B.-E. Berkovich Conflict with: I have no COI. , A. Stark Conflict with: I have no COI. , A. Eliakim Conflict with: I have no COI. , D. Nemet Conflict with: I have no COI. , T. Sinai Conflict with: I have no COI.
OBJECTIVES & STUDY: Undernutrition is seen in 6-32% of hospitalized children in Europe. The prevalence is higher in children with an underlying chronic disease, such as cerebral palsy (CP). STRONGkids is a nutritional screening tool that predicts the risk for undernutrition.

AIM OF THE STUDY: Prevalence of acute/chronic undernutrition in an ambulatory population of children with CP in general, and according to the degree of motor impairment and eating ability. Usefulness of STRONGkids screening tool to predict undernutrition in this population.

METHODS: Acute and chronic malnutrition were defined as WFH and HFA Z-score < -2 (with growth curves for the Flemish population as standard). Gross motor function and eating (in)ability were assessed by the Gross Motor Function Classification system (GMFCS) and Eating and Drinking Ability Classification System for individuals with Cerebral Palsy (EDACS). The STRONGkids score was used in all patients.

RESULTS: 63 patients (39 M, mean age 13 years, range 2-20 y) entered the study after informed consent. None of them had enteral feeding. 43.5% (with 17.7% Z-score < -3) and 20.6% (with 6.4% Z-score < -3) had chronic or acute undernutrition. Chronic undernutrition was more frequently found in children > 12 years of age (50% vs 27% in younger children). Acute and chronic undernutrition prevalence increased with higher GMFCS and EDACS score. Het STRONGkids score revealed a medium vs high risk for undernutrition in resp 90.5-92.1 and 7.9-9.5% of the population.

CONCLUSION: Acute and chronic undernutrition was seen in resp 20.6 and 43.5% of the ambulatory children with CP. There is a clear correlation of the severity of undernutrition with increasing motor and eating disability. The STRONGkids tool does not seem to be discriminative and of additional use in this population.

DISCLOSURE OF INTEREST: None Declared
Objectives & Study: Background: Despite advances in the prevention and treatment of influenza, it is still considered an important factor in morbidity and mortality worldwide. Chronic medical conditions and immunosuppression are risk factors for severe complications. Annual vaccination is the safest and most effective means for influenza prevention. Data regarding the vaccination rates among pediatric patients with chronic diseases and reasons for non-vaccination are limited.

Objective: The objectives of this study to define the rates of seasonal influenza vaccination among children and to define the main reasons for non-vaccination.

Methods: Methods: Between September-October 2011 and March 2012, children and parents seen at the Institute of Gastroenterology, Nutrition, and Liver Diseases at Schneider Children’s Medical Center of Israel completed a questionnaire which included demographic and clinical items, data regarding influenza vaccination and possible reasons for non-vaccination.

Results: Results: The study included 273 patients, 136 boys and 137 girls, at mean age of 10.2 years (range 2-18). The rates of seasonal influenza vaccination among all children were 30.8%. Immunization rates in immunosuppressed patients were 46.1% and 50% IBD patients. The patient’s age, gender, ethnic origin and parent’s education did not significantly affect the vaccination rates. Immunization rates were significantly influenced by the information and knowledge of the patients on this subject, and their personal beliefs (P value <0.001).

Conclusion: Conclusions: Low immunization rates were seen in this study, both in the normal study population and in high risk groups. Patient and parental education by general physicians and gastroenterologists may be a key to increasing the immunization rates.

Disclosure of Interest: None Declared
**Nutrition**

**Observational and Epidemiological Studies**

PO-N-0336

**NUTRITION IN CHILDREN WITH NEUROMOTOR DISABILITIES: STILL A PROBLEM IN AN ITALIAN SERIES**

Maria Sangermano 1, Roberta D’Aniello 1, Grazia Massa 1, Pasquale Pisano 2, Giangennaro Coppola 3, Marco Poeta 1, Luca Pierri 1, Dario Di Salvio 1, Giulia Paolella 1, Pietro Vajro 1,*,

1Paediatrics Section Dept Medicine and Surgery, Univ Salerno, Baronissi - Salerno, Italy,

2Paediatrics, AOU Ruggi D’Aragona, Salerno, Italy, 3Neuropaediatrics Section Dept Medicine and Surgery, Univ Salerno, Baronissi - Salerno, Italy

**Objectives & Study:** Neuromotor disabilities share exclusive and often quite neglected nutritional problems. Our study aims to delineate the frequency of malnutrition in a series of non-hospitalized, neurologically impaired Southern Italy children.

**Methods:** Thirty children (21 M, 9 F; age 2 - 15 years) followed-up as outpatients by neurologists for cerebral palsy (n = 15), epileptic encephalopathy (n = 6), severe psychomotor developmental delay (n= 5), and genetic syndromes (n = 4). Nutritional status was assessed by anthropometric parameters [weight, estimated height by specific body segments measurement, according to Stevenson criteria (Stevenson, 1995) BMI, Plicometry(Samson-Fang and Stevenson, 2007)], blood count, serum levels of iron, albumin, transferrin, calcium, phosphorus. Feeding difficulties and daily calorie intake were assessed by parents’ dietary questionnaires and a 3 days food diary, respectively.

**Results:** Despite massive caregivers commitment [about 90% of patients required constant assistance during meals, usually > 30 minutes/meal (mean 45 minutes)], most patients had an insufficient daily caloric intake with slightly unbalanced composition (Table). Approximately from one third to an half of them was at high risk of malnutrition according to feeding difficulties (44%), reduced albumin and transferrin levels, or < 5th percentile weight (44%), and BMI (33%) and < 10th percentile triceps skinfold thickness (37%). Malnutrition was less severe in the 4 patients with PEG access.

**TABLE.** Calories and diet composition (mean ± SD, and %)

<table>
<thead>
<tr>
<th></th>
<th>Kcal/die</th>
<th>Carbohydrates</th>
<th>Lipids</th>
<th>Proteins</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>1092 ± 215</td>
<td>134.2±19.0 (46%)</td>
<td>45.4±8.9 (37%)</td>
<td>45.9±17.7 (17%)</td>
</tr>
<tr>
<td>Reference</td>
<td>1474 ± 411*</td>
<td>55- 60% (RDI)</td>
<td>22-30% (RDI)</td>
<td>12-15% (RDI)</td>
</tr>
</tbody>
</table>

RDI= Reference Daily Intake; * Krick’s formula (Krick et al, 1996)

**Conclusion:** The results of the present study suggest that during the specialized follow-up of neurologically impaired children nutritional issues, at least in our country, are still rather neglected and need therefore more emphasis in the daily care.

**References:**


**Disclosure of Interest:** None Declared
Nutrition

Observational and Epidemiological Studies

OUTCOME OF NEONATAL SHORT BOWEL SYNDROME (SBS) REQUIRING LONG-TERM PN: NECROTISING ENTEROCOLITIS (NEC), VOLVULUS/ATRESIA & GASTROSCHISIS COMPARED

Vanessa La Vela 1,*, Sarah Macdonald 1, Susan Hill 2

1 Gastroenterology, Great Ormond Street Hospital, London, United Kingdom, 2 Gastroenterology, Great Ormond Street Hospital for Children, London, United Kingdom

Objectives & Study: To review length of time on treatment with parenteral nutrition (PN) in infants presenting with intestinal failure (IF) according to underlying diagnosis.

