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CP-N-0018

MODIFICATION OF MATERNAL FEEDING BEHAVIOR EFFECTS GROWTH OF INFANTS DIAGNOSED WITH FEEDING DISORDERS

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Objectives and Study: In a previous study we have shown that the Role Reversal method for treating Infantile Feeding Disorders (IFD), focuses on maternal feeding behavior modification without any direct intervention in the child's eating habits or his caloric intake, significantly affected maternal feeding patterns and reduced the incidence of child's food refusal (1). In the present study, we examined prospectively the influence of this method on child's growth parameters and the relation to mother's perception and occupation regarding the child's IFD.

Methods: Mothers of infants and toddlers diagnosed with IFD were invited to participate in the study. Mothers filled out a questionnaire recording patient and parents' behaviors, attitudes and perceptions, at initiation and at the end of treatment (after 3-6 months). Anthropometric data of patients was collected and age- and gender-specific z-scores (SDSs) were determined according to Centers for Disease Control and Prevention (CDC) growth charts.

Results: Twenty-nine pairs of IFD patients, 23.1±15.7 months, and their mothers, participated in the study. Mean patients' weight for age was -1.48±1.45 SDS and 18 (60%) of them were diagnosed with Failure to Thrive (FTT) after crossing two major lines of the CDC growth charts. Following treatment, an increase or stabilization of weight gain (∆Weight-Z Score≥0) was found in 15 (52%) patients, 11 (73%) of them had had FTT. Weight gain was inversely correlated with patient's age (p<0.05) and maternal extent of occupation regarding patient's IFD (p<0.05). ∆ Height-Z Score≥0 were found in 12 of 21 patients (57%). Higher levels of maternal education was associated with greater success in the program.

Conclusion: Modification of maternal feeding patterns alone, using the Role Reversal method, can improve growth parameters of patients with food refusal and FTT. This method was found to be more effective when applied in younger children.


Disclosure of Interest: None Declared
ENZYME REPLACEMENT THERAPY IN CYSTIC FIBROSIS: THE CHALLENGE TO ACHIEVE AN OPTIMAL FOOD REABSORPTION COEFFICIENT

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Objectives and Study: Pancreatic Enzyme Replacement Therapy (PERT) is a major challenge in the treatment of Cystic Fibrosis (CF). Recommendations on dosage rely on patient’s age and body weight, but this may be an insufficient evidence-based criterion to successfully adjust it: esteatorrhea stills present in patients, values increasing and decreasing over time. Moreover, patients follow a fixed pattern of PERT-dosage for the different meals. Lipase enzyme contained in oral supplement aims at the hydrolysis of the fats present in meals (its substrate), thus we have hypothesised that dietary fat could be a better criterion to effectively adjust the PERT. The aim of this study is to assess the Fat Reabsorption Coefficient (FRC) with the enzyme/substrate ratio, and find out if there is a correlation.

Methods: Prospective study in which a Food Record (FR) template was specifically developed including questions on oral-supplement dosage per meal and time and description of stool depositions. 16 patients followed a 4-days FR plus a 3 days stool collection, 3-4 times along 1.5 years. Fat in stool test was performed and FRC was calculated according to dietary fat ingested between periods of 24h, coinciding with each day of stool collection. Enzyme/substrate (E/S) ratio (Lipase IU/g of fat) was calculated. We assessed the association between variability in FRC and variability in E/S using a robust linear regression model.

Results: A statistically significant correlation between FRC and E/S ratio variability (p<0.001) was found, being the lowest variability in the E/S ratio pattern, the lowest variability in the FRC value (figure), this being true both for the highest and the lowest values of FRC. Patients who successfully adapted the oral-supplement dose according to the fat content of meals obtained non-variable FRC values, and patients who followed a fixed pattern obtained variable FRC results (table).
Conclusion: It is possible to maintain stable an E/S ratio if oral-supplement dosage is re-adjusted for each meal, but it is not enough to guarantee high values of FRC. The way ahead is find the optimum E/S ratio for each patient plus maintain it stable.

Disclosure of Interest: None Declared
IMPROVED GROWTH, TOLERANCE AND INTAKE IN INFANTS WITH COMPLEX DISEASE ON AN EXTENSIVELY HYDROLYSED FORMULA DESIGNED FOR CATCH UP GROWTH

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Objectives and Study: The aetiology of faltering growth is often multifactorial, including increased requirements, severe malabsorption and poor feed tolerance. Nutrition support strategies include extensively hydrolysed peptide feeds. Historically, these were powdered products, associated with increased risk of contamination and constitution error and were not nutritionally designed to support catch up growth. The aim of this prospective, longitudinal study was to evaluate the tolerance, compliance, intake and growth with a ready to use peptide feed in a group of infants with growth faltering who were unable to tolerate whole protein standard infant feeds.

Methods: 18 infants with a range of complex diseases (mean age of 6.11 ± 4.69 months, weight for age Z Score of -2.67±1.1), recruited from 7 UK hospitals completed the 4 week intervention. The peptide feed was a ready to use, 1 kcal /ml 10.4% protein energy ratio, extensively hydrolysed (whey) peptide feed, containing 48% fat as MCT, osmolality 360mosmol/kg H2O (Infatrini Peptisorb, Nutricia Ltd). Tolerance (measured as gastrointestinal symptoms, ability to consume prescribed feed and healthcare professional opinion), compliance (% of prescribed feed consumed) and anthropometric (weight, length, head circumference) data were recorded during the 28 days on the peptide feed in addition to a comprehensive patient history.

Results: Tolerance to the ready to use peptide feed either improved or remained the same over the 28 days. All 18 babies continued on the peptide feed once the study was complete. Mean compliance was 94.02%±12.60 over the entire study. There were significant increases in mean weight (0.61kg ± 0.31, p=0.0001), length (1.89 ± 1.77 cm, p=0.0001), head circumference (1.33 ± 1.29 cm, p=0.001), weight for length Z score (p<0.05) and weight for age Z Score (p<0.05). 61% (n=11) of infants showed signs of increased growth velocity, moving upwards in terms of their centile charts.

Conclusion: This study showed that the ready to use peptide feed was well tolerated and improved growth in infants with complex diseases, who could not tolerate a whole protein feed. This study was supported by a grant from Nutricia Ltd, Trowbridge, United Kingdom.
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AHP-0003

IODINE STATUS IN INFANTS AND CHILDREN UNDER 2 YEARS OF AGE ALLERGIC TO COW’S MILK PROTEINS

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Objectives and Study:
Allergy to cow’s milk protein is the most common food allergy in small children. A diet without milkproteins is potentially low in many nutrients, and could put the child at risk of malnutrition (1,2). Dairy products are the major source of iodine in most western diets, and excluding these reduces iodine intake (3). A low level of iodine during childhood could potentially be detrimental and puts the child at risk for delays in mental development and growth. Little is known about the iodine status and intake in this group of children.

Aim: To investigate iodine status in infants and children under 2 years of age allergic to cow’s milk proteins.

Methods: Fifty infants and children under 2 years of age following a cow’s milk protein free diet were included from Oslo University Hospital, Department of Paediatric Medicine. To evaluate dietary intake of iodine a 3 day food record and a food frequency questionnaire were used. Two spot urine samples from each child were collected and analysed for iodine. Urinary iodine levels were compared to the WHO cut off values for iodine deficiency (4) and to the dietary intake of iodine.

Results: Preliminary results are indicating a low dietary intake and a high incidence of iodine deficiency in this population.

Conclusion: Exclusion of cow’s milk protein, the major foodsource of iodine, increases the risk of deficiency. Our preliminary results are in line with this notion. Small children in particular are prone to detrimental effects. It is thus important to identify these high risk children for iodine deficiency and ensure alternative sources of iodine in the diet.

References:

Disclosure of Interest: None Declared
Objectives and Study: We aimed to examine the consumption of beverages in a sample of Slovenian pregnant and lactating women.

Methods: We included 167 pregnant and 141 lactating women from the study “My-Milk” (www.moje-mleko.si/en). The diet was assessed by a 4-day weighted dietary record (DR) in pregnant (3rd trimester of pregnancy) and lactating women (4 weeks post partum). The beverages were divided into: a) sugary beverages with: a1) added sugar (sugar sweetened beverages (SSBs): including flavoured water, sports drinks, ice teas, energy drinks, beverages prepared with syrups, sweetened carbonated drinks, fruit nectars and tea with sugar), a2), naturally occurring sugars (fruit juices, smoothies), a3) other beverages with added sugar (cocoa, hot chocolate, coffee with sugar, vegetable drinks (rice drink, soya drink, etc.)); b) sugar-free beverages: b1) water, mineral water, tea and coffee without sugar/honey, b2) coffee, b3) non-caloric beverages with sweeteners; c) alcoholic drinks (wine and beer).

Results: Mean consumption of SSBs (a1) was 230 ml/day (11 % of beverages) in pregnant women and 267 ml/day (11 % of beverages) in lactating women. Consumption of fruit juices and smoothies (a2) was 92 ml/day (4 % of beverages) in pregnant and 66 (3 % of beverages) in lactating women. Consumption of other sugary beverages with added sugar (a3) was 84 ml/day in pregnant women (4 % of beverages) and 70 ml/day (3 % of beverages) in lactating women. Consumption of water and mineral water (b1) was 1,640 (76 %) in pregnant women and 1,942 ml/day (79 % of beverages) in lactating women. Consumption of sugar free coffee (b2) was 95 ml/day (4 % of beverages) in pregnant and 76 ml/day (3 % of beverages) in lactating women. Consumption of non-caloric beverages with sweeteners (b3) was 2 ml/day (0.1 % of beverages) in pregnant and 3 ml/day (0.1 % of beverages) in lactating women. Consumption of alcoholic drinks (c) was 11 ml/day (0.5 % of beverages) in pregnant and 22 ml/day (1 % of beverages) in lactating women. Energy intake (mean (SD)) was 2,083 kcal/day (372) in pregnant women and 2,127 kcal/day (498) in lactating women. SSBs contributed 3 % (61 kcal), fruit juices/smoothies 1.5 % (32 kcal) and other beverages with sugar 1.7 % (36 kcal) to the daily energy intake in pregnant, 3.1% (65 kcal), 1.1% (23 kcal) and 2.0% (43 kcal) in lactating women.

Conclusion: Slovenian pregnant and lactating women drink excessive amounts of sugary beverages, especially SSBs, which pose dangers to their and their children's long-term health as well as to the society as a whole. Reducing the intake of SSBs would need to become a public health priority.
Disclosure of Interest: None Declared
Objectives and Study: We previously defined four subsets of innate lymphocytes (CD45+CD7+CD3-CD14-CD19-) in the human intestinal epithelium, distinguished by the presence or absence of CD56 and IL-7Rα (CD127). Of these four subsets, the CD56+CD127 subset bears strong resemblance to the recently described innate-like lymphoid cells (ILC) type 1 in the epithelium. To investigate the full diversity of intestinal innate lymphocytes and their relationship with the ILC family, we applied high-parameter mass cytometry (cytometry by time-of-flight; CyTOF).

Methods: We designed a CyTOF panel of 32 monoclonal antibodies recognizing lineage markers, activation markers, and chemokine and cytokine receptors, including several markers commonly used to identify ILCs. This panel was used to define and compare the phenotypic diversity of innate and adaptive lymphocytes in intestinal biopsies and blood samples from non-diseased individuals and from patients with inflammatory intestinal diseases (i.e. celiac disease, RCDII and Crohn’s disease). By combining bio-informatics tools that allow unsupervised hierarchical clustering (SPADE) and nonlinear dimensionality reduction (viSNE), we were able to visualize innate and adaptive lymphocytes from ~100 samples at single-cell resolution in a single map that took into account all 32 phenotypic markers concurrently.

Results: From our antibody panel, 20 markers were differentially expressed by innate lymphocytes, including the cell-surface markers CD11c, CD45RA, CD8a, c-Kit (CD117), CD161, NKp46 and several cytokine receptors. We observed two distinct types of marker expression profiles within the innate lymphocyte compartment: (1) Gradients of marker expression indicative of transitional states between cell populations. (2) Highly restricted expression profiles indicative of phenotypically distinct cell populations that were automatically identified in an unbiased, data-driven manner with ACCENSE analysis. In addition, we observed highly distinctive tissue and disease-specific expression profiles both within the adaptive and innate lymphocyte compartments.

Conclusion: We conclude that CyTOF offered unprecedented depth in the analysis of cellular heterogeneity of both the innate and adaptive lymphocyte compartment present in intestinal biopsies, results that can be used to obtain functional insight into the role of innate and adaptive subpopulations in health and disease.

Disclosure of Interest: None Declared
IN THE INTESTINAL MUCOSA OF CHILDREN WITH POTENTIAL COELIAC DISEASE
IL21 IS LESS EXPRESSED THAN IN THE ACTIVE DISEASE

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Objectives and Study: Potential celiac disease is characterized by the presence of anti-tissue transglutaminase2 antibodies and normal small intestinal mucosa despite a Th1 skewed immune response. Interleukin 21 (IL-21) and IL-17A have recently been reported to contribute to the pathogenesis of celiac disease (CD). We aimed to investigate the presence of both IL-21 and IL-17A in potential CD and using the organ culture system, the role of gliadin peptides and IL-15 in their expression.

Methods: Duodenal biopsies from 76 active CD, 90 potential CD and 58 control patients were analyzed for IL-21 and/or IL-17A production by quantitative real-time PCR, immunohistochemistry, flow cytometry and ELISA. The presence of IL-21 receptor was investigated by western blot. Intestinal biopsies from potential CD patients were cultured in the presence of gliadin peptides (PTG) or IL-15 or both and the expression/production of IL-21 and IL-17A assessed by quantitative real-time PCR and immunohistochemistry.

Results: IL-21 RNA expression as well as density of lamina propria IL-21 immunostained cells were significantly lower in potential CD mucosa when compared to active CD (p<0.01, p<0.05, respectively), but similar to controls. IL-21 protein secreted spontaneously into culture medium of biopsies from potential CD was lower in comparison to active CD (p<0.05). Also IL-21R was less expressed in potential CD mucosa. Flow cytometry confirmed that lamina propria CD4+ cells overproduced IL-21 both in active and potential CD although they were not the major sources of the cytokine. Interestingly the majority of lamina propria IL-21+CD4+ cells coexpressed IFN-g but not IL-17A. IL-21 but not IL-17A producing cells, increased after 24 hours of culture with PTG in the mucosa of potential CD patients. The addition of IL-15 to culture medium further increased IL-21 production.

Conclusion: In potential CD IL-21 expression is low, suggesting a key role of the cytokine in the pathogenesis of villous atrophy in CD. The mechanisms involved in the switch of its production in CD remain largely to be elucidated.

Disclosure of Interest: None Declared
Objectives and Study: Coeliac disease (CeD), an immune mediated gluten induced enteropathy affects approximately 1% of the europeans and occurs in genetically susceptible individuals only. Diagnosis in early stages of the disease is challenging, due to the heterogeneity of CeD. If CeD could be detected at an early stage, severe consequences of CeD, such as chronic diarrhoea and failure to thrive could be prevented by quick initiation of a gluten free diet. However, no early biomarkers for CeD previous to enteropathy development are known.

In the search for predictive disease biomarkers, circulating microRNAs (miRNAs) have captured the attention of the medical world. In contrast to mRNA, miRNAs are very stable in blood due to transport in (lipo)protein complexes or exosomes. Changes in plasma miRNA levels have been associated in several other immune-mediated diseases.

In this study we aim to identify circulating miRNAs that could function as early biomarkers for CeD.

Methods: The PreventCD study provides an unique prospective cohort for CeD biomarker discovery. In this study blood was drawn from high risk infants at set timepoints after birth, at time of diagnosis and after start of gluten free diet. miRNA profiles were determined in 253 serial samples of 32 PreventCD participants that developed CeD during the study, 11 subjects in which CeD-antibodies were elevated but did not develop CeD (1 subject with elevated anti-tTG, 10 subjects with AGA), and of 10 children that did not develop CeD (coined controls).

Total RNA was isolated by miRvana Paris kit, miRNAs libraries were prepared using the TruSeq Small RNA Sample Preparation Kit and were sequenced using the Illumina HiSeq2500. Data was preprocessed and SRNAbench was used to trim adapter sequences and align the reads to the human reference genome. The DESeq2 R-package was used to evaluate differential expression. P-values were corrected for false discovery rate (FDR) by Benjamini and Hochberg's method.

Results: Interim analysis of half of the samples identified 25 miRNAs to be significantly differentially expressed (FDR corrected) between the available month 4 samples and samples taken at the time of diagnosis. Some of these miRNAs display a gradual increase or decrease until diagnosis and, intriguingly, normalise to healthy levels after the start of gluten free diet.

Conclusion: Some of the miRNA candidates appear to be potential biomarkers for early CeD development and for diet compliance. In the next few months we will sequence the remaining samples and complete this study. In addition, miRNAs will be correlated to clinical data, such as gender, age, diet, antibodies and PreventCD intervention (gluten challenge versus placebo).
Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PA-G-0032

**DIPOTASSIUM GLYCYPHRIZATE NORMALIZES THE MUCOSAL HEALING GENE EXPRESSION ALTERED BY INFLAMMATION IN A MURINE MODEL OF COLITIS**

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**Objectives and Study:** Dipotassium glycyrrhizate (DPG) is a compound derived from glycyrrhizin, a glycoconjugated triterpene produced by the licorice plant, Glycyrrhiza glabra, whose anti-inflammatory properties are well-known. DPG reduce inflammation though various mechanisms, including the inhibition of the alarmin high mobility group box (HMGB)1 and the enzyme 11beta-hydroxysteroid dehydrogenase 2 (11βHSD2).

We previously demonstrated that DPG significantly reduces the DSS-induced colitis in mice, that showed a surprising recovery of body weight and large intestine length as well as an increase in histological score, the latter indicating the occurrence of a mucosal healing (MH).

The aim of the present study was to deeply investigate the effect of DPG on the expression of genes involved in the mucosal healing (MH) pathway during inflammation.

**Methods:** C57BL/6 mice were divided into 3 experimental groups (5 mice for each group): DSS (3%)-treated mice, DSS (3%)+DPG (8mg/Kg)-treated mice and control mice. After 7 days, mice were sacrificed and the colon removed. Tissue samples were analysed by a PCR array (QIAGEN) able to evaluate 84 key genes central to the wound healing response. To identify the most altered genes, a threshold of 3.5 times was chosen. Selected genes were divided into functional groups. The expression level of the most altered genes inside each group was validated by RT-PCR.

**Results:** DSS treatment significantly up-regulated 19 MH genes, as showed by comparing DSS-treated vs control mice. These genes were significantly down-regulated to control values by DPG treatment, as showed by comparing DSS+DPG mice vs DSS mice.

Altered genes were classified into 6 different functional groups: cytokines (IL-10, IL-1β, IL-6), chemokines (CCL12, CCL7, CXCL1, CXCL3, CXCL5), extracellular matrix (ECM) components/collagen proteins (Col3a1, Vtn), growth factors (Csf3, Fgf2, Fgf7), remodelling enzymes (Mmp9, Timp1, Plat, Plaur, Serpine1), others (Ptgs2). Expression analysis of most altered genes within each functional group was validated by RT-PCR (p<0.001: IL-1β, IL-6; p<0.01: CXCL3, CXCL5, Col3A1, Vtn, Fgf7; p<0.05: Mmp9, Serpine1).

**Conclusion:** We show for the first time that the use of DPG in mice with a DSS-induced colitis strongly improves the MH by modulating the expression levels of genes involved in wound healing response. Due to the total lack of side effects, we believe that DPG could represent a very innovative and useful tool for the management of human intestinal inflammation.
Disclosure of Interest: R. Vitali: None Declared, F. Palone: None Declared, L. Stronati: None Declared, E. Prete: None Declared, M. Costanzo: None Declared, F. Civitelli: None Declared, F. Nuti: None Declared, M. Aloi: None Declared, S. Cucchiara Conflict with: Develop Registry, Johnson & Johnson
DOES ACTIVATION OF CASR REPRESENT A NEW METHOD TO REDUCE SECRETORY AND INFLAMMATORY DIARRHEA?

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Objectives and Study: Treatment of infectious diarrheas remains a challenge, particularly in immunocompromised patients in whom infections usually persist and resultant diarrhea is often severe and protracted. Children with infectious diarrhea who become dehydrated are normally treated with oral or intravenous rehydration therapy. Although rehydration therapy can replace the loss of fluid, it does not ameliorate diarrhea. Thus, during the last decades, there has been continuous effort to search for ways to safely stop diarrhea. The extracellular calcium-sensing receptor (CaSR) is an ancient G protein-coupled receptor that uses nutrients, such as calcium, polyamines and amino acids, as its ligands. This receptor is highly expressed in the gut, and when activated, inhibits intestinal fluid secretion and inflammation suggesting that activating CaSR might represent a way to stop diarrhea, both secretory and inflammatory.

Methods: To test this hypothesis, cholera toxin model of secretory diarrhea and dextran sodium sulfate (DSS) model of inflammatory diarrhea were induced in 4-6 wk-old Sprague-Dawley rats and CaSR wild type and knockout C57BL/6 mice and effects of CaSR agonists were examined. To prove the concept, antidiarrheal effect on patients with infectious diarrheas assessed.

Results: Mice receiving cholera toxin developed diarrhea; the latter was inhibited by the specific CaSR agonist R-568, i.p. in wild type but not in knockout mice. DSS induced inflammatory diarrhea, which was significantly more severe in knockout than wild type mice. In rats, activation of CaSR by calcium, spermine or tryptophan attenuated diarrhea induced by DSS. Six patients with viral, bacterial and/or parasitic diarrhea were treated by administration of calcium (2mEq/kg/day), orally or intravenously. Consistent with active control of intestinal secretion and inflammation by the CaSR, their diarrheas were successfully “halted” within 1 to 2 days following the administration of calcium.

Conclusion: Our results suggest activating CaSR in the gut might represent a new modality to stop diarrhea and treat gut inflammation.

Disclosure of Interest: None Declared
Comparing Serum Bacterial DNA and Lipopolysaccharide in Preterm Infants Randomised to Bifidobacterium breve BBG-001 versus Placebo

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Objectives and Study: Introduction

Under normal circumstances, the intestinal mucosal barrier prevents potentially pathogenic bacteria and toxins from entering the systemic circulation. In preterm babies, the mucosal barrier is immature and factors occurring postnatally may result in further loss of barrier function. This may result in translocation which is regularly cited in the pathogenesis of necrotising enterocolitis (NEC). Probiotics may enhance intestinal barrier function via a number of different mechanisms thereby reducing translocation. Meta-analyses of probiotic studies in preterm babies have reported reduced rates of NEC in babies receiving this intervention but data are controversial. In vivo studies of probiotic mechanisms in this patient group are lacking.

Hypothesis

That randomisation to Bifidobacterium breve BBG-001 is associated with reduced evidence of bacterial and lipopolysaccharide translocation in preterm babies <31 weeks.

Methods: Babies recruited to this study were already enrolled to a randomised controlled trial of Bifidobacterium breve BBG-001 versus placebo for the prevention of NEC, sepsis or death (The PiPS Study). Blood samples were collected weekly for 4 weeks from a cohort of infants starting 14 days after birth. 16S rRNA Real-time PCR and ELISA were used to detect the presence of bacterial DNA and LPS endotoxin in blood and plasma.

Results: Eighty six infants were enrolled [median (range) gestation 26.5 (23-30) weeks and median (range) birth weight 859 (572-1800) g]. One hundred and forty samples were collected from 41 babies randomised to BBG and 152 samples were collected from 45 babies randomised to placebo. Results are presented in Table 1.

Table 1. Results

<table>
<thead>
<tr>
<th></th>
<th>Bifidobacterium breve BBG 001</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive 16S</td>
<td>7/140 (5%)</td>
<td>8/152 (5%)</td>
<td>1.0</td>
</tr>
<tr>
<td>Lipopolysaccharide</td>
<td>27/140 (19%)</td>
<td>24/152 (15%)</td>
<td>0.44</td>
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Conclusion: In this cohort, administration of Bifidobacterium breve BBG-001 was not associated with a reduction in bacterial and endotoxin translocation. To date, there remains no evidence of benefit for probiotic use in babies weighing <1000g at birth. Studies such as this might help inform optimal strain selection for future probiotic trials in preterm babies.

Disclosure of Interest: None Declared
SCREENING FOR IBD IN CHILDREN WITH CHRONIC GASTROINTESTINAL SYMPTOMS IN PRIMARY CARE WITH FECAL CALPROTECTIN, A PROSPECTIVE COHORT STUDY.

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Objectives and Study: Fecal calprotectin (fCal) is a non-invasive diagnostic test in children presenting with gastrointestinal symptoms to rule out inflammatory bowel disease (IBD). The diagnostic accuracy has been extensively evaluated in secondary and tertiary care, but not in primary care. The aim of this study was to evaluate the diagnostic accuracy of fCal as a screening method for IBD in children with chronic gastrointestinal symptoms in primary care.

Methods: We studied two cohorts of children. The general practitioner (GP) cohort consisted of consecutive children with chronic diarrhoea and/or abdominal pain. Subjects in this cohort were primarily seen by their GP and were referred for specialist care when they had increased risk for IBD. The hospital cohort consisted of consecutive children who were primarily seen by a paediatrician. fCal was measured at inclusion (index test) and the results were compared to endoscopy or clinical assessment at 1-year follow-up (reference standard). Both paediatricians and GPs were blinded for the fCal result. The specificity of fCal in primary care was calculated in the GP cohort. The diagnostic accuracy of fCal was calculated in children referred for suspected IBD to specialist care.

Results: We included 103 children (median age 9 years (IQR 5-12)) in the GP cohort and 63 children (median age 12 years (IQR 7-15)) in the hospital cohort. In the GP cohort 35 children had increased risk for IBD and were evaluated by a paediatric gastroenterologist. None of these children was ultimately diagnosed with IBD. fCal was elevated (>50 mg/g) in 13 of 103 children (median 88 mg/g (IQR 69-151)), yielding a specificity of 0.87 (95% CI 0.80-0.92). In the total group of children seen at hospital level (n=63+35=98), IBD was confirmed by endoscopy in 16 patients. All of them had elevated fCal levels (median 711 mg/g (IQR 470-824)). Sensitivity and specificity in children at increased risk for IBD was 1.00 (95% CI 0.81-1.00) and 0.85 (95% CI 0.76-0.91) respectively. A cut-off point of 250 mg/g gave the optimal diagnostic accuracy with a sensitivity of 0.81 (95% CI 0.57-0.93) and specificity of 0.99 (95% CI 0.93-1.00).

Conclusion: fCal showed high specificity in children with chronic gastrointestinal symptoms presenting in primary care and good diagnostic accuracy in children at increased risk for IBD. Our results suggest that fCal testing in primary care is helpful in identifying those children that need referral for specialist care. Children with normal fCal levels do not need to be referred.
Disclosure of Interest: None Declared
**Objectives and Study:** Coeliac disease and type-1 diabetes mellitus (T1D) are often associated and coeliac antibodies are also present in the pancreas. However, it is still unclear whether coeliac autoimmunity directly causes T1D as a complication of coeliac disease. Although manifest T1D does not change anymore in response to a gluten-free diet (presumably because islet cells are already irreversibly lost), coeliac disease may be subclinically present long before clinical T1D appears and timely treatment in such cases may offer a window of opportunity to slow down or reverse pancreatic damage.

**Aim of this study** was to evaluate whether early detection and treatment of coeliac disease in the population would decrease subsequent T1D prevalence in childhood.

**Methods:** The prevalence of T1D was studied in 2014 in a county among schoolchildren (n=21724) in five birth year cohorts born between 1.6.1996 and 31.5.2001 using local school nurse registries and data from diabetes centres. The middle school year cohort born between 1.6.1998-31.5.1999 received screening for anti-transglutaminase and anti-endomysial antibodies in 2005, at the age of 5-6 years (BMJ 2007;335:1244-7), where 78% of the total eligible population took part and coeliac disease cases confirmed by small bowel biopsy were treated by a gluten-free diet and followed by regular serology monitoring at the local gastroenterology unit. The screened and not screened children were exposed to identical other environmental factors.

**Results:** None of the screen-detected and treated coeliac cases (n=45) developed T1D. The prevalence of T1D was 2.69/1000 children (95% confidence intervals [CI] 1.92-3.46) in the not screened control birth cohorts comprising children 1 and 2 years older as well as 1 and 2 years younger than the screened cohort. The prevalence of T1D was 0.93/1000 children (95% CI 0.02-1.85) in the screened cohort, odds ratio 0.35 (95% CI 0.13-0.96). Parents had declined participation in the coeliac screening in 2005 in half of the later T1D cases in the screened cohort. Eighty-two percent of all paediatric T1D cases in the population appeared after the age of 6 years.

**Conclusion:** Early detection and treatment of coeliac disease may prevent a substantial fraction of paediatric T1D cases. Screening at the age of 6 years seems to be still efficient. It also looks equally important to achieve good dietary adherence during coeliac disease treatment.

Grant support: nPOD, TÁMOP-4.2.2.A-11/1/KONV-2012-0023
Disclosure of Interest: None Declared
CLOSTRIDIUM DIFFICILE TOXINS INDUCE CHLORIDE SECRETION, EPITHELIAL DAMAGE AND OXIDATIVE STRESS IN INTESTINAL EPITHELIAL CELLS.

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Objectives and Study: Clostridium difficile (CD) is the leading cause of nosocomial diarrhea and it is the etiologic agent of pseudomembranous colitis. Toxin A (TcdA) and B (TcdB) are thought to play a major role in inducing diarrhea although their role is far to be understood. The aim of this study is to investigate the direct role of CD toxins in inducing one or both chloride secretion and epithelial damage in an in-vitro model of diarrhea in human cell lines. Oxidative stress was also investigated.

Methods: To test the hypothesis that CD toxins induce an increase in chloride secretion (enterotoxic effect) in intestinal epithelial cells, Caco-2 cell monolayers were exposed to TcdA or TcdB at different doses for 1 hour and the short circuit current (Isc) was measured in Ussing Chambers. The cytotoxic effect induced by CD toxins was evaluated by occluding. The oxidative stress was investigated evaluating the reactive oxygen species (ROS) increase. ROS was assessed using dichlorofluorescein (DCF) by fluorimetric method and fluorescence microscopy.

Results: TcdB, but not TcdA, induced a dose-dependent increase in Isc with a maximal effect at 100ng/ml (DIs= +10.63±3.7 vs 1.7±2.9; p<.05) indicating a direct effect on chloride secretion. Immunofluorescence staining of occludin clearly showed the disruption of cell-cell junctions in Caco-2 cell monolayers exposed to TcdA or TcdB compared with untreated cells, indicating that both CD toxins induced the cytotoxic damage. Finally, TcdA and TcdB induced oxidative stress increasing ROS intracellular level (247±57 and 318±45 respectively vs 19±21 DCF fluorescence units, p<.05). Microscopic evaluation confirmed the CD toxins-induced oxidative stress in Caco-2 cells.

Conclusion: Both TcdA and TcdB induced the epithelial damage and cell oxidative stress, but only TcdB is responsible of increase of chloride secretion by alteration of transepithelial ion transport suggesting that plays a key role in CD-induced diarrhea.

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

PA-G-0069

**EFFICACY AND SAFETY OF WIRELESS CAPSULE ENDOSCOPY IN 305 PAEDIATRIC PATIENTS: A TERTIARY CENTRE EXPERIENCE**

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**Objectives and Study:** Wireless capsule endoscopy (WCE) is a useful diagnostic tool proposed to observe small-bowel lesions undetectable by conventional endoscopy.

**Aim:** Assessment of diagnostic yield and safety of WCE in a large cohort of paediatric patients and to compare with magnetic resonance enteroclysis (MRE).

**Methods:** In a retrospective review of consecutive capsule endoscopy studies, 305 studies were performed in 265 patients with a mean age of 11.2 (range 2-18) years during an 8-year period. 47(15%) patients were younger than 6 year old. 136(46%) underwent WCE for suspected or confirmed Crohn’s disease (CD); 13 (4%) anaemia; 55 (18%) obscure gastrointestinal bleeding; 12% (37) polyposis; 13(4%) intestinal lymphangectasia; 30(10%) recurrent and chronic abdominal pain.

**Results:**

**Safety:** 34(11%) patients had delayed passage of the capsule beyond the study period but none necessitated endoscopic removal because of symptoms.

**Efficacy:** 152(51%) had positive findings and 170 WCE findings (57%) led to a change in management of patients.

WCE resulted in reclassification of 15 IBD from indeterminate colitis to CD and another 30 patients to likely UC. 32(64%) of 50 patients with previously diagnosed CD had more extensive small bowel disease identified leading to treatment escalation.

In polyposis: 22(59%) WCE were positive for suspected PJP, and 12(32%) had a positive finding leading to endotherapeutic resection/ablation. In 9(24%) WCE for Familial Adenomatous Polyposis (FAP)/Gardner, 2 had small polyps detected in small bowel but no intervention was necessary.

For obscure GI bleed, 10 patients had had identified bleeding site during conventional endoscopy and 23(42%) patients had positive findings from WCE. All positive cases were followed by DBE/enteroscopy with endotherapeutic intervention.

24 suspected small bowel IBD involvement had both MRE and WCE: 21(88%) cases had similar outcome for both modalities where as 2(8%) cases showed positive WCE finding of extensive luminal Crohn’s and negative MRE finding. One case (4%) had positive MRE finding of small bowel stricture and negative WCE finding. 3 cases showed hold up of the capsule in some areas and correlated with MRE finding of narrowing. Hence WCE had 95% sensitivity and 100% specificity versus 89% sensitivity and 100% specificity for MRE.
**Conclusion:** WCE is a safe and reliable investigation with 51% diagnostic yield in our patient cohort and changed management in 57%. Its use in recurrent or chronic abdominal pain is of no diagnostic value in our cohort.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Management of non-IgE mediated gastrointestinal (GI) multiple food protein allergy (MFPA) in early childhood involves allergen avoidance using either an extensively hydrolysed formula (eHF) or an amino acid-based formula (AAF) as a cow’s milk formula substitute. Whilst eHF and AAF are both hypo- or non-allergenic, clinical anecdote suggests that AAF relieve symptoms more effectively than using an eHF or specific allergen avoidance. The aim of this study was to explore the potential additional immunomodulatory properties of AAF.

**Methods:** Biopsies from the ascending colon of 48 paediatric patients (≤ 5 years) on diets free of cow’s milk, egg, wheat and soya undergoing diagnostic colonoscopy were cultured for 24 hours with media only, 250µg/ml AAF (Neocate), eHF (Nutramigen) or a whole protein feed (Aptamil). Post-stimulation, immune mediators were quantified by qPCR, ELISA and/or multiplex cytokine assay. For each immune mediator multivariable linear mixed effect models were applied.

**Results:** Biopsies from children with AAF supplementation showed a significant reduction in mucosal IL-6 level (estimate -547.88, 95% CI -1116.57 to -33.19, p=0.04) compared to those without AAF. Ex-vivo stimulation with AAF resulted in a significant increase of ‘mucosal repair’ GM-CSF (estimate 16.59, 95% CI 0.63 to 32.56, p=0.04) and ‘Th1 cytokine’ IL-12 (estimate 3.14, 95% CI 0.44 to 5.85, p=0.02) suggesting a propensity towards Th1 immunity as opposed to the typical Th2 response associated with allergy. Interestingly, ex-vivo stimulation with eHF and whole protein formula showed no or minimal effect on mucosal cytokine responses.

**Conclusion:** The data suggest that AAF exerts distinct immunomodulatory effects on the GI mucosal cytokine milieu. The tripartite effect on IL-6, T-cell immunity and repair mechanism(s) may explain the effectiveness and symptom relief seen in patients. These changes were not found with eHF ex vivo stimulation, suggesting that AAF may have additional benefits in comparison to allergen avoidance. Detailed analysis to identify the components of AAF responsible for these effects is ongoing (1).

**References:** (1) The anti-inflammatory potency of an amino acid-based formula (AAF). Hartog et al. ESPHAN 2015.

**Disclosure of Interest:** H. Jones Conflict with: Part of the work was funded by Nutricia, A. Hartog Conflict with: Nutricia, H. Stephenson Conflict with: Part of the work was funded by Nutricia, K. Brunner: None Declared, L. Harthoorn Conflict with: Nutricia, J. Langford Conflict with: Nutricia, J.
Koglmeier: None Declared, N. Shah: None Declared, M. Bajaj-Elliott Conflict with: Part of the work was funded by Nutricia, K. Lindley Conflict with: Part of the work was funded by Nutricia
Objectives and Study: Children with Type 1 Diabetes Mellitus (T1DM) are at increased risk of coeliac disease (CD) compared to the general population [1]. Recently ESPGHAN [1] and BSPGHAN [2] have published guidelines for the assessment of populations at increased risk of coeliac disease, including those with T1DM. The guidelines state that the first line in screening these patients is to perform HLA-DQ2/DQ8 typing. The objective of this study was to determine the frequency of CD associated HLA genotypes. We also performed a cost benefit analysis of HLA screening in this population.

Methods: 176 children with T1DM attending paediatric diabetes out-patient clinics in two Scottish centres were screened by HLA-DQ2/DQ8 genotyping. A pre-existing diagnosis of CD was also recorded. The frequency of CD associated HLA genotype was recorded. We also performed a cost benefit analysis by calculating the additional cost of HLA genotyping compared with the potential saving on regular anti-tTG screening in those with a non-predisposing HLA-DQ2/DQ8 genotype.