There is limited information about the length of time that parenteral nutrition (PN) support may be required for neonates who undergo small intestinal resection for either intestinal necrosis due to volvulus or necrotising enterocolitis (NEC), or for intestinal strictures, atresia or gastroschisis.

Methods: All patients attending an intestinal rehabilitation clinic who underwent intestinal resection for necrotising enterocolitis (NEC) or volvulus and/or atresia or gastroschisis who required long-term PN for >28 days were reviewed. Gestational age was recorded. Length of time on PN was calculated and compared in the two groups.

Results: Eighteen infants (9 male: 9 female) were identified. 9 patients (3 male: 6 female) had NEC. Eight were born prematurely and one at term (range 23-40 weeks, mean 27, median 25 weeks). Three patients had intestinal volvulus (2 male: 1 female) and 4 atresia (2 male: 2 female) born from 27-35 weeks gestation (mean 31, median 30 weeks). Three other male infants had gastroschisis.

Small intestinal length was from 30-85 cm (mean 45 cm, median 40 cm) at time of resection in 8 NEC patients (1 unknown), from 30-120 cm (mean 63, median 60 cm) in volvulus/atresia patients and 22 and 50 cm in 2 gastroschisis cases (1 unknown).

PN treatment was given for 3-42 months (mean 16, median 10 months) in NEC patients, 1-33 months (mean 14, median 8 months) in volvulus/atresia and 7, 137 and 144 months in gastroschisis patients.

There was no significant correlation between remaining length of small intestine and time on PN (Pearson’s R was 0.21, p=0.59 for NEC; -0.01, p=0.99 for volvulus and -0.02, p=0.8 for atresia).

Conclusion: There was no clear correlation between length of remaining small intestine and time on PN.

Children with SBS secondary to NEC, volvulus or atresia with a remaining small bowel length from 30-120 cm who require long-term PN are likely to continue to need PN for on average 15 months and up to 42 months whereas gastroschisis cases may need treatment for over 10 years.

Disclosure of Interest: None Declared
**Nutrition**

*Observational and Epidemiological Studies*

PO-N-0338

**PREVALENCE OF VITAMIN D DEFICIENCY IN MOSCOW ADOLESCENT GIRLS**

Irina Zakharova 1, Svetlana Vasilyeva 1, Yulia Dmitrieva 1,*

1Russian Medical Academy of Postgraduate Education, Moscow, Russian Federation

**Objectives & Study:** Vitamin D is considered to be one of key nutrients related to well-being and growth in pediatric population. At the same time the prevalence of vitamin D deficiency among children and adolescents runs up to 70% with some regional differences. Our study was performed to assess the status of serum vitamin D in healthy adolescent girls living in Moscow.

**Methods:** The serum 25-hydroxyvitamin D 25-OHD was measured in February with chemiluminescence enzyme immunoassay in 100 untreated girls aged 10-17 years (mean age 13.7±0.2). Vitamin D deficiency was defined as 25-OHD below 20 ng/mL; insufficiency as 25-OHD of 21 – 29 ng/mL; and sufficiency as 25-OHD higher than 30 ng/mL.

**Results:** The serum 25-OHD level ranged from 4.42 to 24 ng / ml with mean level of 12.6±0.4 ng/ ml. The prevalence of serum 25-OHD deficiency found to be 98%, in 2 girls (2%) the level of 25-OHD was defined to be insufficient. None of girls had 25-OHD higher than 30 ng/mL. Age related analysis found the lowest level of 25-OHD among 12 years girls (11.7±0.7 ng/ml) while the highest one was detected among 17 years old girls (14.2±1.28 ng/ml).

After evaluating the initial 25OHD level the girls were randomized into 3 groups according to the duration of the vitamin D intake. The 1st one (n=24) took vitamin D3 of 400IU during 1 month, the 2nd one (n=13) - the same dose for 2 months, the 3rd (n=51) one - for 3 months. In all groups we detected significant changes in 25OHD serum level with maximum increase in the 3rd group (12.62±0.6ng/ml and 19.91± 0.61ng/ml, respectively) though we didn't find any significant difference at the end of the therapy between groups. Noone of treated girls at the end of the study demonstrated sufficient level of 25OHD.

**Conclusion:** The study showed 100% of vitamin D deficiency among healthy adolescent girls that indicates the need of regular vitamin D supplementation in winter time. In cases of vitamin D deficiency intake of 400IU might be not enough to increase serum 25OHD to sufficient level.

**Disclosure of Interest:** None Declared
FATTY ACID OXIDATION DEFECTS: A SINGLE-CENTRE EXPERIENCE

Ana Moráis 1*, Lorena Magallares 1, Raquel González 2, Miguel Sáenz de Pipaón 2, Elena Dulín 3, Begoña Merinero 4, Rosa A Lama 1
1Nutrition and Metabolic Diseases Unit, 2Neonatology, Hospital Universitario La Paz, Madrid, Spain, 3Newborn Screening Laboratory, Hospital Universitario Gregorio Marañón, Madrid, Spain, 4Centro de Diagnóstico de Enfermedades Moleculares, Universidad Autónoma de Madrid, Madrid, Spain

Objectives & Study: Expanded newborn screening (ENS) has allowed the early identification of children with fatty acid oxidation disorders (FAOD), contributing to improve prognosis. In addition, novel mutations with uncertain clinical relevance have been identified in involved genes, representing a challenge for clinicians. The aim of this study is to describe the children who presented with biochemical markers of FAOD and are currently followed in a tertiary pediatric hospital.

Methods: All children admitted to the Unit of Metabolic Diseases with clinical or biochemical suspicion of FAOD, and who maintain current follow-up, were included. Age of onset, clinical findings and biochemical and genetic data are described.

Results: At present, 18 children maintain monitoring: 7 patients with homozygous/double heterozygous mutations [3 medium-chain defects (MCAD), 2 very-long-chain defects (VLCAD) and 2 carnitine metabolism disorders], 7 heterozygous carriers (6 MCAD and 1 VLCAD) and 4 infants currently waiting for the result of MCAD gene mutation analysis. One MCAD patient presented with hypoglycemia and high ammonia levels at 16 months; another one was his asymptomatic 8-year-old sister and the third one was identified by ENS. The most frequent mutation was identified in homozygosis in the siblings and in heterozygosis in the third child. All patients with VLCAD and carnitine metabolism disorders, all heterozygous carriers and the 4 with genetic results pending were identified by ENS. 50% MCAD heterozygous carriers have the most frequent mutation. Both VLCAD patients are double heterozygous and both carry the mutation c.848T>C, associated with mild phenotype. Both patients with carnitine defects presented <5 μM on ENS. All patients were treated with diet therapy (avoiding long-fasting periods, restricted long-chain fat when indicated), riboflavin supplementation and carnitine (only when required according to free carnitine plasmatic levels).

Conclusion: At present, most patients with FAOD are identified by ENS, and clinical presentation in the form of metabolic crisis is exceptional in our reference population.

Disclosure of Interest: None Declared
IMPLEMENTATION OF AN ORAL-MOTOR REHABILITATION PROGRAM IN A DEPARTMENT OF PAEDIATRIC GASTROENTEROLOGY AND NUTRITION

Sergio Pinillos 1,*, Raquel García 1, Catalina Ortiz 1, Silvia Meavilla 1, Anna Mila 2, Natalia Egea 1
1 Paediatric Gastroenterology, Hepatology and Nutrition, 2 Paediatric Neurology, Hospital Sant Joan de Deu, Barcelona, Spain

Objectives & Study: Oropharyngeal dysphagia (OD) is a risk for malnutrition, which is specially important in children (stage of growth and development). The oral-motor rehabilitation is part of nutritional therapy. We describe our experience following the implementation of oral-motor rehabilitation program (OMRP) conducted by a speech therapist, in a department of pediatric gastroenterology and nutrition (PGN).

Methods: Prospective study of patients included in the OMRP from January 2011 to November 2012. Distribution by sex, age, underlying disease, therapeutic group and overall results.

Results: 106 patients included, 68 male (64%). Average age 3 years and 2 months (2 months - 17 years). Underlying disease: neurological disease (cerebral palsy, global developmental disorder, traumatic brain injury, cerebral vascular and tumoral disease) n= 64 (60%), non neurological disease (congenital heart disease, functional maturation disorder, craniofacial anomalies, airway abnormalities, others) n=42 (40%). According to the rehabilitation group therapy: Group (G)1: chewing disorders (n= 12, 11.5%), G2: Return to oral feeding from nasogastric tube or gastrostomy (n= 23, 21.5%), all with oral hypersensitivity, G3: moderate-severe oral-motor dyspraxia (n= 54, 51%), G4: Others (n= 17, 16%). The number of sessions varies according to availability and the type and severity of involvement. The overall trend is positive in 95% of children in the first 2 months of treatment, faster and better in groups 1 and 2.

Conclusion: The addition of a speech therapist and an OMRP in a department of PGN, first experience in our country, contributes positively to the nutritional evolution of the child with OD.

Disclosure of Interest: None Declared
Nutrition
Observational and Epidemiological Studies
PO-N-0341

CHANGES IN WEIGHT STANDARD DEVIATION SCORES OF CHILDREN ADMITTED TO A TERTIARY PAEDIATRIC HOSPITAL

Sarah Macdonald 1*
1Dietetics, Great Ormond Street hospital for Children NHS Trust, London, United Kingdom

Objectives & Study: There are very few studies examining the nutritional outcome of children admitted to hospital. Poor nutrition is known to impact in the short term on wound healing, immune function and pressure sores in bed bound patients and on growth and development in the long term.

Aim: As part of the GOSH CQUIN audit for nutrition the weights of a representative sample of children discharged between 01.06.11 to 24.02.12 were compared to their admission weights as a proxy for nutritional sufficiency during their hospital stay. It was hoped that this information would be useful in the future to guide dietetic interventions and service to areas with particularly vulnerable patients.

Methods: Patients were selected that were discharged on a particular day of the week with length of stay>than 7 days and who were known to the dietetic department. The following information was obtained from the dietetic / medical notes: wt on admission, date taken, sex, gestational age if < 2yrs, the last wt taken during the hospital admission, date taken. The LMS growth programme was used to calculate the weight standard deviation (SD) scores on admission and discharge.

Results: Data was collected for 175 children over a 37 week period. The number of children with an identifiable weight on admission and discharge was 154 (88%) The mean variance in SD score for weight from admission to discharge was -0.17. Sub-analysis for different age groups;0–1 year, 59 children(38%), -0.35, 1–2 years, 13 children(8%) -0.08, > 2 years 82 children(53%) -0.06. The specialties with the greatest variance (> -0.25) were: BMT 8 children(5%) -0.55, Cardiology /CICU 27 children(17%) -0.5, Endocrinology 5 children (3%)-0.29 NICU 11 children (7%)-0.26

Conclusion: The data suggests that infants under the age of 1 year have a poorer nutritional status on discharge than those aged >1 year. This is to be expected due to their high nutritional requirements and difficulties maintaining these during the hospital admission.

Because of the small numbers of patients in each specialty it is difficult to draw firm conclusions. Cardiology / CICU patients are known to be nutritionally vulnerable due to increased energy requirements often coupled with fluid restrictions. Patients undergoing BMT have increased LOS, severe mucositis and rely on parenteral nutrition for several weeks of their admission. This data cannot be extrapolated to all children admitted to GOSH as it is unknown whether the most nutritionally vulnerable patients are referred to the Dietetic Department. The Trust wide introduction of a nutrition screening tool in January 2012 should now ensure that all children at nutritional risk are referred and will be included in our future audits. It may be that the very complex nature of the children admitted to GOSH and the procedures that they undergo precludes maintenance of nutritional status.

Disclosure of Interest: None Declared
HEALTH-RELATED QUALITY OF LIFE AMONG CHINESE INFANTS FED INFANT FORMULA EITHER EXCLUSIVELY OR IN COMBINATION WITH HUMAN MILK

Kathleen Yerger 1, Meng Mao 2, John Ge 3, Robert Northington 1, MJ Yao 1, Nicholas P. Hays 1,*
1Nestlé Nutrition, King of Prussia, PA, United States, 2Chengdu Women’s and Children’s Central Hospital, Chengdu, China, 3Wyeth Nutritional (China) Company Ltd., Shanghai, China

Objectives & Study: Choice of feeding regimen (either human milk [HM] or formula) represents an important potential mediator of parent-reported infant health-related quality of life (HRQoL), yet this outcome measure has received relatively little attention. This multi-center, observational cohort study evaluated HRQoL among Chinese infants receiving different feeding regimens. We hypothesized that there would be no difference in HRQoL outcomes among infants exclusively fed formula containing increased sn-2 palmitate and oligofructose, HM, or study formula and HM (mixed-fed).

Methods: Healthy term infants (n=440; 56% boys) age ~42 days were enrolled on their current feeding regimen: study formula (n=142), HM (n=143), or mixed (n=155). The Infant Toddler Quality of Life Questionnaire™ (ITQOL) was used to assess parent-reported infant HRQoL at the beginning and end of the 48-day study period. The ITQOL is a standardized, validated tool designed to assess core infant health concepts along with parent-focused concepts; scores range from 0 (worst) to 100 (best). Since the parent’s own quality of life may influence their perception of the infant’s HRQoL, we used another validated tool (SF-12v2 Health Survey®) to assess and adjust for the parent’s Mental Component Summary score using ANCOVA.

Results: Infant and parent demographics were generally comparable among groups. Scores for 4 of 9 concepts were significantly different among groups at day 48 (Table), with differences ranging from 3 – 6 units. No significant differences were seen at study day 1 except for Temperament and Moods and Parent Impact-Time scores; these scores were slightly but significantly lower in the formula-fed group compared with the HM-fed group, but mean values were high (>71).