Results: The overall frequency of CD associated HLA genotypes was 165/176 (94%). This was consistent across the two centres (95% v 93). 12/176 (6.8%) had a pre-existing diagnosis of CD and all of these patients had a CD predisposing HLA genotype. Cost-benefit analysis based on a non-predisposing HLA genotype was largely dependent on the cost of HLA-typing across different laboratories and resulted in an additional cost of £21.96 per patient in order to prevent regular anti-tTG screening in 6% of our paediatric T1DM population.

Conclusion: We demonstrate a very high frequency (94%) of CD associated HLA genotypes in a Scottish paediatric T1DM population. The benefit of implementing HLA screening appears marginal with only 6% of patients excluded from future testing in our population – HLA cost is also key to the implementation of such a strategy. This highlights the practical limitations in using HLA screening in certain ‘at-risk’ groups and these limitations should be considered for individual populations.


Disclosure of Interest: None Declared
ANTIGI-XANTHINASE 6 ANTIBODIES IN CHILDREN WITH COELIAC DISEASE.

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Objectives and Study: Anti-transglutaminase 6 antibodies (anti-TG6) represent a marker associated with gluten-related neurological dysfunctions. The anti-TG6 prevalence in children suffering or not from celiac disease (CD) and without neurological manifestations is not known. Our aims were: 1) to investigate the anti-TG6 prevalence in serum samples from children without neurological disorders undergoing gastrointestinal biopsy; 2) to calculate the anti-TG6 prevalence in CD patients with or without another autoimmunity; 3) to correlate in CD patients the anti-TG6 concentrations with anti-TG2 concentrations and with gluten exposure duration (GED).

Methods: Sera from 267 patients with untreated CD, 147 with other diseases (46 gastritis, 17 eosinophilic esophagitis, 26 Crohn disease, 58 minor gastrointestinal complaints) and 6 with foreign body ingestion (controls) were analyzed for IgA anti-TG6.

IgG anti-TG6 were measured in 249 patients with untreated CD, 132 with other diseases (47 gastritis, 17 eosinophilic esophagitis, 19 Crohn disease, 49 minor gastrointestinal complaints) and 5 controls. Anti-TG6 were detected by ELISA assay. A measurement >75 U/ml for IgA or >34 U/ml for IgG was considered positive. Differences between groups were evaluated with Pearson’s χ² test.

Results: Pathological concentrations of IgA anti-TG6 were found in 29/267 (11%) patients with CD, 13/147 with other diseases (9%; 7 with Crohn, 1 gastritis, 5 minor gastrointestinal complaints) and 0/6 controls. 13/267 CD patients were suffering from another autoimmune disease (thyroiditis, diabetes or dermatitis herpetiformis) and 3/13 (23%) were tested positive for IgA anti-TG6.

IgG anti-TG6 were found in 25/249 (10%) patients with CD, 17/132 (13%; 6 with Crohn, 3 with eosinophilic esophagitis, 2 with gastritis, 6 minor gastrointestinal complaints) with other diseases and 0/5 controls. 10/249 CD patients were suffering from another autoimmune disease and IgG anti-TG6 were found in 3/10 (30%).

In CD patients there wasn’t a correlation between IgA/IgG anti-TG6 and anti-TG2 concentrations. The correlation of GED with IgA and IgG anti-TG6 concentration was statistically significant only with IgG isotype (r = 0.3; P<0.0001).

Conclusion: Pathological concentrations of IgA/IgG anti-TG6 were found in patients even if neurological disorders were not reported. We are monitoring the anti-TG6 positive CD patients during the gluten free diet in order to evaluate the anti-TG6 gluten-dependency. The anti-TG6 presence in CD patients without neurological complaints might be a consequence of a widespread gluten-dependent immune response as we found for the organ specific auto-antibodies.
Disclosure of Interest: None Declared
**Objectives and Study:** Crohn's disease (CD) is a chronic relapsing inflammatory condition of the gut that primarily affects young individuals, often leading to significant impairment of quality of life. The major objective of medical therapies in CD is the modification of the clinical course of the disease. Mucosal healing (MH) has recently arisen as a therapeutic goal able to predict sustained clinical remission.

Our aim was to evaluate the clinical outcome, after 2 years of follow-up (FU), of a cohort of pediatric CD patients according to the achievement of MH during maintenance therapy with anti-TNFα antibodies.

**Methods:** Pediatric CD pts starting infliximab (IFX) or adalimumab (ADA) from January 2009 were enrolled. All pts were naïve to biological therapies. An endoscopy was performed before starting biologics and after 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 the endoscopic FU. A further 1-year clinical FU was performed to evaluate differences in relapse rates, surgical rates and corticosteroid (CS) need according to the achievement of MH at endoscopic FU.

**Results:** Thirty-seven patients were enrolled. At two years, 26 of 30 patients in maintenance treatment with anti-TNFα were in clinical remission, 4 were not; and the remaining 7 (22%) had stopped therapy for either surgery (4 pts) or loss of response (3 pts).

All of the patients that had achieved a complete MH and 75% of those that had achieved a partial MH were in clinical remission at this further FU. Two pts that had obtained a complete MH and 4 of those that had obtained a partial MH needed a course of CS.

Kaplan Meier survival curves showed no statistical difference at two years from therapy introduction dividing patients according to treatment (ADA vs IFX) for risk of disease relapse.

**Conclusion:** In pediatric Crohn's disease, biologics are effective in inducing clinical remission and in achieving MH. The achievement of MH appears able to predict a better clinical outcome at least in the short term. Larger studies will highlight the effect of MH on the long-term disease evolution.

**Disclosure of Interest:** None Declared
Objectives and Study: Persistence of transmural inflammation in Crohn’s disease (CD) may lead to irreversible bowel damage requiring surgery and causing disability. Biologic therapy with anti-TNFα agents is effective in achieving mucosal healing (MH) and, in a smaller percentage of patients (pts), transmural healing (TH). We describe the clinical outcome of a cohort of paediatric CD pts receiving anti-TNFα therapy who achieved MH and/or TH after one year of maintenance therapy.

Methods: CD pts, naïve to biologics, were prospectively followed-up for 24 months (mts). They were evaluated before starting anti-TNF-α (T0), after 12 (T1) and 24 mts of treatment (T2). At T0 and T1 endoscopic activity (simple endoscopic score, SES-CD) and transmural disease, as assessed by small intestine contrast ultrasonography (SICUS), were evaluated. SES-CD of 0-1 was defined as complete MH, its decrease of 50% versus baseline as partial MH. TH was defined as a bowel wall thickness (BWT) <3 mm and normalization of other US parameters: BW vascularity, BW stratification, presence of strictures and prestenotic dilatation. After the T1 follow up we conducted a further 1-year observation period to evaluate clinical outcome in terms of disease activity (paediatric CD activity Index: PCDAI), rate of relapses, use of corticosteroids (CS) and need for surgical resection.

Results: 24 pts (mean±SD age [years] 12.2± 4; 15 males) were included. At T1, 8(33%) had complete MH, 9(38%) partial MH and 7(29%) no MH, while TH was present in 4 pts (17%), all with endoscopic complete MH. There was no US normalization in the remaining pts with complete MH and in those with partial MH. At T2, 21 pts were still on anti-TNF therapy, 2 pts required combined therapy with an immunomodulator, 1 discontinued biologic therapy before colectomy; moreover, pts that had achieved both complete MH and TH at T1 were in clinical remission without relapses or need of CS/surgery in the 12 mts pre-T2; whereas pts with partial MH ad no TH exhibited higher rates of relapses and need for CS (78%), higher rate of hospitalization (44%) and surgery (22%).

Conclusion: Biologics are effective in inducing clinical remission and in achieving MH and TH in paediatric CD. In our preliminary experience, complete MH and TH are associated with a better clinical outcome. The persistence of transmural inflammation may lead to higher rate of relapses and need for CS and surgery. Further long term prospective studies are needed to evaluate the actual role of TH in modifying the natural course of paediatric CD.
Disclosure of Interest: None Declared
THE ASSOCIATION BETWEEN SLEEP DURATION AND OBESITY IS AGE- AND GENDER-DEPENDENT AMONG CHILDREN IN URBAN GUANGZHOU, CHINA

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Objectives and Study: There is limited information on sleep duration and obesity among children in urban Guangzhou, China. The aim of this study is to examine the relationship between sleep duration and obesity in children aged 6-18 years.

Methods: Randomly, 11800 students aged 6-18 years, from 13 schools in 3 urban districts of Guangzhou, were examined and surveyed during September to November, 2013. Height and weight of all students were measured. Adiposity status was estimated using body mass index (BMI) according to the cut point in China criteria [1]. With a structured questionnaire, students reported sleep hours (less than 7 hours, 7-9 hours or more than 9 hours) each day, food intake (including vegetable, fruit, sugar beverage and meat), physical activity/inactivity and household income. If a student was under 9 years old, the caretaker would answer the questionnaire on the student’s behalf.

Results: Overall, 8760 students aged 6 to 18 years (mean±SD: 11.37±3.39 years, 49.0% boys) completed both height & weight measurement and questionnaire survey. The prevalence of obesity was 8.3% (9.8% in boys and 5.7% in girls). Comparing sleeping <7 hours with ≥9 hours, the odds ratio (OR) for obesity was 0.89 (95% Confidence Interval: 0.89-0.90) among boys, 1.86 (95% CI: 1.85-1.87) among girls, and 1.48 (95% CI: 1.47-1.49) in both genders. When comparing sleeping 7-9 hours with ≥9 hours, the ORs for obesity were 1.29 (95% CI: 1.28-1.30), 1.45 (95% CI: 1.44-1.46) and 1.40 (95% CI: 1.39-1.40) (boys, girls and both genders, respectively). The association between short sleep (<7 hours) and obesity was stronger in the elder age group (13-18 years: OR=1.97) than in younger age group (6-12 years: OR=1.60, both genders). Among younger children, 7-9 hours sleep each night means lower risk of obesity relative to ≤7 hours sleep (both compared with ≥9 hours sleep, OR: 1.34 versus 1.60, both p<0.01); while for elder children, 7-9 hours sleep and ≤7 hours sleep have similar risks for obesity (both compared with ≥9 hours sleep, OR: 1.98 versus 1.97, both p<0.01). All the OR values mentioned above are based on multivariate analysis after adjusting for age, household income, intake of fruit, vegetables, sugar beverage and meat and physical activity/inactivity.

Conclusion: Short sleep duration is associated with increased risk of obesity among girls but decreased risk of obesity among boys. Relative to children aged 6-12 years, the association between short sleep duration and obesity is stronger among children aged 13-18 years.

Disclosure of Interest: None Declared
BRAIN PROCESSING OF RECTAL SENSATION IN CHILDREN WITH FUNCTIONAL DEFECATION DISORDERS

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**Objectives and Study:** The pathophysiology underlying functional defecation disorders (FDD) such as functional constipation (FC) and functional nonretentive fecal incontinence (FNRFI) is poorly understood. Both groups often report fecal incontinence (FI) and a lack of sensation of urge to defecate, although only FC is characterized by low defecation frequency, hard stools and fecal impaction. Impaired brain processing of visceral sensory stimuli might play a role in the loss of rectal sensation in both disorders. The aim of this study was to investigate the cerebral activity in response to rectal distension in children with FNRFI and FC.

**Methods:** 10 patients with FNRFI (8 boys, mean age 13.7 yrs, range 12-17 yrs) and 15 patients with FC (8 boys, mean age 14.3 yrs, range 12-18 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. During acquisition of blood oxygenation level-dependent (BOLD) fMRI, subjects received 2 sessions of 5 stimulations consisting of repetitions of 30 sec of rectal stimulation with previous defined threshold pressures, followed by 30 sec of rest. 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 covering the whole brain. Analyses were performed 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:** Defecation frequency per week was 5.2 for FNRFI patients and 1.8 for FC patients. The mean number of FI episodes per week was 4.5 for FNRFI patients and 3.3 for FC patients. FC patients required a mean pressure of 18 mmHg above minimal distension pressure (MDP) to provoke urge sensation, for FNRFI patients this was 16 mmHg above MDP. During rectal distension, FC patients showed activation in anterior cingulate cortex, dorsolateral prefrontal cortex, inferior parietal lobule and putamen. In contrast, FNRFI patients showed no activation of brain areas during rectal distension. FNRFI patients showed significant deactivation in the hippocampus, parahippocampal gyrus, fusiform gyrus, lingual gyrus, posterior parietal cortex and precentral gyrus. While no significant deactivation was detected in FC patients.

**Conclusion:** Children with FNRFI differ significantly from children with FC with respect to neural processing of rectal urge sensation in brain regions. This conforms that FNRFI is a different clinical entity compared to FC.
Disclosure of Interest: None Declared
Bowel Preparation for Colonoscopy in Children: One Day PEG 3350 Plus Bisacodyl Versus Three Day Sennosides

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Objectives and Study: Effective bowel preparation (BP) is required for an accomplished colonoscopy. Oral bowel cleansing agents, along with 2 or 3 days of arduous dietary restrictions are widely used for BP. An efficient BP protocol should be easy to complete and successful in whole bowel cleanout without affecting histological findings, besides drugs used should be palatable with negligible adverse effects. Current protocol used in our center includes 3 days of sennosides and strict dietary restrictions, and is very successful. However, prolonged dietary restrictions decrease quality of daily life and compliance of the patients. A recent NASPghan report suggested 1-day bowel preparation with polyethylene glycol 3350 (PEG) plus bisacodyl and liquid diet as an option, but clinical practice is limited. In this study, our current protocol was compared to 1-day BP with PEG plus bisacodyl for efficacy, adverse effects and patient comfort.

Methods: Consecutive colonoscopy patients were block randomized into two groups. PEG group received oral 2 g/kg/day PEG (max. 55.2 g/day, dissolved in max. 2 L water) plus bisacodyl and clear liquid diet for one day. Senna group received oral sennoside A+B 2 ml/kg/day (max. 150 ml/day) for 3 days with liquid diet for 2 days and clear liquid diet on the last day. The sufficiency of bowel preparation was assessed according to Ottawa and Boston BP scales. Bowel movements, remarks and adverse effects during BP were recorded, and biochemical changes were monitored.

Results: Patient characteristics in 2 groups were demonstrated in table 1. In both groups, minor adverse effects such as nausea (15.7%), abdominal discomfort (13.9%), encopresis (4.6%) and sleep disturbance (3.7%) were similar. Biochemical changes monitored during BP were within normal limits in all patients.

Table 1 – Demographic characteristics, BP scores and patient remarks on BP of the study group

<table>
<thead>
<tr>
<th></th>
<th>PEG Group (n=53)</th>
<th>Senna Group (n=55)</th>
<th>p</th>
</tr>
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<tbody>
<tr>
<td>Age ± SD (years)</td>
<td>10 ± 4.7</td>
<td>10.3 ± 4.3</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Girls (%)</td>
<td>47.1</td>
<td>49.1</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Ottawa BP scale total score ± SD</td>
<td>2.6 ± 2</td>
<td>3 ± 2.3</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Boston BP scale total score ± SD</td>
<td>8 ± 2.1</td>
<td>7.8 ± 2</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Incomplete colonoscopy caused by poor BP n (%)</td>
<td>2 (3.7)</td>
<td>4 (7.2)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Taste (well or very well) n (%)</td>
<td>44 (83)</td>
<td>44 (80)</td>
<td>&gt; 0.05</td>
</tr>
<tr>
<td>Disrupted regular daily activities n (%)</td>
<td>30 (56.6)</td>
<td>42 (76.3)</td>
<td>0.04</td>
</tr>
<tr>
<td>Ease of administration (very easy and easy) n (%)</td>
<td>41 (77.3)</td>
<td>24 (43.6)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Desire to repeat the same BP if needed n (%)</td>
<td>37 (69.8)</td>
<td>19 (34.5)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>
**Conclusion:** The efficacy, safety and adverse effect profile of 1-day BP with PEG plus bisacodyl was found similar to 3-day BP with sennosides. Short duration, ease of administration and better patient comfort are the advantages of 1-day BP with PEG plus bisacodyl over 3-day BP with sennosides.

**Disclosure of Interest:** None Declared
**Gastroenterology**  
**Peptic Disease and Helicobacter Pylori**  
PA-G-0087

**RANDOMISED OPEN TRIAL WITH SACCHAROMYCES BOULARDII CNCM I-745 IN HELICOBACTER PYLORI ERADICATION IN CHILDREN**  
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**Objectives and Study:** This study aims to investigate the effect of *Saccharomyces boulardii* CNCM I-745 (S. boulardii) during *Helicobacter pylori* (*H. pylori*) eradication treatment in children.

**Methods:** A total of 194 *H. pylori* positive children were randomized in two groups. A 14-day triple therapy (omeprazole + amoxicillin + clarithromycin, or omeprazole + metronidazole + clarithromycin for participants with penicillin allergy) was given to both groups. In the "Treatment group" *S. boulardii* was added to the triple therapy, while the "control group" only received triple therapy. The incidence, onset, duration and severity of diarrhoea and compliance to the eradication treatment were compared.

A 13C urea breath test was done 4 weeks after the end of the eradication treatment in 2 groups of 21 patients aged 12 years and older to test *H. pylori* eradication rate.

**Results:** In the Treatment group, diarrhoea was less frequent, started later and was of shorter duration than in the control group (Table). Compliance was significantly better in the *S. boulardii* group. Although there was a 10% better eradication rate, this was not statistically significant.

<table>
<thead>
<tr>
<th></th>
<th>S. boulardii (n:102)</th>
<th>Control (n:92)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number children</td>
<td>12 (11.8%)</td>
<td>26 (28.3 %)</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Onset diarrhoea (days)</td>
<td>6.25 ± 1.24</td>
<td>4.05 ± 1.11</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Duration diarrhoea (days)</td>
<td>3.17 ± 1.08</td>
<td>4.02 ± 0.87</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Compliance</td>
<td>100 %</td>
<td>93%</td>
<td>&lt; 0.05</td>
</tr>
<tr>
<td>Eradication rate</td>
<td>71.4 %</td>
<td>61.9%</td>
<td>NS</td>
</tr>
</tbody>
</table>

**Conclusion:** *S. boulardii* has a beneficial effect on the prevention and treatment of diarrhoea occurring during *H. pylori* eradication in children. Even though *S. boulardii* did not significantly increase the *H. pylori* eradication rate, the compliance to anti-*H. pylori* treatment was improved.

**Disclosure of Interest:** B. ZHANG: None Declared, Y.-Z. XU: None Declared, Z.-H. DENG: None Declared, C. BO: None Declared, L.-R. JIANG: None Declared, Y. Vandenplas Conflict with: Biocodex and United Pharmaceuticals
**Gastroenterology**

**Coeliac Disease**

PA-H-0024

**HBS VACCINE VERSUS PRE-S VACCINE IMMUNIZATION IN CHILDREN WITH COELIAC DISEASE (CD) PREVIOUSLY VACCINATED AGAINST HBV - A RANDOMIZED CONTROLLED TRIAL**

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**Objectives and Study:** Previous studies have suggested that HBV vaccine may be less immunogenic in coeliac disease (CD) patients. Pre-S containing vaccine has shown superior immunogenicity than standard HBs recombinant vaccines in several disease states. We conducted a randomized, patient-blinded, study to compare the short term immunogenicity of a Pre-S-vaccine (Sci-B-Vac) versus an HBs vaccine (Engerix B) for re-vaccination of sero-negative, previously immunized CD patients.

**Methods:** Eligible participants were 1-18 year old children with a confirmed diagnosis of CD who received a course of standard HBV vaccines in infancy but had non-protective HBs-antibody (HBs-AB) concentrations (≤10mIU/mL) at inclusion. Patients were randomized to receive either HBs vaccine or Pre-S vaccine. Serum anti-HBs concentrations were measured one month after the first dose and again after the third injection for those who had not responded to the initial dose. The primary outcome was HBs-Ab concentrations following vaccination.

**Results:** A total of 82 patients were randomized (42 and 40 to Pre-S vaccine and HBs vaccine respectively). Baseline characteristics showed no significant differences between the groups, including the gluten free diet status (p=0.45). Both arms showed high response rate with no significant difference: 41 (97.6%) vs. 35 (87.5%) among Pre-S vaccine and HBs vaccine recipients, respectively, following the first injection (p=0.08). At the completion of the study, there was a 100% response in both arms. However, HBs-Ab concentrations (mIU/ml) were higher in the Pre-S vaccine group (median=925, IQR=424-1000) than the HBs vaccine group (median=363, IQR=106-996; p=0.005). Furthermore, 20 (47.6%) of the Pre-S vaccine arm were “high responders” (>1000mIU/ml), versus only 10 (25%) in the HBs vaccine arm (p=0.008).

**Conclusion:** Both vaccines elicited an adequate booster response in most previously vaccinated CD patients with non-protective anti-HBs concentrations. Pre-S vaccine administration resulted in higher anti-Hbs concentrations than the HBs vaccine; however, the clinical significance of the improved immunogenicity remains to be proven in a long term follow up. Our data suggest that a single dose of either vaccine is sufficient to raise titers to protective levels in the vast majority of CD patients.
Disclosure of Interest: None Declared
**Efficacy and Safety of Sebelipase Alfa in Children and Adults with Lysosomal Acid Lipase Deficiency: Results of a Phase 3 Trial**

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**Objectives and Study:** Lysosomal Acid Lipase (LAL) Deficiency is a progressive multisystem disease that is an underappreciated cause of cirrhosis, severe dyslipidemia and early onset atherosclerosis.

**Methods:** A phase 3, double-blind, placebo-controlled trial (NCT01757184) randomized affected children and adults (N=66) to placebo or sebelipase alfa 1 mg/kg every other week for 20 weeks. Primary endpoint was ALT normalization. Secondary endpoints included additional important efficacy assessments, safety and immunogenicity. Medically important abnormalities were common at baseline including fibrosis (100%), bridging fibrosis (Ishak score 3 or 4; 47%) and cirrhosis (31%) in biopsied patients (n=32) and a median LDL-C of 204.0mg/dL (range 70-378mg/dL). Mean age of biopsied patients was 12 yr. LDL-C was ≥190mg/dL in 58% (38 of 66 of patients, including 24% (9 of 38) who were on lipid lowering medications.

**Results:** After 20 weeks, ALT normalization (ULN range 34-43 U/L) was achieved in 31% of the sebelipase alfa group and 7% of the placebo group. Multiple secondary efficacy endpoints were also met including relative reduction in LDL-C, non-HDL-c, and triglycerides and relative increase in HDL-C. Over 350 infusions of sebelipase alfa were given during the double-blind period. The number of patients with AEs was similar in each arm. During the double-blind period, most AEs were mild and unrelated to sebelipase alfa; 6 patients experienced infusion-associated reactions (4 placebo; 2 sebelipase alfa). Dosing was paused in 1 patient after an atypical infusion-related reaction following sebelipase alfa treatment.
**Conclusion:** Sebelipase alfa for 20 weeks demonstrated statistically significant improvements in ALT normalization and in a number of other important disease related abnormalities including marked reductions in LDL. The safety profile appears favorable and infusions were generally well tolerated.

INCREASED CIRCULATING ZONULIN IN CHILDREN AND ADOLESCENTS WITH BIOPSY-PROVEN NONALCOHOLIC FATTY LIVER DISEASE

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Objectives and Study: Alteration in gut microbiota followed by impairment of intestinal wall integrity may play an important role in the pathogenesis of non-alcoholic fatty liver disease (NAFLD). Zonulin is a mediator known to regulate intestinal permeability by modulating intracellular tight junctions. The current study was designed to investigate the potential association of circulating zonulin with the stage of liver disease in obese children with biopsy-confirmed NAFLD.

Methods: A case-control study was performed. Cases were 40 obese children with NAFLD. The diagnosis of NAFLD was based on magnetic resonance imaging (MRI) with high hepatic fat fraction (HFF ≥ 5%), and confirmed by liver biopsy with ≥ 5% of hepatocytes containing macrovesicular fat. Controls were selected from obese children with normal levels of aminotransferases, and without MRI evidence of fatty liver as well as of other causes of chronic liver diseases. Controls were matched (1 to 1) with the cases on age, gender, pubertal stage and as closely as possible on body mass index (BMI)-standard deviation score (SDS). All participants underwent clinical examination, laboratory tests including zonulin, inflammatory and metabolic parameters, and MRI for measurement of HFF and visceral adipose tissue (VAT).

Results: Zonulin values were significantly greater in obese subjects with NAFLD than in those without NAFLD. In patients with NAFLD, zonulin concentrations increased significantly with the severity of steatosis and the Spearman’s coefficient revealed a positive correlation between zonulin values and steatosis (r = 0.372; P < 0.05); however, we did not find a significant correlation between zonulin and lobular inflammation (P = 0.23), ballooning (P = 0.10), fibrosis score (P = 0.18), or presence of nonalcoholic steatohepatitis (NASH)(P = 0.17). Within the entire study population, zonulin levels were positively associated with GGT (P < 0.05), 2-h insulin (P < 0.01), HFF (P < 0.01), and negatively associated with whole-body insulin sensitivity index (WBISI)(P < 0.05), after adjustment for age, gender and pubertal status. When the associations were restricted to the group of NAFLD patients, 2-h insulin (P < 0.01), HFF (P < 0.01), and WBISI (P < 0.05) retained statistical significance.

Conclusion: Circulating zonulin is increased in children and adolescents with NAFLD and correlates with the severity of steatosis.

Disclosure of Interest: None Declared
TARGETING THE INNATE IMMUNE RESPONSE USING CYTOTOPIC THERAPEUTIC AGENTS TO PREVENT EARLY CELL LOSS AFTER HEPATOCYTE TRANSPLANTATION

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Objectives and Study: Hepatocyte transplantation is a promising alternative to orthotopic liver transplantation for children with liver-based metabolic disease. Its success is limited partly due to early cell loss shortly after transplantation. This is mainly due to the instant blood-mediated inflammatory reaction (IBMIR), resulting in activation of complement and coagulation pathways. A novel cytotopic therapeutic agent, thrombalexin (PTL004α), which is a direct inhibitor of thrombin enzyme activity that binds to cell surfaces, has shown both local anticoagulant effects and may also affect the complement cascade. We set out to investigate the potential of this agent to overcome IBMIR in the context of hepatocyte transplantation.

Methods: HepG2 cells or donor primary hepatocytes isolated from donor organs unsuitable for transplantation were treated with 0.1µM, 0.5µM, 1µM, 2.5µM and 5µM thrombalexin for 20 minutes at 4°C. Immunofluorescence microscopy and flow cytometry were used to measure fluorescein-conjugated thrombalexin bound to the lipid membrane of hepatocytes. The effect of thrombalexin on cell viability was determined by flow cytometry using 7-AAD and MTT assays. Any effect on cell function was determined with albumin and urea immunoassays. Thrombin time (TT) and activated partial thromboplastin time (APTT) were measured on an automated coagulation system (STAR-Evolution) to determine the effect on coagulation of human plasma.

Results: Thrombalexin (0.5µM-5µM) bound readily to the phospholipid membrane of both HepG2 cells and fresh primary hepatocytes. Cryopreserved primary hepatocytes showed internalization of thrombalexin which co-localized with the plasma membrane marker CellMask™ suggesting injury to the cell membrane. Viability of primary hepatocytes was not significantly affected at any concentration of thrombalexin (0.1µM-5µM (P>0.05). HepG2 viability was significantly lower when cells were treated with 5µM thrombalexin (P<0.0001). Both albumin and urea production were maintained in primary hepatocyte cultures at all concentrations of thrombalexin. Both TT and APTT significantly increased in plasma containing hepatocytes treated with 2.5µM and 5µM thrombalexin, suggesting an inhibition of coagulation (P<0.0001 and P<0.01 respectively).

Conclusion: Initial results suggest treating hepatocytes with thrombalexin before transplantation may provide local inhibition of coagulation and improve cell engraftment without affecting their viability or function. This could contribute significantly to overcoming IBMIR which is a major barrier to the success of the technique.
Disclosure of Interest: None Declared
ALGINATE BIOMATERIAL PROTECTS FROM ACETAMINOPHEN-INDUCED LIVER INJURY IN MICE

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Objectives and Study: Acetaminophen (APAP)-induced liver toxicity is the most prevalent cause of acute liver failure in the western world. Overdose may be intentional or unintentional due to the various medications containing APAP. Currently, the accepted treatment for APAP over-dose is N-acetylcysteine (NAC), which has several drawbacks, mainly due to its limited therapeutic window. Therefore, even with NAC treatment 40% of patients will undergo liver transplantation or die. There are currently no commercially available formulations of acetaminophen which intended to reduce the risk of liver toxicity. Alginate is an anionic polysaccharide derived from brown algae. Previously we demonstrated in mice that alginate scaffolds prevented liver damage after 90% partial hepatectomy. The aim of this study was to assess the ability of a special formulation of alginate hydrogel (Very Low Viscosity and high of Guluronic acid, VLVG) to prevent APAP toxicity.

Methods: After overnight fasting, male C57BL/6 mice were orally administered 4mg of VLVG. Thirty minutes later, APAP (160mg/kg) syrup diluted in PBS, was orally administered. Control mice received vehicle (saline). All mice were scarified the next day and various parameters were studied in the liver and in the sera.

Results: VLVG- treated mice presented normal ALT levels while 20-40 fold increase was demonstrated in control mice. Accordingly, liver histology was normal in the VLVG group while massive centrlobular necrosis and increased nitortyrosine staining appeared in the control group. High proliferation appeared in livers stained with KI-67 in the control group, implying increased liver regeneration in response to hepatic damage. In VLVG-treated mice no proliferation was presented in livers. Importantly, APAP blood levels were comparable in the two groups. When VLVG was administered an hour after APAP it showed no effect.

Conclusion: VLVG powerfully prevented acute liver damage caused by high dose of APAP. Further studies are warranted to elucidate the mechanism of VLVG in this model.

Disclosure of Interest: None Declared
Hepatology
Hepatology
PA-H-0058

SERUM BILE ACIDS IN CHILDREN AND ADOLESCENTS WITH TYPE 1 DIABETES
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Objectives and Study: High levels of bile acids (BA) stimulate insulin release and therefore decrease serum glucose levels via the TGR5/GLP1 pathway; contrariwise, high glucose levels can upregulate BA synthesis from cholesterol by forcing transcription of the rate-limiting enzyme Cyp7a1. Type 1 diabetes (T1D) leads to hyperglycemia due to lack of endogenous insulin. We hypothesized that in children and adolescents with T1D BA levels vary coordinately with HbA1c, a longtime marker of glycemic control.

Methods: Concentrations of glucose, HbA1c, and serum total BA (tBA) were measured in 119 fasted children and adolescents with T1D (age 3 - 20 years) under insulin therapy. Patients were divided into three groups: Group 1: low HbA1c (< 59 mmol/mol; n=25); Group 2: medium HbA1c (59 – 75 mmol/mol; n=62) and Group 3: high HbA1c (> 75 mmol/mol; n=16). These groups were further subdivided according to age (3 - 5 years, 6 - 11 years, and > 11 years) and tBA values were compared with reference ranges (Jahnel et al. 2014, unpublished data). Using 10 μl of serum we determined by high-performance liquid chromatography – high-resolution mass spectrometry a BA profile including 15 unconjugated and taurine- or glycine-conjugated BA; summed, the values for these analytes yield the tBA value.

Results: In Group 1, with low glucose and HbA1c values, mean tBA values generally lay below reference ranges: 3 - 5 years, 3.8 μmol/l (reference range 4.3 - 6.4 μmol/l; p<0.01), 6 - 11 years, 3.8 μmol/l (3.6 - 5.1 μmol/l) and > 11 years, 2.8 μmol/l (3.1 - 4.1 μmol/l; p<0.01). In Group 2, with normal HbA1c values, mean tBA values were lower than in Group 1 and generally lay below normal ranges for age: 3 - 5 years, 2.7 μmol/l (p<0.01), 6 - 11 years, 4.7 μmol/l (3.6 - 5.1 μmol/l) and > 11 years, 2.1 μmol/l (3.1 - 4.1 μmol/l). Group 3 comprised only patients with high HbA1c values in the age group > 11 years, which showed the highest tBA concentration at 5.5 μmol/l (p<0.01).

Conclusion: This study shows that insulin therapy in T1D may influence the concentration of serum tBA. Adequate insulin therapy, as judged by HbA1c values, is associated with normal or low tBA levels, whereas chronically high glucose levels are associated with high tBA levels. The pathways leading to changes in BA metabolism in T1D remain to be defined.

Disclosure of Interest: None Declared
**Hepatology**

**Basic Science**

PA-H-0059

**MIR-124 SUPPRESSES BILIARY HYPERPLASIA BY TARGETING IL-6/STAT3 SIGNALLING**

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**Objectives and Study:** Normal cholangiocyte proliferation is a typical feature of biliary atresia (BA) in children. Others and our team recently reported that the dysregulation of microRNAs (miRNAs) has been associated with pathogenesis of BA. However, whether miRNAs are involved in the biliary hyperplasia remains unknown.

**Methods:** Biliary hyperplasia was induced in rats following ligation of the bile duct (BDL). The expression of miRNAs in liver tissues from rats and BA patients were examined with miRNA array and quantitative real-time polymerase chain reaction (qRT-PCR) assays. The biological functions of miRNAs were studied with immunoblot, immunohistochemical and proliferative assays. Western blot and luciferase reporter assays were performed to determine the targets of the miRNAs.

**Results:** In the liver, interleukin-6 (IL-6) is significantly elevated in BA patients and in rats subjected to BDL compared to controls. In contrast, the expression of miR-124 is dramatically decreased in the livers of BA subjects and BDL rats compared to controls. The mRNA levels of signal transducer activator of transcription 3 (STAT3) and IL-6 receptor (IL-6R) are inversely correlated with that of miR-124. The ectopic expression of miR-124 inhibited IL-6-mediated cholangiocyte proliferation in vitro and cholangiocytes hyperplasia in vivo by directly targeting the 3'-untranslated region (3'-UTR) of STAT3 and IL-6R.

**Image:**
Conclusion: Our findings provide a clearer understanding of the underlying mechanism by which miR-124 inhibits bile duct proliferation that might be therapeutically targeted for the treatment of BA.

Disclosure of Interest: None Declared
METABOLOMICS REVEALS METABOLITE CHANGES IN BILIARY ATRESIA INFANTS

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Objectives and Study: Biliary atresia (BA) is a severe neonatal cholestatic disorder caused by obstruction of extra and intra hepatic bile ducts. If untreated, progressive liver cirrhosis will lead to death within two years of age. Early diagnosis and operation improve the outcome significantly. Infants with neonatal hepatitis syndrome (NHS) present similar symptoms, confounding the early diagnosis of BA. However, there is no non-invasive diagnostic method to differentiate BA from other causes of neonatal cholestasis. This study is aimed to determine if plasma metabolite profiles can be potential diagnostic markers of BA.

Methods: We performed a metabolomics study in plasma of 45 BA, 15 NHS, and 6 healthy infants using gas chromatography-time-of-flight mass spectrometry (GC-TOFMS). Orthogonal partial least square discriminate analysis (OPLS-DA) was used to identify the differential metabolites between each group. Ingenuity pathway analysis (IPA) was introduced to analyze pathway and network of the differentially expressed metabolites. The altered metabolites were validated using ultra-performance liquid chromatography-tandem mass spectrometry in plasma of 53 BA and 28 NHS infants.

Results: BA was clearly separated from the OPLS-DA scores plots from NHS infants and healthy infants using GC-TOFMS analysis (Figure). A total of 18 metabolites (L-Glutamic acid, L-Ornithine, L-Isoleucine, 2-hydroxy-3-methylbutyric acid, L-Lysine, L-Valine, D-Mannose, L-Tryptophan, gluconolactone, L-Serine, phosphate, succinic acid, glycerol 3-phosphate, D-Glucose, citric acid, oxalic acid, ribitol, and pentanoic acid) were found differentially expressed between BA and NHS. IPA analysis revealed the network of amino acid metabolism was altered most significantly, and they were quantitatively validated.

Conclusion: In this study, we identified 18 metabolites, including 7 amino acids particularly, were significantly altered in BA. These results suggest that plasma metabolic profiling has great potential in differentiating BA from NHS.

Disclosure of Interest: None Declared
Objectives and Study: To investigate predictors of clinical evolution in PFIC-II patients and their relationship to BSEP expression and (re)targeting

Methods: 23 children with established PFIC-II were retrospectively included. Clinical, biochemical and histological characteristics were reviewed at presentation and following treatment with Ursodeoxycholic acid (UCDA) only (10 mg/kg TDS) (n=20) or UCDA and Partial Biliary Diversion (PBD) (n=3). BSEP immunostaining was obtained in 20/23 patients. Response to treatment was defined as normalization of pruritus, disappearance of jaundice, and normalization of alanine amino transferases (ALT) (<1.5 upper limit of normal-ULN). The duration of remission was also recorded. Six responders had a paired biopsy with BSEP immunostaining, 2 after PBD

Results: Twelve of 23 patients were non-responders, 1 partial responder and 10 responded to treatment. Non-responders had earlier onset of jaundice (<9months), neonatal cholestasis and higher ALT levels. ALT > 165 IU/L had sensitivity of 72% and specificity of 55% to predict non-response. 8/12 non-responders had no BSEP expression, 1 cytoplasmic, 1 canalicular, 2 not done. Amongst 10 responders, 5 had cytoplasmic BSEP expression and 5 absent. Paired biopsies were obtained after treatment in 6/10: De novo canalicular expression of BSEP occurred in 4/6, 2 with baseline cytoplasmic expression and 2 with no baseline expression.

Seven patients were still responders at last follow up (median 20 months, range 5-67 months), one of them died from unrelated cause, and 3 did relapse after 56, 72 and 82 months. Amongst the 9 living responders a median relapse free survival time of 72 months (CI 95% 48 to 96 months) was observed and the five years Kaplan Meier relapse free survival was of 75% (CI 95 % 33-100%)

Conclusion: PFICII children with late onset presentation, ALT <165 IU/L and cytoplasmic BSEP are likely to respond at least transiently to non-transplant treatment while patients with neonatal cholestasis do not. All but one PFIC II patients had abnormal or no BSEP expression. De novo or retargeted canalicular expression of BSEP can occur under treatment amongst the responders

Disclosure of Interest: None Declared
**Objectives and Study:** No consensus exists about the optimal immunosuppression after paediatric liver transplantation. We aimed to reevaluate efficacy and side effects in our current individualized Tacrolimus (TAC) based monotherapy as compared to historical alternative regimens in children undergoing primary liver transplantation in our centre in 2012/2013.

**Methods:** Children were analysed who underwent primary isolated liver transplantation in our centre in 2012 + 2013. Exclusion criteria were change of immunosuppression and pre-existing renal disease. Patients were retrospectively divided into three subgroups (TAC vs TAC + Mycophenolate Mofetil (MMF) vs. Ciclosporin A (CSA) + Prednisolone). Clinical and laboratory data on histopathologically proven rejection rates, renal function (Creatinin Clearance (Schwartz-formula (2009), Cystatin-C-Clearance), treatment-requiring impaired wound healing, systemic infections with evidence of pathogens and treatment-requiring hypertension was collected before (regarding renal function) and for one year after transplantation. Data was processed using MS Excel and SPSS.

**Results:** 71 paediatric liver transplantations in 66 patients (32f) were performed in 2012/13 (26.8% living donor). Diagnoses were biliary atresia (N=22), ALF (5), hepatoblastoma (5), PFIC I/II (4), CFALD (4), PSC/AIH (3), Alagille’s syndr. (2), PFIC III (2). 19 patients had to be excluded. Creatinine clearance and Cystatin C clearance showed no significant differences.

<table>
<thead>
<tr>
<th>Mean values</th>
<th>Group I (TAC, n=15, 9f)</th>
<th>Group II (TAC/MMF, n=21, 10f)</th>
<th>Group III (CSA, n=11, 4f)</th>
<th>T-Test Group I vs. Group II</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at LTX (y.m)</td>
<td>4.8</td>
<td>6.5</td>
<td>4.4</td>
<td>P = 0.280</td>
</tr>
<tr>
<td>Rejection rate (%)</td>
<td>20 (n=3)</td>
<td>28.6 (n=6)</td>
<td>27.3 (n=3)</td>
<td>p = 0.260</td>
</tr>
<tr>
<td>Infection rate (%)</td>
<td>53.3 (n=8)</td>
<td>71.4 (n=16)</td>
<td>63.6 (n=7)</td>
<td>p = 0.155</td>
</tr>
<tr>
<td>Wound healing defects (%)</td>
<td>13.3 (n=2)</td>
<td>23.8 (n=5)</td>
<td>0</td>
<td>p = 0.221</td>
</tr>
<tr>
<td>Hypertensive treatment (%)</td>
<td>53.3 (n=8)</td>
<td>63.6 (n=14)</td>
<td>72.7 (n=8)</td>
<td>p = 0.335</td>
</tr>
</tbody>
</table>
Conclusion: Overall there were only insignificant differences between the three subgroups regarding efficacy and side effects of the respective treatments. Tacrolimus monotherapy in our hands had marginally better results regarding rejection rates and systemic infections. There is a significantly higher rate of wound healing defects in patients treated with TAC + MMF compared to the group treated with CSA (p=0.021), whereas we could not detect a significant benefit in the renal function of the MMF group. Our data supports the importance of individualised, patient-adapted immunosuppression and is reassuring different regimes used provide an effective and safe treatment though we see a benefit for Tacrolimus monotherapy.

Disclosure of Interest: None Declared
TRANSJUGULAR INTRAHEPATIC PORTO-SYSTEMIC SHUNT (TIPSS) INSERTION FOR THE MANAGEMENT OF PORTAL HYPERTENSION IN CHILDREN: A SINGLE-CENTRE EXPERIENCE.

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Objectives and Study: TIPSS has an established role in the management of portal hypertension in adults. There is however a paucity of evidence outlining the indications for and long term outcomes of TIPSS in childhood. Our aim was to assess the use of the TIPSS procedure in the management of portal hypertension at a supra-regional paediatric liver unit.

Methods: Retrospective review of all children (age 0-18 years) that had undergone a TIPSS procedure at Birmingham Children's Hospital since 1995. Subjects were identified from the liver unit database and radiology information system. Data was collated and analysed following review of patients' medical records and imaging.

Results: 35 TIPSS procedures were performed on 34 patients, over a 19 year period. The median age at time of TIPSS was 12 years (range 7 months-17 years). 20 of the procedures were performed to palliate symptoms of recurrent or active variceal bleeding; 6 were done as a bridge to transplant and 9 were performed to both palliate symptoms and act as a bridge to transplant. In 2 cases the procedure was performed as an emergency measure due to life threatening bleeding. There was successful placement of a covered stent with creation of a porto-systemic shunt in 29 cases. In 6 patients it was a failed procedure. In 16 cases there was a measurable reduction in hypersplenism with a rise in platelet count and a reduction in spleen size. Complications occurred in 11 cases and included encephalopathy (3), hepatic pseudo aneurysm requiring placement of a covered stent (1), secondary infarction and liver failure (1), bile leak (1), infection (1) and minor symptoms (4). In all but 5 patients variceal bleeding came under control; of the remaining patients 3 had persistent bleeding but at a reduced volume, 1 had persistent hypersplenism requiring splenic artery embolization and 1 had no improvement and so required early liver transplantation. 5 of the initially successful TIPSS later required further intervention due to thrombus formation and occlusion (2) or narrowing of shunt (3). 1 patient has been lost to follow up. Of the remaining patients 14 have subsequently undergone liver transplant and 6 have died (3 from sepsis and 3 from progressive deterioration of liver disease whilst awaiting transplantation).

Conclusion: This study represents the largest series of paediatric TIPSS procedures to date. It demonstrates that TIPSS can be successful in palliating patients with variceal bleeding and also acting as a bridge to later transplantation. However, it is not without risk and therefore patients must be appropriately selected and counselled for the procedure.
Disclosure of Interest: None Declared
TRANSIENT LIVER ELASTOGRAPHY IMPROVED DURING FOLLOW-UP OF CHILDREN SUFFERING FROM WILSON’S DISEASE.

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Objectives and Study: Accurate assessment of the degree of fibrosis is important in Wilson’s disease (WD) to evaluate prognosis and follow-up of the hepatic disease. Non-invasive assessment of liver fibrosis with Transient Elastography (TE) by Fibroscan has been validated in several chronic liver diseases and recently validated in WD (1). But to date there is no data regarding TE in monitoring liver disease progression of WD patients during follow-up under treatment.

Methods: The aim of our study was to compare mean values of liver stiffness (LS), at diagnosis and during a 4 years follow-up, in a cohort of 23 children with WD on stable condition with medical treatment according to their therapeutic observance.

LS measurements were performed at diagnosis (T0), 1 year (T1), 2 years (T2), 3 years (T3) and 4 years (T4).

Results: Fibroscan mean value in WD children at diagnosis was 25 +/- 14 kPa in hepatic forms (N=10), 16,2 +/- 8 kPa in presymptomatic forms with ALT > 80 UI/L (N=4), 3,6 +/- 0,3 kPa in presymptomatic forms with ALT < 80 UI/L (N=3), and 20,4 +/- 11 kPa in neurologic forms (N=6). Mean LS measurement improved significantly between T0 and T1 in WD children (presymptomatic forms with ALT < 80 excluded): 22,2 +/- 11,7 kPa versus 12,4 +/- 4,6 kPa (p<0,05).

Mean LS at T2 continued to decrease and was 9,5 +/- 2,7 kPa. After 3 and 4 years Fibroscan mean values tended to stabilize, respectively 9,4 +/- 3 kPa and 8,1 +/- 0,9 kPa.

Mean Fibroscan values were significantly different at T0 vs T1, T0 vs T2, T0 vs T3, T1 vs T2 and T1 vs T3 (p<0,05).

According to observance, a significant difference between good and mild observant patients at 2 years was shown, with a -5,4 +/- 3,1 kPa decrease of mean FB value between 1 and 2 years in good observant patients versus a 0,24 +/- 2,3 kPa increase in mild observant patients (p=0,009).

No correlation was found between AST and Fibroscan values at T0, T1, T2 et T3 (p >0,05).
**Conclusion:** Fibroscan values dramatically improved during the first year after diagnosis in children with WD on treatment. Between 1 and 2 years on treatment Fibroscan values continued to improve to a lesser extent.

Our study confirms that TE could be a useful non-invasive method to monitor liver disease evolution in WD, and that liver fibrosis could regress in pediatric WD patients on stable condition with medical treatment.

Further studies are needed with higher number of patients to confirm our results.


**Disclosure of Interest:** None Declared
BODY IMAGE PERCEPTION IN YOUNG PEOPLE WITH CHRONIC LIVER DISEASE

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Objectives and Study: Body image (BI) is a normative discontent in adolescence. Researchers have hypothesised that the physical effects of chronic liver disease (CLD) and its treatment would exacerbate BI dissatisfaction in this population, but this has never been investigated.

Methods: The study investigated BI in young people with CLD of 'transition age' (16-24 years). 4 validated questionnaires were used to assess these constructs in 80 young people (42 female) with various diagnoses of CLD; the Multi-dimensional Body Self-Relations Questionnaire (MBSRQ), the Screening Tool for Psychosocial Distress (STOP-D), The Coping Responses Inventory (CRI) and the Basel Assessment of Adherence Scale to Immunosuppressives (BAASIS). The role of surgical scars and immunosuppressive medication side-effects in appearance dissatisfaction was examined using linear regression. The study also investigated the association between medication non-adherence with appearance dissatisfaction, psychosocial distress, and coping response style.

Results: Compared to the general population, young females with CLD are less satisfied with their overall appearance. Young males are more dissatisfied with discrete parts of their body (particularly muscle tone and mid-torso) but not their overall appearance. No evidence was found that immunosuppressive medication side-effects or scarring from surgery impacts upon BI. High levels of psychosocial distress were reported; 46% screened positively for depression, 51% for stress, 39% for anxiety, 23% for anger and 18% for perceived lack of social support. Young people who reported feeling more vulnerable to physical illness (Health Evaluation) reported higher psychosocial distress. Just 26.7% reported full adherence to their immunosuppressive regimen over the past 4 weeks, which challenged comparisons between ‘adherent’ and non-adherent' individuals.

Conclusion: BI is poorer in young people with CLD than the general population. The findings also indicate high rates of non-adherence in young people with CLD. Psycho-social factors should be considered alongside physical indicators of health. Detection of, and subsequent early intervention for issues could prevent these impacting upon the self-management of their condition and potentially influence their overall outcome.

Disclosure of Interest: None Declared
Objectives and Study: Non-alcoholic steatohepatitis (NASH) is the most severe form of a common hepatic condition known as non-alcoholic fatty liver disease (NAFLD). NASH is histologically characterized by hepatic fat accumulation, inflammation and ballooning, and eventually coupled with fibrosis, which in turn may progress to end-stage liver disease even in young individuals. Hence, there is a critical need for specific non-invasive markers to predict hepatic inflammation at an early age. We investigated if plasma levels of cathepsin D (CatD), a lysosomal protease, correlated with severity of liver inflammation in pediatric NAFLD.

Methods: Liver biopsies from children (n = 96) with NAFLD were histologically evaluated according to the criteria of Kleiner (NAFLD activity score) and the Brunt’s criteria. At the time of the liver biopsy, blood was taken and levels of CatD, alanine aminotransferase (ALT) and cytokeratin-18 (CK-18) were measured in plasma.

Results: Plasma CatD levels were significantly lower in subjects with liver inflammation compared to subjects with simple steatosis. Furthermore, we found that CatD levels were gradually reduced and corresponded with increasing severity of liver inflammation, steatosis, hepatocellular ballooning and NAFLD activity score. CatD levels correlated with pediatric NAFLD disease progression better than ALT and CK-18. In particular, CatD showed a high diagnostic accuracy for differentiation between steatosis and hepatic inflammation with a ROC-AUC of 0.94 (95%CI: 0.85-1.03) and a sensitivity and specificity of 100% and 89.5%, respectively.

Conclusion: Plasma CatD holds an extremely high diagnostic value to distinguish pediatric patients with hepatic inflammation from children with simple steatosis.

Disclosure of Interest: None Declared
PREVALENCE OF TWO INBORN ERRORS OF PRIMARY BILE ACID SYNTHESIS IN EUROPE: RESULTS OF AN ESPGHAN SURVEY

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Objectives and Study: Bile acid synthesis defects (BASD) are rare genetic disorders leading to impaired biliary secretion and accumulation of atypical bile acid (BA) metabolites. Untreated errors cause progressive chronic liver disease and serious morbidity. In this study we sought to determine the prevalence in Europe of the two main deficiencies (3β-hydroxy-Δ5-27-steroid dehydrogenase [3β-HSD / HS D3B7] and Δ4-3-oxosteroid-5β-reductase [Δ4-3-oxoR / AKR1D1]) and to identify treatment strategies.

Methods: 62 paediatric european centres were surveyed in an ESPGHAN wide call for contribution. An electronic survey comprised 10 questions regarding general information, number of cases, methods of analysis and laboratories and current treatment strategies. Results from 36 centres in 20 countries were obtained.

Results: Among 37 clinical paediatric centres, 19 reported 72 cases with BASD. 64 patients were diagnosed with a 3β-HSD and 8 with a Δ4-3-oxoR defect. Diagnosis was made by fast atom bombardment-mass spectrometry (12 centres) or gas chromatography–mass spectrometry (8 centres), one centre used both methods. 11 centres performed confirming genetic analysis in 40 patients. Most centres (n=13) treated 3β-HSD patients with cholic acid (CA), six centres also gave chenodeoxycholic acid and 7 centres ursodeoxycholic acid (UDCA) or 2 BA in combination. 7 of 8 Δ4-3-oxoR patients were treated with CA, partly in combination with UDCA (3 centres). In each disease group, one patient received a liver transplantation before diagnosis of BASD was made. Most colleagues (11 centres in charge of 59 patients) will not change the treatment strategies in both diseases. 4 centres will not continue to use UDCA in 3β-HSD and 1 centre in Δ4-3-oxoR patients. The major obstacles to diagnosis reported were lack of experience (64%) and lack of appropriate laboratory technology (45%).
Conclusion: We identified 72 patients with 3β-HSD or Δ4-3-oxoR deficiency in Europe. CA seems to be the therapy most commonly used, although several centres prescribe other BA. Diagnostic approach and treatment strategies for these BASD in Europe differ considerably. Consensus guidelines are needed to further improve patient care.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Total parenteral nutrition (PN) is a vital support for neonatal infants with congenital or acquired GI disorders and requiring small bowel resection. An adverse outcome associated with prolonged PN use is parenteral nutrition associated liver disease (PNALD). We previously showed that enteral chenodeoxycholic acid (CDCA) treatment reduced PNALD and induced intestinal mucosal growth. We hypothesized that the protective CDCA effects were mediated by dual activation of FXR-mediated induction of intestinal fibroblast growth factor 19 (FGF19) and TGR5 receptor-mediated glucagon-like peptide 2 release. The aim of the current study was to compare the physiological effects of obeticholic acid (OCA)(selective FXR agonist) vs CDCA (dual FXR and TGR5 agonist) on hepatic bile acid homeostasis and intestine growth in PN-fed piglets.

METHODS: Term, newborn piglets were assigned to receive complete TPN (PN), PN + enteral CDCA (30 mg/kg), or PN + enteral OCA (0.5, 5, 15 mg/kg) daily for 19 d. Endpoints of PNALD, bile acid homeostasis, intestinal growth and crypt cell proliferation (in vivo BrdU labeling) were measured.

RESULTS: Compared to control PN pigs, treatment with OCA5 and OCA15, but not CDCA, reduced serum PNALD markers (bilirubin, GGT, total bile acid, triglyceride, and VLDL). Gallbladder bile content was increased in CDCA and OCA15 vs PN. Compared to PN, hepatic expression of CYP7A1 protein was suppressed, whereas bile salt export pump (BSEP) mRNA was increased by OCA5 and OCA15, but not CDCA. Liver mass was higher in CDCA compared to PN and all OCA groups. However, both CDCA and OCA dose-dependently increased intestinal mass, villus height, and crypt cell BrdU-labeling indices. Also, CDCA, OCA5 and OCA15 increased ileal expression of FXR-target genes (FGF19, intestinal fatty acid binding protein (IBABP), and organic solute transporter (OSTα).

CONCLUSION: We conclude that enteral OCA is more effective than CDCA in prevention of PNALD. Both bile acids induced intestinal trophic effects but OCA has greater potency than CDCA.

DISCLOSURE OF INTEREST: B. Stoll: None Declared, Y. Jiang: None Declared, Z. Fang: None Declared, H. Wang: None Declared, G. Guthrie: None Declared, D. Burrin Conflict with: Mead Johnson, Fresenius Kabi
BOVINE LACTOFERRIN REGULATES CELL SURVIVAL, CELL DEATH AND ENERGY METABOLISM IN INTESTINAL EPITHELIAL CELLS

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Objectives and Study: Lactoferrin is a multifunctional protein present in both human (1-7 g/L) and bovine milk (0.1-2 g/L). It has a potential to attenuate intestinal inflammatory diseases in early life, such as necrotizing enterocolitis (NEC). Previous studies have shown that low doses (0.01-1 g/L) of bovine lactoferrin (bLF) increased intestinal epithelial cell (IEC) proliferation whereas high doses (10 g/L) triggered inflammation and exacerbated intestinal inflammation in preterm pigs.

Methods: To further elucidate the cellular mechanisms of these effects, we profiled the porcine IEC proteome stimulated with bLF at 0, 0.1, 1 and 10 g/L (0, 1.25, 12.5 and 125 µM) by iTRAQ-LC-MS-based proteomics.

Results: bLF was internalized into the IECs with the uptake correlating with increasing doses of bLF from 0 to 1 g/L, but without further uptake at 10 g/L. Among 122 differentially expressed porcine proteins, we focused on and grouped 31 proteins according to their biological functions: a) cell survival and cell death, b) energy metabolism, c) hypoxia inducible factor 1 (HIF-1) pathway, and d) aminoacyl-tRNA ligase activity. At 0.1-1 g/L, bLF up-regulated some proteins involved in cell survival and energy metabolism (cathepsin D, pyruvate dehydrogenase). At 10 g/L, bLF increased three proteins involved in cell death (apoptosis inducing factor, annexin 1, cyclophilin), two proteins of the HIF-1 pathway (ubiquitin carboxyl-terminal hydrolase, DNA lyase), and six aminoacyl-tRNA ligases. The high dose also down-regulated two anti-apoptotic proteins (catalase, huntingtin-interacting protein 1), three proteins involved in proliferation (CD63, granulins, 7-dehydrocholesterol reductase), and ten proteins involved in energy metabolism. Most differentially expressed proteins were regulated to a greater extent by 10 g/L of bLF than by lower doses.

Conclusion: Low bLF doses increase bLF uptake and signaling to facilitate cell survival, protection against stress and energy metabolism. Conversely, high doses may inhibit proliferation, stimulate apoptosis and cell death, and trigger inflammation. Careful selection of bLF dose is therefore crucial for its supplementation to infant formula with the aims to stimulate intestinal maturation and defense in preterm neonates.

Disclosure of Interest: None Declared
PRE-DIGESTION OF FAT FROM MILK FORMULA WITH IMMOBILIZED MICROBIAL LIPASE ENHANCES PUFA ABSORPTION IN A MODEL OF EXOCRINE PANCREATIC INSUFFICIENT (EPI) YOUNG PIGS

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Objectives and Study: The efficacy of pre-digestion with immobilized microbial lipase (ML) to improve fat absorption was tested in a porcine EPI model. Surgical ligation of pancreatic ducts in pigs causes impaired excretion of pancreatic enzymes, and thus mimics conditions in pre-term and/or term human babies (Goncharova et al, 2014). The purpose of this study was to confirm that consumption of an infant formula containing hydrolyzed fats in the form of fatty acids and monoglycerides is effective in increasing absorption of total fat and long-chain polyunsaturated fatty acids (LCPUFA).

Methods: EPI pigs (duct-ligated at an age of 6 weeks) were fed for 6 weeks with a baby formula (NAN, Nestle, Sweden) enriched with LCPUFA (1% docosahexaenoic acid (DHA) and 2% arachidonic acid (AA) from fish oil). The EPI pigs were divided into 2 groups where the 1st group was fed the formula only (EPI, n=6) while the 2nd group fed the formula pre-hydrolyzed with immobilized ML on acrylic beads (EPI+ML, n=7). As a control group un-operated pigs of the same age was fed with the formula (Control, n=6). The effect of pre-digestion of dietary fat was monitored by reduction of total and LCPUFA faecal fats, together with increases in the absorption of AA and DHA expressed as changes of their levels in plasma, erythrocytes, liver, fat, and heart.

Results: No adverse clinical signs and pathological findings along the gut or in the liver were observed after the 6 weeks of feeding the pre-hydrolyzed formula. Moreover, feeding with pre-hydrolyzed formula resulted in a significant reduction in faecal fats (total fat with 43%, omega-3 with 38%, omega-6 fats with 53%, AA with 66% and DHA with 50%), and improved absorption of LCPUFA in plasma (35% increased level) and tissues (heart, liver and fat tissue accretion of AA, 26%, 46% and 30% respectively, and DHA: 37%, 56% and 53% respectively), compared to the group of EPI pigs fed non-hydrolyzed formula.

Conclusion: An efficient way to increase fat and LCPUFA absorption, in particular, in newborn babies is to feed with a formula pre-hydrolyzed with immobilized ML just before consumption. Serving formula pre-hydrolyzed leads to an improved fat absorption resulting in reduced fat in the stool and tissue fat accretion, that together present the hallmark for an effective treatment for newborn babies.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Human milk contains exosomes, i.e. microparticles consisting of microRNAs (miRs) with sizes of ~22 nts. Exosome-mediated transfer of miRs is a novel mechanism of genetic exchange between cells. miRs bind to the 3'-untranslated region of target mRNAs and cause translational block or mRNA degradation. We hypothesized that milk exosomes can resist digestion in the gastrointestinal tract and be taken up by enterocytes and thus have the potential to regulate gene expression.

METHODS: Human milk samples from donors at different stages of lactation were collected into tubes with RNAse inhibitor. Exosome RNA isolated by ExoQuick-TC was eluted in RNAse-free Exosome lysis buffer. CD9 was used as positive control and calnexin as negative control. miRs of 22 nts extracted from isolated exosomes were verified by BioAnalyzer. Sequencing was done using Illumina HiSeq 2500. miRDeep2 was used to find miRNA signatures from the read alignments to known miR sequences (miRBase) and to quantify expression.

RESULTS: Only a few miRs were differentially expressed during lactation. In vitro digestion (pepsin + pancreatin) under conditions mimicking those in infants showed a significant proportion of the exosomes surviving digestion as verified by TEM. Human intestinal epithelial cells were incubated with digested exosomes and intracellular localization was determined by anti-CD9 antibodies using confocal microscopy. The exosomes localized to the nucleus as visualized by Topro3.

CONCLUSION: Human milk exosomes are capable of surviving digestion and being taken up by enterocytes where they localize to the nucleus and may affect gene expression.

DISCLOSURE OF INTEREST: B. Lonnerdal Conflict with: Mead Johnson Nutrition, X. Du: None Declared, Y. Liao: None Declared, J. Li: None Declared
POLYMORPHISMS IN THE FATTY ACID DESATURASE (FADS) GENE CLUSTER ALTER THE EFFECTS OF FISH OIL SUPPLEMENTATION ON ERYTHROCYTE DHA LEVELS.

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Objectives and Study: The enzymes encoded by fatty acid desaturases (FADS) 1 and FADS2 determine the desaturation of the essential fatty acids including linoleic acid (LA; 18:2n-6) and alpha-linolenic acid to their longer-chain counterparts including arachidonic acid (AA; 20:4n-6), eicosapentaenoic acid (EPA; 20:5n-3) and docosahexaenoic acid (DHA; 22:6n-3) respectively. This desaturation process, along with dietary consumption, will determine the LCPUFA status of an individual. In recent years it has been debated whether specific genotype carriers of the FADS1 and 2 genes will have altered requirements for supplementation, due to differences in desaturation rates. Our aim was to investigate if single nucleotide polymorphisms (SNPs) in FADS1 and FADS2 can influence plasma phospholipid and erythrocyte EPA, DHA and AA status in infants who received either fish oil or placebo supplementation from birth to six months of age.

Methods: Children enrolled in the IFOS study (Infant Fish Oil Supplementation Study) were randomly allocated to receive either fish oil supplementation or placebo from birth to six months of age. A blood sample was collected at six months of age for the measurement of plasma phospholipid and erythrocyte fatty acids, along with DNA. Twenty three FADS1 and FADS2 SNPs were selected for an exploratory study on the basis of previous association with fatty acids, neurodevelopment or immune function. In a multivariable analysis, the infant genotype effect was adjusted for the effect of the supplementation group to determine the strength of the influence of infant fatty acids.

Results: A total of 276 participant DNA samples underwent genotyping. A total of 145 paired plasma fatty acid measurements and 133 paired red blood cell fatty acid measurements were available for analysis. Infant FADS genotypes influenced the effect of the supplementation; with only minor allele homozygous carriers receiving a significant benefit of supplementation (p <.05). This was found for SNPs of the FADS1, FADS2 and intergenic regions including; rs174548, rs174556, rs99780, rs174574, rs174576, rs174578, rs174579 and rs17448.

Conclusion: Genotypic variations of the FADS 1 and 2 genes may influence the requirements for DHA supplementation, with minor allele homozygous carriers receiving the greatest benefit of supplementation. Targeted supplementation of the carriers may result in greater effects of DHA supplementation on neurodevelopmental, cardiovascular and immune outcomes.

Disclosure of Interest: None Declared
**Objectives and Study:** A majority of acute lymphoblastic leukemia (ALL) survivors develop treatment-related late-onset complications such as metabolic syndrome (MetS), which is potentially mediated by epigenetic alterations caused by chronic inflammation and chemo/radiotherapy treatments. Our aim was to investigate the DNA methylome of ALL survivors affected with MetS in order to characterize specific patterns of DNA methylation associated with MetS.

**Methods:** Our study, part of the PETALE project, draws its subjects from a pool of 350 French-Canadian ALL patients aged under 19 at diagnostic that have been in remission for at least 5 years post-diagnostic and did not undergo hematopoietic stem cell transplantation. Twelve patients (6 men and 6 women) with MetS, as determined by the NCEPIII criteria, were sex- and age- (±5y) matched to 12 healthy survivors. Age was not different between groups, with cases 24.2±8.3yo and controls 22.8±8.1yo (p=0.09). DNA methylation in whole leukocytes was analyzed on Infinium HumanMethylation450 BeadChips (Illumina). Differential methylation between groups was assessed using Illumina’s GenomeStudio software (custom model). P-values were corrected for multiple testing using the Benjamini and Yekutieli procedure, and CpG sites with associated false discovery rate <0.05 were considered as differentially methylated.

**Results:** All measured metabolic data, with the exception of blood pressure, were significantly altered in survivors with MetS as compared to controls: waist circumference 80±9 vs. 108±16cm (p<10^{-3}), fasting glucose 5±0.4 vs. 5.4±0.6mM (p<0.05), HDL-cholesterol 1.38±0.15 vs. 1.08±0.25mM (p<0.01) and triacylglycerol 0.8±0.46 vs. 1.65±0.77mM (p<10^{-3}). Differential methylation was observed at 1099 CpG sites associated to 874 genes. Unsupervised clustering of sites associated with metabolic genes did not discriminate between MetS and control groups. However, 117 differentially methylated genes are involved in functions related to energy metabolism, stress, or inflammation; indeed, oxidative stress (SLC25A24, GSTM1), inflammation (PRKCZ, TRIM15), carbohydrate (GCK, INS-IGF2, CASR), triacylglycerol (GPLD1, AGPAT1), and cholesterol metabolism (ABCA1, ABCA6) genes were differentially methylated, indicating potential metabolic alterations.

**Conclusion:** We observed alterations in DNA methylation patterns of metabolism-related genes specific to ALL survivors affected with MetS, as compared to non-affected ALL survivors, which may contribute to explain the increased prevalence of MetS in that population. This study could help to define biomarkers to predict late-onset MetS susceptibility in childhood ALL survivors.

**Disclosure of Interest:** None Declared
Obesity and Early Markers of Metabolic Syndrome in Children Born with Marginally Low Birth Weight

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Objectives and Study: Low birth weight correlates to increased risk of obesity and metabolic syndrome. However, the magnitude and emergence of adverse health outcome in marginally low birth weight (MLBW, 2000-2500 g) subjects is not known. The aim of the present study was to examine if being born with MLBW is a risk factor for obesity and other early signs of metabolic syndrome already in childhood.

Methods: This was a prospective cohort study including 285 Swedish MLBW children. Of included infants, 44% were born small for gestational age (SGA, < -2 SD for weight) and 56% were born preterm. When the children were 3.5 years and 7 years of age, we measured weight, height, and BMI, and calculated the prevalence of overweight and obesity. Furthermore, we measured blood pressure and skinfold thickness and analysed serum levels of glucose, insulin and lipids. At 7 years, a dual energy X-ray (DXA) was performed and fat mass index (FMI) and fat free mass index (FFMI) were calculated. All analyses were also performed on 95 matched controls born term with normal birth weight (2500-4500 g).

Results: At 3.5 years, mean height, weight, and BMI in MLBW children were 2.1 (95% CI: [1.2-3.1], p<0.001) cm, 1.1 ([0.7-1.6], p<0.001) kg and 0.47 ([0.17-0.76], p=0.002) kg/m² lower in MLBW children compared to controls. At 7 years, the corresponding mean differences were 2.5 ([0.9-4.1], p=0.003) cm, 1.7 ([0.6-2.8], p=0.002) kg, and 0.48 ([0.01-0.94], p=0.046) kg/m². Stratified analyses showed that these differences were larger in the subgroup of children born SGA but the trends were similar in those born AGA. Body composition analyses suggested that the differences in BMI corresponded to lower values of both FFMI and FMI in MLBW children. At 3.5 years, the prevalence of obesity or overweight was 5.2% and 7.4% (p=0.427) in MLBW children and controls respectively, and at 7 years, the corresponding proportions were 6.7% and 5.0% (p=0.631) respectively.

Analyses of blood pressure, skinfold thickness and laboratory measures presented no significant differences between the groups.

Conclusion: At 3.5 and 7 years of age, MLBW children do not show any increased risk of obesity or signs of metabolic syndrome. Instead, their BMI, FMI and FFMI were lower compared to controls, findings most pronounced in those born SGA. The findings are in contrast with our hypothesis and further long term follow up trials are needed to determine the metabolic risks profile in this large subgroup of LBW children.
Disclosure of Interest: None Declared
ABDOMINAL CIRCUMFERENCE OR GASTRIC RESIDUAL VOLUME AS MEASURE OF FEED INTOLERANCE IN VLBW INFANTS: A RANDOMISED CONTROL TRIAL

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Objectives and Study: Background: Up to 2/3rd of VLBW infants have been reported to experience feed intolerance. Traditionally volume and nature of prefeed gastric aspirates have been used to define feed intolerance; however there is no unanimity for its definition. In very preterm infants prefeed gastric residues up to 3 ml may be inconsequential and even greenish aspirates may be physiological. Prefeed abdominal circumference measurement has been suggested as an alternative to gastric aspirates for assessment of feed intolerance. However, its utility in clinical practice has not been evaluated systematically.

Objective: To compare prefeed abdominal circumference and gastric residual volume as a measure of feed intolerance in very low birth weight infants (VLBW).

Methods: Eighty VLBW infants were randomized to two groups; Feeding protocol was standardized and feed intolerance was monitored by measuring either gastric residual volume (GRV group) or prefeed abdominal circumference (AC group). The primary outcome was time to full enteral feeds (180 ml/kg/day). Other main outcome measures were feed interruption days, duration of parenteral nutrition, incidence of culture positive sepsis, NEC, mortality and duration of hospital stay.

Results: The median (IQR) time to achieve full feeds was 10 (9,13) vs. 14 (12,17.5) days in AC and GRV groups, respectively, (p <0.001). The hazard ratios of possible confounding factors affecting time to reach full feeds in the 2 groups were comparable. On reliability analysis there was a good intra-observer and inter-observer agreement among the assessors with ICC (intraclass correlation coefficient) ranging between 0.93 to 0.98. Infants in AC group had fewer feed interruption days [0 (0, 2) vs. 2.0 (1, 5), p <0.001] and shorter duration of parenteral nutrition (p <0.001). The incidence of culture positive sepsis in AC and GRV groups was 17.5 % and 30 %, respectively (p = 0.18). Duration of hospital stay and mortality were comparable in both the groups.

Conclusion: Our study suggests that abdominal circumference monitoring is a better marker of feed intolerance than pre feed gastric residual monitoring. Use of abdominal circumference monitoring as a measure of feed intolerance may result in earlier achievement of full feeds and lesser feed interruption days.

Disclosure of Interest: None Declared
EFFECT OF PROBIOTIC CECT7210 SUPPLEMENTATION OF INFANT FORMULA IN HEALTHY INFANTS.

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Objectives and Study: Breast fed infants develop a specific microbiota pattern, characterized by a predominance of bifidobacterium and lactobacillus, which is related with advantages in terms of gastrointestinal infections, intestinal immunity and more frequent and softer depositions compared to formula fed infants. Our aim was testing the improvement on infections incidence by the supplementation of an infant formula with the bifidobacterium longum CECT7210.

Methods: Randomized double blind clinical trial in which formula fed healthy term infants (< 3 months) were randomized to an infant formula supplemented with 10^7 cfu/g of Bifidobacterium longum (infantis CECT7210) (SUP group) or to a standard formula (CO group) during 3 months. Anthropometry, clinical history, tolerance, immunity biochemical markers and stool bifidobacteria were assessed.

Results: 97 and 93 infants were included in the CO and SUP groups respectively. Birth anthropometry, gender, age at enrolment, delivery type and clinical and socioeconomic variables were equally distributed within study groups. There were no differences in any of anthropometric variables during the study period between groups; both groups of children grew similarly and properly. Supplemented study formula was well tolerated as no differences were observed in total volume intake, regurgitation, flatulence or sleeping and crying behaviour. Children fed the SUP formula showed less constipation incidence (22.6% vs 9.9% p=0.033) as well as higher stool depositions/day (2.6 ± 1.3 vs 2.2 ± 1.0, p=0.038) after 4 weeks of supplementation. In both study groups, stool depositions/day were decreased with age along the study period, however, this reduction was higher among the CO group (p=0.046). We didn’t find significant differences between groups in the frequency of infections or adverse events. However, we found less diarrhea episodes among the supplemented infants compared to CO being significant after two months of supplementation (0.12 ± 0.56 vs. 0.00 ± 0.00, p=0.047). Bifidobacterium longum in stool samples was increased among supplemented infants after 4 weeks of supplementation and secretor immunoglobulin A concentration increased in parallel with the bifidobacterium longum count, even adjusting by the number of vaccinations received by the infant in a linear regression model (p=0.019).

Conclusion: Infant formula supplementation with bifidobacterium longum CECT7210 is safe and well tolerated among infants and is related with a reduction of diarrhea episodes, less constipation frequency and an increase in immunoglobulin A.
INTESTINAL FAILURE IN NEONATES - CAUSES AND OUTCOME.

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Objectives and Study: In adult and paediatric patients, there are clear definitions around provision of PN and the diagnosis of intestinal failure. There is no definition in neonatal patients and it is unclear at what stage these infants could or should be classed as having intestinal failure.

The aim of this retrospective cohort study was to identify and describe the number of neonates who require PN for greater than 28 days in a level 3 neonatal unit and describe their outcomes for growth, mortality, and time taken to achieve enteral autonomy.

Methods: Neonates receiving PN for greater than 28 days between January 2009 to December 2013 were included. The cases were identified from Badgernet (version 2.8.0.0). Accuracy of ascertainment was assessed using pharmacy data. Data on each eligible case was collected recording their demographics, gestation age, diagnosis, duration of use of PN and anthropometry. Statistical analysis variables were completed using Statistical Package for Social Sciences 19.0 (SPSS: An IBM Company, Chicago, IL). Differences between weight and variables of interest were analysed using Wilcoxon-Mann-Whitney Test to determine statistical significance.

Results: A total of 128 cases were identified where neonates had received PN for greater than 28 days. The mean gestation age was 26 weeks with 119 cases being preterm. There were 69 males and 59 females. The indication for use of PN was congenital or acquired gut disorder in 65 cases with 63 cases needing PN because of gut immaturity associated with prematurity. Prematurity in absence of GI disease required PN for a median duration of 35 days and they were able to achieve enteral autonomy by the corrected gestation age of 29.6 weeks. No case in absence of GI disease required PN for 90 days or more. Infants with GI disease required a significantly longer duration of PN with the median being 45 days (p 0.02).

109 cases were discharged home, 3 transferred out to another hospital and 16 died. 8 cases were on PN at the time of discharge from neonatal unit. Of these there were 3 males and 5 females. 4 cases had congenital gastrointestinal disorder with 4 requiring bowel resection because of complications associated with prematurity.