<table>
<thead>
<tr>
<th>Concept</th>
<th>Formula-fed</th>
<th>HM-fed</th>
<th>Mixed-fed</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Overall Health</td>
<td>79.0±1.4</td>
<td>78.9±1.4</td>
<td>79.5±1.4</td>
</tr>
<tr>
<td>2. Physical Abilities</td>
<td>93.9±7.5</td>
<td>86.2±7.1</td>
<td>74.4±7.4</td>
</tr>
<tr>
<td>3. Growth and Development</td>
<td>84.5±1.2</td>
<td>84.7±1.3</td>
<td>83.8±1.3</td>
</tr>
<tr>
<td>4. Bodily Pain/Discomfort</td>
<td>93.8±0.8</td>
<td>95.1±0.9</td>
<td>94.4±0.9</td>
</tr>
<tr>
<td>5. Temperament and Moods</td>
<td>74.2±0.7</td>
<td>77.9±0.7</td>
<td>77.2±0.7</td>
</tr>
<tr>
<td>6. General Health Perceptions</td>
<td>80.8±0.9</td>
<td>84.9±0.9</td>
<td>85.6±1.0</td>
</tr>
<tr>
<td>7. Parent Impact-Emotional</td>
<td>87.5±1.0</td>
<td>92.3±1.1</td>
<td>90.2±1.1</td>
</tr>
<tr>
<td>8. Parent Impact-Time</td>
<td>85.4±1.2</td>
<td>90.4±1.2</td>
<td>91.1±1.3</td>
</tr>
<tr>
<td>9. Family Cohesion</td>
<td>80.4±1.4</td>
<td>79.4±1.5</td>
<td>80.8±1.5</td>
</tr>
</tbody>
</table>

Adjusted mean ± SE values within a row that do not share the same superscript are significantly different (p<0.05).

Conclusion: Healthy Chinese HM-fed infants and infants fed term infant formula with increased sn-2 palmitate and OF had similar scores for the majority of HRQoL concepts, and small differences in scores for remaining concepts. Mean scores for all groups (71 – 95) were towards the upper end of the score range. These data indicate positive physical, mental, and social well-being in these infants and parents.
ECTOPIC EXPRESSION OF METHYLATION PATTERN IN GATA-4 PROMOTER REGION OF VITAMIN A-INSUFFICIENT OFFSPRING’S HEART

Yi Feng¹,*, Li Hong¹, Li-ya Pan¹, Pan-pan Chang¹

¹Dept. of Clinical Nutrition, Shanghai Children’s Medical Center, Shanghai, China

Objectives & Study: Vitamin A (VA) regulates several transcription factors, including GATA-4, linked to cardiogenesis through many signaling pathways. The mutation of GATA-4 is associated with congenital heart defect (CHD). More and more attention is paid to epigenetics for interpretation of correlations between lifestyle and risk disease. Changes of maternal diet have been shown to alter epigenetic regulation such as affecting DNA methylation status. Our hypothesis is that GATA-4 gene methylation would lead to CHD in vitamin A insufficient offspring.

Methods: Ten weaning female SD rats (VAN group) were maintained on the American Institute of Nutrition 93 Growth Purified Diet (AIN-93G) which contains 4 IU VA per gram diet, while 20 female SD rats (MVAD) were fed with a modified diet based on AIN-93G which contains 0.4 IU VA/g diet. All the female rats were mated with normal males rats at the 10th week. All the VAN group rats and 10 of the MVAD group rats (MVAD) were maintained the same diet as before mating, while the rest of 10 MVAD rats (MVADS) were transferred to a diet with added 10 IU VA/g diet for the pregnancy cycle. The embryo hearts were dissected out at embryonic day 13.5 (E13.5) for observation of cardiac ultrastructural changes, GATA-4 gene methylation status and the expression of DNA methyltransferases (DNMTs).

Results: Embryos from MVAD group exhibited a disoriented arrangement of myocardium and mitochondria swelling with broken cristae and vacuoles (Figure 1). With the NCBI genome database and online tools, the CpG loci of GATA-4 containing 43 CpG sites were characterized. The methylation percentage of the VAN group was 0.93% (4/430), whereas the percentage of the MVAD and MVADS group was 1.63% (7/430) and 1.40% (6/430), respectively ($\chi^2=0.835, P=0.659$). High methylation was present in the CpG loci of GATA-4 gene with down-regulated expression of GATA-4 mRNA from MVAD and MVADS group compared to VAN group (P<0.01) (Figure 2). Moreover, down-regulated DNMT3a (P<0.01) and DNMT3b (P<0.05) expression were found in VA insufficient groups.

Image:
**Conclusion:** These findings show that aberrant methylation is one of key mechanisms to abnormal heart development in VA insufficient offspring. DNMTs play a critical role in this process.

**Disclosure of Interest:** Y. Feng Grant / Research Support for: This work was supported by grants from the National Nature Science Foundation of China (No. 81100622) and Project HOPE (US non-profit health organization) “The Abbott Fund Instituted of Nutrition Science (AFINS)” program grant., L. Hong: None Declared, L.-Y. Pan: None Declared, P.-P. Chang: None Declared
VITAMIN D RESCUES AUTOPHAGY AND REDUCES CYTOTOXIC EFFECTS IN ROTAVIRUS-INFECTED HUMAN ENTEROCYTES

Emanuele Nicastro 1,*, Francesca Wanda Basile 1, Vittoria Buccigrossi 1, Carla Russo 1, Serena Orlando 1, Maria Cristina Fedele 1, Alfredo Guarino 1

1Department of Translational Medical Science, University of Naples Federico II, Naples, Italy

Objectives & Study: Autophagy is a highly conserved lysosomal degradation pathway essential for cell survival and homeostasis. It is also a component of innate immunity against intracellular pathogens. Rotavirus (RV) has been shown to block the maturation from initial to degradative autophagosome and to use the initial autophagosomes for viral replication. Vitamin 1,25(OH)2D3 (1,25D3) has been described to induce autophagy thus promoting antimicrobial clearance via the human cathelicidin LL-37. In this study we investigated the role of autophagy and its regulation by 1,25D3 in Rotavirus (RV)-related enterocyte damage.

Methods: Caco-2 cells monolayers were infected with activated RV strain SA11 at 50 PFU. Autophagy was evaluated by western blot and confocal microscopy using an anti-LC3 mAb (autophagosomal staining) and an anti-LAMP2 mAb (lysosomal staining). To understand whether RV infection caused either upregulation of autophagosome formation or blockage of autophagic degradation, the inhibitor of lysosome-mediated degradation Bafilomycin A1 (BafA) was used. Cells were pretreated with 1,25D3 (in a range of 20nM to 100nM) at 37°C overnight. LL-37 expression was assessed by ELISA and seen by immunofluorescence with a specific mAb. Epithelial integrity was monitored by transepithelial electrical resistance (TER) in Ussing chambers.