Conclusion: Our results suggest that the use of PN for up to 90 days in extremely preterm infants is very prevalent. Failure to achieve enteral autonomy in neonates by 90 days is seen in presence of GI disease only. Nearly half of all infants in a neonatal unit require prolonged PN (>28 days) because gut immaturity associated with prematurity. All preterm infants would achieve enteral autonomy in absence of gastrointestinal disease with the median age being 30 weeks. This data would suggest that intestinal failure in neonates would be better described as use of parenteral nutrition for greater than 90 days.
Disclosure of Interest: None Declared
ABDOMINAL FAT AND METABOLIC PROFILE IN OBESE CHILDREN: A CASE-CONTROL STUDY

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Objectives and Study: In adults an excess of visceral adipose tissue, to which preperitoneal fat is highly related, seems to be associated with metabolic alterations. This association in children is controversial. The aim of this study was to determine preperitoneal and subcutaneous fat thickness in obese children, compared to normal weight children (control group), and evaluate their association with metabolic profile.

Methods: Twenty-seven obese and 26 normal-weight children (mean age (SD), 11.09 (0.98) years), sex and age- matched, were recruited. Anthropometry, fasting blood glucose, insulin and lipids were measured. Children were defined as obese or normal weight according to WHO (World Health Organization) criteria. Insulin resistance and insulin sensitivity were evaluated calculating HOMA (Homeostasis Model Assessment) and QUICKI (Quantitative Insulin-Sensitivity Check Index) indexes. Subcutaneous and preperitoneal fat thickness were measured using ultrasonography.

Results: BMI (Body Mass Index) z-score was 3.04 (0.62) in obese children and -0.04 (0.57) in normal-weight children (P < 0.001). Compared to control group, obese children showed higher subcutaneous (17.15 [4.32] vs. 5.58 [2.44] mm, P < 0.001) and preperitoneal (11.25 [2.81] vs 5.77 [1.71] mm, P < 0.001) fat thickness. In the obese group, subcutaneous fat thickness was associated positively with BMI z-score (P = 0.04), fasting insulin (P = 0.005), HOMA index (P = 0.005) and negatively with QUICKI index (P = 0.006). No association between preperitoneal fat thickness and BMI z-score, fasting insulin, HOMA and QUICKI indexes was found. Neither subcutaneous nor preperitoneal fat thickness were associated with lipid profile.

Conclusion: Compared to normal-weight children, obese children showed higher subcutaneous and preperitoneal fat thickness. Subcutaneous fat thickness was associated positively with HOMA index and negatively with QUICKI index, differently from what is described in adults. Further studies are needed to understand if subcutaneous fat thickness could be considered a marker of abnormal glycaemic-insulinemic metabolism in paediatric obese population.

Disclosure of Interest: None Declared
CHARACTERISATION OF THE HUMAN MILK WHEY PROTEOME ACROSS POPULATIONS AND LACTATION STAGES: A GEHM STUDY OF THREE GLOBAL COHORTS

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Objectives and Study: Improved understanding of the human milk proteome may provide novel insights into milk composition and function during breastfeeding. Mass spectrometry (MS)-based proteomic approaches have largely facilitated our systemic understanding of the composition and biological function of milk proteins, though there is little information available regarding the developing milk function across populations at different stages of lactation. The goal of this study is to characterize the temporal proteomes of human milk collected from three global cohorts to understand the proteomic similarities and differences between distinct populations over time.

Methods: We employ tandem mass tag (TMT) for differential labeling of milk proteins in order to quantitate relative protein abundances using mass spectrometry. We have compared milk proteomes among three populations (Shanghai, China, Mexico City, Mexico and Cincinnati, United States; n = 9 for each population) at two different stages of lactation (4 and 26 weeks), with all samples collected as part of the Global Exploration of Human Milk (GEHM) study.

Results: At each of the two lactation stages, the profiles of milk proteins are largely similar among the three populations. Unsupervised hierarchical clustering showed greater differences in proteomic profiles between the two lactation stages than between populations. Interestingly, proteins with significant abundance changes over time show patterns of regulation that are broadly similar among populations. Examples include immunoglobulin IgA2 and IgM, which are more abundant at 4 weeks of lactation, and IgG1 and IgG2, which are more abundant at 26 weeks of lactation. Regardless of temporal pattern, IgA2, IgG1, IgG2 and IgM are present at higher levels in both 4 and 26 week milk from China and Mexico compared to the U.S. with fold changes between China and U.S. samples of 2.0, 1.6, 2.3 and 2.1, respectively, and fold changes between Mexico and U.S. samples of 1.8, 1.3, 1.1 and 2.0, respectively. Similar observations can be made for the antimicrobial protein lactoferrin.

Conclusion: Our findings suggest broad congruency in milk protein composition among mothers from three global cohorts in China, Mexico and the United States. This study also suggests that a number of host-defense proteins may be more abundant in human milk from developing countries.

LONGITUDINAL ANALYSIS OF 12 MINERALS IN HUMAN MILK: A GEHM STUDY OF THREE GLOBAL COHORTS THROUGH THE FIRST YEAR OF LACTATION

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Objectives and Study: Elemental composition of human milk is likely influenced by multiple factors, including dietary intake and genetic background, though mineral content and variation in human milk over the course of lactation and by geographic region has not been well characterized. As part of the Global Exploration of Human Milk (GEHM) collaboration, this study investigates the mineral composition of human milk collected from mothers in three geographic regions over the first year of lactation.

Methods: Mother-infant pairs participated in the GEHM study from three distinct geographies (Shanghai, China, Mexico City, Mexico, and Cincinnati, United States), and breast milk was collected from study mothers throughout the first year of lactation. For this mineral characterization, milk samples from 4, 26 and 52 weeks lactation were simultaneously analyzed for 12 elements including P, Na, K, Ca, Mg, Mn, Cu, Zn, Fe, Mo, Cr, and Se using an internally validated inductively coupled plasma-mass spectrometry (ICP-MS) method. Collision cell technology was utilized during analysis to suppress known polyatomic interferences, which could otherwise contribute to measurement bias of elemental concentrations.

Results: Milk from distinct geographic regions exhibited similar mineral concentrations as well as temporal patterns between 4 and 52 weeks of lactation. Among several observations, some elements showed consistent decreases in concentration between 4 and 52 weeks postpartum, including Ca (295 to 220 µg/mL, ↓25%), K (545 to 431 µg/mL, ↓21%), P (163 to 130 µg/mL, ↓20%), Cu (416 to 140 ng/mL, ↓66%) and Zn (2520 to 617 ng/mL, ↓76%), while Fe and Mn remained fairly stable with ≤10% change in concentration over the course of lactation.

Conclusion: Though the twelve analyzed minerals show differing patterns of milk concentration over the course of lactation, overall concentrations and temporal trends for the minerals are markedly congruent in human milk collected from three geographically distinct populations. The data generated in this study provides new insights into the content and variability of 12 minerals in human milk during the first year of lactation from a global perspective.

Johnson Nutrition, R. McMahon Conflict with: Mead Johnson Nutrition, B. Davidson Conflict with:
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Objectives and Study: Previously, HMOs were shown to reduce the duration of rotavirus (RV)-induced diarrhea in formula-fed pigs\(^1\). Herein, the effects of HMOs on systemic and gut mucosal immune cell populations from non-infected (N) and RV-infected pigs were investigated.

Methods: Colostrum-deprived, newborn pigs were fed: formula (FF) or formula with 4g/L HMO (2'-FL, LNnT, 6'-SL, 3'-SL, free sialic acid). On d10, half of the pigs were infected with swine OSU strain RV. Peripheral blood (PBMC) and mesenteric lymph nodes (MLN) were collected 5 days post-infection, and immune cell populations were assessed by flow cytometry. Interferon-gamma (IFN-gamma)-producing cells were assessed by ELISpot.

Results: Diet affected some immune cell populations independent of infection status. FF had more MLN B cells than HMO. Whereas, HMO had more PBMC NK cells and MLN effector memory T cells. PBMC of HMO_N had twice as many IFN-gamma-producing cells than PBMC of FF_N. Innate immune cells or antigen-presenting cell populations of FF_N differed from those of HMO_N, but differences were not always maintained following RV-infection. FF_N had more PBMC and MLN granulocytes than HMO_N, but this effect was lost with infection. FF_N also had more PBMC monocytes/macrophages than HMO_N and infected pigs. Furthermore, the MLN of FF_N had more plasmacytoid dendritic cells (DC) than HMO_N; this population, which is vital to the anti-viral immune response, did not differ between FF_I and HMO_I pigs. Finally, FF_N MLN had fewer immature DC and more mature DC compared to HMO_N and both RV-infected groups. Differences in immune cell populations between FF_N and HMO_N indicate that dietary HMO affected baseline immunity. These baseline effects may be due to differences in the gut bacterial populations\(^1\) or direct effects on mucosal immune cells\(^2\). Importantly, HMOs induced increases in PBMC NK cells and MLN effector memory T cells, IFN-gamma-producing cells, were maintained during infection.

Conclusion: Our results show for the first time that dietary HMOs induce changes in immune cell populations in non-infected piglets, and that changes in immune cell populations may mediate the effects of dietary HMOs on reducing the duration of RV-induced diarrhea. (Supported by NIH grant R01 HD061929).

BULK 15N NATURAL ISOTOPIC ABUNDANCE IN A MOUSE MODEL OF PROTEIN RESTRICTION

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Objectives and Study: The values of the bulk natural isotopic abundance (NIA) of 15-nitrogen, which is a stable isotope, partly depends on the intensity of protein metabolism. The bulk 15N NIA values can be measured in all tissues, like hair and nails using isotopic ratio measurement mass spectrometry. Our aim was to investigate the impact of an early protein restriction on the protein metabolism in adulthood.

Methods: Pregnant Balb/c mice were fed a low protein diet (10% protein) during gestation and lactation (LPD, n=6), gestation but not lactation (LPD-ND, n=8) or lactation only (ND-LPD, n=8). They were compared to control mice feeding a 22% protein diet (ND, n=4). After weaning (at 1 month), all offspring were fed the same standard diet (A03, ad libitum) until sacrifice at 16 months. Offspring’s hair samples were weighed into tin capsules. The bulk 15N NIA values for hair were measured by isotope ratio measurement mass spectrometry coupled with an elemental analyser.

Results: The weight of mice at 16 months was significantly different between groups, LPD, LPD-ND, ND-LPD and ND respectively: 30.1±2.3g, 35.4±5.9g, 30.5±1.8g and 34.4±1.3g; P=0.03 (Anova). A difference was found in the bulk 15N NIA values, respectively: 7.0±0.5‰, 6.6±0.9‰, 7.4±0.8‰ and 7.9±0.2‰, p=0.03 (Anova) although all mice were fed the same diet since weaning.

Conclusion: These data suggest that a protein restriction during gestation and/or lactation leads to an imprinting of the protein metabolism, regardless of the diet at sacrifice.

Disclosure of Interest: None Declared
MALNOURISHED PARENTERALLY-FED PIGLETS SHOW ALTERED ACUTE PHASE REACTION FOLLOWING ENDOTOXIN EXPOSURE

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Objectives and Study: Malnutrition has been associated with adverse outcomes in both hospitalized paediatric patients and in children experiencing severe acute malnutrition (SAM) in low income countries. Small bowel bacterial overgrowth and release of endotoxin to the systemic circulation may play a role for disease in both groups of children. Endotoxemia induces multiple hemodynamic and acute phase reactions associated with septic shock. Altered fluid homeostasis including formation of oedema in the interstitial compartment is also known to be associated with endotoxemia. Using parenterally-fed piglets as a model for malnourished children, we hypothesized that endotoxin-induced acute phase response would be altered following malnutrition.

Methods: Three-day old piglets were given total parenteral nutrition (TPN) with optimal (OPT) or suboptimal (SUB) nutritional composition. Relative to OPT, the SUB group was given TPN with lower amino acid (5.5 vs 47 g/L) but higher fat (34 vs 10 g/L) and dextrose (97 vs 86 g/L) contents, and all micronutrients were lower. After seven days, half of the pigs from each group were co-infused with endotoxin (LPS, given 10 μg kg⁻¹ h⁻¹ for 9 h; OPT-LPS, n=10 and SUB-LPS, n=8), whereas the rest were co-infused with saline (OPT-SAL, n=10 and SUB-SAL, n=8). Oedema formation was assessed with abdominal ultrasonography before and after LPS infusion.

Results: There was a marked reduction in body weight gain in SUB vs OPT pigs (120 vs. 567 g, P<0.001), and biochemical and haematological profiling showed higher CRP, bilirubin, cholesterol, globulin, gamma-tocopherol and lactate, whereas malondialdehyde, albumin, haptoglobin, glutathione, ALP, ASAT, CK, urea, Fe, Mg, P, Na, platelets and lymphocytes were lower (all P<0.05) in SUB, relative to OPT. Following LPS infusion, perirenal oedema formation was higher in SUB-LPS than OPT-LPS (P<0.01), whereas no oedema was detected before LPS infusion or in the saline-infused control groups. Among the measured biochemical and haematological markers, TNF-α increased in both OPT-LPS and SUB-LPS, relative to saline-controls, but with the highest increase in OPT-LPS at 2h after start of LPS infusion (all P<0.01).

Conclusion: The combination of endotoxemia and insufficient nutrition may play an important role for altered acute phase responses and excessive oedema formation as seen in malnourished children.

Disclosure of Interest: None Declared
ELECTROMAGNETIC-GUIDED POST-PYLORIC TUBE PLACEMENT IN CHILDREN: A SAFE AND EFFECTIVE METHOD

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Objectives and Study: Postpyloric enteral tube (PET) placement can be cumbersome. Fluoroscopic and endoscopic placement are required when unguided placement fails. We aimed to evaluate the feasibility and safety of PET placement in children, using an electromagnetic (EM) guided system as a rescue strategy in case unguided tube insertion fails.

Methods: In a single center prospective study we included all children (>2.5 kg) in which unguided PET placement failed between 2009 and 2012. EM guided PET placement was attempted before regular fluoroscopic and endoscopic placement was attempted.

Results: Forty-nine children were included (mean age 3.5 yrs). EM guided PET placement was successful in 82% of the children. No adverse events occurred. Age or indication for the PET did not influence the success rate of the procedure. A trend of a learning curve of 25 patients was noticed. Costs of EM placement were slightly higher than those of fluoroscopic placement in our hospital setting.

Conclusion: EM guided PET placement is safe and can prevent fluoroscopic or endoscopic tube placement in 82% of children.


Disclosure of Interest: None Declared
A NOVEL MILK-DERIVED COMPONENT WHICH CAN SPECIFICALLY SUPPRESS TH2 RESPONSES MAY HAVE AN APPLICATION IN ENHANCING RESOLUTION OF COWS MILK PROTEIN ALLERGY.

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Objectives and Study: In Europe, 20 to 30% of infants are diagnosed with an atopic (allergic) disease. The majority of first atopic responses are directed towards food proteins that are observed during the first months of life, such as cows milk protein. Cows milk protein allergy (CMPA) affects 2.2 % to 7.5 % of infants worldwide and is a growing public health problem in Western Europe and USA. Existing hypoallergenic formula solutions adopt avoidance strategies such as the extensive hydrolysis of whey or casein proteins (using proteolytic bacteria or enzymes). However, allergic responses are associated with a dominant T helper type 2 (Th2) response, which plays a key role in triggering IgE production by B cells. Therefore the aim of this study was to assess whether novel milk-derived component can suppress Th2 responses which may enhance resolution of CMPA and lower the risk of developing a further allergy.

Methods: Murine spleenocytes were isolated from the spleens of 8-14 week old BALB/c mice and purified for CD4+ T-cells using magnetic negative isolation. Cells were activated using plate bound anti-CD3 and anti-CD28 antibodies in fully supplemented RPMI for 3 days during differentiation. For a Th2 phenotype cells were differentiated by the addition of rIL-2, rIL-4 and anti-IFN-γ. For a Th1 phenotype cells were generated in the presence of rIL-12, anti-IL-4 and rIL-2. The novel milk-derived component was added during T helper cell differentiation. Th1 and Th2 subsets were confirmed using ELISA analysis of cytokine production after 3 days.

Results: The novel milk-derived component specifically suppressed the secretion of IL-4 from differentiated Th2 cells in a dose dependent manner. A regenerated form of the novel milk-derived component also had the same effect. Interestingly, the novel component had no effect on Th1 cells and the level of secretion of IFNγ was not affected by the presence of the component. This suggests that the component specifically suppresses Th2 responses. Not all component fractions showed this activity, highlighting the fact that functional activity can vary greatly between different component preparations.

Conclusion: We have identified a novel milk-derived component that can specifically suppress secretion of IL-4 by differentiated Th2 cells. The presence of such a component in hypoallergenic infant formula may act to suppress the over activated Th2 response associated with allergy and could enhance resolution of CMPA or lower the risk of developing a further allergy later in infancy.
Disclosure of Interest: None Declared
**Follow-up of Malnourished Hospitalised Children: A Dutch Multicenter Study**

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**Objectives and Study:** Follow-up studies of malnourished children after discharge from the hospital are lacking. The aim of this study was to evaluate the course of the nutritional status of these children during and after hospital stay.

**Methods:** A prospective observational multicenter study was performed in 9 Dutch general paediatric wards, during a period of 3-5.5 months. Admitted children were screened for risk of malnutrition using STRONGkids and weight-for-age (WFA, ≤1y), weight-for-height (WFH, >1y) and height-for-age (HFA). SD-scores were calculated to classify acute or chronic malnutrition respectively. Follow-up of nutritional status was performed at discharge, and 4-8 weeks after discharge for malnourished and high risk children.

**Results:** Preliminary data of 6 wards were analyzed; 1226 children, median age 2.6 years (0.02-19.1y). Acute and chronic malnutrition on admission was present in 14% and 8% respectively (overall 18%). Based on STRONGkids, 7% were at high risk (37% medium risk, 56% low risk). Hospital stay was longer in high compared to medium/low risk children (3 days vs. 2 days, p < 0.001). Weight was measured at discharge in 59% of children; weight loss was found in 23% (1% lost > 5%). In those children with malnutrition or at high risk seen at the outpatient clinic (n=107), mean WFA/WFH SD-scores significantly improved compared to admission (-2.4 vs. -1.5 SD for WFA (<1y)) and -2.4 vs. -1.1 SD for WFH (>1y), p < 0.001). There was no difference in WFA/WFH improvement between children with (n=63) and without nutritional intervention. At follow-up, 39 of 107 children (36%) were still acutely malnourished. These children were younger and had lower WFA/WFH SD scores on admission than those who were not malnourished at follow-up.

**Conclusion:** This multicenter study shows that 4-8 weeks after hospital discharge, significant improvement of nutritional status is found in children with (high risk of) malnutrition on admission. However, still 36% of these children were acutely malnourished, so attention is needed for malnutrition in the outpatient setting.

**Disclosure of Interest:** None Declared
EARLY INFANT FEEDING AND COELIAC DISEASE: UPDATED SYSTEMATIC REVIEW

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Objectives and Study: In 2012, as part of PREVENTCD (an EU-funded project investigating the possibility of inducing tolerance to gluten in children genetically predisposed to celiac disease [CD] through changing infant feeding practices), we summarized, in a systematic review (1), evidence on the possible relationship between early feeding practices (breastfeeding and gluten introduction) and the risk of developing CD during childhood. In the last few years, new evidence has emerged, prompting an updated systematic review of the evidence. We aimed to systematically review the evidence on early feeding practices and the prevention of CD.

Methods: The Cochrane Central Register of Controlled Trials (CENTRAL, the Cochrane Library), MEDLINE, and EMBASE were searched from July 2012 (end of last search) to November 2014. Researchers working in the field were contacted for any unpublished data. Letters to the editor, abstracts, and proceedings from scientific meetings were excluded, unless a full set of data was available from the authors. No language restriction was imposed. Interventions eligible for assessment involved the consumption of gluten-containing products of any type (cereals, flour, or any other foods containing gluten; preparations manufactured for research purposes). The primary outcome measure was the development of CD or the development of CD–related autoimmunity (i.e., anti-transglutaminase or anti-endomysial antibodies).

Results: In addition to the previously identified 12 studies, 4 new studies were found, including two, new, randomized controlled trials (RCTs) performed in high-risk infants. Overall, the current evidence indicates that exclusive or any breastfeeding does not reduce the risk of developing CD during childhood. Breastfeeding at the time of gluten introduction does not reduce the risk of developing CD. For infants at high risk of developing CD, gluten introduction at 4 or 6 or 12 months of age results in similar rates of CD diagnosis in early childhood. Finally, but this comes from observational studies only, consumption of a higher amount of gluten at weaning increases the risk of developing CD.
Conclusion: Current evidence suggests that infant feeding practices (breastfeeding, time of gluten introduction) have no effect on the risk of developing CD during childhood, necessitating an update of current ESPGHAN recommendations.


Disclosure of Interest: None Declared
**Nutrition**

**Neonatal Nutrition**

PA-N-0076

**ROUTINELY PROBIOTIC MIXTURE ADMINISTRATION, LACTOBACILLUS ACIDOPHILUS AND BIFIDOBACTERIUM BIFIDUM IN PRETERM VERY-LOW-BIRTH-WEIGHT NEONATES: A HISTORICAL CONTROL STUDY.**

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**Objectives and Study:** Probiotics are important in preventing gut microbiota disturbances. Neonatal studies disclose efficacy of certain mixtures of probiotics in preventing NEC (necrotizing enterocolitis). Nevertheless, concerns exist about safety and efficacy of routinely administration of living microorganisms in immature patientes. Objective: To test that oral administration of prophylactic *Lactobacillus acidophilus* and *Bifidobacterium bifidum* to preterm neoantes in an intensive care unit, would be safe and decrease the incidence of NEC and sepsis.

**Methods:** A retrospective review of a database collected prospectively on infants with birth weight < 1250g admitted to a single NICU (Neonatal Intensive Care Unit) during two years, after the implementation of a standard protocol of administration of *Lactobacillus acidophilus* and *Bifidobacterium bifidum* consisted of 10⁹ UFC/Kg of each of the probiotics enteral, twice a day, maximum 10⁹ UFC per dosis, since the 1 th day of life, for 6 week courses, were compared with histoical controls admitted during two years before probiotic use. Nutritional policy in the two periods relied on administration of fresh, expressed maternal milk, whenever possible, and supplementation of premature formulae when needed. Data about safety of probiotic administrtion, concomitant sepsis an necrotizing enterocolitis, were retrieved and analyzed.

**Results:** 273 infants (mean birth weight 1041 (±288) g; mean gestational age 38.5 (±2.1) weeks), 142 infants < 28 wks gestation. In this study, 308 infants were used as controls (mean birth weight 1059 (±289) g; mean gestational age 28.6 (±2.1) weeks, 168 infants were born < 28 wks gestation. No significant differences were found between the two periods. Over the study period, none of the clinical cultures ever grew *Lactobacillus acidophilus* or *Bifidobacterium bifidum* or other *Lactobacilli* or *Bifidobacteria*, no episode of sepsis was attributable to probiotics. In the historic control group, there were 7 cases of NEC (4%) and 62 cases (37%) of nosocomial sepsis compared to 9% (p=0.17) and 30% (p= 0.41) respectively in the group that received probiotic prophylaxis.

**Conclusion:** Routinely use of probiotic mixture was safe. No isolation of probiotics from clinical cultures occurred. No clinical episode of sepsis attributable to probiotics was recorded. No effect on NEC incidence or sepsis was observed. Our study does not support the use of *Lactobacillus acidophilus* and *Bifidobacterium bifidum*.

**Disclosure of Interest:** None Declared
Objectives and Study: Feeding very low birth weight (VLBW) infants is a challenge and the optimal timing, volume and diet remain controversial. The NeoNutriNet database gives an overview of differences in feeding practice for preterm infants around the world. This will help to identify optimal feeding regimens and design appropriate intervention studies.

Methods: Fourteen hospitals in ‘Western’ (USA, Denmark, Netherlands, UK, Australia, New Zealand) and ‘non-Western’ (China, India, Taiwan) regions participated. Infants with a birth weight <1500g born between Jan 2011 and Sept 2014 were included. Collected data include timing and composition of (par)enteral nutrition and anti-/probiotics, anthropometrics and clinical complications from birth until a gestational age (GA) 37 weeks or discharge from hospital. Here we present preliminary results from seven hospitals, four non-Western (A-D) and three Western (E-G).

Results: Birth weight, GA, gender distribution and mortality rates differed significantly among hospitals (Table). Nutritional regimes and outcomes (time to full enteral feeding (TFF; 150 ml/kg/day), incidence of necrotizing enterocolitis (NEC), weight gain, anti-/probiotics use) also differed markedly. Infants from Western hospitals had lowest birth weight, but reached full enteral feeding earlier (median 13 vs. 27 d).

Image:

Conclusion: Nutritional practices and associated clinical outcomes in VLBW infants show marked differences among hospitals. The variations may relate to differences in infant biology, culture or clinical practice between Western and non-Western regions. This is important to clarify because it is
suggested that early enteral feeding influences later outcomes. Results from the NeoNutriNet database will be a valuable tool to help design future intervention studies in this field.

**Disclosure of Interest:** None Declared
How an Optimised Feeding Protocol Influences the Risk of Necrotising Enterocolitis in Extremely Low Birth Weight Infants?

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Objectives and Study: To evaluate if optimizing feeding practices with a standardized protocol that includes early introduction from the first day of life, 20-25 ml/kg/d feeding advancement, and human milk fortification from 50 ml/kg/d may be detrimental to extremely low birth weight (ELBW) infants.

Methods: This study is a single-centre comparative cohort study in ELBW infants born before (2005-2007) and after (2010-2012) the implementation of a new feeding protocol. Inclusion criterion was all newborns with a birth weight (BW) <1250g. Exclusion criteria were congenital malformations, functional intestinal diseases (meconium ileus, meconium plug and spontaneous neonatal intestinal perforation), and early neonatal death before day 7. Feeding practices (age of first feeding, age when parenteral nutrition (PN) was stopped, and PN duration), neonatal mortality after day 6, Bell stage 2 necrotizing enterocolitis (NEC) and transient feeding intolerance (>48h feeding withholding and no NEC) were evaluated.

Results: Gestational age, BW and the incidence of transient feeding intolerance were similar in the 2 cohorts (Table). The age for the first feeding and the need for PN were significantly reduced after the implementation of the new optimized feeding protocol (p<0.001). The incidence of NEC was significantly reduced (p<0.01) as well as neonatal mortality after day 6 (p=0.04). The severity of NEC was also decreased with a significant reduction of Bell stage 3 NEC (6/123 versus 0/120, p=0.02). The reduction in the incidence of NEC is particularly significant in infants with BW <1000g (7/58 versus 0/58, p=0.01).

<table>
<thead>
<tr>
<th></th>
<th>Before (N=123)</th>
<th>After (N=120)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gestational age, weeks (SD)</td>
<td>28.1 (2.0)</td>
<td>28.1 (2.3)</td>
<td>0.84</td>
</tr>
<tr>
<td>Birth weight, grams (SD)</td>
<td>995 (171)</td>
<td>963 (197)</td>
<td>0.18</td>
</tr>
<tr>
<td>Age for first feeding, days (IQR)</td>
<td>3 (1-5)</td>
<td>1 (1-1)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age when PN was ended, days (IQR)</td>
<td>19 (12-29)</td>
<td>12 (9-17.5)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>PN duration, days (IQR)</td>
<td>22 (13-36)</td>
<td>13 (10-20)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Transient feeding intolerance, n (%)</td>
<td>13 (10.6)</td>
<td>12 (10.0)</td>
<td>0.90</td>
</tr>
<tr>
<td>Necrotizing enterocolitis, n (%)</td>
<td>11 (8.94)</td>
<td>1 (0.8)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Death after day 7, n (%)</td>
<td>7 (5.7)</td>
<td>1 (0.8)</td>
<td>0.04</td>
</tr>
</tbody>
</table>

SD: standard deviation, IQR: interquartile range, PN parenteral nutrition

Conclusion: Implementing an optimized feeding protocol significantly reduces the need for PN in ELBW infants and do not increase their risk of NEC or their mortality. In addition, this study shows a significant decrease in the incidence of both NEC and mortality after the implementation of the new protocol.
optimized feeding protocol suggesting a potential protective effect. Further studies are required to better understand the pathophysiology of NEC and to define the optimal feeding strategy in premature infants.

Disclosure of Interest: None Declared
BOVINE COLOSTRUM AS NUTRITION FOR PRETERM INFANTS IN THE FIRST DAYS OF LIFE: A PILOT FEASIBILITY STUDY (PRECOLOS-NEOMUNE)

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Objectives and Study: The optimal feeding regimen for preterm infants is not clear, especially when mother’s own milk (MM) is not available. Infant formula (IF) and donor milk (DM) are potentially inferior to MM in promoting feeding tolerance, growth and intestinal maturation. Bovine colostrum (BC) contains large amounts of protein, growth factors and immuno-regulatory components (IGFs, IgG, lactoferrin) which may be beneficial. We investigated whether feeding BC to preterm infants during the first days of life is safe, well tolerated and may promote nutrient uptake and gut maturation when MM is limited. PreColos is a three-phase (A, B, C), dual-site (Rigshospitalet, RH and Foshan Women and Children’s Hospital, FWCH), pilot feasibility study (ClinicalTrials.gov NCT02054091). The protocol and preliminary results of phases A and B are summarized here.

Methods: In phases A and B, 12 infants delivered with gestational age (GA) between 27+0 and 32+6 weeks (RH) or birth weights (BW) 1000-1800 g (FWCH) were recruited before the first feeding. BC was administered as a supplement to MM for up to 10 d with maximum total protein intake of 4.5 g/kg/d. In phase C, a randomized controlled trial, 40 infants will be recruited to BC intervention or control feeding (DM at RH and IF at FWCH). Outcomes are feeding intolerance (FI), time to enteral feeding at 120 ml/kg/d (TTF120), growth, combined incidence of serious infections/NEC, plasma amino acids, plasma bovine IgG, intestinal functions, and faecal microbiota. Data are presented as median (interquartile range).

Results: The BW and gestational age (GA) for the 12 infants (7/5, female/male) were 1499 (1231-1650) g and 30.4 (29.8-31.9) week. Infants received BC for 7.5 (5.8-9.0) d at a dose of 17.7 (12.2-25.3) ml/kg/d and 1.4 (1.0-2.0) g/kg/d protein from BC. At 37 weeks or discharge, body weight reached 2280 (2112-2510) g and average growth velocity was 12.3 (10.3-13.8) g/kg/d. TTF120 and days on PN were 10.0 (6.0-14.5) and 11.0 (0.0-15.5) d. Seven infants showed FI in the first week and 1 infant in the second. Total volume of gastric residual was 39 (6-79) ml in the first week and 4 (1-12) ml in the second. On day 7, 5 infants showed a transient hypertyrosinemia, which disappeared on day 14 for all infants. Plasma bovine IgG was below the detection limit (5µg/ml, n=7). No adverse reactions to BC were observed.

Conclusion: Feeding BC as a supplement to MM during the first 10 d of life was well tolerated in preterm infants with GA between 27+0 and 32+6 weeks or BW 1000-1800 g. Phase C will proceed as planned and plasma tyrosine will be closely monitored.
Disclosure of Interest: Y. Li: None Declared, S. M. Petersen: None Declared, X. Ye: None Declared, R. L. Shen: None Declared, P. T. Sangild Conflict with: Univ of Copenhagen has filed a patent regarding the use of bovine colostrum for pediatric patients, G. O. Greisen: None Declared
**Nutrition**

**Neonatal Nutrition**

PA-N-0091

**FAT MASS IN EXTREMELY PRETERM INFANTS: RELATIONSHIP WITH NEONATAL WEIGHT GAIN**

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¹Princess Margaret Hospital, Perth, Australia, ²Neonatology, ³Centre Hospitalier de l'université Laval, Quebec, Canada

**Objectives and Study:**

**Background:** Early growth impairment of preterms is associated with growth retardation and increased rate of neurodevelopmental impairment.

**Objective:** To compare fat % measured by Dual-Energy X-ray Absorptiometry (DXA) in extreme preterms at term corrected age (TCA) with those of terms and to assess weight gain velocity contribution during the neonatal period on preterm body composition at TCA.

**Methods:** Preterms (< 29⁰⁷ wks) and terms (37-40 wks) were prospectively enrolled in a longitudinal study from October 2012 to October 2013. Nutritional parameters, anthropometry and body composition were evaluated using DXA at TCA in preterms and before day 10 of life in terms. Group differences were assessed by Student t-test (Wilcoxon rank-sum test when appropriate) for continuous data and Chi-square (Fisher exact test when appropriate) for categorical. Multivariate general linear regression modelling was performed to determine the effects of studied factors on fat %. Statistical significance was p<0.05.

**Results:** 68 infants (29 preterms, 39 terms) were included. Preterms at TCA were shorter, lighter with a smaller head circumference compared with similar age terms. Weight estimated by DXA was significantly lower in preterms at TCA (2960g±551.9 vs 3843g±377.1;p<0.01 for preterm and term respectively). Lean mass was reduced in preterms (2488g±370.8 vs 3207g±321.4;p<0.01 for preterm and term respectively). Fat mass was reduced but not significantly in preterms at TCA compared to terms (430.3g±228.5 vs 567.6g±152.2). Fat % (14.0±5.4%) and lean mass % (84.7±5.6%) in preterms were similar to those of terms (14.7±3.5 and 83.5±3.6 for fat and lean % respectively). Triceps, biceps, suprailliac and subscapular skinfold thickness were significantly increased in preterms compared to terms. Preterm's weight gain speed from birth to DXA evaluation was 12.0±1.4g/kg/d and positively related to preterm fat % in a multivariate regression model (Reg coef=1.58, 95% CI 0.45–2.71).

**Conclusion:** Under our nutritional regimen, preterms at TCA had lean and fat mass in similar proportion than terms. However, fat distribution was different, as preterms had more subcutaneous fat than terms. Even if they have a growth velocity close to the intrauterine one, they do not achieve an extraterterine growth similar to terms. Therefore, there is a need to better understand fat deposition in preterms and its childhood impact.

**Disclosure of Interest:** None Declared
FIFTH ANNUAL PAEDIATRIC NUTRITION WEEK: E-PINUT 2014

Arnaud De Luca 1 2 3, Michel Fischbach 4, Dominique Guimber 5, Noël Peretti 6, Hugues Piloquet 7, Virginie Colomb 8, Régis Hankard 9, 10

1 Inserm CIC 1402, 2 CHU, 3 University of Poitiers, Poitiers, 4 CHU, Strasbourg, 5 CHU, Lille, 6 CHU, Lyon, 7 CHU, Nantes, 8 Vaincre la mucoviscidose Association, Paris, 9 F. Rabelais University, 10 CHU, Tours, France

Objectives and Study: Protein-energy malnutrition (PEM) remains poorly reported and then under-diagnosed in hospitalised children. We conducted our 5th annual survey of systematic nutritional assessment in hospitalised children. Our aim was to assess the evolution of PEM frequency and focus on mid-upper arm circumference (MUAC) and disabilities.

Methods: All hospitalised child admitted the same week were weighed and measured, including MUAC measurement. ICD10 diagnoses (reason of hospitalisation and chronic disease if any), disabilities (WHO definition) and nutritional support were recorded. Children below the 3rd centile of body mass index for age and sex had full diagnostic procedure, according to the 2012’s guidelines of the French Paediatric Society. The data recording was performed using e-Pinut web-based tool (www.epinut.fr). An organisational questionnaire was sent after the survey.

Results: This cross-sectional survey involved 144 wards (72 hospitals) in 7 countries. Among the 2204 collected observations, 2115 were analysed (55% boys, median age: 3.8 years). Eleven per cent had weight-for-height z-score (Z-WFH) <-2SD (compatible with PEM): Ivory Coast (IC) 40%, Gabon (G) 28%, Democratic Republic of the Congo (DRC) 22%, Belgium (B) 11%, France (F) 10%, Canada (Ca) 7% and Colombia (Co) 6%. Height-for-age z-score <-2SD was found in 14% of the whole population: DRC 28%, G 21%, Co 21%, IC 20%, Ca 14%, F 13% and B 11%. For Z-WFH <-2SD, the negative predictive value of Z-MUAC <-2SD was 93%. Among the 2003 documented diagnoses, PEM was more frequent in digestive diseases (14%), neurological diseases (12%) and surgical diseases (12%). The PEM frequency was higher in children with chronic disease (52% of the population) (12.3% vs. 8.8%,  P=0.01) and in children with disability (21% of children) (15.6% vs. 9.4%,  P<10^-3). Overweight and obesity frequency was 8.4%. Among the 39 received questionnaires, 85% of centres claimed e-Pinut promoted malnutrition awareness in their wards. A written procedure was declared in 38% of centres.

Conclusion: e-Pinut is an annual rendezvous promoting the nutritional assessment since 2010. The number of participating centres and countries is still rising, showing a growing and lasting mobilisation, helping with standardisation of the diagnostic procedure. PEM frequency was similar to previous surveys. Gastroenterology is the number 1 disease leading to PEM. MUAC may provide a simple screening tool but specific studies are needed. Our next step is a European nutrition week.
Disclosure of Interest: A. De Luca Conflict with: Nutricia, Advanced Medical Nutrition-France, M. Fischbach: None Declared, D. Guimber: None Declared, N. Peretti: None Declared, H. Piloquet: None Declared, V. Colomb: None Declared, R. Hankard: None Declared
**ORAL SUPPLEMENTATION WITH PROBIOTICS IN VERY LOW BIRTH WEIGHT NEONATES- THE EFFECTS ON LATE ONSET SEPSIS AND GROWTH**

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¹University Medical Centre, ²University of Maribor, Faculty of medicine, Maribor, Slovenia

**Objectives and Study:** Late onset sepsis in very low birth weight neonate (VLBW; < 1,500 g) is associated with increased morbidity and mortality. It has been suggested that probiotics may decrease late onset sepsis and has positive impact on growth. The aim of our study was to establish whether the administration of probiotic combination (*Lactobacillus acidophilus*, *Enterococcus faecium* and *Bifidobacterium infantum*) with the ratio of 1.5:1:1.5 at a dosage of 0.6 x 10⁷ CFU twice a day decreases the number of late onset sepsis in VLBW infants and to determine the impact of probiotics on growth. The study protocol was approved by national ethics board and informed written parental consent was obtained.