Results: RV induced autophagosome formation as judged by immunofluorescence - showing an increase in LC3 puncta at 8 hours post-infection (HPI) - and western blot densitometry (0.39±0.01 vs 0.33±0.01 LC3-II/tubulin ratio, P<.05), which was not modified with BafA, indicating a blockage of autophagy. At confocal microscopy, LC3+ vesicles did not localize with LAMP-2 in RV-infected cells, indicating that autophagosome maturation to degradative structures was inhibited. Overnight pretreatment with 1,25D3: a) reduced LC3-II 8 HPI (0.21±0.01 vs 0.39±0.01 LC3-II/tubulin ratio, P<.0001) but determined an increased LC3-II in BafA-treated cells; b) induced colocalization of LC3 and LAMP-2 in intracellular vesicles, indicating restored autophagic flux; c) upregulated LL-37 as observed in ELISA (1.56±0.03 vs 1.42±0.03 AU, p<.02) in cell supernatants, and in immunofluorescence at 6 HPI (74% vs 41% LL-37+ cells, P<.01); d) reduced the RV-dependent epithelial damage as shown by TER compared with control infected cells (275±6 vs 180.1±2 Ω/cm², p<.0001).

Conclusion: Autophagy is involved in the response to RV infection in human enterocytes, but there is evidence for a blockage of the autophagosome maturation. Vitamin D restores competent autophagy and this is associated with LL-37 upregulation, ultimately determining an increase in epithelial integrity in RV-infected enterocytes. This data suggest that vitamin D may be effective in adjunct to oral rehydration against RV infection.

Disclosure of interest: None Declared
LACTOBACILLUS RHAMNOSUS GG INTERVENTION EXPANDS IMMUNOREGULATORY MICROBIOTA IN INFANTS WITH COWS MILK ALLERGY

Roberto Berni Canani 1, Andrew T. Stefka 2, Tiffany J. Patton 3, Rita Nocerino 1, Rosita Aitoro 1, Lorella Paparo 1, Antonio Calignano 4, Rosaria Meli 4, Giuseppina Mattace Raso 4, Raffaele Simeoli 4, Margherita Di Costanzo 1, Stefano Guandalini 3, Dionysios Antonopoulos 5,6, Cathryn R. Nagler 2

1Department of Translational Medical Science-Paediatric Section and European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy, 2Departments of Pathology, 3Department of Paediatric Gastroenterology, University of Chicago, Illinois, United States, 4Department of Pharmacy, University of Naples "Federico II", Naples, Italy, 5Department of Medicine, University of Chicago, Illinois, United States, 6Argonne National Laboratory, Argonne, Illinois, United States

Objectives & Study: Treatment of cow’s milk allergic (CMA) infants with an extensively hydrolyzed casein formula (EHCF) supplemented with the probiotic Lactobacillus rhamnosus GG (LGG) accelerates tolerance to cow’s milk. The mechanistic basis for this effect is not known. We tested the hypothesis that it is attributable, at least in part, to an influence of this dietary intervention on the composition of the gut microbiota.

Methods: We used high throughput sequencing technology (16S rRNA-based sequence analysis) to compare fecal samples from newly diagnosed CMA infants (n=12, 9 male, mean age 4.33 m)(before and after treatment with EHCF plus LGG) to those obtained from 20 healthy age and weight matched controls. Gut butyrate production was assessed in the same stool samples by gas chromatography. A murine model of CMA (4-week-old female C3H/HeOuJ mice) was used to explore the protective effects of the short chain fatty acid, butyrate, produced by gut microbiota.

Results: Treatment with EHCF plus LGG expanded gut microbiota populations associated with immunoregulatory effects and increased butyrate production at intestinal level. We found a significant positive correlations between fecal butyrate concentration and the abundance of four clostridial genera: Faecalibacterium, Blautia, Roseburia, and Coprococcus (p<.05). All four genera resulted increased in CMA infants after treatment with EHCF plus LGG. Oral butyrate treatment (20 mg/kg/day) alleviates allergic reaction to β-lactoglobulin in C3H/HeOuJ mice, as demonstrated by a significant inhibition of acute allergic skin response, anaphylactic symptom score, body temperature decrease, intestinal permeability increase, and specific-IgE production (p<.05).

Conclusion: Our data suggests that EHCF containing LGG promotes oral tolerance, in part, through its influence on gut microbiota.

Disclosure of Interest: None Declared
Common ESPGHAN Topics

Basic Science

PO-CT-0346

EXTENSIVELY HYDROLYZED CASEIN FORMULA ALONE OR IN COMBINATION WITH LACTOBACKILLUS RHAMNOSUS GG IS ABLE TO PREVENT AND TREAT COWS MILK ALLERGY IN A MURINE MODEL

Rosita Aitoro 1, Margherita Di Costanzo 1, Raffaele Simeoli 2, Antonio Calignano 2, Giuseppina Mattace Raso 2, Rita Nocerino 1, Riccardo Troncone 1, Rosaria Meli 2, Roberto Berni Canani 1,*

1Department of Translational Medical Science-Paediatric Section and European Laboratory for the Investigation of Food Induced Diseases (ELFID), 2Department of Pharmacy, University of Naples "Federico II", Naples, Italy

Objectives & Study: Cow’s milk allergy (CMA) is the most common food allergy in children. Extensively hydrolyzed casein formula (eHCF) has been proposed for prevention and treatment of CMA. We have recently demonstrated that a new formulation of eHCF containing the probiotic Lactobacillus rhamnosus GG (eHCF+LGG) is able to accelerate tolerance acquisition in infants with CMA. The present study was performed to look into the potential mechanisms underlying tolerance acquisition in a murine model of CMA. To investigate the effects of eHCF and eHCF+LGG given before or after sensitization to β-lactoglobulin (BLG), a major cow milk protein allergen, in a murine model of CMA.

Methods: 4-week-old female C3H/HeOuJ mice were sensitized by oral administration of BLG (20 mg) using cholera toxin (10 ug) as an adjuvant at weekly intervals for 5 weeks (sensitization period). Two experimental phases: 1. eHCF or eHCF+LGG given daily by gavage for 2 weeks before and then continually during the whole sensitization period; 2. eHCF or eHCF+LGG given daily by gavage for 4 weeks soon after the sensitization period. Acute allergic skin response (ear thickness at 1 h after intra-dermal challenge with 10 μg BLG), anaphylactic symptom score, body temperature, intestinal permeability (determined by FITC dextran concentration in plasma), serum specific IgE against BLG, IL-4 and IL-10 concentrations from spleen lysates were assessed soon after oral challenge with BLG (20 mg).

Results: Treatment with eHCF, provided before or after sensitization, was able to counteract BLG response, as demonstrated by a significant inhibition of acute allergic skin reaction, anaphylactic symptom score, body temperature decrease, IL-4 and specific-IgE production; as well as improved intestinal barrier integrity and a significant increase in IL-10 production (p<.05). These beneficial effects of eHCF were augmented by the addition of LGG (p<.05).

Conclusion: The data support dietary intervention with eHCF for the prevention and treatment of CMA through a favorable inhibition of Th2 response. The observed effects were found to be even more pronounced with LGG supplementation.