**Methods:** 80 randomly chosen VLBW infants were enrolled. 40 infants received their milk feedings supplemented with probiotic combination (*Lactobacillus acidophilus*, *Enterococcus faecium* and *Bifidobacterium infantum*) from the first feeding until the discharge. Another 40 infants received only milk. There were no significant differences between the groups in regard to maternal and labour characteristics, anthropometric data and clinical characteristics. In case of suspected sepsis, aerobe and anaerobe blood cultures with serial CRP and procalcitonin measurements were performed. Sepsis was defined as period of clinical infection together with elevated inflammatory indices with or without positive blood culture. The growth of bodyweight, length and head circumference was followed by observing the dynamics at 1st, 2nd, 4th, 8th and 12th week after admission and at discharge.

**Results:** Infants receiving probiotic supplements had a lower prevalence of late onset sepsis. In the group with probiotic supplementation 16 infants (40%) had at least one episode of sepsis in comparison with 29 infants (72.5%) in the group without probiotics (p=0.006). The total number septic episodes was significantly lower in infants receiving probiotics (30 episodes) than in the group without them (69 episodes) (p=0.003). There was no difference in bodyweight, length and head circumference, but infants who received probiotics were discharged with smaller postmenstrual age (37 weeks) than infants without probiotics supplement (38 weeks). None of the added probiotics was isolated in any of the blood or other cultures.

**Conclusion:** Children receiving prophylactic probiotics *Lactobacillus acidophilus*, *Enterococcus faecium* and *Bifidobacterium infantum* with a ratio 1.5:1:1.5 at a dosage of 1.2x 10⁷ CFU from their first milk feeding until discharge had less late onset sepsis episodes. There was no effect on growth, but VLBW neonates were discharged at a smaller gestational age.

**Disclosure of Interest:** None Declared
SAFETY OF A NEW AMINO ACIDS FORMULA IN INFANTS WITH COW’S MILK ALLERGY AND INTOLERANT TO EXTENSIVELY HYDROLYSED FORMULAS

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2 Department of Pediatrics, Saint Vincent de Paul Hospital, Lille, France.
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4 Gastroenterology, Hepatology and Nutrition Unit, University and Pediatric Hospital of Lyon, Lyon, France.
5 Pulmonology and Allergology Department, Regional University Hospital, Strasbourg, France.
6 Allergologist, Illkirch-Craffenstaden, France.
7 Pediatrician allergologist, Forbach, France.
8 Allergology Department, Queen Fabiola Children’s University Hospital, Brussels, Belgium.

Objectives and Study: Amino acids formulas (AAF) are recommended for children with cow’s milk protein allergy (CMPA) failing to respond to extensively hydrolysed formulas (eHFs). This study compared a thickened AAF (TAAF; Novalac®, United Pharmaceuticals, Paris), containing a pectin-based thickener, to a reference AAF (RAAF; Neocate®, Nutricia, Germany) on allergy symptoms and their impact on family life. Safety was assessed through growth and blood biochemistry analysis.

Methods: Infants aged <18 months with CMPA symptoms failing to respond to eHFs were randomised in a double-blind manner to receive TAAF or RAAF for 3 months. All infants were then fed TAAF for 3 additional months. Paediatricians assessed symptoms at 1, 3 and 6 months. Blood samples were collected at inclusion and 3 months.

Results: Results at 1 month, previously described, showed tolerance to both formulas by all of the 75 infants with proven CMPA and eHF intolerance. Tolerance to both formulas persisted for 3 months. For the last 3 months, all infants were fed and tolerated TAAF, including infants who switched from RAAF to TAAF. At 3 months, the dominant allergic symptom had disappeared in 76.2% of infants with TAAF and 51.5% with RAAF (p=0.03). SCORAD improved more with TAAF than with RAAF (-27.3 ±2.3 vs -20.8 ±2.2, p=0.05). 92.9% of infants had normal stools (soft/formed consistency) with TAAF vs 75.8% with RAAF (p=0.05). Daily sleeping time increased in the TAAF group (p=0.01). More infants in TAAF group had better quality of nighttime sleep (p=0.04) and low frequency of irritability signs (p<0.01). Growth parameters did not differ between groups. No difference in essential amino acid plasma concentrations was noted between groups, except higher valine in RAAF group (p=0.05), but not clinically significant. With both formulas, plasma eosinophils decreased by 3 months (p<0.05); all biochemical parameters were within normal ranges.

Conclusion: Both formulas were tolerated by all infants with CMPA and intolerance to eHFs, the TAAF improving more daily family life. Anthropometric and clinical data showed that both formulas were safe.
Disclosure of Interest: C. Dupont Conflict with: Coordinator fees, N. Kalach: None Declared, P. Soulaines: None Declared, E. Bradatan: None Declared, A. Lachaux: None Declared, F. Payot: None Declared, F. de Blay: None Declared, L. Guénard-Bilbault: None Declared, R. Hatahet: None Declared, S. Mulier: None Declared
Differences in triglyceride load and number of chylomicrons in breast- or formula-fed infants

Inga C. Teller 1,* Stefanie Schoen 1 Bert MJ van de Heijning 1 Eline M van der Beek 2 Pieter JJ Sauer 3
1 Danone Nutricia Research, Utrecht, Netherlands, 2 Danone Nutricia Research, Singapore, Singapore, 3 UMCG, Groningen, Netherlands

Objectives and Study: Milk fat globules in human milk (HM) are large complex structures with multilayered membranes and embedded functional proteins that surround the triglyceride (TG) core, whereas the smaller lipid droplets in infant milk formula (IF) have no membrane but mostly proteins adhering to the lipid-water interface. During breastfeeding, fat globules are increasingly released over time with higher lipid content in hindmilk versus foremilk, whereas IF lipids are provided constantly. We hypothesised that these differences in lipid delivery may affect lipid handling in early life.

Methods: In this exploratory observational single-centre pilot study, two blood samples were collected from eight week old healthy term infants, either exclusively breast (BF-group) or formula fed (FF group) by parent’s choice: One before, the other 30, 60, 90, 120, 180, or 240 min after the 2nd morning feeding after 06:00. Ethical approval was obtained from the hospital Independent Review Board.

Results: Feeding frequency per day was lower in FF compared to BF resulting in a 30 min longer intermeal interval. Subjects consumed similar amounts, established by test weighing and bottle weights. Despite the longer feeding interval in FF, pre-feeding TG concentrations were similar in both groups. ApoB48 concentrations (indicative for chylomicron number) were higher in FF compared to BF resulting in lower TG:ApoB48 ratios (proxy for chylomicron load/ Figure)). Post-feeding TG:ApoB48 ratios in BF were numerically consistently but not significantly higher than FF; a meal response was not detected for the ratio.

Conclusion: These observational data indicate that although similar TG concentrations are present prior to the 2nd morning meal in normally fed healthy infants, lipid metabolism may differ: FF subjects seem to have a higher number of chylomicrons carrying plasma lipids consistently whereas BF chylomicrons contain a higher TG load per carrier. This observation is not influenced by meal intake or intermeal interval, shown by the consistent increased post-meal concentrations, especially those
closer to the next feeding at the end of the observational period. Taken together, these findings suggest consistent effects of feeding mode and complex lipid matrix of HM on infant lipid metabolism that may be related to the long-term benefits of breastfeeding.

**Disclosure of Interest:** I. Teller Conflict with: CTMM/ PREDICt consortium, Conflict with: Danone Nutricia Research, S. Schoen Conflict with: Danone Nutricia Research, B. M. van de Heijning Conflict with: Danone Nutricia Research, E. M. van der Beek Conflict with: Danone Nutricia Research, P. J. Sauer: None Declared
BOVINE COLOSTRUM REDUCES DOXORUBICIN-INDUCED INTESTINAL TOXICITY IN PIGLETS RELATIVE TO FORMULA

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Objectives and Study: Chemotherapy-induced gastrointestinal (GI) toxicity is a common adverse effect of cancer treatment. Using piglets as models for infants, we hypothesized that the immunomodulatory and gastrointestinal tropic effects of bovine colostrum would reduce the severity of GI complications after doxorubicin treatment.

Methods: Thirty-two 5-day-old piglets were given an intravenous infusion of doxorubicin (DOX, 1 x 100 mg/m², n=18) or an equivalent infusion of saline (SAL, n=14) and subjected to formula feeding (DOX-Form, n=9, SAL-Form, n=7) or feeding with bovine colostrum (DOX-Colos, n=9, SAL-Colos, n=7). Pigs were euthanized five days after initiation of chemotherapy to assess markers of intestinal function and inflammation.

Results: DOX-treated animals developed diarrhea, growth deficits, and had reduced intestine, colon and spleen weights (all P<0.05). DOX-Colos pigs had higher lactose digestion and absorption capacity than DOX-Form (37 vs. 8 uM plasma galactose after lactose bolus, P<0.01), corresponding with longer intestinal villi and higher activities of brush border enzymes (lactase, maltase, DPP-IV, all P<0.05). Intestinal permeability was reduced (0.03 vs. 0.30 for urinary lactulose/mannitol ratio, P<0.01) with reduced intestinal tissue IL-8 levels (33 vs. 76 ng/g, P < 0.05) and reduced levels of plasma C-reactive protein (CRP), relative to DOX-Form (118 vs. 170 mg/L, P<0.05).

Conclusion: A single dose of doxorubicin induces intestinal toxicity in suckling pigs. The toxic response is diet dependent with beneficial effects of bovine colostrum compared with a suboptimal formula. Systemic inflammatory responses may result partly from damage to intestinal structure and functions. It is important during chemotherapy to provide an enteral diet that adequately supports intestinal growth, function and defense mechanisms. Bovine colostrum may be considered as an interventional diet for infants and children subjected to chemotherapy.

Disclosure of Interest: None Declared
POLYUNSATURATED FATTY ACID STATUS IN OBESITY REVISITED: A SYSTEMATIC REVIEW AND META-ANALYSIS OF THE LITERATURE

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Objectives and Study: Long-chain polyunsaturated fatty acid (LCPUFA) status has been related to the pathogenesis of obesity. Our aims were to extend our previous report on 10 studies identified on the subject (Győrei et al, JPGN 52: E68, 2011), and to systematically review observational studies investigating LCPUFA status from different blood compartments in overweight or obese subjects and to assess the relationship between LCPUFA profile and obesity.

Methods: The Ovid MEDLINE, Scopus and Cochrane Library CENTRAL databases were searched from inception to January 2014 for observational studies in which LCPUFA status of overweight or obese subjects and normal weight controls were investigated.

Results: Data of 21 studies form 19 publications were analyzed. The meta-analysis showed significant alterations in the LCPUFA composition of total plasma, plasma phospholipid (PPL) and plasma cholesteryl ester. Dihomo-gamma-linolenic acid (DGLA) values were significantly higher in overweight or obese subjects compared to controls in all investigated biomarkers. In addition, DGLA/linoleic acid ratio (estimated Δ6 desaturase activity) in PPL was significantly elevated (mean difference (MD): 0.05; 95% confidence interval (CI): 0.02, 0.08; n = 280), while arachidonic acid/DGLA ratio (estimated Δ5 desaturase activity) was significantly decreased (MD: -0.55; 95% CI: -0.71, -0.39; n = 347) in overweight or obese subjects.

Conclusion: The results of the present meta-analysis confirm that LCPUFA profile is altered in obesity. The differences observed in the desaturase activities may be responsible for the disturbed LCPUFA metabolism.

Disclosure of Interest: None Declared
POST-PARTUM ANTIBIOTIC TREATMENT DISTURBS DEVELOPMENT OF THE INTESTINAL MICROBIOTA

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Objectives and Study: The acquisition and development of the infant gut microbiota can be influenced by numerous factors, of which early antibiotic treatment is an important one. However, studies on the effects of antibiotics on the development of the gut microbiota of term infants are limited. The aim of this study was to determine the impact of empiric antibiotic use in the first week of life on microbial acquisition and development.

Methods: Faecal samples of 45 vaginally term-born and exclusively breastfed infants, of which 21 received antibiotics in the first week of life (AbT) and 24 were healthy controls (CtR), were obtained at three time points: T1, one week; T2, one month; T3, three months. We used IS-pro, a high-throughput bacterial profiling technique that was optimized for the complex microbiota of the human intestinal tract. Differences in bacterial phylum abundance and diversity (Shannon index) of the resulting profiles were assessed by conventional statistics. Stability was calculated as cosine distances. Discriminative species were detected by LDA Effect Size.

Results: Infants were clustered into two subgroups, Bacteroidetes- or Firmicutes-dominant microbiota (subgroup B and F, respectively), regardless of treatment group. Abundance and diversity of Bacteroidetes were reduced at all time points in AbT infants of subgroup B. Bacteroidetes’ colonization was delayed in AbT infants of subgroup F. *Escherichia coli*, a marker for antibiotics effect, was more prevalent and more stable over time in controls. *Staphylococcus epidermidis* was more prevalent in controls at T1 and *Enterococcus faecium* was more prevalent in AbT infants at T2 and T3. AbT infants had a less stable microbial composition over time, reflected by increased cosine distances.

Conclusion: Postpartum antibiotic treatment disturbs the microbiota development in infants, mostly evident in Bacteroidetes species. The effects of antibiotics on the development of the infant gut microbiota are dependent on the initial predominant bacterial acquisition. As the long-term health implications of these effects are yet unknown, follow-up studies are warranted.

References:
Disclosure of Interest: None Declared
Gastroenterology
Inflammatory Bowel Disease
PL-G-0005

THALIDOMIDE EFFICACY AND SAFETY IN CHILDREN AND ADOLESCENTS WITH ULCERATIVE COLITIS REFRACTORY TO OTHER IMMUNOSUPPRESSIVES: PILOT RANDOMISED CLINICAL TRIAL

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Objectives and Study: Thalidomide has shown to be effective in refractory Crohn’s disease in children. This pilot study aimed at evaluating thalidomide’s efficacy and safety in refractory paediatric ulcerative colitis.

Methods: Double-blind, placebo-controlled, randomized clinical trial (clinicaltrials.gov Identifier: NCT00720538) on thalidomide 1.5-2.5 mg/kg per day in children with active ulcerative colitis despite multiple immunosuppressive treatments. In an open-label extension, non-responders to placebo received thalidomide for an additional 8 weeks; all responders were followed up for a minimum 52 weeks.

Results: Twenty-six children with refractory ulcerative colitis were randomized to thalidomide or placebo. Clinical remission at week 8 was achieved by significantly more children treated with thalidomide (10/12 [83.3%] vs 2/11 [18.8%]; risk ratio [RR], 4.5 [95%CI 1.2 to 16.4]; P = .005; number needed to treat [NNT] 1.5). Of the non-responders to placebo who were switched to thalidomide, 8/11 (72.7%) subsequently reached remission at week 8 (RR 4.0 [95%CI 1.1-14.7]; NNT = 2.45; P = .01). Clinical remission in the thalidomide group was maintained for a mean of 135.0 weeks (95% CI 32 to 238), compared with 8.0 weeks (95% CI, 2.4 to 13.6) in the placebo group (p<0.0001). Cumulative incidence of severe adverse events was 3.1 per 1000 patient-weeks. Peripheral neuropathy and amenorrhea were the most frequent adverse event.

Conclusion: In this pilot RCT on cases of ulcerative colitis refractory to immunosuppressive therapy thalidomide compared with placebo resulted in improved clinical remission at 8 weeks of treatment and in longer-term maintenance of remission.

References: ON THE BEHALF OF THE THALIDOMIDE STUDY GROUP: Giuseppe Magazzù, Salvatore Pellegrino, Maria Cristina Lucanto, Arrigo Barabino, Angela Calvi, Serena Arrigo, Paolo Lionetti, Monica Lorusso, Francesca Mangiantini, Massimo Fontana, Giovanna Zuin, Gabriella Palla, Giuseppe Maggiore, Maria Chiara Pellegrin, Massimo Maschio, Vincenzo Villanacci, Stefania Manenti, Giuliana Decorti, Sara De Iudicibus, Rossella Paparazzo, Marcella Montico

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and interpretation of the data; nor in the preparation, review, or approval of the manuscript, S. Martelossi: None Declared, M. Bramuzzo: None Declared, A. Ventura: None Declared
**Gastroenterology**

**Peptic Disease and Helicobacter Pylori**

PL-G-0006

**SEQUENTIAL VERSUS 10-DAY TRIPLE THERAPY TARGETED TO ANTIMICROBIAL SUSCEPTIBILITY FOR HELICOBACTER PYLORI ERADICATION IN CHILDREN**

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**Objectives and Study:** Background: The sequential regimen appeared to be more effective than a 7-day triple therapy in the eradication of *Helicobacter pylori* in children, but not better than the 10 or 14 days triple therapies, as it was shown in a recent meta-analysis. The bias in this review were the small number of children given the 10-day triple therapy and the absence of interpretation of factors known to increase the risk of failure such as antimicrobial resistance and adherence to therapy. Aim: to compare, in naïve infected children, the eradication rates with a sequential regimen and a 10-day tailored triple therapy, as well as factors that may affect the treatment outcome.

**Methods:** Prospective randomized controlled trial conducted between November 2010 and December 2013 in a tertiary hospital in Brussels, Belgium, included children aged 2 to 17 years with a positive *Helicobacter pylori* culture. Children infected with a strain susceptible to clarithromycin and to metronidazole were randomly assigned to receive either a sequential regimen or a 10-day triple therapy. Children infected with a strain resistant to clarithromycin or metronidazole received a 10-day triple regimen tailored to the antimicrobial susceptibility. The eradication rate was assessed by a negative 13C-Urea breath test performed at least 8 weeks after the end of the treatment.

**Results:** 177 children (85 girls/92 boys, median age 9.7 years) were enrolled in the study. 147 were infected with multisensitive, 11 with clarithromycin resistant and 19 with metronidazole resistant strains. The eradication rate was significantly higher in the sequential regimen arm compared to the triple therapy arm in the Intention-To-Treat (60/73, 82.2% - 70/104, 67.3% - OR 2.24, *p* = 0.037) and in the Full-Analysis-Set (60/68, 88.2% - 70/93, 75.2% - OR 2.46, *p* = 0.044) but not significantly higher in the Per-Protocol analysis (55/59, 93.2% - 60/80, 85% - OR 2.43, ns). In a multivariate analysis, a higher eradication rate was observed with the sequential regimen (OR 3.73, *p* = 0.036) and in children that adhere more strictly to the treatment (compliance >=90% vs <90% OR 23.6, *p* < 0.001).

**Conclusion:** The sequential therapy, when administered to naïve children infected with multisensitive strains is more effective than the 10-day tailored triple therapy and should be proposed as first-line treatment. When infected with a strain resistant to at least one antimicrobial agent, a tailored triple therapy can be proposed but the eradication rate remains below the target of 85% in per-protocol analysis (the same was observed for the sequential regimen in a previous study performed in the same center).
Disclosure of Interest: None Declared
DUODENAL BULB BIOPSIES IN COELIAC DISEASE: SPECIAL EMPHASIS ON MUCOSAL MORPHOMETRY AND INFLAMMATION

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Objectives and Study: Recent coeliac disease guidelines recommend including duodenal bulb specimens in the diagnostic evaluation. However, previous studies exploring the value of bulb in diagnostics have shown inconsistent results. Further, clinical experience suggest that bulb might be more difficult to interpret than distal duodenum due to inferior specimens and differences in the mucosal morphology. We addressed these issues in a prospective pediatric cohort with our validated histological methods.

Methods: 115 consecutive children with positive serum transglutaminase 2 (TG2) and/or endomysial antibodies were evaluated in clinical centers in Finland and Romania. Upon gastrointestinal endoscopy 6-8 biopsies were taken from anatomic duodenal bulb and distal duodenum irrespective of the macroscopic findings. Special attention was devoted to representative biopsies and correct orientation and cutting of the paraffin-embedded specimens. Quantitative villous height: crypt depth (VH:CrD) ratio was used for the morphometric measurements (normal ratio >2.0). Further, density of mucosal CD3+ and γδ+ intraepithelial lymphocytes (IEL) and presence of TG2 targeted IgA-deposits were evaluated in frozen mucosal samples.

Results: Altogether 103 (90%) out of the 115 children had diagnostic mucosal lesion in at least one biopsy site (median age 7 years, range 2.6 -17.6, 66% girls). Although several samples were taken, in 33% of the patients the bulb specimens were of inadequate quality for accurate morphometric measurements; altogether these were possible from both bulb and duodenum biopsies in only 61% of the patients. Three patients (4.7%) showed mucosal damage only in bulb specimens and 2 (3.2%) only in the distal duodenal specimens. There was no significant difference in the mean VH:CrD ratio between the bulb and duodenum (0.4 vs 0.6, p=0.500) but the crypts were deeper in bulb (p=0.020). Also, no differences were observed in the mean density of either CD3+IELs (76.3 vs 74.5 cells/mm, p=0.750) or γδ+ IELs (27.3 vs 25.7 cells/mm, p=0.485) between the bulb and duodenum. All coeliac disease patients showed TG2 targeted mucosal IgA deposits in both bulb and distal duodenum samples.

Conclusion: Our study confirmed that coeliac patients may have lesions only in the duodenal bulb. However, diagnosis based solely on bulb histology should be used with caution because the samples are often more difficult to interpret and may differ morphologically from the distal duodenum. Markers of mucosal inflammation and coeliac disease-specific IgA deposits are valuable in both biopsy sites.
Disclosure of Interest: None Declared
**Objectives and Study:** Infections in early life may disrupt the mucosal barrier function and the establishment of oral tolerance. Previous studies, primarily based on inpatient infectious data, have been inconclusive on the risk of celiac disease (CD) after infections in early life.

**Methods:** In the prospective Norwegian Mother and Child Cohort Study with children born between 1999 and 2009, CD were identified through reporting by parental questionnaires and by linkage to the Norwegian Patient Register. The ESPGHAN diagnostic criteria were required for diagnosis. We collected detailed questionnaire data on infectious diseases when the child was 6 and 18 months old. Complete 6-month-questionnaire data were available in 89,588 children, and out of these 679 had developed CD by end of follow-up (December 31st, 2013). Infectious data assessed at 18 months were available in 73,471 children (out of which 583 developed CD). At time of analysis the median age of the cohort was 8.5 years. We used logistic regression to estimate odds ratios (ORs) for CD according to earlier infections with adjustment for children's age, sex and maternal CD.

**Results:** The mean number of infections before age 18 months was 8.8 in children with later CD as compared to 8.0 in reference individuals (P-value <0.001, T-test), corresponding to a significantly increased adjusted (a) OR of 1.03 per infectious episode (95% confidence interval [CI] = 1.02-1.04). The aOR for later CD per infectious episode in the first 6 months of life was 1.05 (95% CI=1.00-1.10; P-value=0.06). Children with gastroenteritis first 6 months of life (aOR=1.20; 95%CI 0.95-1.51) or from 6-18 months of life (aOR 0.97, 0.81-1.15) were not at a significantly increased risk of CD as compared with children with no gastroenteritis. Before age 6 months, lower respiratory tract infections (aOR=1.33; 95%CI=0.97-1.83) and recurrent (>2) upper respiratory tract infections (aOR=1.09; 95%CI=0.89-1.34) were not associated with later CD. From 6-18 months, both lower (aOR=1.39; 95%CI=1.10-1.75) and recurrent upper (aOR=1.37; 95%CI=1.13-1.65) respiratory tract infections were associated with later CD. Adjustments for previous use of antibiotics in the child as well as analyses restricted to CD diagnosed after age 2 years revealed largely unchanged risk estimates (data not show).

**Conclusion:** Overall number of infectious episodes as well as respiratory tract infections between age 6 and 18 months were associated with a modestly increased risk for later CD.

**Disclosure of Interest:** None Declared
CHARACTERISATION OF INTRACELLULAR TRAFFICKING PATHWAYS IN MICROVILLUS INCLUSION DISEASE

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

Methods: The above mentioned Rab GTPases were knocked-down and MyosinVb was depleted using Zinc Finger Nucleases in polarized CaCo2 cells, an enterocyte model, to analyze their role in the establishment of epithelial polarity, such as the formation of a distinct apical membrane and formation as well as maintenance of brush border microvilli.

Results: Co-immunoprecipitations followed by Western blotting revealed, that all Rab GTPases of interest as well as MyosinVb co-immunoprecipitated Syntaxin3, a t-SNARE protein, which localises at the apical plasma membrane in epithelial cells. Loss of Syntaxin3 was recently shown to cause a variant form of MVID in patients negative for mutations in MYO5B [3], adding additional relevance to this discovery. Furthermore, the interaction of the v-SNARE Slp4a with Syntaxin3 is lost upon deletion of MyosinVb. This is also reflected by a sub-apically retained hemagglutinin-reporter.

Conclusion: Together, these findings outline the necessity of MyosinVb for correct apical exocytosis and shed new light on the pathophysiology of MVID.

Disclosure of Interest: None Declared
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IDENTIFICATION OF A HYPOMORPHIC LRBA MUTATION AS A CAUSE OF AN IBD-LIKE PHENOTYPE WITHOUT AFFECTING B-CELL HOMEOSTASIS

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Objectives and Study: Inflammatory bowel disease (IBD) is a heterogeneous disorder associated with an imbalance of gut microbiome and immune system. Early-onset IBD represents a distinct subgroup with more severe disease course and often insufficient response to treatment, suggesting that a considerable proportion of patients suffer from monogenic disorders heritable in a Mendelian fashion. This was best exemplified by the discovery of IL10 receptor deficiency which led to a very early-onset IBD unresponsive to standard therapy.

Methods: Here, we studied a patient born to consanguineous parents who suffered from severe intestinal manifestations since 6 months of age and later diagnosed as IBD. Eventually, she presented features of autoimmunity including thyroiditis validated by the presence of autoantibodies. Consanguineous pedigree allowed for SNP-array based homozygosity mapping combined with exome sequencing to identify the underlying genetic defect. Predictions of protein structure were calculated using I-TASSER online algorithm. Immunoblot was performed to assess protein expression. B-cell subpopulations were analyzed with flow cytometry.

Results: We identified a homozygous missense mutation (p.Ile2812Pro) in lipopolysaccharide-responsive and beige-like anchor (LRBA) affecting the C-terminal WD40 domain of the protein, with perfect segregation assuming an autosomal-recessive mode of inheritance. Mutant protein was expressed at a similar level to a healthy control, in contrast to all previously published LRBA-deficient patients presenting with common variable immunodeficiency (CVID) in which identified mutations have led to non-detectable protein. Neither immunophenotype nor clinical presentation of the index patient confirmed a diagnosis of CVID. However, the patient presented with elevated numbers of CD21 low B cells associated with autoimmunity, which were not observed in any of the previously published LRBA-deficient patients.

Conclusion: In sum, we here for the first time identify a (hypomorphic) missense mutation in LRBA as a novel genetic etiology of early-onset IBD (-like) disease presenting with an absence of typical signs of immunodeficiency. Genetic analysis of LRBA in patients with early-onset IBD should thus be performed in particular if the phenotype of affected individuals extends to autoimmunity.
Disclosure of Interest: None Declared
CLINICAL CONSEQUENCES OF EPCAM MUTATIONS IN CONGENITAL TUFTING ENTEROPATHY

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Objectives and Study: Congenital Tufting Enteropathy is a rare and severe congenital enteropathy recently associated with mutation of EPCAM gene in its non syndromic form. We previously described a genotype-phenotype correlation and were next interested in understanding the pathophysiology of the disease and how the cellular abnormalities could explain the presented symptoms.

Methods: We analyzed intestinal biopsies of patients (n=15) and cellular models of patient’s mutated in EPCAM and compared it 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 have been conducted following a lentiviral shRNA strategy on Caco2 cells, and knockdown clones have been analyzed.

Results: The loss of strong cell-cell contact as well as the large intercellular spaces could well explain, at least partially, the continuous hydroelectolytic diarrhea present in CTE, that persists at fasting. Nevertheless, the abnormal filling of these intercellular spaces with proteic materials such as ZO1, crb3, villin, ezrin, could prevent infectious agents from passing through, thus explaining why no increased inflammatory cells are described in the CTE chorion, and why infections via this defective intestinal tract are not more frequent in this population than in other diseases. A second important anomaly is the intestinal insufficiency in CTE, that leads to parenteral nutrition dependency. We suggest in this study how the unstructured apical domain impairs the absorbing capacity of CTE enterocytes. We show here how different hydrolases are or not misplaced and discuss how these observations could impact on the choice of pertinent feeds for these children. We also report a severe lipid metabolism anomalies in EPCAM mutated enterocytes. Moreover, the expected deficience in electrolytic pumps usually situated at the brush border may not only account for the defect in electrolytes absorption, or for the coupled Amino-acid/Na+ absorption, but also in the intestinal osmolality regulation involved in the diarrhea.

Conclusion: The description of such a deep misorganization of the CTE enterocytes reported in our study shows the multiple key roles played by EPCAM. Moreover, as the maintenance of the enteral route could be associated to a better evolution in these children, our study could help adapting the enteral and parenteral feeding of these children.

Disclosure of Interest: None Declared
Objectives and Study: Crohn’s disease and ulcerative colitis, collectively known as inflammatory bowel disease (IBD), are chronic bowel disorders characterised by recurrent relapses alternating with periods of remission. Traditionally, children with IBD are asked to attend regular face-to-face hospital appointments for their routine out-patient follow up. This means that, even when they are well, they have to travel to the hospital and this may involve travelling long distances. We tested the hypothesis that telephone consultation is an effective and safe alternative to face-to-face consultation for children and adolescents with IBD.

Methods: Patients with IBD (aged 8-16 years) were randomly assigned via a computer-generated randomisation schedule to receive telephone consultation or face-to-face consultation for 24 months. The primary outcome measure was the paediatric IBD-specific IMPACT quality of life (QOL) scores. Secondary outcome measures included patient satisfaction with consultations, disease course, anthropometric measures, proportion of consultations attended, and duration of consultations. Analysis was by intention to treat.

Results: 86 patients were randomised to receive either telephone consultation (n=44) or face-to-face consultation (n=42). Baseline characteristics of the two groups were well balanced. 86% and 83% of patients completed follow-up in the telephone and face-to-face consultation groups respectively. After 12 months, there was no clinically relevant difference in QOL scores (estimated treatment effect in favour of the telephone consultation group was 5.7, 95% confidence interval -2.9 to 14.3; P=0.188). No differences were seen in secondary outcomes between the groups, except that there was a statistically significantly lower mean consultation time for telephone consultation compared to face-to-face consultation (estimated reduction 4.3 minutes, 95% confidence interval 2.8 to 5.7; P<0.001).

Conclusion: Telephone consultation reduced consultation time and did not have any negative impact on outcomes. Telephone consultation can be an effective and safe alternative to face-to-face consultation for the routine out-patient follow up of children and adolescents with IBD.

Disclosure of Interest: None Declared
**Hepatology**

ADENO-ASSOCIATED VIRUS VECTOR-MEDIATED LIVER GENE THERAPY FOR CRIGLER-NAJJAR SYNDROME

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**Objectives and Study:** Crigler-Najjar syndrome (CN) is an autosomal recessive rare disorder caused by mutations in the UDP-glucuronosyltransferase 1 isotype A1 (UGT1A1) gene. In severe CN, lack or reduced activity of UGT1A1 results in high levels of serum unconjugated bilirubin (UCB), which can lead to brain damage and death. Treatment of CN consists of phototherapy for 10-12 hours per day, which presents several limitations and has a major impact on the quality of life of patients. Liver transplantation is the only curative option for CN. The limited therapeutic options available prompted us to develop a new therapy for CN based on the transfer of a corrected copy of the UGT1A1 gene to hepatocytes.

**Methods:** Adeno-associated virus (AAV) vectors are the most attractive vectors for in vivo gene transfer. Clinical trial results demonstrate long-term correction of inherited diseases with AAV vectors, particularly for liver-directed gene therapy.

An AAV vector optimized for the liver expression of the UGT1A1 transgene was developed (AAV-UGT1A1). Safety and efficacy of correction of CN with AAV-UGT1A1 were assessed in mouse and rat models of CN.

**Results:** We demonstrated that a single intravenous administration of AAV-UGT1A1 resulted in efficient targeting of the liver and was sufficient for the long-term correction of CN in affected rats and mice, resulting in UCB levels undistinguishable from wild-type animals. Correction of CN was documented for at least 6 months post-gene transfer (observation ongoing) with no need for immunosuppression or additional interventions.

**Conclusion:** Long-term correction of the pathological accumulation of UCB in animal models of CN can be achieved at AAV-UGT1A1 vector doses similar to those safely tested in previous human gene therapy trials. Based on these encouraging results, efforts towards a multicenter clinical trial for AAV-UGT1A1 vector-mediated gene transfer to the liver in severe CN patients have been initiated. Orphan Drug Designation was obtained, and vector manufacturing in GMP and mandatory GLP toxicity studies are ongoing. Screening of CN patients to identify subjects potentially eligible for enrollment in the proposed trial has started in four European countries.
Disclosure of Interest: None Declared
IMPACT OF SEBELIPASE ALFA ON SURVIVAL AND LIVER FUNCTION IN INFANTS WITH RAPIDLY PROGRESSIVE LYSOSOMAL ACID LIPASE DEFICIENCY

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Objectives and Study: Lysosomal Acid Lipase Deficiency (LAL D) in infants, historically known as Wolman Disease, is a medical emergency with rapid disease progression and death occurring within the first 6 months (mo) of life. In a natural history study, failure to thrive, liver complications, massive hepatomegaly, and mortality were confirmed in LAL D infants. Disease progression was frequently accompanied by rapidly progressive liver failure. In addition to steatosis and foamy histiocytes, fibrosis was prominent and seen in 4 infants before 6 mo of age and in 1 infant as early as 1.5 mo of age. In infants with evidence of growth failure who did not undergo transplant, the K-M estimate (95% CI) of survival past 1 year of age was 0 (0, 0). Those treated with HSCT or liver transplant survived slightly longer but still died before 1 year of age (median age 8.6 mo).

Methods: A phase 2/3 trial (LAL-CL03) assesses the safety and efficacy of sebelipase alfa (SA) in 9 LAL deficient infants with growth failure in the first 6 mo of life. Median baseline liver function tests reveal significant underlying liver dysfunction with a median ALT and AST of 145 IU/L and 125 IU/L respectively. At symptom onset, subjects had diarrhea/vomiting (n=6), hepatomegaly (n=9), splenomegaly (n=8), or adrenal calcification (n=6).

Results: As of November 1, 2014, 6 subjects have met the primary endpoint of survival at 12 mo of age with a mean age of 22 mo and 5 continue to receive SA. Deaths (n=4) were unrelated to SA and were deemed to be either related to underlying disease or, in 1 subject, due to complications of an abdominal paracentesis. 3 subjects died after receiving ≤4 doses. In addition to improved survival relative to the historical cohort, all subjects demonstrated improved weight gain, improvement of GI symptoms, and reductions in hepatosplenomegaly. Rapid improvements in biochemical and hematological markers including ALT, AST, hemoglobin, and bilirubin were observed. One SA-related SAE occurred: an infusion reaction of malaise with tachycardia and fever. The majority of the infusion associated reactions were reported as fever, diarrhea, or vomiting. To date, 4 subjects tested positive to anti-SA antibodies and all 4 continue weekly infusions of SA.

Conclusion: Analysis suggests that SA rapidly improves weight gain and many of the disease activity parameters observed in infants with LAL D. These improvements appear to be accompanied by a substantial survival benefit compared to a matched historical control group.
**Objectives and Study:** Pancreatic fat has been identified as a novel obesity-related fat depot, which may contribute to the development of β-cell dysfunction. The aims of the current study were to compare pancreatic fat fraction (PFF) in overweight/obese Caucasian children with and without NAFLD, and to assess the interrelations among pancreatic fat and liver fat, abdominal visceral (VAT), as well as insulin sensitivity and β-cell function.

**Methods:** We performed magnetic resonance imaging (MRI) for measurement of hepatic fat fraction (HFF), PFF and VAT, along with insulin sensitivity in 140 obese children, 70 with (HFF ≥ 5%) and 70 without NAFLD. Whole-body insulin sensitivity index (WBISI), insulinogenic index (IGI), and disposition index (DI) were obtained from oral glucose tolerance test. Prediabetes was diagnosed on the basis of fasting glucose of 100-125 mg/dL and/or 2-hour glucose of 140-199 mg/dL, and/or haemoglobin A1C 5.7-6.4%.