Common ESPGHAN Topics

Basic Science

PO-CT-0347

DECREASE IN IL-15 PRODUCTION BY CORD BLOOD MONONUCLEAR CELLS AS A MARKER OF ATOPIC DISEASE DURING CHILDHOOD

Catherine Lombard 1, Floriane André 1, Jérôme Paul 2, Catherine Wanty 3, Olivier Vosters 4, Pierre Bernard 5, Charles Pilette 6, Pierre Dupont 2, Etienne Sokal 3, Françoise Smets 3.

1Paediatrics, Université Catholique de Louvain, IREC, 1200 Brussels, Belgium, 2INGI, Machine Learning Group, Université Catholique de Louvain, ICTEAM, 1348 Louvain-La-Neuve, Belgium, 3Paediatrics, UCL, IREC, Cliniques universitaires Saint-Luc, 1200 Brussels, Belgium, 4IRIBHM, Université Libre de Bruxelles, 1070 Brussels, Belgium, 5Obstetrics, 6Pneumology, UCL, IREC, Cliniques Universitaires Saint-Luc, 1200 Brussels, Belgium

Objectives & Study: Allergy afflicts one third of children, negatively impacting their quality of life and generating a significant socio-economical burden to society. To this day, this disorder remains difficult to diagnose early in very young patients, and there is no predictive test available. This study was designed to correlate cytokine profiles with clinical phenotypes of allergy development.

Methods: Three hundred patients were recruited and followed from birth to 18 months of age. They were given a clinical exam at birth and at 2, 6, 12, and 18 months of age, with skin prick tests at 6, and 18 months, in order to have a record of their medical history and determine their allergic status. In addition, mononuclear cells were isolated from cord blood samples at birth and from peripheral blood samples at 2, 6 and 18 months of age, to analyse their cytokine and chemokine production. These analyses were performed on a subgroup of 131 patients.

Results: CBMCs from future atopic children produced significantly less IL-12p70 and IL-15 than cells from non-atopic children. Multivariate analyses revealed that the best predictive model of allergy was built on cytokine data, whereas the best predictive model of atopy was built on clinical parameters.

Conclusion: Although univariate analyses can yield interesting information regarding the immune responses of allergic or atopic children, finding predictive markers of the disorders will likely rely on monitoring multiple parameters. Nonetheless these analyses suggest a potential key role for IL-15 in the development of atopy. In addition, the study highlights the importance of clinical parameters such as a history of allergy and breastfeeding in predicting the development of atopy.

Disclosure of Interest: None Declared
EARLY COLONIZATION OF FUNCTIONAL GROUPS OF MICROBES IN HEALTHY INFANTS GUT
Van Pham 1, 2,*, Christophe Chassard 1, Rebekka Koller 2, Christian Braegger 2, Christophe Lacroix 1

1Laboratory of Food Biotechnology, Institute of Food, Nutrition and Health, ETH Zürich, Switzerland, 2Division of Gastroenterology and Nutrition, University Children’s Hospital Zürich, Zürich, Switzerland

Objectives & Study: The colonization process of the infant gut microbiota is crucial for the present and future health of infants. However, little is known about the sequence of colonization, abundance and diversity of different functional bacterial groups in the infant gut. The present study investigated the colonization pattern of healthy infant gut microbiota using a combination of cultural and molecular methods, focusing on the functional groups of microbes contributing to a healthy trophic chain, and the fate of lactate as an important intermediate.

Methods: Faecal samples were obtained from 40 healthy infants at 2 weeks, 1, 3, and 6 months after delivery. Major populations of the gut microbiota were analysed with molecular methods (qPCR). Functional groups of microbes were enumerated using a combination of both cultural methods and qPCR.

Results: Our results indicated that a dense microbiota had established in all infants after 2 weeks of life (total bacteria: 11.9 log g⁻¹ faeces). The lactate producing bacteria population was dominated by Bifidobacterium, which reached 9.3 log g⁻¹ after 2 weeks and slightly decrease in the next 6 months. Other lactate producing populations were also detected after 2 weeks, including Lactobacillus (6.4 log g⁻¹) and Bacteroides (7.6 log g⁻¹). Interestingly, there was an uneven distribution of Bacteroides levels in the first 2 weeks of life and infants could be classified into two groups: one harboured high levels of Bacteroides (9.3 log g⁻¹), whereas the other showed significant lower levels (5.7 log g⁻¹).

We were able to detect early colonization of different groups that are able to reutilize lactate. Veillonella dominated the ecological niche at high levels after 2 weeks (7.8 log g⁻¹) and strongly increased to 9.0 log g⁻¹ after 6 months. Lactate-utilizing sulphate-reducing bacteria (SRB) population, which are involved in the pathogenesis of colonic diseases, already reached adult level of 6.3 log cfu g⁻¹ at week 2 and gradually increased to 7.2 log cfu g⁻¹ after 6 months. The lactate-utilizing bacteria non-SRB population increased from 2 weeks (5.8 log cfu g⁻¹) to 6 months (7.1 log cfu g⁻¹) but remained significantly lower than adult levels. Eubacterium hallii, detected after 2 weeks (7.0 log g⁻¹), remained stable over time and represented one of the predominant butyrate producers in the infant gut.

Conclusion: Our data revealed for the first time the complexity of early colonization until 6 months of age and the competition between functional groups involved with lactate production and reutilization. The competitive interactions among functional microbes could cause microbial and metabolic dysbiosis which may directly impact on infant gut health.

Disclosure of Interest: V. Pham Grant / Research Support for: This study is supported by the Swiss National Foundation (SNF), Switzerland, C. Chassard Grant / Research Support for: This study is supported by the Swiss National Foundation (SNF), Switzerland, R. Koller Grant / Research Support for: This study is supported by the Swiss National Foundation (SNF), Switzerland, C. Braegger Grant / Research Support for: This study is supported by the Swiss National Foundation (SNF), Switzerland, C. Lacroix Grant / Research Support for: This study is supported by the Swiss National Foundation (SNF), Switzerland
Common ESPGHAN Topics
Basic Science
PO-CT-0349

THE ROLE OF PHOSPHORYLATED MYOSIN REGULATORY LIGHT CHAIN IN EPITHELIAL BARRIER DYSFUNCTION IN THE COMMON BILE DUCT OF PATIENTS WITH CHOLEDOCHOCYST

Jian Wang 1*, Wan-liang Gu 1
1Paediatric Surgery, Children's Hospital of Soochow University, Suzhou, China

Objectives & Study: A principal function of epithelial surfaces is the maintenance of a barrier to hydrophilic solutes. There are no related reports about common bile duct epithelium barrier dysfunction in choledochocyst (CCC). Previous study showed that the expression of phosphorylated myosin regulatory light chain (P-MLC20) is high common bile duct in CCC. The aim of this study was to determine if there is epithelium barrier dysfunction and the relationship between P-MLC20 and epithelial barrier function in common bile duct in CCC.

Methods: Twenty-one specimens of the common bile duct from pediatric patients with CCC were collected. The expression of P-MLC20, MLCK and ZO-1 was also examined with Western blot. Twenty-one specimens of the common bile duct from pediatric patients without CCC were used as controls.