**Results:** Children with NAFLD had higher VAT, and PFF than those without NAFLD. After adjustment for age, gender and pubertal status, PFF was significantly associated with HFF (Standardized β, 0.215; P< 0.001), and VAT (0.2560; P< 0.001), but not with BMI-SDS (0.152; P= 0.061). In multiple linear regression analyses with WBISI or DI as the dependent variable, against the covariates of age, gender, pubertal status, BMI-SDS, VAT, PFF, and HFF, we found that HFF and VAT were significantly associated with WBISI (β, -0.270; P< 0.001 and -0.215; P< 0.05, respectively). DI was associated only with HFF (-0.199; P= 0.049). We identified 15 children (13 with NAFLD and 2 without NAFLD) as being prediabetic. These children had a higher PFF, HFF, and VAT than those without prediabetes. To gain understanding of the predictors of prediabetes, we employed multiple logistic regression using age, gender, pubertal status, BMI-SDS, VAT, PFF, and HFF as predictors. This analysis revealed that pancreatic fat and hepatic fat independently predicted prediabetes [OR, 1.54 (95% CI,1.11-2.08); P<0.001 and 1.06 (1.05-1.12); P<0.001, respectively].

**Conclusion:** Overweight/obese children with NAFLD have higher pancreatic fat accumulation than obese children without NAFLD. Moreover, ectopic fat in pancreatic and hepatic depots are associated with diabetes risk.

**Disclosure of Interest:** None Declared
CHOLINE ALLEVIATES PARENTERAL NUTRITION-ASSOCIATED LIVER DISEASE IN INFANT RATS

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Objectives and Study: Choline deficiency is associated with parenteral nutrition–associated liver disease (PNALD). However, the molecular mechanisms remain unknown. This study was aimed to investigate the role of choline in alleviating PNALD in infant rats on parenteral nutrition (PN).

Methods: SD male rats (aged 3 weeks) were randomly assigned to 3 groups: PN, PN with intravenous choline (1.2 g/kg) and controls (0.9% saline). Rats underwent jugular cannulation for infusion of PN solution or 0.9% saline for 7 days. Liver pathology, hepatic biochemical indicators, oxidative stress status and antioxidant capacity were assayed. The methylation status of peroxisome proliferator activated receptors (PPARα) gene promoter, the mRNA and protein expression levels of PPARα and its target gene carnitine palmitoyltransferase-I (CPT-I) were also evaluated. Data were analyzed using the Student’s t test or ANOVA test and bivariate correlations analysis.

Results: PN induced cholestasis and steatosis at early stage histologically, whereas choline supplement attenuated the elevated serum alanine aminotransferase, aspartate aminotransferase, direct bilirubin, total bilirubin and triglyceride by 70%, 33%, 40%, 58% and 52% respectively, compared with PN feeding alone (all p<0.05). The enhanced reactive oxygen species and malonaldehyde elicited by PN were also relieved by 40% and 36% respectively with 1.5-fold increased superoxide dismutase activity and 1.2-fold enhanced glutathione peroxidase activity under co-treatment of choline and PN (all p<0.05). Moreover, choline reduced hypermethylation of PPARα promoter by 39% and up-regulated mRNA and protein expression of PPARα by 2.8-fold and 2.6-fold respectively with its downstream target CPT-I mRNA expression increased by 1.9-fold and its protein synthesis elevated by 1.8-fold, relative to PN feeding alone (all p<0.05).

Conclusion: Choline could alleviate PN-induced disordered metabolism, excessive lipid peroxidation and oxidative stress in liver, which is partially related to lower PPARα gene promoter methylation, higher PPARα and CPT-I expression and higher antioxidative activities.

Disclosure of Interest: None Declared
ACUTE LIVER FAILURE AND SEVERE APLASTIC ANEMIA IN CHILDREN
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Objectives and Study: Children with acute liver failure (ALF) are at high risk for developing life-threatening bone marrow failure (BMF). We aimed to compare the outcome of children with severe aplastic anemia (SAA) with and without liver failure.

Methods: All children who presented with ALF (INR > 2, Bilirubin > 150 µmol/l) and BMF (according to the Definition of the European SAA working group) seen in our centre between 1986 and 2013 were analyzed. As a comparison group we collected data of patients with isolated severe aplastic anemia of unknown etiology.

Results: Over the 27-year observation period a total of 15 children (8m, median age 8.07 years (range 1.42-16.22)) developed BMF and ALF, of these n=11 were listed for liver transplantation. Of a total of n=550 children underwent liver transplantation (LTx) 63 children were transplanted for ALF. Of these ALF was idiopathic in n=40 children. Ten of these 40 children (25%) developed BMF. In addition 4 patients had an ALF of unknown origin and severe aplastic anemia but recovered without LTx. One patient with ALF and BMF died on the liver transplant waiting list. No case of BMF was identified in patients liver transplanted for ALF, secondary to other specific causes. First symptoms of bone marrow disease occurred 0-22 days (median 7) after the diagnosis of liver disease. All patients were treated with immunosuppression (GPOH-SAA 94 or EWOG-SAA 2010 study protocol) and/or haematopoietic stem cell transplantation (HSCT). Overall 8 patients reached bone marrow remission, 4 required HSCT, 3 children died before hematological recovery. Bleeding and infections were the two most frequent causes of death. Thrombocytopenia and leucopenia as first signs of BMF occurred before LTx in all cases. During follow up (range 0.2-19.8 years, median 10) there were no hepatological or hematological relapse. All children with spontaneous liver remission survived. Controls were 54 SAA patients, treated in our hospital from 1984 – 2011; 15 patients of the total cohort (11 males; age 8.3, range 1.4-17.3 years) had isolated acquired aplastic anemia. None of these had significant hepatic involvement (elevated transaminases > 3x ULN or impaired liver function). Four of the children from the control group were treated with HSCT, the other 11 obtained an IST. None of the 15 patients died in a follow up time of 5.6 (range 2-14.9 years).

Conclusion: Full blood count to detect thrombocytopenia and/or leucocytopenia should be examined early and regularly in patients with idiopathic acute liver failure. Aggressive management of affected patients with LTx, IST and BMT may reduce the morbidity and mortality. Patients with isolated SAA have no increased risk of liver involvement.

Disclosure of Interest: None Declared
HEPATITIS B VIRUS-INDUCED HISTONE HYPOACETYLATION IN NON-TRANSFORMED MURINE HEPATOCYTES IS ASSOCIATED WITH UPREGULATED SIRTUIN ACTIVITY AND DECREASED CHROMATIN ACCESSIBILITY

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Objectives and Study: Virus-host interactions result in altered gene expression profiles in host cell nuclei enabling virus particle production, thus obligatorily involving changes in their epigenomes. Virus-induced epigenetic changes that contribute to genetic dysregulation and subsequent development of secondary diseases such as hepatocellular carcinoma (HCC) have not yet been understood.

We investigated the influence of the hepatitis B virus (HBV) on post-translational histone acetylation patterns in the promoter region of key genes for the development of HCC.

Methods: We analyzed gene expression of 84 key genes for HCC oncogenesis in a HBV-negative (MMH-D3) and a HBV-positive (HBV-Met) immortalized, non-transformed murine hepatocyte cell line using qPCR. Chromatin immunoprecipitation was carried out to assess histone acetylation levels before and after anti-viral treatment with lamivudine and HBV knockdown experiments using ectopic expression of antiviral siRNA. HAT, HDAC and sirtuin activity was measured using ELISA and luminiscence reporter assays, respectively. Chromatin accessibility was analyzed with a micrococcus nuclease digestion assay.

Results: HBV-positive murine hepatocytes showed selective gene deregulation when compared to HBV-negative hepatocytes. HBV-positive cells revealed a global hypoacetylation state at all analyzed loci which was reversible by nucleoside and siRNA anti-viral therapy. While there was no difference in histone acetyltransferase activity, histonedeacetylase (class III HDACs/sirtuins) were significantly more active in HBV-Met. Chromatin purified from MMH-D3 cells was better accessible for MNase when compared to HBV-Met chromatin.

Conclusion: Reversible hypoacetylation of histones in liver cell nuclei accompanies pre-cancer transregulatory gene expression induced by HBV. These changes are possibly driven by upregulation of class III HDACs/sirtuins and subsequent decreased chromatin accessibility.

Disclosure of Interest: None Declared
PRE-EMPTIVE STRATEGY IS AS VALUABLE AND MORE COST-EFFECTIVE THAN PROPHYLAXIS FOR CMV DISEASE IN PAEDIATRIC LIVER TRANSPLANT RECIPIENTS

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Objectives and Study: Strategies to prevent Cytomegalovirus (CMV) disease in liver transplantation (LT) are still matter of debate. Most paediatric liver transplantation centres currently administer long courses of CMV prophylaxis (P) to susceptible subjects, that bear the disadvantages of significant antiviral drug exposure and costs. Our aim is to assess the long-term efficacy and cost-effectiveness of the anti-CMV test/pre-emptive (T/PE) strategy in children who underwent LT at our Centre in the last 4 years in comparison with the historical cohort that received P+T/PE protocol.

Methods: Clinical records of all consecutive children (0-18 years) who underwent LT between 2011 and October 2014 were reviewed and compared with a historical group who received P+T/PE with 30 days gancyclovir (years 2003-2006). Patients with <200 days of follow up, retransplantation, oncologic diseases and HIV were excluded. The outcomes considered were CMV infection and disease, antiviral exposure, adverse effects and costs. Pre-emptive (gancyclovir 10 mg/kg/day or valgancyclovir 30 mg/kg/day) therapy was started at a threshold of >100,000 CMV-DNA copies/ml and maintained for at least 15 days and until CMV-DNA resulted negative twice consecutively.

Results: 58 children (28/30 F/M, age at LT 0.25-17 years) were considered for analysis, 49 in the T/PE and 9 in the P+T/PE group, respectively. The two groups did not differ in age at LT, donor age and risk status. The incidence of CMV infection (T/PE 69.4% vs P+T/PE 77.8%, p=1) and CMV disease (T/PE 6.1% vs P+T/PE 11.1%, p=0.5) did not differ in the two groups. CMV infection in the T/PE group occurred at 47.5±46 days post-OLT vs 74.5±33 in the P+T/PE (p=0.09), and required pre-emptive therapy in 12.2% and 33.3% of cases in the T/PE and in the P+T/PE group, respectively (p=0.13). The incidence of acute graft rejection, EBV infection and sepsis were not different in the two groups. Instead, children managed with the T/PE strategy had a significantly shorter exposure to antiviral drugs than P+T/PE group (6.6±15 vs 42.9±18 days, p<0.0001), whereas the calculated CMV-related costs were lower in patients managed without prophylaxis (7,311±10,930 vs 1,586±5,459 € per patient, p=0.019).

Conclusion: Our study shows that virologic surveillance with adequate pre-emptive therapy is as safe and effective as prophylaxis-based regimen in preventing CMV disease and its complications in paediatric LT recipients. This strategy is also cost-effective and reduces the exposure of these children to nucleoside analogues.
Disclosure of Interest: None Declared
MATERNAL HIGH-PROTEIN DIET DURING GESTATION IMPAIRS RAT PUPS GLUCOSE TOLERANCE

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Objectives and Study: Early life environment, especially nutrition from beginning of gestation, has a programming effect on the offspring adult health (Gluckman et al., 2008). Suboptimal nutrition, like protein restriction during gestation, is known to be a risk factor for developing type 2 diabetes (Martin-Gronert et al., 2012). The aim of this study, performed in two independent experiments (exp), is to characterize maternal high-protein (HP) diet influence during gestation or lactation on rat pup after weaning.

Methods: In exp 1, Wistar rat dams received either HP diet (55% protein) or control (C) diet (20% protein) during gestation and/or lactation, forming 4 groups (C-C, C-HP, HP-C, HP-HP). In exp 2, three dam groups were constituted: C-C, C-HP, HP-C. After weaning, pups received C or HP diet, groups were composed of 16 and 8 rats in exp 1 and 2. Litters were sacrificed at postnatal day (PND) 42 in exp 1 and at PND70 in exp 2. Results were analyzed using a mixed model with the MIXED procedure of SAS.

Results: Whatever the dams’ diet, pups receiving HP compared to C diet after weaning gain less weight (p<0.0001 at PND 38 in exp 1 and 2 and p=0.0002 at PND65 in exp 2), eat less (p<0.0001 for both exp) and have less adipose tissue (p<0.0001 in absolute and relative weight for both exp) than rats receiving C diet. In addition, pups receiving HP diet after weaning have a higher fasted blood glucose (p<0.0001 at PND38 in exp 1 and at PND65 in exp 2) and a higher glycaemia during oral glucose tolerance test (OGTT, p=0.008 at PND65 in exp 2).

Maternal gestation HP compared to C diet reduces pup weight after weaning (PND38 exp1: p=0.079, exp2: p=0.0001, PND65 exp 2: p=0.06) and lower food intake from weaning to PND39 (p=0.04 and p=0.07 in exp 1 and 2). Maternal HP diet during gestation also increases fasted blood glucose in the pups at PND38 (p=0.046, exp 1) and enhances the effect of HP diet after weaning resulting in higher glycaemia during OGTT at PND65 (gestation diet*diet after weaning effect: p=0.01). Finally HP diet during gestation increases plasma insulin response in pups receiving C diet after weaning (gestation diet*diet after weaning effect: p=0.02 in exp 1).

Conclusion: Maternal HP diet during gestation leads to lower glucose tolerance in the offspring. HP diet after weaning induces weight and fat loss as described in adults, but also induces higher glycaemia and this effect was enhanced by maternal HP diet during gestation. These findings show that HP diet during gestation period can program the offspring metabolic health, impairing glucose tolerance.
Disclosure of Interest: C. Desclée De Maredsous Conflict with: Danone Nutricia Research, R. Oozeer Conflict with: Danone Nutricia Research, C. Delteil: None Declared, F. Blachier: None Declared, P. Barbillon: None Declared, T. Mary-Huard: None Declared, D. Tomé: None Declared, E. van der Beek Conflict with: Danone Nutricia Research, A.-M. Davila: None Declared
FISH OIL SUPPLEMENTATION OF HEALTHY TERM INFANTS DURING THE FIRST SIX MONTHS OF LIFE HAS NO EFFECT ON NEUROCOGNITIVE DEVELOPMENT AT SIX YEARS: A RANDOMISED CONTROL TRIAL

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Objectives and Study: There has been widespread promotion of fish oil supplements for enhancing intelligence and other elements of cognitive functioning. However there is little peer-reviewed, empirical information concerning the utility of these products in healthy term infant populations, particularly with respect to lasting effects into early childhood. We evaluated the impact of fish oil supplementation during early infancy by utilising a variety of sensitive neurocognitive tests which were motivated from the extant literature. Testing was conducted at a mean age of 6 years, 0 months (SD: 7 months).

Methods: This randomised control trial compared high dose post-natal omega-3 long-chain polyunsaturated fatty acid supplementation (containing >250 mg DHA and 60 mg EPA) vs. placebo daily; these treatments were administered from birth to 6 months. At the end of the supplementation period, the fish oil group had significantly higher concentrations of DHA within plasma phospholipids (P = 0.003) relative to those infants in the placebo group. Of the 420 neonates who were enrolled into the study, 80% of these participants were followed-up at 6 years of age using a battery of neurocognitive tests that were aimed at evaluating higher intellectual functioning in well-educated families of moderately high socio-economic status. The main areas of inquiry were: language and communication, higher-order executive functions including working memory and behavioural traits associated with anxiety and/or depression.

Results: Our results suggest that in healthy, full-term infants high dose fish oil supplementation provides no significant benefit at 6 years of age for any of the neurocognitive outcomes measured. However, fish oil treatment is associated with negative externalising- and oppositional/defiant behaviour (P = 0.035, P = 0.006), particularly in boys.

Conclusion: On the basis of these findings, infant fish oil supplementation is not recommended for the purposes of enhancing neurocognitive outcomes in early childhood. Furthermore, effect of fish oil supplementation on externalising and oppositional/defiant behaviours in childhood deserves more consideration. Overall, it may be concluded that in well educated, Western populations, there is no long-term neurocognitive or behavioural benefit to be gained from supplementation with fish oil during infancy. Therefore, our results do not support routine fish oil supplementation of healthy term infants.

Disclosure of Interest: None Declared
**Nutrition**

**Neonatal Nutrition**

PL-N-0039

**EFFECT OF IRON SUPPLEMENTATION IN INFANCY ON COGNITIVE DEVELOPMENT AND BEHAVIOURAL PROBLEMS AT 7 YEARS OF AGE IN MARGINALLY LBW CHILDREN – A RCT FOLLOW UP**

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**Objectives and Study:** Iron deficiency (ID) in infancy is associated with impaired cognitive and behavioural development in childhood. One important risk group is marginally LBW infants (MLBW, 2000-2500g). We recently showed that MLBW infants benefit from supplements with improved iron status at 6 months and reduced behavioural problems at 3 years of age (1,2). Based on those results, we hypothesized that ID can be an important contributing mechanism to impaired neuropsychological development previously observed in MLBW children. In the present paper, we analysed the long term effect on cognition and behaviour.

**Methods:** In a randomized, controlled trial, 285 healthy MLBW infants received 0, 1, or 2 mg/kg/day of iron supplements from six weeks to six months of age. Another 95 normal birth weight controls were included at 3 years of age. At 7 years of age, a subgroup of 62 controls and 174 MLBW children were assessed by a pediatric psychologist with Wechsler Intelligence Scale of Children (WISC-IV) and parents of 64 controls and 191 MLBW filled in the validated behavioral questionnaire Child Behavioral Checklist (CBCL).

**Results:** In analyses controlled for maternal age and education, MLBW children showed significantly lower scores compared to controls in verbal comprehension (104.3 [10.3] vs. 107.7 [9.4], p=0.017), but not in perceptual reasoning (p=0.202), working memory (p=0.356), processing speed (p=0.976) or full scale IQ (100.4 [11.3] vs. 102.9 [9.6], p=0.123). There were no significant differences between the iron groups in the five scales respectively (p=0.599, p=0.365, p=0.965, p=0.385, and p=0.418). The prevalence of behavioural problems (above CBCL cut-off for clinical problems) was 3.1% in controls and 5.8% in MLBW children (p=0.527). However, the latter prevalence was 10.4% in the placebo group, 1.8% in the 1 mg-group, and 4.5% in the 2 mg group, p=0.114. The RR (95% CI) for a pathological score in un-supplemented cases was 3.2 (0.98-10.7), p=0.053 compared to those supplemented.

**Conclusion:** MLBW children have lower verbal scores in school age compared to children born at term with normal weight. These cognitive scores are not affected by early iron supplements. We observed a non-significant trend of increased behavioural problems in non-supplemented MLBW children, a trend that together with the previously observed significant differences at 3 years of age suggests that iron supplementation of these infants may be beneficial.
References:

Disclosure of Interest: None Declared
BRANCHED CHAIN FATTY ACIDS OF HUMAN MILK: INFLUENCED BY MATERNAL DIET?
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Objectives and Study: Human milk (HM) fatty acid (FA) composition differs between mothers. The FA of HM include branched chain fatty acids (BCFA). HM BCFA may be influenced by maternal consumption of ruminant products, but data are lacking. We tested the hypotheses that the BCFA concentrations of HM differ among populations, are influenced by maternal diet, and in turn influence the infant gut microbiome.

Methods: We examined BCFA concentrations in HM from three urban populations with differing diets: Cincinnati, Ohio; Shanghai, China; and Mexico City, Mexico. Sample collection was standardized as part of the GEHM study. Enrollment was limited to healthy mothers of term, singleton infants. FA were extracted from milk using Bligh-Dyer technique and analyzed by gas chromatography. Dietary analysis included three 24 hour dietary recalls, limited to Cincinnati mothers. Statistical analysis was done using ANOVA. Samples from ~115 women were analyzed per site at postpartum week 4.

Results: Cincinnati, Shanghai and Mexican mothers, respectively, had mean age in years of 32, 29, and 25; prepregnancy BMIs of 28, 21, and 24; and parity of 2, 1, and 2. The BCFA iso14:0, iso16:0, iso18:0, iso20:0, anteiso15:0, anteiso17:0 all differed in concentration (p<0.0001) among the three cohorts. The most abundant BCFA was iso20:0; mean (± SD) concentrations (mol-wt%) were 0.28±0.06 Cincinnati, 0.19±0.06 Mexico City, and 0.11±0.04 Shanghai. Using linear regression models of BCFA, site differences persisted after controlling for delivery mode, maternal age and BMI. Dietary intake of dairy was associated with iso14:0, anteiso15:0 and iso16:0 but not the longer BCFA. Beef intake was not associated with any BCFA. Higher BCFA in milk was significantly associated with increased relative abundance of phylum Firmicutes, family Ruminococcaceae at 4 weeks postpartum in infant.

Conclusion: The BCFA concentration of HM differs across populations. Higher concentration of BCFA is associated with significant differences in the infant microbiota, increasing relative abundance of specific beneficial microbiota, the Ruminococcaceae and the Bifidobacteria. The health consequences of this variation requires further investigation.

**Nutrition**

**Neonatal Nutrition**

PL-N-0041

**ARACHIDONYL SPECIES OF PHOSPHOLIPID ARE AFFECTED BY FADS GENOTYPE AND DIETARY ARACHIDONIC ACID INTAKE ALTERING B CELL ACTIVATION MARKERS IN INFANTS**

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**Objectives and Study:** Whether all infants require a source of arachidonic acid (ARA) is controversial as conversion of 18:2n-6 to 20:4n-6 may occur in term neonates. Infants having FADS1 and FADS2 polymorphisms exhibiting reduced enzyme activity may require more dietary ARA to maintain plasma ARA levels. The study objective was to determine if ARA intake or FADS polymorphisms alter plasma ARA levels and immunoregulation in term infants fed infant formula.

**Methods:** Eighty-nine infants between 12 and 25 days were enrolled in this prospective, randomized double-blind controlled study. Infants consumed formula containing 0, 25 or 34mg ARA/100kcal. Each formula contained 17mg 22:6n-3 (DHA)/100kcal. After 10 weeks of formula consumption, blood was drawn for separation of plasma, red blood cells and lymphocytes. Fatty acid composition and fatty acid species of phospholipids were determined along with immune cell phenotypes. SNPs in FADS1 and FADS2 to characterize higher vs. lower Δ6 and Δ5 desaturase activity were identified.

**Results:** Plasma PE and PC species containing 16:0/20:4 and 18:0/20:4 increase in a dose-dependent manner. Consuming formula with supplemental ARA decreases plasma levels of 16:0/18:2 species and 18:0/18:2 in PC and PE. In minor allele carriers for FADS1 and FADS2, plasma ARA content is increased only at the highest level of ARA consumed. Expression of B cell activation markers and CD80 appears to be affected by diet intake of ARA or genotypes affecting ARA level.

**Conclusion:** The level of ARA in infant plasma is influenced by level of ARA consumed and the presence of minor alleles in FADS1 and FADS2. Dietary ARA may exert an immunoregulatory role on B cell activation by decreasing 16:0/18:2 and 18:0/18:2 phospholipid species.

**Disclosure of Interest:** J. Miklavcic: None Declared, B. Larsen: None Declared, V. Mazurak: None Declared, D. Scalabrin Conflict with: Mead John Nutrition, I. MacDonald: None Declared, G. Shoemaker: None Declared, L. Casey: None Declared, J. VanAerde: None Declared, T. Clandinin: None Declared
STUDY OF MORPHOLOGICAL AND FUNCTIONAL MYOCARDIAL ABNORMALITIES IN OBESE CHILDREN

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Objectives and Study: Obesity in childhood is associated with cardiac abnormalities (left ventricular hypertrophy (LVH), increased posterior wall thickness) and arterial changes (increased intima-media thickness and endothelial dysfunction). The factors causing impaired arterial function have been studied (importance of obesity, insulin resistance, inflammation) but those explaining the cardiac morphological abnormalities and their possible links with impaired arterial function remain to be determined. The aim of this study was to investigate the changes of echocardiographic parameters in obese children and to study the origin and possible links with impaired arterial function and metabolic cardiovascular risk factors.

Methods: Two hundred and seven severely obese children (BMI Zscore = 4.55 ± 0.07 SD), aged 5 to 17 years (mean 11.9 ± 0.17 years) were studied. Each patient underwent an echocardiography, a study of arterial function by high-resolution ultrasound, a Dual energy X-ray absorptiometry, an oral glucose tolerance test and a blood sample to assess lipid, ferritin and leptin concentrations.

Results: Thirteen percent of obese children had a high blood pressure and 22% had a dyslipidaemia. Mean HOMA-IR was 2.76 ± 0.2. Seventy-two patients (34.7%) had a left ventricular hypertrophy and 120 patients (58.0%) had a right ventricular dilation. The diastolic right ventricular diameter positively correlated with age ($r^2=0.19; p<0.0001$), obesity duration ($r^2=0.22; p<0.0001$), and pulse blood pressure ($r^2=0.39; p=0.0025$). The left ventricular mass did not correlate with any metabolic factors or blood pressure. In multivariate analysis, after adjustment for anthropometric and blood parameters, there was no correlation between myocardial and arterial changes.

Conclusion: Our study confirms the existence of myocardial morphological abnormalities in obese children. Those abnormalities are not due to metabolic cardiovascular risk factors or arterial changes. LVH may be a physiological adaptation to the increased hemodynamic load induced by obesity. Right ventricular dilation, rarely reported in previous studies, could be the consequence of an underlying sleep apnoea syndrome, which existence remains to be confirmed in further studies.

Disclosure of Interest: None Declared
Objectives and Study: To evaluate associations between currently available paediatric malnutrition screening tools (MSTs) and baseline body composition (BC) measurements and clinical outcomes (length of stay-LOS; nutrition status on discharge-NS) in children admitted to a tertiary referral hospital.

Methods: 128 children (mean age 10.7yr; 49.2% male; 54.7% surgical) admitted to Great Ormond Street Hospital (GOSH) under any specialty and expected stay >3 days were enrolled. 3 MSTs (Paediatric Yorkhill Malnutrition Score-PYMS; Screening Tool for the Assessment of Malnutrition in Paediatrics-STAMP; Screening Tool for Risk of Impaired Nutritional Status and Growth-STRONG) were implemented on admission. Weight (WT) and BC measurements (lean (LM) and fat mass (FM)) by dual Energy X-ray Absorptiometry) were obtained within 48 hours of admission and SD scores (SDS) calculated from UK BC reference data. WT and LOS were recorded on discharge.

Results: STAMP classified more patients as high risk (HR) compared to PYMS and STRONG. Most patients were identified as moderate risk (MR) by both STAMP and STRONG, and low risk (LR) by PYMS. STAMP and STRONG classified more surgical patients in HR and MR categories respectively. STAMP and STRONG showed the best agreement (60.9% agreement, 0.427 kappa), followed by STRONG and PYMS (48.4% agreement; 0.321 kappa) and STAMP and PYMS (46.1% agreement; 0.284 kappa). Children classified HR by STRONG had significantly lower WT, LM and FM SDS compared to LR and MR patients. The HR category in STAMP also had significantly lower LM SDS. MSTs did not correlate significantly with LOS and discharge NS (WT change), although there was a tendency for HR patients to stay longer than predicted.

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<th>% patients</th>
<th>Baseline BC *</th>
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<tr>
<td></td>
<td>LR</td>
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<tr>
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<tr>
<td>STAMP</td>
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<td>STRONG</td>
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*ANOVA p-value; mean SDS between HR, MR and LR groups.

Conclusion: STAMP and STRONG seem to show the best agreement, and identify HR patients with abnormal BC (especially low LM). GOSH patients are generally short and have multiple and chronic diagnoses, possibly explaining the proportion of patients classified as LR by PYMS, which used body mass index scores and does not consider underlying diagnosis. Although HR patients showed a
tendency for worse clinical outcomes, these were not significant, probably reflecting the limitations of these generic outcomes for this heterogeneous group. Thus, further research is needed in specific patient groups to establish the usefulness of each MST in different conditions.

References: ¹Wells JC et al. AJCN 2012;96:1316-26

Disclosure of Interest: None Declared
VITAMIN D INTAKE SHOULD BE INCREASED IN SWEDEN DURING WINTER, WHERE CHILDREN WITH DARKER SKIN NEED TWICE THE DOSE OF VITAMIN D COMPARED TO THOSE WITH FAIR SKIN

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Objectives and Study:
Children living in northern Europe with few hours of sunlight are at increased risk of vitamin D deficiency and are therefore more dependent on vitamin D from food and supplements. We hypothesized that children living in Sweden would benefit from vitamin D supplement during winter and that children with dark skin and those living at higher latitudes would have a greater need. The aim of this study was to evaluate the level of vitamin D supplement needed to ensure that 97.5% of five to seven-year-old children attain serum 25-hydroxy vitamin D [S-25 (OH) D] levels > 50 nmol/L, taking latitude and skin colour into account.

Methods: In a two-centre (Umeå, 63°N and Malmö, 55°N) longitudinal, double-blinded randomized, intervention study, 206 five to seven-year-old children with fair and dark skin were randomized, stratified by skin colour to a milk-based vitamin D₃ supplement³ providing 10 µg or 25µg vitamin D/day, or placebo during three months. At baseline and at follow-up dietary intake was assessed by a food frequency questionnaire (FFQ), blood samples taken and anthropometrics measured.

Results: Whereas dietary intake only covered around 60 % of the national recommended daily vitamin D intake of 10 µg, supplements resulted in a total mean intake (diet and supplement combined), daily vitamin D intake of 16 and 29 µg at follow-up in the intervention groups supplemented with 10 µg/day and 25 ug/day, respectively.

Serum-25(OH) D levels of ≥50 nmol/L was attained in 97% and 88% of children with fair and dark skin, respectively, when 10 µg/day of supplements was given during at least 60 days, whereas a supplement of 25 µg/day was needed to reach the same level for 95 % of children with dark skin. Skin colour, but not differences in latitude between northern and southern Sweden, influenced our results.

Conclusion: An daily supplement of 10 µg vitamin D seems to be needed in fair skinned children whereas an increased daily intake of >25 µg/ will be s needed in children with dark skin beyond the age of five years to reach S-25(OH) D levels ≥50 nmol/L in most children in Sweden during winter.

³Study products were a kind gift from Valio OY, Helsinki

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PAEDIATRIC GASTROESOPHAGEAL REFLUX DISEASE: ACIDIC AND NON-ACIDIC GASTRIC JUICE MODULATES BRONCHIAL EPITHELIAL IL-8 RESPONSE

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Objectives and Study: Acid suppression aims to prevent and treat complications of gastroesophageal reflux (GOR) disease. However, acid-suppressed gastric juice (GJ) was found to induce IL-8 production by primary bronchial epithelial cells (PBEC). We assessed to what extent IL-8 responses are modulated when bronchial epithelial cells are exposed to GJ collected from children without or with acute or long-term acid suppression treatment.

Methods: Gastric juice was collected from 16 pediatric long-term proton pump inhibitor users (LTPPI), 16 controls (C) and from 9 children admitted to the pediatric intensive care unit (PICU), before and 72h after starting proton pump inhibitors (PPI).

To assess the pro-inflammatory capacity of GJ, airway epithelial-like H292 cells and PBEC cultures were obtained by brush from paediatric patients without respiratory problems, and were exposed to GJ for 18h (serial dilutions 1/10-1/640). To assess whether GJ modulates pro-inflammatory responses, GJ was added to cells stimulated with TNF-α (5 ng/mL). Stimulation index (SI) is the fold-increase of IL-8 after TNF-α over that without TNF-α. IL-8 in cell culture supernatant was measured by ELISA and cytotoxicity by MTT (3-[4,5-dimethylthiazol-2-yl]-2,5 diphenyl tetrazolium bromide) analysis.

Results: Exposure of H292 cells and PBEC to GJ of LTPPI users and C induced similar high levels of IL-8. GJ was not cytotoxic for H292 cells at dilutions ≥1/80, but was cytotoxic for PBEC at dilutions ≤1/640. SI was reduced by GJ, but no differences were found comparing SI from LTPPI users and C. In PICU patients, GJ was not cytotoxic for H292 cells at dilutions ≥1/40. GJ of PICU-on therapy induced more IL-8 (>1/80 dilution, p <0.05) and reduced SI more (p=0.05 in 1/320 dilution) in H292 cells compared to PICU-before therapy. PICU GJ was cytotoxic to PBEC (dilution ≤ 1/640) limiting IL-8 production. Cytotoxicity was greater in PBEC exposed to GJ from PICU-on as compared to PPI-before (p=0.02). SI for PBEC culture was not more suppressed after PPI (p=0.12 at 1/640 dilution).

Conclusion: GJ of long-term PPI users and controls (<18yr) is equally pro-inflammatory and inhibits IL-8 response to TNF-α, which could lead to inadequate anti-bacterial responses in both groups. GJ from PICU patients on PPI therapy, however, induces more IL-8, is more cytotoxic and reduces SI even more compared to PICU before therapy. Acid suppression therapy in paediatric patients might not prevent extra esophageal GOR symptoms and potentially increases the risk of (secondary) respiratory infections, especially in PICU patients.

Disclosure of Interest: None Declared
GASTRO-ESOPHAGEAL REFLUX DISEASE IN CHILDREN AND ADOLESCENTS: CORRELATION BETWEEN SYMPTOM SEVERITY AND IMPEDANCE PARAMETERS

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Objectives and Study: Gastroesophageal reflux disease (GERD) is defined by the passage of gastric contents into the esophagus causing troublesome symptoms and/or complications. Over the last years, questions have been raised about the usefulness of new diagnostic questionnaires and their consistency with objective tools. The validated Pediatric GERD Symptoms & Quality of Life Questionnaire (PGSQ) is the first questionnaire developed for a wide range of age but it was never compared with objective parameters such as pH-impedance characteristics of reflux. The primary aim of the study was to investigate the relationship between the clinical picture severity and the main impedance reflux parameters in both children and adolescents investigated for GERD. The secondary aim was to compare the score obtained in patients with symptoms suggestive of GERD and healthy children.

Methods: Fifty-nine children, aged between 2-8 years (G1), and 39 children, aged between 8-17 years, (G2) were enrolled in the study for symptoms suggestive of GERD. All patients underwent multichannel intraluminal impedance (MII) monitoring and were asked to complete the PGSQ questionnaire, a symptomatic score was deduced for each patient (range 0-40). Moreover, an equal number of healthy children were enrolled from General Pediatrician and well-baby clinic and registered the questionnaire (C1: 2-8 years; C2: 8-17 years). A possible relationship between PGSQ scores and MII values was searched by statistical analysis.

Results: Based on the main MII/pH parameters (pHmetric parameters, impedance parameters, number and height of the reflux) we distinguished, in both the age groups (G1: mean age: 56.3 months; range: 24-96 months; 35 boys; G2: mean age: 127.9 months; range: 98-168 months; 29 boys) positive and negative patients. In G1 we found 28 patients (47.5%) positive to MII/pH, nevertheless, these patients had PGSQ score equal to those resulted negative (p=0.39). A similar result was found in the G2 in which 20 patients (51.3%), resulted positive to MII/pH with a PGSQ score superimposable to those resulted negatives (p= 0.09). Conversely, both groups (G1 and G2) and the related results (positive and negative) showed a PGSQ score significantly higher than the correspsective control group (p< 0.001).

Conclusion: The main finding of our study on children and adolescent with symptoms of GERD is the lack of correlation between the complained symptom severity and the main impedance reflux
parameters. However, the PGSQ seems to be useful in order to evaluate the presence of symptoms but not to discriminate between GER and GERD.

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EARLY DETECTION OF NECROTISING ENTEROCOLITIS BY FECAL GAS ANALYSIS AND ITS ASSOCIATION WITH INTESTINAL MICROBIOTA

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Objectives and Study: Necrotizing enterocolitis (NEC) is the most common severe gastro-intestinal disease in very low birth weight infants with incidence rates between 3-15%. Currently available biomarkers lack accuracy to detect NEC in pre-clinical stage and do not allow discrimination from sepsis. Alterations in microbiota are considered an essential factor in pathogenesis of NEC. We hypothesized that analysis of fecal volatile organic compounds (VOC), reflecting microbial composition, by means of an electronic nose (eNose) allows for early discrimination of children with NEC, sepsis and controls.

Methods: Fecal samples of infants born at gestational age <30 weeks were collected daily, from birth to 28 days, in three neonatal intensive care units in The Netherlands. Included infants were allocated in three groups: NEC, matched controls or sepsis. Fecal samples of different subgroups were analyzed by eNose and ISpro up to 5 days prior to diagnosis of NEC. Furthermore, fecal microbiota composition at same time-intervals was assessed by means of ISpro, to link measured fecal VOC profiles to microbial shifts.

Results: Fecal VOC profiles of infants with NEC (n=13) differed significantly from matched controls (n=26) 2 to 3 days prior to clinical onset of NEC (AUC ± 95% CI, p-value, sensitivity, specificity: 0.79 ± 0.95, p=0.002, 83%, 75%). NEC could also be discriminated from sepsis (n=31) at the same time-interval (0.73 ± 1.0, p=0.015, 90%, 83%). We observed differences in microbiotal profiles between the groups at every measured time-point, up to 5 days before clinical onset of NEC, within the phyla Firmicutes and Proteobacteria. Shannon diversity indices of Proteobacteria in the sepsis-subgroup were significantly lower at all time-points.

Conclusion: Fecal VOC profiles of infants with NEC could firmly be discriminated from controls and sepsis, 2 to 3 days prior to onset of clinical symptoms. Microbiota profiles of NEC-subjects differed from controls at all measured time-intervals, up to 5 days prior to NEC. Our observations indicate that microbiota- and VOC profiling have potential as non-invasive method to detect NEC in early stage. Timely diagnosis allows for early initiation of (novel) therapeutic strategies, potentially decreasing mortality and morbidity of NEC.

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Objectives and Study: A diverse group of monogenic conditions can present with IBD-like phenotype. Very early onset IBD refers to children with disease onset before the sixth year of life. Considering the orphan nature and phenotypic heterogeneity of VEOIBD, detecting a causative gene is challenging and can be both time and resource consuming. Next-generation sequencing (NGS) technologies such as whole exome sequencing (WES) or targeted gene panel sequencing (TGPS) might therefore be attractive genetic screening modalities.

Methods: We retrospectively reviewed the phenotype data of all VEOIBD patients registered in our IBD database and recruited candidates who fulfilled the study criteria for further molecular evaluation. Over an 18 month-period, 25 patients were recruited for WES and 40 for TGPS. Samples for whole exome analysis were sequenced using the SureSelect Human All Exon Kit Version 4. Forty TGPS samples were sequenced in house (SureSelect XT Custom Capture protocol).

Results: Over the last 14 years, 85 VEOIBD patients (56% male) were treated at our center. The median age of disease onset was 7 months [IQR: 1 to 22] with a median age at diagnosis of 2.5 years [IQR: 1 to 3.8]. Out of all children, 78% had pancolonic, 14% extensive perianal and 8% stricturing disease. 15% of patients underwent abdominal surgery and 33% required TPN (>28 days). Hematopoietic stem cell transplantation (HSCT) was performed in 25% of children. 52% of children were treated with 2 or more biologics and/or immunomodulators. 3 patients deceased. Prior to the launch of our program, 9 patients were diagnosed through Sanger sequencing (genes: IL10, IL10RA, IL10RB, XIAP, IPEX). Since then, NGS revealed 10 diagnoses in 6 genes (EPCAM, IL10RA, TTC37, SKIV2L, LRBA, TTC7A). Subgroup analysis revealed that patients with monogenic IBD were more likely to come from consanguineous families (53 % vs. 20%, p=0.007), had earlier disease onset (1 month [IQR: 0 to 4] vs. 12 months [IQR: 3 to 30], p<0.0001) and were more likely to undergo HSCT (63% vs. 14%, p<0.0001), when compared to children with non-monogenic IBD. When screening for known VEOIBD genes, TGPS performed better than WES (% of exons with coverage deficiency: 1.3% vs. 13.8%, p<0.001).

Conclusion: Children with VEOIBD frequently present with extensive and treatment resistant disease. The comprehensive screening approach through NGS has revealed unexpected phenotypes with high impact on patient management. Early disease onset (under 6 months) and consanguinity are positive predictive factors for monogenic VEOIBD. Careful considerations of different NGS technologies should precede genetic screening.

Disclosure of Interest: None Declared
RANDOMISED, CONTROLLED STUDY OF CARBON DIOXIDE INSUFFLATION DURING COLONOSCOPY IN SEDATED CHILDREN

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Objectives and Study: Several studies in adults have shown that post procedural abdominal pain is reduced with the use of carbon dioxide (CO₂) instead of air for insufflation during colonoscopy, but no studies exist in pediatrics. Our aim was to compare abdominal pain and girth in children undergoing colonoscopy using CO₂ and air for insufflation.

Methods: This was a prospective randomized double-blind study. Seventy six consecutive patients undergoing colonoscopy under moderate intravenous sedation with ketamin and midazolam were included. Patients were randomly assigned to either CO₂ or air insufflation group. They were assessed for abdominal pain before and at 2, 4, and 24 hours post examination using a validated numeric rating scale (NRS-11). Waist circumference was measured before, and then 10 minutes, 2 and 4 hours after the procedure. Scale variables were compared between the two groups using independent samples t-test and Mann-Whitney U test. Chi-squared test was used to compare descriptive variables.

Results: There were no statistically significant differences in patients' demographic characteristics between the CO₂ and air groups. The use of CO₂ did not prolong the colonoscopy (p = 0.574) or the time to reach terminal ileum (p = 0.969). The mean NRS-11 abdominal pain score of patients in CO₂ group was significantly lower at both 2 and 4 hours post procedure when compared to the air group (0.526 vs. 2.579 (p<0.001), and 0.105 vs. 1.211 (p=0.001), respectively). The proportion of patients who had no abdominal pain was significantly higher in the CO₂ group at both 2 and 4 hours after examination compared to the air group (82% vs. 37% (p < 0.001), and 95% vs. 63% (p = 0.001), respectively). None of the patients reported pain 24 hours after examination. We found no statistically significant difference in waist circumference at all time points. No significant adverse events were noted in either group.

Conclusion: CO₂ insufflation during colonoscopy in children significantly reduces abdominal pain when compared to insufflation with air at 2 and 4 hours post procedure. The use of CO₂ did not prolong the colonoscopy or affect the extent of the examination.

Disclosure of Interest: None Declared
CLEAR LIQUID VS LOW-FIBER DIET IN BOWEL CLEANSING FOR COLONOSCOPY IN CHILDREN: A RANDOMISED TRIAL

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Objectives and Study: There is a paucity of clinical trials of bowel cleansing regimens in the pediatric population and in particular little is known about the role of diet in this process in children. The aim of the study was to compare the efficacy of clear liquid diet versus low-fiber diet prior to macrogol bowel preparation for colonoscopy in pediatric patients.

Methods: We conducted a prospective, randomized, single-blind trial in children aged 6-18 years. Patients were randomly assigned to receive clear liquid diet or low-fiber diet on the day preceding colonoscopy. Polyethylene glycol 3350 (1 L per 15 kg of body weight, 4 L max.) was administered in the afternoon. The primary endpoint was cleansing efficacy measured using the Boston bowel preparation scale (BBPS).

Results: Seventy-one patients (median age 14.8 years) were enrolled in the study; 35 were allocated to clear liquid diet and 36 received low-fiber diet. The mean BBPS scores provided by the endoscopist and the nurse did not differ between the two groups (p=0.64 and p=0.78, respectively). The length of time between the last dose of bowel preparation and the start of colonoscopy correlated with cleansing efficacy (r=-0.25, p<0.05).

Conclusion: Clear liquid diet and low-fiber diet provided to children on the day before colonoscopy were associated with similar bowel cleansing efficacy. (ClinicalTrials.gov Identifier: NCT02102373)

Disclosure of Interest: None Declared
CROHN DISEASE LOCALISATION DOES NOT CONTRIBUTE TO THE COURSE OF MAINTENANCE THERAPY WITH INFLIXIMAB IN CHILDREN

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**Objectives and Study:** The primary and secondary loss of efficacy are major problems during anti TNF-α maintenance therapy. It's documented that complete remission, concurrent immunomodulators, are the predictors of prolonged remission. It is questionable if ileal or colonic localization can contribute the CD flare. The aim of the study was to explore the contribution of CD gut localization to the course of maintenance therapy with infliximab in children.

**Methods:** This is a per protocol subanalysis of CIMIT study. 77 patients with PCDAI>30 pts and endoscopic evaluation (using Simple Endoscopic Score for Crohn's Disease (SES-CD), based on 4 endoscopic variables (ulcer size, ulcerated and affected surfaces, stenosis) in 5 ileocolonic segments (ileum, right colon, transverse colon, left colon, rectum) and the endoscopic parameters are scored from 0–3) performed, who finished one year maintenance therapy with infliximab 5 mg/kg were involved to the study. Clinical (PCDAI score) remission (PCDAI<10) were assessed at Week 52. Scorings in each ileocolonic segment were used as five independent variables in analysis of discrimination between: groups with clinical remission (with or without rescue therapy n=57) vs. no remission (n=20) and groups with CD flare during maintenance therapy present (n=34) vs. absent (n=43).

**Results:** None of the analyzed variable had significant impact on discrimination between group with clinical remission vs. no remission – all partial Wilks' Lambda > 0,97. The optimal model of discrimination had sensivity 0,98 and specificity 0,17.

None of the analyzed variable had significant impact on discrimination between group with CD flare during maintenance therapy present vs. absent – all partial Wilks' Lambda > 0,99. The optimal model of discrimination had sensitivity 0,78 and specificity 0,42.

**Conclusion:** Crohn Disease localization does not contribute to the course of maintenance therapy with infliximab in children

**Disclosure of Interest:** None Declared
**Gastroenterology**  
**Inflammatory Bowel Disease**  
SP-G-0101

**INTRAVENOUS CORTICOSTEROID (IVCS) DOSING IN PAEDIATRIC ACUTE SEVERE ULCERATIVE COLITIS (ASC): A MULTICENTRE PROPENSITY SCORE STUDY**

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**Objectives and Study:** There are no available data to support dosing of intravenous corticosteroids (IVCS) in pediatric acute severe ulcerative colitis (ASC). We thus aimed to explore the optimal dosing of IVCS in pediatric ASC using a robust statistical method on the largest pediatric cohort of ASC to date.

**Methods:** 283 children treated with IVCS for UC were included from the retrospective and prospective OSCI studies and further newly reviewed patients from Jerusalem and Liverpool. Patients were followed for 1yr (46% males, age 12.1±3.9 years, disease duration 2 (IQR 0-14) months, baseline PUCAI 69±13 points). Confounding by indication bias was addressed by matching high and low IVCS dose patients according to the propensity score (PS) method, using 3 cutoffs (1mg/kg methylprednisolone to 40mg/day, 1.25mg/kg to 50mg/day and 2mg/kg to 80mg/day).

**Results:** The median IVCS dose in the entire cohort was 1.0 mg/kg (IQR 0.8-1.4) and 44 mg/day (32-60). 218 children were matched in the 1.25mg/kg cutoff, 94 children were matched in the 1mg/kg cutoff and 86 children were matched in the 2mg/kg cutoff. No differences were found in 25 pretreatment baseline variables in the three cutoffs, implying successful matching. There were no statistical differences in all outcomes of the two lower cutoffs (including need for salvage therapy during admission and by 1 year after discharge, admission duration, day-5 PUCAI and day 5 CRP, ESR and albumin; all P>0.05). In the high cutoff, the higher doses were somewhat better but this benefit reversed after excluding one center in a sensitivity analysis that routinely used very high doses and reported better outcomes. In a PS-weighted regression model on the entire cohort, high doses were not associated with better effectiveness in any of the outcomes (all P>0.1).

**Conclusion:** Our data support current guidelines of dosing IVCS in the range of 1-1.5mg/kg/d to a maximum of 40-60mg/d

OUTCOMES OF A LARGE COHORT OF CHILDREN WITH IBDU COMPARED TO OTHER IBD SUBTYPES AND TREATMENT OPTIONS- A LONGITUDINAL REPORT FROM THE PORTO PAEDIATRIC IBD GROUP OF ESPGHAN

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Objectives and Study: Inflammatory bowel disease unclassified (IBDU) is the rarest subtype of IBD and as such treatment options for patients are based mainly on extrapolation from ulcerative colitis (UC) and Crohn’s disease (CD) treatment studies. We aimed to look at treatment choices for IBDU compared to other patients with colonic IBD and to compare patient outcomes at 3 years.

Methods: This was a multicentre retrospective longitudinal study including 23 centres affiliated with the Porto IBD working group of ESPGHAN. Data on 797 children with colonic IBD were collected on a standard proforma at diagnosis and follow up with strict diagnostic (Porto) criteria (mean age 10.5±3.9): 250 with CD, 287 with UC and 260 with IBDU. Disease severity was assessed by Physician Global Assessment (PGA).

Results: IBDU treatment significantly differed from that of UC for lower use of corticosteroids (CS) [154 (59%) vs. 204 (71%), p=0.004] but higher use of exclusive enteral nutrition (EEN) [26 (10%) vs. 2 (0.6%), p<0.0001]. Compared to CD, IBDU patients received less EEN and immunomodulators [26 (10%) vs. 93 (37%), p<0.0001 and 67 (26%) vs. 129 (52%), p<0.0001, respectively] but more aminosalicylates [228 (88%) vs. 159 (64%), p<0.0001]. At 3-year follow-up, 135 (69%) IBDU patients had a remission or a mild disease, compared to 100 with CD (46%, p<0.0001), and 174 with UC (64%, p=0.3). CD patients were more commonly treated with biologics than those with IBDU and UC [82 (34%) vs. 24 (12%) and 47 (17%); p<0.0001 vs. IBDU and UC]. Four patients with IBDU (1%) underwent surgery during follow up, vs. 22 (5%) with UC (p=0.009) and 20 (5%) with CD (p=0.008 vs. IBDU), while no significant differences for time for surgery were reported among the three groups. A significantly higher proportion of IBDU patients treated with CS at the diagnosis required biologics and cyclosporine at follow-up, compared to those treated with other therapies (p=0.04 and p=0.05, respectively).

Conclusion: Children with IBDU receive less 5ASA/steroids than UC but more than CD yet receive less EEN and immunomodulators than CD but more than UC. The need for biologics and surgery at
follow up is lower in IBDU than CD. CS use at the diagnosis in IBDU patients is related to worse clinical outcomes. Despite these differences a mild disease course in IBDU patients at follow-up is common.

**Disclosure of Interest**: None Declared
MANAGING PAEDIATRIC CROHN’S DISEASE IN SE ASIA – EVALUATING THE EFFICACY OF ENTERAL NUTRITION INDUCTION THERAPY AND THE EFFECT OF EARLY ADMINISTRATION OF AZATHIOPRINE ON RELAPSE RATE.

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Objectives and Study: Recent reports suggested that Asian children with IBD have a more aggressive disease phenotype compared to Caucasian. Exclusive enteral nutrition (EEN) is well described in the West as an effective induction therapy in Paediatric Crohn’s Disease (PCD). The efficacy of EEN therapy in Southeast-Asian (SEA) children remains largely unknown. Recent adult literature had raised controversies regarding early use of azathioprine in maintaining remission. Our study aims to evaluate the efficacy of EEN induction therapy in newly-diagnosed SEA PCD. Secondary aim was to study the effect of early azathioprine on relapse rate.

Methods: Patients were recruited from a single paediatric tertiary hospital in Singapore over 3 years (2011-13). All SEA children newly diagnosed with PCD who received EEN with whole casein polymeric diet (ModulenIBD, Nestle) were identified. Pediatric Crohn Disease Activity Index (PCDAI) was calculated before and after EEN therapy. Remission was defined as PCDAI <15. Rate of relapse at 6 months and 1 year was compared between 2 groups: Early administration of azathioprine (EAZ) group: azathioprine started within 1 month of diagnosis vs Late Azathioprine (LAZ) group: azathioprine not started or started after EEN if clinically indicated.

Results: All results expressed in mean±SD.

A total of 40 newly diagnosed PCD patients were started on EEN (25 boys, age 11.6±3.6y). Disease location: Colonic=13; Ileocolonic=25; Small Bowel=2.

33/40 patients completed 6-8 weeks EEN course (15/33 EAZ and 18/33 LAZ).

30/33 (91%) achieved remission: 14/33 EAZ and 16/33 LAZ.

Mean PCDAI reduced from 33.75±8.95 to 3.03±4.51 (p<0.001) following EEN. There were significant improvements in inflammatory markers (p<0.001 for all): ESR (46.2±25.4 to 13.3±7.06), CRP (49.0±56.4 to 5.16±3.89), albumin (30.6±7.58 to 38.7±3.89) and platelets (463.5±160.8 to 369.9±111.1). Growth improved significantly after EEN: weight increased from 36.9kg±14.36 to 38.18kg±12.62 (p <0.001) and height from 147.1cm±18.8 to 149.2cm±18.72 (p=0.009).

Overall rate of relapse: 9/30(30%) within 6 months and 14/30(47%) with 12 months. Rate of relapse in EAZ: 2/14(14%) within 6 months and 4/14(29%) within 1 year. Rate of relapse in LAZ: 7/16(44%) within 6 months and 10/16(63%) within 1 year. The rate of relapse was lower in EAZ compared to LAZ: (First 6mths, p=0.046; first year, p=0.065).

Conclusion: EEN is an effective induction therapy for newly diagnosed PCD in SE Asian children with significant improvements in PCDAI, inflammatory markers, and growth. However almost half the
patients relapsed within a year. Our data suggests that early use azathioprine in PCD was associated with a lower rate of relapse although a larger study is needed for evaluation.

Disclosure of Interest: None Declared
**Objectives and Study:** Relationship between coeliac disease (CD) and allergy has been investigated but is still a matter of controversy. Some reports suggested that patients with CD have an increased frequency of allergic manifestations compared to the normal population, but more recent studies have denied this association. Aim of this study was to evaluate the prevalence of CD in a selected population of children with very severe food allergy.

**Methods:** A retrospective study was conducted on a collection of serum samples and clinical records of patients seen between October 2007 and October 2014 at the Paediatric Department of the IRCCS “Burlo Garofolo” in Trieste. 308 subjects (mean age 9±4) with very severe food allergy were included in our study. Inclusion criteria were represented by elevated IgE levels against food proteins (milk, egg or wheat) and a positive history for severe allergic reactions after exposure to the causal food (e.g. anaphylactic shock, bronchospasm). All the subjects underwent a specific oral tolerance induction. Sera were analysed for determination of both IgA anti-endomysial (EMA) and anti-tissue transglutaminase (anti-tTG) antibodies. Patients found to be positive to serologic tests underwent endoscopy with duodenal biopsy.

Prevalence of CD in our population was compared with the prevalence of CD in a control group of 76 age-matched subjects affected by non-complicated allergic disorders: mild food allergy, rhinoconjunctivitis, asthma. Furthermore the prevalence data were compared with those of the CD screening study evaluated in the schoolchildren population of Trieste.

**Results:** Thirteen patients with severe food allergy were tested positive for both EMA and anti-tTG, and for the HLA DQ2/8 haplotypes. Eight/13 underwent duodenal endoscopy, which confirmed the diagnosis of CD. Furthermore 6 subjects were known to be coeliac and were in gluten free diet. The overall prevalence of CD in our population is 6.2% (19/308). One subject (1/76, 1.3%) with mild food allergy was diagnosed as having CD.

**Conclusion:** In subjects with severe food allergy the CD-prevalence is 6-fold higher than in both healthy population and subjects with mild allergic manifestations. From a clinical point of view, the subjects with severe food allergy should be screened for CD. The association between CD and severe food allergy might be explained by the pathological intestinal mucosal permeability, which may lead to the production of reaginic antibodies and gastrointestinal hypersensitivity. Finally, the efficacy of gluten free diet to cure coeliac with severe food allergy should be verified by prospective studies.

Disclosure of Interest: None Declared
TOLERANCE ACQUISITION IN CHILDREN WITH IGE-MEDIATED COW'S MILK ALLERGY IS CHARACTERIZED BY A DIFFERENT TH1 AND TH2 CYTOKINES DNA METHYLATION PATTERN

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Objectives and Study: Epigenetic changes in DNA methylation have recently been demonstrated to be involved in the control of several allergy-related genes expression. We aimed to investigate whether tolerance acquisition in children with IgE-mediated cow’s milk allergy (CMA) is characterized by a different DNA methylation profile of Th2 (IL-4, IL-5) and Th1 (IL-10, IFN-γ)-associated cytokine genes.

Methods: DNA methylation of CpGs in the promoter regions from peripheral blood mononuclear cells and respective serum level of IL-4, IL-5, IL-10 and INF-γ, were assessed in patients with IgE-mediated CMA (Group 1), in children who outgrew CMA (Group 2) and in healthy controls (Group 3).

Results: 40 children (24 male, aged 3-18 months) were enrolled: 10 in Group 1, 20 in Group 2 and 10 Group 3. DNA methylation profiles of all cytokines clearly separated active CMA patients from healthy controls. Active IgE-mediated CMA patients showed significantly lower rate in IL-4 and -5 and higher rate in IL-10 and INF-γ DNA methylation, respectively. Meanwhile healthy controls showed significantly lower rate in IL-4 and -5 and higher rate in IL-10 and INF-γ DNA methylation profile, respectively. DNA methylation analysis of these cytokine genes clearly also separated CMA patients by disease-state. In fact, subjects with a recent evidence of oral tolerance acquisition presented a significant different profile if compared to active CMA patients. This profile was similar but not identical to that observed in healthy controls. A strong correlation between gene promoter DNA methylation rates and respective serum levels was also demonstrated for all cytokines.

Conclusion: Tolerance acquisition in children with IgE-mediated cow’s milk allergy is characterized by a different Th1 and Th2 cytokines DNA methylation pattern. Our results suggest new epigenetic biomarkers for preventive and therapeutic interventions in CMA.

with: Mead Johnson Nutritionals, L. Greco Conflict with: Mead Johnson Nutritionals, F. Salvatore
Conflict with: Mead Johnson Nutritionals
PAEDIATRIC ACHALASIA: DIAGNOSIS, MANAGEMENT AND FOLLOW-UP IN THE NETHERLANDS

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Objectives and Study: Paediatric achalasia is a rare oesophageal motility disorder. Data on prevalence, incidence, presenting symptoms, treatment success and follow up are scarce.

Methods: Medical charts of registered Dutch paediatric achalasia patients (<18yrs) diagnosed between January 1990 and December 2013, were retrospectively reviewed for data on presenting symptoms, treatment, relapses and follow up.

Results: In total, 87 Dutch paediatric achalasia patients (mean age at diagnosis 11.44 +/- 3.43 years, 60% male) were included. Mean incidence was 0.10/100,000 per year (range, 0.03 and 0.21). No significant increase in incidence was observed over the study period. The prevalence of paediatric achalasia in The Netherlands in 2012 was 0.90/100,000. Presenting symptoms included dysphagia (83%), regurgitation (69%), weight loss (44%) and chest pain (37%). Initial treatment (IT) was pneumatic balloon dilation (PD) in 68 (79%) patients and Heller’s Myotomy (HM) in 18 (21%) patients. In 4 patients, achalasia was diagnosed as part of Triple A syndrome. Complications of IT occurred more after HM compared to PD (10/18 vs 1/68 P<0.0001, n=4 perforations). Similarly, complication rate was higher for HM after relapse treatments (20/22 vs 3/135, P<0.0001, n=7 perforations). However, the cumulative amount of complications of re-treatment(s) after IT PD is higher compared to IT HM (n=21/229 vs n=13/24). Re-treatment was required more often after initial PD (n=59, 88%) compared to initial HM(n=4, 22%), P<0.0001. First re-treatment after initial PD was re-PD in 90% and HM in 10% of patients. After initial HM, first relapse treatment was PD in 50% and re-HM in 50%.

Median (interquartile range) follow-up after initial treatment was 3.9 years (1.4 - 10.2). Four years after IT 46% of patients <18 years were lost to follow up.

Conclusion: Incidence of paediatric achalasia in the Netherlands is 0.10/100.000/year. PD is the predominant initial treatment of choice, however high relapse rates indicate the need for prospective studies comparing HM and PD for paediatric achalasia. Many patients are lost to follow up.
up. Considering the long term risks of uncontrolled achalasia, there is a need for a standardized follow up regime to improve clinical outcome and transfer to adult care.

Disclosure of Interest: None Declared
GLUTEN CONSUMPTION HABITS AMONG YOUNG CHILDREN OF DIFFERENT EUROPEAN COUNTRIES.

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Objectives and Study: After we previously assessed significant differences in mean daily gluten intake (MDGI) among infants from Spain, Germany, The Netherlands, Italy and Hungary, we aimed at evaluating the gluten containing foods (GCF) consumed up to 36 months of age in these countries.

Methods: Subjects from the PreventCD project (www.preventcd.com), a randomized placebo controlled trial on timing gluten introduction (100 mg gluten versus placebo between week 16-24) were instructed to gradually increase the amount of gluten from month 7 (500 mg/day) to 9 months (1500 mg/day) but from 10 months onwards gluten intake was unrestricted. The MDGI was assessed by specific food records (FRs). The products were grouped in bread, infants’ cereals, biscuits, pasta, pastries and “others”. We report the percentage each food group contributed to total MDGI.

Results: 6132 FRs pertaining to 637 children were assessed. We have observed differences in the consumption of GCFs and in the average age these products are introduced. Bread is the first GCF introduced in The Netherlands, at 8 months, and the gluten consumption from bread is the highest at any age varying from 57% at 11 months to 73% at 36 months. For the other countries, bread consumption increases with age but is lower: in Spain it varies from 11% at 11 months to 42% at 36 months, in Italy from 8% at 11 months to 19% at 36 months, in Hungary from 36% at 11 months to 56% at 36 months. The Italians are the first to introduce pasta (at 9 months), reaching 50% of total MDGI at 11 months and presenting the highest consumption at any age with relevant differences respect to the other countries: in Spain, 2% at 11 months and 18% at 36 months, in The Netherlands and Hungary, respectively 2% and 11% at any age. Infants’ cereals are the first GCF introduced into infants’ diet in Spain (7 months). However, as opposed to bread and pasta, consumption of infants’ cereals decreases with age in all countries. The introduction of biscuits (8 months), pastries (16 months) and “others” (15 months) is similar for all countries as well as the pattern of consumption at any age. The biscuit consumption decreases with age whereas consumption of pastries and “others” increases with age.

Conclusion: True differences are observed among European countries in the percentage each food group contributes to total MDGI and also in the age of introduction. This information could be of value to further assess the impact of gluten intake in coeliac disease development.
Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

SP-G-0117

**CLINICAL FEATURES ARE NOT HELPFUL FOR CASE FINDING OF COELIAC DISEASE IN YOUNG CHILDREN AT GENETIC RISK: RESULTS FROM THE TEDDY STUDY**

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**Objectives and Study:** To investigate whether clinical features of celiac disease (CD) distinguish young children at the time of first tissue transglutaminase antibodies (tTGA) positivity from age matched children with no CD autoimmunity and to evaluate the association of these features to known risk factors for CD in a birth cohort at genetic risk (TEDDY study).

**Methods:** Children from six clinical centers in four countries positive for HLA-DR3-DQ2 and/or DR4-DQ8 were annually screened for tissue transglutaminase antibodies (tTGA) and assessed for symptoms by questionnaires. Associations of symptoms were examined to anthropometric measures, known risk factors for CD, tTGA levels, and mucosal lesions in those biopsied.

**Results:** Of 6706 screened children, 914 developed persistent positive tTGA, 406 underwent biopsies and 340 had CD. Compared with age matched tTGA negative children, those with persistent tTGA had more frequently symptoms when tested first positive at two (34% vs 19%, p<0.001) and three years of age (28% vs 19%, p=0.009), but not at four years of age (27% vs 21%, n.s.). In both groups the most common symptoms were abdominal pain, constipation and loose stool, with significantly higher frequency in tTGA positive children for constipation at 2 years (11% vs 6%) and abdominal pain at 3 years of age (16% vs 8%). Z-scores for height, weight and body mass index or percentage of children below the 10th percentile did not differ between groups. In children with persistent tTGA, having ≥1 symptom was associated with family history of CD (OR=2.59, 95% CI=1.21-5.57), but not with age, sex, or HLA-DR3-DQ2 homozygosity. At seroconversion, tTGA levels were higher in symptomatic than asymptomatic children (p<0.001), in those from CD families (p<0.001), and US participants (p<0.001), but not associated with age, sex or HLA-type. TTGA levels correlated with severity of mucosal lesions both in symptomatic (r=0.53, p<0.001) and asymptomatic children (r=0.22, p=0.01).

**Conclusion:** At least two thirds of screening identified children has no symptoms at the time of seroconversion to tTGA positivity by four years of age. Symptoms are not associated with HLA-
genotype. Prospective screening for CD enables the diagnosis before adverse effects on growth develop in at genetic risk children. Our findings may have implications for future screening of the general population and case finding strategies in at risk groups.

**Disclosure of Interest:** None Declared
Objectives and Study: The worldwide incidence of paediatric-onset inflammatory bowel disease (PIBD) is rising, with Scotland having the highest rate in the UK. Scottish PIBD data over the last 40 years has shown a consistent increase, including a 76% rise over 13 years around the millennium (1). The aim of this study was to calculate current PIBD incidence rates in Scotland and to determine if the temporal trend of significant increase has been maintained.

Methods: Historical data from 2003-2008 (cohort 1) was compared to prospective, nationwide data of all incident cases diagnosed in paediatric services (under 16 years of age) from 2009-2013 (cohort 2). Age-sex adjusted incidence rates were calculated using population data from the General Registrar's Office for Scotland. Cases were classified as Crohn's disease (CD), ulcerative colitis (UC) or inflammatory bowel disease unclassified (IBDU) and diagnosed according to the Porto criteria. Statistical analysis was performed using Poisson regression.

Results: A total of 436 patients were diagnosed with PIBD over six years in cohort 1 (265 CD, 115 UC, 56 IBDU) compared to 478 children over five years in cohort 2 (286 CD, 126 UC, 66 IBDU). Median age at diagnosis in cohort 2 (60% males) was 12.3 years, similar to cohort 1 (58% males) at 11.9 years. The adjusted incidence rate increased from 7.8/100,000/year (95%CI 7.1-8.6) in cohort 1 (2003-2008) to 10.4/100,000/year (95%CI 9.6-11.5) in cohort 2 (2009-2013) (p<0.001). This significant increase was also seen individually for CD (4.7/100,000/year [95%CI 4.2-5.4] compared to 6.3/100,000/year [95%CI 5.6-7.0][p<0.0001]) and UC (2.1/100,000/year [95%CI 1.7-2.5] compared to 2.7/100,000/year [95%CI 2.3-3.3][p=0.009]). There was a non-significant increase in IBDU from 1.0/100,000/year (95%CI 0.7, 1.3) in cohort 1 to 1.4/100,000/year (95%CI 1.1, 1.8) in cohort 2 (p=0.07).

Conclusion: There continues to be an ongoing rise in incident PIBD (and both CD and UC) in 2009-13 in this national, population-based study compared to recent historical data, with a further significant rise of 33%. The reasons behind this continued increase remain unclear and further research is needed to elucidate potential factors in aetopathogenesis.


Disclosure of Interest: None Declared

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Objectives and Study: Little is known on change in the characteristics of paediatric IBD over time. The aim of the present study was to assess the evolution of incidence, age at diagnosis, location and behaviour of pediatric-onset IBD during a 21-y period in a population-based cohort.

Methods: Data from patients <17 y at diagnosis of definitive or probable IBD were extracted from our population-based EPIMAD Registry (Northern France) between 1988 and 2008. Age groups and location at diagnosis were defined using the Paris classification, with age <10 y or >10 y and location: 1) for Crohn's Disease (CD): pure small bowel involvement (L1); pure colonic (L2); ileocolonic involvement (L3); 2) for Ulcerative Colitis (UC): proctitis (E1); left sided colitis (E2); extensive colitis (E3), pancolitis (E4). CD behaviour was defined as nonstricturing nonpenetrating (inflammatory (B1); stricturing (B2); or penetrating (B3).

Results: 1147 cases of incident paediatric-onset IBD were recorded (8% of all IBD cases over the study period): 846 CD (73.8%), 271 UC (23.6%) and 30 IBD unclassified (2.6%). Median age at diagnosis was similar in CD (14.5 y) and UC (14.1 y) with no change over time. Median time to diagnosis did not change over time at 3 months. Incidence increased in teenagers (10-16 years) over the study period: CD (4.3 in 1988-90 to 9.6/ 10^5 in 2006-08 (+123%; p<10^-3)) and UC (1.6 in 1988-90 to 2.9/10^5 in 2006-08 (+81%; p<10^-3)). IBD location did not change over time in CD (L1= 12.2%, L2=14.5%, L3=73.3%) and UC (E1=31.1%, E2=25.4%, E3=10.5%, E4=33%). Overall, the most common behaviour was B1 (76.5%) that significantly increased (63.6% in 1988-90 to 82.3% in 2006-08; p<10^-3), while B2 showed a progressive and significant decrease (33.8% in 1988-90 to 10.1% in 2006-08; p<10^-4).

Conclusion: The incidence of IBD (both CD and UC) increased dramatically in teenagers (10-16 y) between 1988 and 2008. No change was observed in age, location and time to diagnosis over the same study period, but a change in CD behaviour was found with an increase of inflammatory form.
These data strongly suggest the presence of environmental factors predisposing to IBD at work in this population.

**Disclosure of Interest:** None Declared
IL-10R2 MUTATIONS IN PORTUGAL: IDENTIFICATION OF A FOUNDER EFFECT AND OF A NOVEL DE NOVO MUTATION

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Objectives and Study: Mutations affecting the receptor of interleukin 10 (IL-10R) or IL-10 are a cause of early-onset inflammatory bowel disease (EO-IBD) and were systematically screened in our cohort of EO-IBD.

Methods: IL-10R function was tested using exogenous IL-10 to inhibit IL-8 production in LPS-stimulated peripheral blood monocytes (PBMC). IL-10R expression and STAT3 phosphorylation were tested by flow cytometry. Sequencing of IL-10R2 was performed on genomic DNA and cDNA. JAK1 and Tyk2 phosphorylation was analysed by Western Blot.

Results: Three patients P1, P2 and P3 with EO-IBD starting before 9 months had PBMC unresponsive to the inhibitory effect of IL-10. They were born in 3 distinct families from Portugal. In P1 and P2 families, parents were distantly related. Sequencing of IL-10R2 revealed a large deletion encompassing exon 3 (delE3) with an insertion of 2 nucleotides resulting in a stop codon and precluding protein expression. P1 and P2 were homozygous for delE3 while their parents were heterozygous. P3 and P3’s mother were heterozygous for delE3 but P3 carried also a de novo mutation on the paternal allele characterized by a duplication of exon 6 with a frameshift at the end of the first exon 6. The predicted protein had normal extracellular and transmembrane domains but, except for 22 amino acids, an abnormal intracellular domain. IL-10 stimulates the phosphorylation of JAK1 and Tyk2 kinases, which next cooperate to phosphorylate STAT3 transcription factor. JAK1 and Tyk2 are known to associate with the intracellular domains of IL10Rα and IL10Rβ respectively. Flow cytometry analysis of P3’s PBMCs revealed normal IL-10Rβ surface expression, but no phosphorylation of STAT3 in response to IL-10. Western blot analysis of EBV lines stimulated by IL-10 showed comparable phosphorylation of JAK1 in P3, in his parents and in a control. Phosphorylation of Tyk2 could also be induced in control and parents cells by IL-10 or IFNα. In contrast, only IFNα but not IL-10 induced Tyk2 phosphorylation in P3 cells. These results confirm the putative function of the intracellular domain coded by exon 7 of IL-10R2 in the recruitment of Tyk2 and explains that IL-10 signalling is absent despite normal surface expression.

Conclusion: We have identified 2 novel loss-of-function mutations in IL-10R2: a deletion of exon 3 common to 3 unrelated Portuguese families, with micro-satellites homology suggesting a founder effect, and a mutation resulting in the loss of exon 7, which led us to better delineate the necessary interactions between the intracytoplasmic part of IL-10Rβ and Tyk2.
Disclosure of Interest: None Declared
ASSESSMENT OF SAFETY AND EFFICACY OF BIOSIMILAR INFlixIMAB IN CHILDREN WITH CROHN'S DISEASE: A PRELIMINARY REPORT.

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Objectives and Study: Biosimilar infliximab (Remisma/Inflectra) was introduced into therapy in Poland and other selected European countries at the beginning of 2014. Biosimilar infliximab (BI) was authorised based on preclinical and clinical studies and is considered therapeutically equivalent in terms of safety and efficacy to the reference infliximab. We present first, to our knowledge, observation on the safety and efficacy of BI in children with Crohn disease.

Methods: A total of 12 children diagnosed and treated at 3 Polish hospitals with Crohn disease who started therapy with BI were assessed. Patients received BI 5 mg/kg at weeks 0, 2, and 6. Pediatric Crohn disease activity index (PCDAI) and laboratory values (CRP, ESR, platelet count) were assessed at qualification for the biological treatment and after induction treatment at week 10. Due to small number of cases, median and range of clinical values are reported for descriptive purposes only.

Results: Median age was 15.1 years (range 2-18). At BI start median PCDAI was 52.5 (range 5-65); CRP, ESR, platelet count values were 0.9 mg/dL (0.15-6.4), 18 mm (10-93), 327x10⁹/L (235-602x10⁹), respectively. Five out of 12 patients were previously treated with a biologics (4 with reference infliximab, 1 with adalimumab). Time of previous treatment was 6-59 months with biologic-free interval of 7-72 months. Treatment was discontinued in 2/12 patients (17%) after first BI dose due to lack of response, accompanied by adverse event in one patient and withdrawal of consent in second patient. In 10/12 patients (83%) response was observed as assessed by significant PCDAI and inflammation markers decrease. As of November 2014, 6 out of 12 patients (50%) received all 3 induction doses. For those patients, median initial PCDAI was 52.5 (15-62.5) and decreased to 5 (2.5-10). Before treatment and at week 10 CRP, ESR and platelet count were 1.0 (0.15-6.4), 28 (16-93), 309x10⁹ (255-553) and 0.2 (0.04-0.82), 16 (8-29), 263x10⁹ (220-340), respectively. Adverse events during infusion were observed in 2/12 patients (17%) : one anaphylactic reaction leading to treatment discontinuation and one blood pressure rise that resolved after infusion rate lowering. In the latter case patient received all 3 doses of BI.

Conclusion: In this preliminary report BI appears to be safe and efficacious in inducing remission in Crohn disease paediatric patients. No unexpected safety and product quality issues were identified.

Disclosure of Interest: None Declared
Objectives and Study: Gene therapy [GT] has great potential for the treatment of liver based metabolic diseases [LBMD]. For most LBMD GT would be necessary in early childhood, where episomal transgenes would be lost due to a growing liver. Therefore we want to show proof of concept for AAV8 based GT aiming for target integration via Zinc Finger nuclease [ZFN] enhanced homologous recombination in the Fah−/− mouse model, resembling human hereditary tyrosinemia. Liver physiology and function in Fah−/− mice can be maintained with the drug 2-(2-nitro-4-trifluoromethylbenzoyl)-1,3-cyclohexanedione [NTBC] and the animals die within 2 weeks after withdrawal.