Results: The expression of P-MLC20 was significantly higher in the CCC group (0.68 ± 0.31) than in the control group (0.34 ± 0.29; P<0.05). The expression of MLCK was significantly higher in the CCC group (1.90 ±1.20) than in the control group (1.07 ± 0.90) (P<0.05). Whereas the expression of ZO-1 was significantly lower in the CCC group (0.36 ± 0.12) than in the control group (0.63 ± 0.19; P<0.05). The expression of ZO-1 was negatively correlated with the expression of P-MLC20 (r= -0.63).

Conclusion: The common bile duct epithelium barrier function is compromised in CCC. The higher expression of P-MLC20 in the common bile duct probably contributes to epithelial barrier dysfunction in CCC via the MLCK pathway.

Disclosure of Interest: None Declared
Objectives & Study: There is increasing research regarding specific biological activities of peptides in human and bovine milk proteins, which goes beyond their nutritional value. These peptides can be naturally present in human milk, formed during gastrointestinal digestion, or formed through processes of protein hydrolyses for specific nutritional applications. Many of these milk protein-derived peptides have been demonstrated to affect our digestive, immune and nervous system. Prompted by the accumulating evidence on bioactive moieties of milk derived peptides, we developed novel methods to compare the peptide composition amongst commercially available hydrolysate formulations, as well as determining batch-to-batch variations of protein hydrolysate products. Despite the availability of general methods to measure e.g. the degree of hydrolysis and peptide mass-distribution at a high level, the objective of the present study was to more qualitatively compare peptide sequences and composition.

Methods: By a comprehensive approach combining peptidomics technologies and bioinformatics analyses, the peptide profiles of hydrolyzed milk protein samples were compared. Moreover, production of various hydrolysate batched over a five year period was included. Coupling of identified peptide sequences to the position in their corresponding milk proteins produced numerical data-sets that subsequently were utilized for multivariate data analyses.

Results: Principal component analyses revealed that hardly any batch-to-batch variation was present in the peptide profiles of an extensively hydrolyzed casein preparation. In formulae, on average several hundreds of peptides could be identified with a number of differentiating peptide sequence amongst the various hydrolysates. Some sequences even appeared to be unique to the peptide profile of certain hydrolysates. Moreover, extensive multivariate evaluations revealed that the peptide profiles of different commercially available hydrolyzed milk protein formulations provide a descriptive signature.

Conclusion: A combination of peptidomics and multivariate data analyses allows for a comprehensive comparison of hydrolyzed milk protein formulations at the peptide level. Overall, the descriptive methodology may contribute to the field of peptide research as observed dissimilarities in peptide profiles of similar products may determine differences in overall functionality.

**Common ESPGHAN Topics**

**Other Topics**

PO-CT-0351

**HOSPITAL ADMISSIONS FOR FOOD-INDUCED ANAPHYLAXIS IN ITALIAN CHILDREN ARE INCREASING: NEW REPORT FOR THE YEARS 2006-2011**

Rita Nocerino 1, Linda Cosenza 1, Ludovica Leone 1, Vincenza Pezzella 1, Tommaso Cozzolino 1, Margherita Di Costanzo 1, Gianluca Terrin 2, Riccardo Troncone 1, Roberto Berni Canani 1,*,

1Department of Translational Medical Science-Paediatric Section and European Laboratory for the Investigation of Food Induced Diseases (ELFID), University of Naples "Federico II", Naples, Italy,

2Department of Women’s Health and Territorial Medicine, University "La Sapienza", Rome, Italy

**Objectives & Study:** The food allergy (FA) pattern is changing in many western countries with an increased severity of manifestations. We reported an increased incidence of hospital admission because food-induced anaphylaxis (FIA) in Italy from 2001 to 2005. We aimed to explore if this trend was sustained during the most recent years.

**Methods:** The Italian Ministry of Health database was asked about hospital admissions for FIA from the year 2006; data were available up to year 2011. We identified hospital admissions for FIA using dedicated codes for FA and anaphylaxis (ICD-9 codes: 99560, 99561, 99562, 99563, 99564, 99566, 99567, 99568, 99569). We investigated the total number of hospital admissions over the 6 years period, and the food responsible for the disease. The number of deaths for FIA was also recorded.

**Results:** A total of 3,121 hospital admission for FIA from 2,552 subjects (56.5% male; mean age 15.5 years; minimum 0-maximum 92 years) occurred during the 6 years study period. For the age group 0-14 years, a total of 2,252 admissions for FIA from 1,785 subjects occurred during the study period. In the age group 0-4 years a continuous increasing trend was observed: in the year 2006 the total number of hospital admissions for FIA was 163, comparing to 235 admissions for the year 2011 (+44.2%, p<0.01). Similarly, in the age group 5-14 years we found an increase in the number of hospital admissions for FIA, from 107 in the year 2006 to 244 in the year 2011 (+128%, p<0.01). For the age group 0-4 years and 5-14 years the major foods responsible for anaphylaxis were cow’s milk and hen’s egg (cow’s milk 45.2% and 28.8% respectively; hen’s egg 22.4% and 20.8% respectively). We found a rate of subjects who received a final diagnosis of FIA but the particular food was not indicated in 18.4% in the age group 0-4 years and 28.5% in the age group 5-14 years. We identified 4 deaths for FIA, all occurred at hospital in patients aged >14 years. The food responsible were peanuts, crustaceans, fruits and vegetables; in one case the food responsible was not identified.

**Conclusion:** A persistent increase of number of hospital admission because of FIA occurred in the last decade in Italy. Our data suggest the importance of more research to investigate the causative factors and possible preventive strategies. An improvement of healthcare services for this condition is also advocated.

**Disclosure of Interest:** None Declared
CROSS- CULTURAL ADAPTATION OF A DISEASE-SPECIFIC, HEALTH RELATED QUALITY OF LIFE QUESTIONNAIRE (CDDUX) FOR ITS USE IN SPANISH COELIAC CHILDREN

J. Barrio 1,*, E. Román 2, M.L. Cilleruelo 3, C. Fernández 4, M. Marquez 5, ML Mearin 6

1Paediatrics, H.U. Fuenlabrada, Spain, 2Paediatrics, H. U. Puerta Hierro, Mexico, 3Paediatrics, H.U. Puerta Hierro, Mexico, 4Epidemiology, H.U. Clínico, 5ACM, Madrid, Spain, 6Paediatrics, LUCM, Leiden, Netherlands

Objectives & Study: The purpose of this study is 1. to develop a cross-cultural adaptation of a disease-specific health related quality of life (HRQOL) questionnaire (CDDUX) for its use in spanish celiac children, 2. to assess the validity and reliability of the CDDUX version for celiac patients aged 8-18 years, and 3. to evaluate the HRQOL and related factors.

Methods: A cross-sectional study about quality of life in celiac patients 8-18 years. Children members of the Madrid Celiac Association were invited by e-mail to participate. Previously, the CDDUX questionnaire was adapted following the systematic methodology of translation and reverse translation. The questionnaire consists of 12 items grouped into 3 subscales: having celiac disease (CD), communication and diet. There were two versions: one for parents and one for children. We analysed the psychometric properties using the Cronbach’s alpha coefficient with global analysis and by scales, in both children and parents. Demographic and clinical variables associated with HRQOL were also assessed. The scores were recoded into a scale from 1 to 100 by using a 5-point scale where 1-20 is consider very bad, 41-60 neutral, 61-80 good and 81-100 very good.

Results: 1602 celiac children out of 3122 censored members (from 8-18 years) were asked. The questionnaire was completed by 480 families (30%): 214 only by parents, 214 by matched parents and children and 52 only by children. The Cronbach’s alpha coefficient obtained from the overall score for parents was 0.90, and for children 0.88 (ranged from 0.75 to 0.90 by the scales). The mean (DS) HRQOL scores obtained in children were: 55.5 (12.7) overall, 46.5 (13.1) having CD, 72.0 (16.9) communication and 51.7 (17.3) diet. No significant differences were detected in the paired comparison between children and parents. According to a linear regression model, the only factors independently associated with a reduced HRQOL were non classical presentation (-3.71; 95% CI 6.44; -0.98; p=0.008) and finding it difficult to follow the diet (-6.69; 95% CI 10.59; -2.78; (p=0.001). Adherence to treatment was associated with a higher score of HRQOL (+6.03; 95% CI 0.62; 12.69; p=0.075).

Conclusion: The CDDUX questionnaire is a reliable HRQOL measurement instrument for our study population. Children with CD and their parents have a neutral experience of their HRQOL when they consider living with CD. The factors related to a worse HRQOL were non classical presentation and having difficulties to keep the diet.


Disclosure of Interest: None Declared
A FUNCTIONAL PROGNOSTIC SCORE FOR RESIDUAL BOWEL IN SHORT BOWEL SYNDROME NEWBORNS: A PRELIMINARY EVALUATION

Federico Scottoni 1,*, Andrea Conforti 1, Antonella Diamanti 2, Chiara Grimaldi 3, Manila Candusso 2, Giuliano Torre 2, Pietro Bagolan 1, Fabio Fusaro 1

1Medical and Surgical Neonatology, 2Hepatology, Gastroenterology and Nutrition Unit, 3Paediatric Surgery and Transplantation, Bambino Gesù Children Hospital, Rome, Italy

Objectives & Study: Anatomical site and length of residual bowel are usually considered predictors for prognosis and parenteral nutrition (PN) dependency in patients affected by short bowel syndrome (SBS). Aim of the present study is to evaluate a new prognostic bowel functional score for infants affected by intestinal failure related to SBS.

Methods: All infants at 1 year of age with neonatal SBS were enrolled. Retrospective analysis of medical chart was performed.

Residual Bowel Functional Score (RBFS) was defined by the following equation:

\[
\text{RBFS} = \frac{\text{Mean daily enteral Kcal}}{\text{Mean daily parenteral Kcal}} \times \frac{\text{weekly effective growth}}{\text{weekly expected growth}}.
\]

Expected growth has been conventionally considered 150 g/week.

RBFS was calculated at 2 (T1) and 3 (T2) months following the definition of SBS status.

Mann-Whitney test was used as appropriate. P<0.05 was considered significant.

Results: Eleven patients meet the inclusion criteria. Causes of SBS: multiple intestinal atresia (4 patients), volvulus (3 patients), necrotizing enterocolitis (2 patients), extended Hirschsprung’s disease (1 patient), mesenteric ischemia (1 patient). All patients underwent SBS related intestinal surgery before 4 months of age.

Mean residual bowel length was 30.6 cm (range 4-86).

At 1-year of age, 7 infants were off PN, while 4 persistently needed PN. Those off PN has a significantly higher RBFS at T1 (RBFS off-NP: 3.0; IQ range 0.75-6.3 vs on-NP 0.24; IQ range 0.0004-0.56; p 0.006) and T2 (RBFS off-NP: 2.2; IQ range 1.5-2.9 vs on-NP 0.15; IQ range 0.06-0.29; p 0.03)

Conclusion: Our data suggest that RBFS correlates with prognosis and PN dependency in infants affected by neonatal SBS. However, the intrinsic limit of the present study (retrospective data collection and limited number of patients) have to be considered. Prospective validation of the proposed score is warranted.

Disclosure of Interest: None Declared
HEPATO CYTES TRANSPLANTATION FOR AN INFANT OF ORNITHINE TRANSCARBAMYLASE DEFICIENCY USING CELLS ISOLATED FROM LIVING DONOR REDUCED-GRAFT TISSUE

Akira Matsui 1,*, Reiko Horikawa 1, Akiko Yamamoto 1, Seisuke Sakamoto 1, Takanobu Shigeta 1, Shunsuke Nosaka 1, Junichiro Fujimoto 1, Akito Tanoue 1, Kazuaki Nakamura 1, Akihiro Umezawa 1, Yoichi Matsubara 1, Mureo Kasahara 1

1National Center for Child Health and Development, Tokyo, Japan

Objectives & Study: Hepatocyte transplantation (HT) has been indicated in patients with metabolic liver disease as an alternative or bridge to liver transplantation (LT) in children. Limitation to wide application of HT is availability of hepatocytes. We performed HT for 11-days baby with ornithine transcarbamylase deficiency (OTCD), using cryopreserved hepatocytes from segment III of liver reduced-graft procedure in a living donor surgery.

Methods: Cell donor was an unrelated volunteer with same blood type, who had undergone reduced left lateral segmentectomy as a living donor. Segment II was used as a monosegmental liver graft for his son who suffered end-stage liver disease. Separately, the remnant segment III was used for hepatocyte isolation and the cells were cryopreserved until HT under informed-consent. Hepatocytes were transplanted twice from umbilical vein at 11 and 14 days of age. Amount of hepatocyte at each HT was 74 million cells/body and 66 million cells/body with a viability of 89.1% and 82.6%, respectively. The posttransplant protocol included immunosuppressant therapy with tacrolimus and low dose steroid. All procedures were conducted under the permission of Institutional Review Board.

Results: The baby was delivered vaginally as a first child. At 3 days of age, hypothermia, low oxygen saturation, and finally, respiratory arrest happened. The patient was incubated and given artificial respiration. Concurrently, hyperammonemia (1.940μg/dL) was found and continuous hemodiafiltration started in addition to alimentotherapy (protein withdrawal) and medications. Whenever the administration of essential amino acid restarted, blood ammonia level elevated and at 9 day of age, in spite of suspension of essential amino acid administration, the level was increased. Continuous hemodiafiltration and the ventilator were weaned at 26 and 30 days of age, respectively, with a stable serum ammonia level of 40μg/dl. The patient was ultimately discharged 56 days after HT. During the three months of follow-up, the baby has been doing well with protein restriction (2g/kg/day), medication for OTCD and immunosuppression. No neurological sequelae related to hyperammonemia have so far been observed.

Conclusion: Hepatocyte from remnant liver from living donor reduced-graft procedure deserves consideration as a method to extend the pool of available cells for transplantation.

Disclosure of Interest: None Declared