Methods: rAAV8 vector genomes expressing the Fah cDNA under transcriptional control of transthyretin promoter, a second construct with the same transgene cassette, but flanked by homologous sequences (620 bp left and 749 bp right) of the ROSA26 locus and a third construct expressing ZFNs for this sequence were generated. Virus was produced according to published method (cesium chloride centrifugation) and was injected into the tail vein of Fah−/− (C57BL/6 Fah δ-exon 5) mice, organized in 3 groups (A,B,C) a 4 mice. Group A injected with rAAV8 Fah (2.1x10^8 VP), group B injected with rAAV8 Fah ROSA26 (2.1x10^8 VP ) and group C injected with rAAV8 Fah ROSA26 (2.1x10^8 VP) plus rAAV8 ZNF (7.6 x10^10 VP). 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 all treated mice, whereas non treated mice die within 2 weeks. At PH we observed clusters of hepatocytes expressing FAH equal for the 3 groups. Mice, who survived PH, survived until end of study (282 days) without NTBC. From secondary recipients for group A and B only 1 out of 5 mice showed repopulation of the liver indicating only rare integration events of rAAV8, but in group C 6 out 6 survived, indicating clear superiority of the target integration approach with ZFN.

Conclusion: Target integration is a highly efficient approach for creating a stable phenotypic correction in Fah−/− mouse model, if mediated by rAAV8 ZFN enhanced homologous recombination and is superior to episomal gene therapy in state of an extensive hepatocyte proliferation.
Disclosure of Interest: None Declared
PROGRESSIVE PORTAL AND LOBULAR FIBROSIS IN LONG TERM SURVIVING PAEDIATRIC LIVER GRAFTS: DIFFERENT COMPARTMENTS WITH DIFFERENT BACKGROUNDS

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Objectives and Study: Long-term survival after pediatric liver transplantation (LTx) has improved, a 10-year survival rate of more than 80% is reported. Multiple studies have shown that long-term graft survival is associated with increasing histological abnormalities, predominantly fibrosis and hepatitis. We previously reported the presence of graft fibrosis in 2 studies of CSA treated patients who showed a high incidence of progressive fibrosis at 1 and 10 years after LTx. The aim of this study was to evaluate graft fibrosis according to the acinar distribution and establish a correlation with clinical characteristics in a new cohort of patients who all received tacrolimus as the main immunosuppressive therapy. We hypothesize that the portal, perisinusoidal and centrilobular distribution of graft fibrosis results from different underlying conditions.

Methods: We reviewed the histological features in protocol liver biopsies taken at 1 and 5 years after transplantation of 47 children. Fibrosis was assessed according to the Liver Allograft Fibrosis Scoring system (LAFSc).

Results: Normal histology was found in 8% of the 1-year biopsies and in 6% of the 5-year biopsies, whereas fibrosis was present in 84% of the 1-year biopsies and 86% of the 5-year biopsies. An increased incidence of all 3 types of fibrosis was observed between 1 and 5 years. At 5 years centrilobular fibrosis was present in 85% of cases, sinusoidal fibrosis in 79% and portal fibrosis in 62%. The number of biopsies that showed histological hepatitis or minimal reactive changes decreased between 1 and 5 years after transplantation and were not related to fibrosis. There was a trend toward an association between biliary complications and portal fibrosis at 5 years (p=0.06) while total bilirubin and γGT were clearly associated with portal fibrosis (p=0.02 for both). Other liver function tests were not related to fibrosis. Centrilobular fibrosis was related to HLA mismatches (p=0.05), primarily at the HLA class I level. Rejection was related to the development of sinusoidal fibrosis (p=0.02). Previously described relation between fibrosis and (pre)transplant related factors, e.g. CMV status, cold ischemia time, donor age and graft type could not be confirmed in this study.

Conclusion: Using the LAFS scoring system, we found in this new cohort of tacrolimus treated patients a high incidence of progressive fibrosis in the 1 year and 5 year protocol biopsies after LTx. Progression of fibrosis was observed in all acinar compartments and each of the 3 locations is associated with different clinical conditions. Portal fibrosis with biliary complications, centrilobular fibrosis with HLA class I mismatch and sinusoidal fibrosis with previous rejection episodes.

Disclosure of Interest: None Declared
HEALTH STATUS AND PATIENT REPORTED OUTCOMES IN TEN YEAR SURVIVORS OF PAEDIATRIC LIVER TRANSPLANTATION

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Objectives and Study: Less than 1/3 of patients alive 10 years after paediatric liver transplantation (LT) in the Studies of Pediatric Liver Transplant (SPLIT) database fulfilled a research composite definition of an “ideal ten-year survivor”. However, missing within this composite profile were patient-reported subjective outcome variables such as Health Related Quality of Life (HRQOL). We hypothesized that ideal survivors of paediatric LT have higher HRQOL than non-ideal survivors.

Methods: This was an international multi-center cross-sectional analysis characterizing patients who have survived >10 years from LT enrolled in the Pediatric Liver Transplant Quality of Life (PeLTQL) Study Group database. Subjects were categorized as an “ideal survivor” of LT if “yes” answers were obtained from all 13 historically, clinically, and biochemically obtainable variables (Table 1). HRQOL was assessed with both well-validated pediatric disease-specific tools for pediatric LT (PeLTQL) and generic (PedsQL) HRQOL instruments. Data from completed Screen for Child Anxiety Related Disorders (SCARED) scales and the Children’s Depression Inventory Short Form (CDI-S) were also reviewed.

Results: A total of N= 57 (56% female, median patient age 14, range 11-18 years) subjects were reviewed, with 13 (22%) identified as an “ideal survivor”. Total PeLTQL scores were not significantly different between ideal (median 68.8, range 52.8-88.4) and non-ideal (median 69.6, range 27.9-96.1, p=0.8) survivors. The generic PedsQL scores were also not significantly different between ideal (median 79.4, range 28-90) and non-ideal (median 83.7, range 9-99, p=0.4) survivors. While there were no significant differences in SCARED (anxiety) or CDI-S (depression) scores between ideal and non-ideal survivors, SCARED (anxiety) scores above the established clinical cut-scores were found in 6/12 (50%) ideal survivors compared to 12/44 (27%) in non-ideal survivors. In addition, higher CDI-S (depression) scores above the clinical established cut score were found in 2/13 (15%) ideal survivors compared to 5/44 (11%) non-ideal survivors.

Image:
Conclusion: Amongst subjects meeting the recently proposed “ideal survivor” profile, defined as a first allograft stable on immunosuppression monotherapy, normal growth, and absence of common immunosuppression-induced sequelae, HRQOL assessment was not significantly better in ideal survivors compared to non-ideal survivors. Attention to the risk for anxiety remains an important finding for the long-term survivor of pediatric LT.


Disclosure of Interest: None Declared
ETHNIC DISPARITY IN INCIDENCE AND OUTCOME OF BILIARY ATRESIA IN NEW ZEALAND CHILDREN

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Objectives and Study: Biliary atresia (BA) is the commonest liver disease in infancy. Incidence in Europe and North America is approximately 1/20,000 live births but commoner in Taiwan (1/8000) and French Polynesia (1/3000). Corrective Kasai portoenterostomy can prevent or delay the need for liver transplantation (LT) but is most successful if performed before 6-8 weeks of age. Aim was to investigate the incidence of BA in New Zealand children

Methods: Casenote review of all new presentations of BA at Starship Hospital 2002-2013 and comparison to Statistics New Zealand birth rate data for Auckland-born children. Ethnicity was recorded according to parental report. Outcomes for Kasai success (bilirubin < 20 mmol/L by 6 months), need for liver transplantation and overall survival were calculated overall and according to ethnicity.

Results: 75 children (36M; 39F) presented with BA. Ethnicity was European in 25 (33%), Maori in 31 (41%), Pacific in 12 (16%), South East Asian in 4 (5%) and Other in 3. Overall incidence was 1/8,002 but 1/17,893 for European babies and 1/5,430 for Maori children. Maori babies presented earlier than European babies (median 31 days versus 46 days), were more likely to have a successful outcome following Kasai (62% successful versus 20%) and proceeded to LT later (4.8 years compared to 0.8 years). Need for LT was high overall with transplant-free survival being 70%, 49% and 30% at 1, 2 and 5 years of age respectively but overall survival was 92%, 87% and 86% at these timepoints.

Conclusion: BA is commoner in New Zealand likely due to an excess incidence in Maori children who have better outcomes related to earlier presentation and operation. It is important that Maori infants with prolonged jaundice are promptly investigated for BA.

Disclosure of Interest: None Declared
OUTCOME IN ADULTHOOD OF BILIARY ATRESIA CHILDREN WHO WERE NOT TRANSPLANTED AFTER THE KASAI OPERATION: A 20 TO 39 YEARS EXPERIENCE AT A CHILDREN’S HOSPITAL.

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Objectives and Study: to assess outcome into adulthood after Kasai Portoenterostomy (PE) for biliary atresia (BA), with a follow-up ranging from 20 to 39 years.

Methods: Medical records of 156 patients who had undergone Kasai Portoenterostomy (KPE) at our Department between 1975 and 1994 were retrospectively reviewed. For patients actually alive with their native liver, data (weight, height, body mass index (BMI), pregnancies, possible use of assisted reproduction techniques, level of education, any sport practiced, reports of recent blood tests, abdominal ultrasound and esophagogastroduodenoscopy) were collected by telephone interviews or email or social networks.

Results: Twenty-four (15%) out of 156 patients were lost before they reached the intended follow-up: at the last control 15 of these were jaundice free and 9 were icteric; all were alive with their native liver. Median time of the last follow-up was respectively 11 year (range: 4 months-19 years) in jaundice free group and 9 months (range: 3 months-16 years) in icteric group. Thirty (19%) out of the remaining 132 patients died when all were less than 20 years old. 102 patients are alive: 85 (54%) were transplanted and 17 patients (11%) have their native liver. We were able to contact only 11/17 patients, 6 males and 5 females: of whom 10 are actually alive without jaundice and 1 is sub-icteric (total bilirubin 2.95). Survivor median BMI is 20.2 (range from 18.3 to 28.8). Three out of 6 female patients had sons, all naturally conceived. Level of education and occupation of all patients are in line with national rates. Six patients make regular sporting activity.

Conclusion: KPE is universally accepted as the first therapeutic choice for neonates and infants with biliary atresia, but its long-term efficacy remains controversial. Ten-years survival rates in BA patients with their native liver after PE have been reported to range from 13% to 60%, but there are few data on their outcomes into adulthood. All patients we were able to contact who surviving longer than 20 years with their native liver, referred excellent quality of life; normal growth, and level of education, procreative capacity and occupation which are in line with national ones.

Disclosure of Interest: None Declared
LOW IMMUNOGENICITY OF ALGINATE MICROENCAPSULATED HUMAN HEPATOCYTES IN VITRO AND IN VIVO

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Objectives and Study: Transplantation of alginate microencapsulated human hepatocytes (human hepatocyte microbeads; HMBs) is an attractive approach for the management of acute liver failure. The biocompatibility and immunogenicity of the HMBs is an important issue for efficacy following intraperitoneal transplantation. Aim: To investigate the alloimmune response towards clinical grade HMBs after exposure to human ascitic fluid to mimic the intraperitoneal environment in vitro and also test the suitability of HMBs for transplantation in vivo.

Methods: Empty microbeads (EMBs) and HMBs were produced using sterile, ultrapure sodium alginate. Peripheral blood mononuclear cells (PBMCs) and ascitic fluid were obtained from patients with acute-on-chronic liver disease. Five experimental sets were carried out; PBMCs monoculture (control), EMBs-PBMCs co-culture, EMBs (ascites-exposed)-PBMCs co-culture, HMBs-PBMCs co-culture, and HMBs (ascites-exposed)-PBMCs co-culture groups. Microbeads morphology was examined before and after co-culture with PBMCs. The activation of PBMCs and the intracellular cytokines production were analysed 24h post co-culture using flow cytometry (FACS). Microbeads were transplanted intraperitoneally into two groups of normal rats; HMBs (n=3) and EMBs (n=3) and followed up for 7 days.

Results: Microbeads were of uniform in shape and size (500±SD100μm). After 24hr in co-culture with PBMCs, EMBs and HMBs (both exposed and non-exposed to ascitic fluid) were intact without any PBMCs adherent to their surface. The percentage of T-cells, B cells, NK cells and monocytes positive for surface activation markers was not significantly different between all groups. There was no difference in the frequency of cells producing cytokines (IL-2, IL-4, IL-6, IL-10, IL-17, IFN-g, and TNFα) after PBMCs stimulation with cell stimulation cocktail (plus protein transport inhibitors) in the five groups. When transplanted into rats, there were no signs of inflammation or adhesion of microbeads to any structure within the peritoneal cavity and a large proportion of the transplanted microbeads (60-80%) could be retrieved from the rats after 7 days. Microbeads were intact without any deformity and less than 1% of EMBs were minimally covered with adherent host cells. Explanted HMBs in culture still showed hepatocytes viability, and function (albumin and urea synthesis and cytochrome P450 activity).

Conclusion: This study has demonstrated that clinical grade human hepatocyte microbeads were biocompatible with the human PBMCs in vitro and did not provoke reaction when transplanted in vivo. These findings support the clinical application of hepatocyte microbeads transplantation without the need for immunosuppression.
Disclosure of Interest: None Declared
DYSFUNCTION OF TREG SUBSETS WAS ASSOCIATED WITH ABERRANT IMMUNE RESPONSES IN BILIARY ATRESIA

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Objectives and Study: Deficiency of regulatory T cells (Tregs) has been reported to result in exaggerated inflammatory and immune responses in biliary atresia (BA). CD45RA⁺FoxP3⁻ resting Treg cells (rTreg cells) and CD45RA⁻FoxP3⁺ activated Treg cells (aTreg cells) are new definition of Treg subsets, which are highly informative in assessing the dynamics of Treg differentiation. The aim of this study was to identify the frequencies of Treg subsets in BA patients at different stages and whether dysfunction of Treg subsets was associated with aberrant immune responses in BA.

Methods: Between 2013 and 2014, PBMCs were collected from 20 early-stage BA patients (age from 1m to 3m), 25 late-stage BA patients (age from 6m to 8m) and 14 age-matched control patients. 12 of the late-stage patients were followed up at 2 weeks after liver transplantation. Treg subsets, IFN-γ-producing T cells and IL-4-producing T cells were detected by flow cytometry. Tregs were isolated by a high-gradient magnetic cells sorting system.

Results: Deficiencies of rTreg cells were detected in both BA groups compared to controls, with striking deficit in late-stage group (proportion among CD4⁺ T cells: early-stage: 4.16±0.51%, late-stage: 3.22±0.98%, control: 5.75±0.89%), while the decrease of Tregs was only observed in late-stage group. Notably, there was an increase in the proportion of aTreg cells in early-stage BA group (0.36±0.28% versus 0.16±0.09% in controls, P=0.032). Furthermore, simultaneous increase in IFN-γ-producing T cells and IL-4-producing T cells were observed in 90% (18/20) of early-stage BA patients and 88% (22/25) of late-stage BA patients. A positive correlation was identified between the proportions of IFN-γ-producing T cells and IL-4-producing T cells in all BA patients (r=0.634; p<0.001). We also found that compared with preoperative values, the percentage of rTreg cells apparently increased at 2 weeks after liver transplantation (3.21±1.13% versus 4.42±2.02%, P=0.012), combined with a notable decrease in IFN-γ-producing T cells (14.08±10.23% versus 6.35±3.72%, P=0.025) and IL-4-producing T cells (2.68±1.81% versus 1.84±1.30%, P=0.042). Further exploring the role of Tregs to regulate effector T cells, purified Tregs from controls were cultured with PBMCs from BA patients. The results revealed that transfer of Tregs apparently suppressed IFN-γ-producing T cells (6.85±1.28% versus 3.89±1.08%, P<0.001) and IL-4-producing T cells (2.53±0.83% versus 1.83±0.68%, P=0.041).

Conclusion: Deficiencies of rTreg cells were persistent over time in BA patients, with elevation of aTreg cells in early-stage BA patients. Tregs transfer study and postoperative values demonstrated that dysfunction of Treg subsets was associated with aberrant Th1 and Th2 immune responses in BA.
Future studies aimed at expanding Treg subsets in vivo may eventually translate to clinical therapies for BA.

References:

Disclosure of Interest: None Declared
DETERMINATION OF BIFIDOBACTERIUM AND LACTOBACILLUS IN BREAST-MILK OF HEALTHY WOMEN BY DIGITAL PCR

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Objectives and Study: Breast-milk has been shown not only to provide nutrients and bioactive/immunological compounds, but also commensal bacteria, including gut-associated probiotic bacteria. Quantitative real-time polymerase chain reaction (qRT-PCR) is currently used for quantitative analysis of probiotic 16S ribosomal RNA (16S rRNA) gene in human breast-milk. However, it relies on standard curves and its precision is low when quantitating low abundant target DNA. Droplet digital PCR (DD-PCR) provides absolute quantitation without the need for calibration curves. A comparison between DD-PCR and qRT-PCR was conducted for the quantitation of Bifidobacterium and Lactobacillus 16S RNA gene in human breast-milk.

Methods: Samples of breast-milk were collected on 42 days postpartum from 25 mothers in sterile tubes by manual expression using sterile gloves. Then, total DNA was isolated from the pellets using the QIAamp DNA Stool Mini Kit. Genus-specific primers and probes were designed according to the 16S rRNA regions. Taqman-based qRT-PCR and DD-PCR was run on 7300 real-time PCR system and QX100™ droplet digital PCR system, respectively.

Results: From the standard curves, qRT-PCR and DD-PCR exhibited high linearity from $10^3$ to $10^6$ and from $10^4$ to $10^5$ copies of rDNA standards, respectively. DD-PCR showed a 100-fold greater sensitivity than qRT-PCR. From our study, DD-PCR reported 0~34460 copies of Bifidobacterium and 1108~63400 copies of Lactobacillus in 1 ml human breast-milk (Fig.1). The variations of Bifidobacterium and Lactobacillus copy number in all milk samples were obvious. The copy number of Lactobacillus species was much more than that of Bifidobacterium species in human breast-milk (P<0.05). A high correlation was exhibited in Lactobacillus quantitation between qRT-PCR and DD-PCR ($R^2$=0.829, P<0.05). However, the correlation of Bifidobacterium quantitation between qRT-PCR and DD-PCR was poor ($R^2$=0.265, P>0.05). The DNA counts obtained from qRT-PCR was 6.16-fold higher than that obtained from DD-PCR for Bifidobacterium quantitation (P<0.05), but this value was as much as 62.9% lower for Lactobacillus quantitation (P<0.05).
Conclusion: This study confirmed that breast-milk contains *Bifidobacterium* and *Lactobacillus* species that may promote healthy microbiota development, and DD-PCR may be a better tool to precisely quantitate the bacterial DNA in breast-milk in comparison to conventional qRT-PCR.

Disclosure of Interest: None Declared
IMPACT OF DIFFERENTIAL ENTERAL PROTEIN INTAKE ON GROWTH IN PRETERM INFANTS LESS THAN 32 WEEKS

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Objectives and Study: Impact of differential enteral protein intake on growth in preterm infants less than 32 weeks

Methods: Study design Randomized controlled trial.

Study population: All preterm Babies <1500 gm or less than 32 weeks of gestation admitted in Neonatal intensive care unit (NICU) of Sir Ganga Ram Hospital.

Intervention

All babies less than 1500 gm or < 32 weeks were enrolled in this when they reached a feed volume of 100 ml/kg/day. They were randomly assigned to either group A with high enteral protein intake or to the group B with standard enteral protein intake. In Group A neonates received higher protein containing fortifier (1 gm/100ml Expressed breast milk (EBM)). In group B, neonates received standard protein fortifier (0.4 gm protein/100ml EBM).

Results: A total of 120 infants were randomized, 60 in each group. Baseline characteristics of the enrolled babies were similar. In group A, the mean gestation (SD) was 29.93±2.1 weeks which was comparable to mean gestation of 30.43±2.3 weeks in group B. Mean birth weight was 1197±298 gms in group A as compared to 1241±243 gms in group B. Age at enrolment was 6.7±4.7 days in group A and 6.49±4.6 days in group B.

The neonates in group A received higher percentage of EBM as compared to those in group B (57.8% vs 47.1%, P=0.039). The protein intake of the babies from enrolment to discharge was significantly higher in Group A (4.2±0.47gm/kg/d) as compared to group B (3.6±0.37gm/kg/d, P<0.001), however the calorie intake was comparable.

At 40 weeks corrected age the weekly increase in occipto frontal circumference (OFC) was also significantly higher in group A (0.66±0.16) as compared to group B (0.60±0.15), P=0.04. Weight gain in group A was 11.94±2.2 gm/kg/day as compared to 10.79±2.6 gm/kg/day in group B, (P=0.01). However no significant difference was observed in the length between the two groups.

The enrolment weight, median days to regain birth weight and days to reach full feeds were comparable in two groups. The incidence of feed intolerance and NEC was also similar in infants in the two groups. Biochemical parameters were comparable in two groups except for Blood urea nitrogen (BUN) which was significantly higher in higher protein fortification group.

Conclusion: High enteral protein intake resulting from fortification of human milk with higher protein fortifier in preterm babies results in better weight gain and head growth at 40 weeks corrected age.

References: _
Disclosure of Interest: None Declared
THE ABILITY TO ATTEND IN SOCIAL INTERACTION IS INFLUENCED BY LONG-CHAIN SATURATED AND MONOUNSATURATED FATTY ACIDS IN PREMATURE INFANTS

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Objectives and Study: Long chain saturated and monounsaturated fatty acids are important for the development of white matter during the last trimester of gestation and the first years of life. Milk of mothers to premature infants has high concentrations compared to donor human milk (PLEFA 2013), which might indicate important role for nutrition of premature infants. We have earlier reported (ESPGHAN 2014) that nervonic acid (NA, 24:1w9) influenced the mental and motor development in the second half of the first year. Regarding lignoceric (LiA, 24:0) and oleic (OA, 18:1w9) acids, which also are important for myelination, no data about relation to early infant development are reported. The aim of this study was to investigate whether there was a relation between LiA, and/or OA and early development in a prospectively followed cohort of premature infants.

Methods: Forty-four infants born after 29-36 w gestation (59 % late premature) were investigated at 1 m corrected age (44 w) with Brazelton Neonatal Behavioral Assessment Scale (BNBAS). Fatty acid pattern in breast milk at 1 w (n=50) and in plasma phospholipids at 44 w (n=44) were determined with GLC. The results were analyzed involving 7 background factors and the influence of major omega-6 and omega-3 fatty acids, which results have been earlier reported (Early Human Devel 2010).

Results: Alertness was correlated to three factors: OA in plasma (β 0.32, p 0.019), the ratio in breast milk of omega-6/omega-3 (β -0.30, p 0.026) and gestational age (β 0.27, p 0.043), R² 0.34. The item animate visual orientation in BNBAS correlated with LiA concentration in plasma (r= 0.50, p 0.001). Multiple linear regression analyses showed significant correlation to LiA (β 0.33, p 0.024) and with gestational age, accounting for 28% of the variability. Similarly, the item animate visual and auditory orientation was related to OA concentration in plasma (β 0.30, p 0.020), and with LiA β 0.27, p 0.049) and sex of infants, accounting for 40% of the variability (R² 0.40).

Conclusion: The results indicate that early plasma levels of LiA and OA, which are important for myelination, are associated with early social interaction assessed by the BNBAS, also when long-chain polyunsaturated fatty acids are included in the analyses The infant’s ability to interact is of great importance for the attachment process with the mother (infant bonding), which is considered to influence further development.

Disclosure of Interest: None Declared
Objectives and Study: Maternal obesity can result in negative outcomes with long term consequences for both, women and child. Children have higher risk of obesity, heart disease and type 2 diabetes (Leddy et al., 2008). Little is known about the linkage between mothers’ body fat percentage (BFP) and the fatty acid composition of human milk. We aimed to test the hypothesis that fatty acid content and composition of human milk is linked on mothers’ body fat, focusing on skinfold thicknesses.

Methods: 106 women, included in the "My Milk" project (www.moje-mleko.si/en), who exclusively breastfed their singleton infants for at least one month, were included in the study. We determined fatty acid content and composition (weight percent; wt. %) of their mature human milk (equal mixture of fore- and hind-milk) at one month post partum. Anthropometric measurements of mothers were performed at the same time (body mass, body height, and skinfold thicknesses) by which BFP (according to Slaughter et al., 1988) was calculated. Women were classified by BFP (cut-off point set at 30%) into two subgroups, whose fatty acid composition of human milk was compared by t-test.

Results: In total, we identified 31 fatty acids in human milk. Total fat percentage in human milk was (mean (SD))2.6(0.5) in a group of <30% body fat, and 4.3(0.8) in a group of >30% body fat. BFP in a group of <30% body fat was 26.1(2.6), in a group of >30% body fat was 33.9(2.8)). Significant positive association between BFP and fatty acid composition of human milk was observed for the following fatty acids in human milk: C10:0, C22:1n-9, C20:5n-3, C24:1n-9, as well as for total fat % in human milk (p<0.05 for all). No further associations were found between BFP and other fatty acid or the n-6/n-3 ratio.

Conclusion: Lactating women with higher BFP synthesised human milk with higher fat content. BFP of lactating mothers was positively associated with fatty acid composition of human milk at one month post-partum for four fatty acids (C10:0, C22:1n-9, C20:5n-3 and C24:1n-9). In the future, total volume and energy content of ingested human milk (ml/day, kcal/day) would be of interest to compare with anthropometrical characteristics of infant-mother pairs.


Disclosure of Interest: None Declared
**Nutrition**

*Clinical Nutrition*

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**THE RELATION BETWEEN INTERLEUKIN-6 174 G/C GENE POLYMORPHISM AND CHILD OBESITY**

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**Objectives and Study:** The etiology of obesity is much more than the imbalance between intake and energy expenditure, obesity is a plurifactorial condition, resulting from the interaction of multiple factors, of which genetic aspects are increasingly studied lately. The polymorphism of Interleukin 6 (IL-6) gene influences the production, as well as level of this cytokine. **The aim** of the study was to establish the relation between IL-6 174 G/C gene haplotype and obesity in a group of obese children from Romania, inflammation associated with obesity being an issue much studied in recent years, but less in children.

**Methods:** A number of 183 patients consecutively hospitalized in a tertiary emergency pediatric hospital were assessed in terms of IL-6 174 G/C gene polymorphism, as well as anthropometrical and biochemical. The patients were divided depending on the nutritional status in two groups: group I, the witness group included 101 patients with normal BMI, and group II included 82 children with obesity (BMI over 95 percentile). The evaluated anthropometric parameters were middle upper arm circumference (MUAC) and tricipital skin-fold thickness (TST), while paraclinical tests included protein, albumin, leptin and adiponectin.

**Results:** We observed that in obese children, for polymorphism IL-6 174 gene there was a association of CG alleles in 62.7% of cases (p = 0.001), whereas the CC genotype of IL-6 174 was a protective factor for obesity. We applied a multivariate regression in which leptin was the dependent variable, and the others - independent variables; leptin was dependent of IL-6 174 polymorphism and of albumin [p = 0.01, OR 2.3776 95% CI (1.456-5.367)], while adiponectin was dependent only of gene IL 6-174 polymorphism [p=0.0120, OR 1.394 95% CI (1,131-2,356)]. Adiponectin correlated only with phenotype GC (p = 0.001), while regarding anthropometric indices, MUAC correlated with G/C phenotype and TST with all phenotypes.

**Conclusion:** CC genotype of IL-6 174 may be a protective factor for obesity. Leptine and also adiponectine were dependent of IL 6-174 polymorphism. MUAC was correlated with C/G genotype, while TST correlated with all phenotypes. Further studies are needed to clarify the role of these polymorphisms in child nutritional disorders.

**References:**

**Disclosure of Interest:** None Declared
Nutrition

THE ASSOCIATION OF PERINATAL GROWTH WITH ENERGY INTAKE AND SATIETY RESPONSE AT 5-6 YEARS OF AGE – THE ABCD STUDY

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Objectives and Study: Low birth weight and accelerated postnatal growth are associated with an increased risk of obesity and subsequent cardiometabolic disease in later life. The mechanisms how birth weight and postnatal growth influence later obesity risk are unknown, but effects on energy intake and eating behavior have been proposed to play a role. Our objectives were to assess the independent associations of birth weight and postnatal weight and height during different periods with energy intake and satiety response at 5-6 years of age.

Methods: We used data from 2,227 healthy children (52% male), mean age 5.6 (±0.4) years participating in a prospective birth cohort study (the Amsterdam Born Children and their Development study). Energy intake and satiety response were parent-reported through Food Frequency Questionnaires and Child Eating Behavior Questionnaires, respectively. Exposures were birth weight z-score and conditional weight and height between 0-1, 1-3, 3-6, 6-12 months and 12 months to 5 years, which are residuals of current weight and height regressed on prior growth data, to represent deviations from expected growth. Analyses were adjusted for sex, gestational age, smoking during pregnancy, infant feeding, parental BMI, socio-economic status, ethnicity, and current age, BMI and height.

Results: Children had a mean energy intake of 1531 (±338) kcal/day, and a satiety response subscore of 2.37 (±0.50) on a 4-point Likert-scale. Conditional weight gain in early infancy (1-3 and 3-6 months) and childhood (12 months to 5 years) were negatively associated with energy intake, with 24.0 kcal/day (95% CI: 1.8; 46.1. P=0.03) and 79.5 kcal/day (95% CI: 29.4; 129.7. P=0.002) more intake for each Z-score conditional weight gain in infancy and childhood, respectively. Conditional height gain during 0-1, 1-3 months and 12 months to 5 years was negatively associated with energy intake (β at least -35.1 kcal/day per Z-score conditional height gain [95% CI: -58.4; -11.8. P=0.003]). Conditional weight gain in all periods was negatively associated with satiety response, with effect sizes from -0.03 (95% CI: -0.06; -0.002. P=0.03) in early infancy to -0.12 (95% CI: -0.19; -0.06. P<0.001) in childhood. Birth weight was not associated with either energy intake or satiety response.

Conclusion: Our findings suggest that excessive infant and childhood weight gain are associated with increased energy intake and diminished satiety response at 5-6 years. Rapid height gain seems to be beneficial for childhood energy intake. Public health strategies addressing childhood obesity prevention through optimization of feeding patterns should also focus on optimization of childhood growth.
References:

Disclosure of Interest: None Declared
FEEDING DIFFICULTIES IN CHILDREN WITH A TRACHEOSTOMY TUBE

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Objectives and Study: Nutritional deficiencies and swallowing difficulties in young children with tracheostomy have been unrecognized for years. The aim of this study is to identify which feeding and swallowing problems occur among children with a tracheostomy tube.

Methods: Descriptive analysis. Medical history and data on feeding and swallowing difficulties were obtained from the electronic patient record and/or during an outpatient visit to the multidisciplinary team. The results of logopedic consultations and additional investigations including Fibre Endoscopic Evaluation of Swallowing (FEES) and Video Fluoroscopic Swallowing Study (VFSS) were evaluated.

Results: 35 non-ventilated children (57% male) with a tracheostomy tubes for various causes of upper airway obstruction were included. Mean gestational age was 36 5/7 weeks, 9 preterm born and 9 children with a clinical syndrome.

In 27 children the tracheostomy tube was placed in the first year of life. Twenty-two children received tube feeding.

Physical examination depicted that 10 children (27%) were drooling and 20 (57%) patients showed feeding difficulties in the oral and/or pharyngeal phase; 17% (all with tube feeding) in the oral phase, 14% in the pharyngeal phase and 26% in oral and pharyngeal phase. Additionally, in 9 children aspiration was confirmed using FEES and/or VFSS. In the other 11 children, aspiration was so obvious that no additional studies were done. Children who received a tracheostomy tube within their first year of life showed the most logopedic problems. Children who didn't receive tube feeding had no feeding difficulties.

Conclusion: Feeding difficulties both in the oral and pharyngeal phase are common in children with tracheostomy tubes. Early logopedic examination and treatment should be part of the standard care in children with a tracheostomy tube.

Disclosure of Interest: None Declared
THE MILK OLIGOSACCHARIDE 2'-FUCOSYLACTOSE MODULATES BRAIN FUNCTION BY ACTIVATION OF THE GUT-BRAIN AXIS THROUGH THE VAGUS NERVE.

Enrique Vazquez 1 Alejandro Barranco 1 Maria Ramirez 1 Maria Luisa Jimenez 1 Agnes Gruat 2 Jose Maria Delgado-Garcia 1 Pedro Prieto 3 Rachael Buck 3 Ricardo Rueda 1

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Objectives and Study: Human milk is unique regarding its diversity, quantity and complexity of human milk oligosaccharides (HMOs), and 2'-fucosyllactose (2'-FL) is the most abundant HMO. Recently, we reported that orally administered 2'-FL modulates brain function, as measured by behavioral tests and hippocampal long term potentiation (LTP). The ability of synapses to change strength is considered one of the major mechanisms underlying learning and memory. Experimentally-induced LTP has been proposed as a model to replicate the cellular changes in synapses that occur during cognitive function. Moreover, electrical stimulation of the vagus nerve induces a stronger hippocampal LTP.

Aim: To investigate if vagus nerve stimulation is involved in modulating central nervous system functions induced by dietary supplementation with 2'-FL.

Methods: Young adult Sprague Dawley rats underwent bilateral subdiaphragmatic vagotomy or sham surgery. Rats were fed AIN93M diet control or supplemented with 2'-FL (350 mg/kg BW) for five weeks. Animals (n = 8-10 per group) were checked with an instrumental conditioning test in the Skinner box, as well as with experimentally evoked LTP. Electrodes were surgically implanted in the hippocampus (CA1 area). To evoke LTP, we used a high frequency protocol (HFS). After the HFS protocol, field excitatory post-synaptic potentials were recorded again for 30 min. Additional recordings were carried out for 15 min during the 3 following days.

Results: The 2'-FL-Sham group presented a better performance in the Skinner box test as well as a significantly larger LTP, as compared with the Control Sham group. Vagotomy diminished the potentiating effects of 2'-FL, both on LTP and in instrumental conditioning learning.

Conclusion: These results confirm our previous observation that oral 2'-FL facilitates hippocampal LTP and enhances cognitive skills. Since vagus nerve integrity is required for this effect, oral 2'-FL may improve brain function by direct modulation of enteric neurons, and subsequently transmission to the brain through the vagus nerve.

HIPPOCAMPAL METABOLITES CORRELATE WITH NEUROIMAGING OUTCOMES IN THE PIGLET

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Objectives and Study: By combining magnetic resonance imaging (MRI) and metabolomic profiling techniques, the objective of this study was to elucidate relationships between brain structure and hippocampal metabolites in the piglet.

Methods: Two-day-old, vaginally-delivered male piglets (n=24) were artificially reared using standardized procedures and feeding a custom milk replacer formulated to meet piglet nutrient requirements. At 30 d of age, piglets underwent MRI procedures, and brain tissue was collected 24 h post-imaging for metabolomic and lipodomic profiling of hippocampal tissue. Analysis of MRI data in 19 brain regions yielded volumetric estimates as well as microstructural details measured by diffusion tensor fractional anisotropy (FA), and radial (RD), axial (AD), and mean (MD) diffusivities, which provide directional characterization of water movement within axons.

Results: Comparison of fatty acids in n-3, n-6, and n-9 categories with MRI measures yielded correlations (P < 0.05) in 150 of 2726, 162 of 3596, and 129 of 2494 possible outcomes, respectively. Neuroimaging outcomes that were highly correlative across fatty acid categories included MD, RD, and AD in the internal capsule and right hippocampus, suggesting ongoing myelination in the piglet brain. Nervonic acid, a fatty acid known to be prevalent at peak myelination, was correlated with 26 of 58 total outcomes, further supporting the link between metabolism and neurodevelopment.

Conclusion: Significant correlations between metabolic and structural outcomes in the neonatal piglet brain emphasize targets whereby dietary manipulation may alter neurodevelopmental patterns. (Supported by Mead Johnson Nutrition).

Objectives and Study: Identifying nutritional strategies to optimize early-life development is a relevant and important focus of pediatric nutrition research. The piglet has been accepted as the best pre-clinical model of infant development. The goal of the current study was to investigate a novel mixture of prebiotics and bioactive whey components on piglet intestinal and brain development.

Methods: Beginning at 2 d of age, 24 male pigs received either a control formula (CONT) or test formula containing a prebiotic blend of polydextrose and galactooligosaccharides with bioactive whey protein fractions (TEST) for 30 days. Neuroimaging was used to quantify brain composition and structure while intestinal histomorphology, vasoactive intestinal peptide (VIP) expression, and disaccharidase activity were measured as markers of gut development and function.

Results: Pigs fed TEST had greater (P < 0.05) jejunal lactase activity, increased (P < 0.05) ileal VIP expression and small intestine morphology comparable to CONT. Analysis of brain microstructure by diffusion tensor imaging indicated lower (P < 0.05) mean and radial diffusivities values in the internal capsule (IC) of TEST-fed pigs, suggesting advanced white matter development in TEST-fed pigs. Since the IC is one of the first subcortical structures to myelinate, these data may indicate advanced brain maturation in the TEST-fed pigs.

Conclusion: A combination of nutritional technologies elicited changes in gut functions and brain microstructure that may translate into functional benefits. However, future research is warranted to explore how these changes may impact other aspects of piglet development. (Supported by Mead Johnson Nutrition).

ACUTE UPPER GASTROINTESTINAL BLEEDING IN CHILDHOOD: DEVELOPMENT OF THE SHEFFIELD SCORING SYSTEM TO PREDICT NEED FOR ENDOSCOPIC THERAPY.

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Objectives and Study: Acute upper gastrointestinal bleeding (AUGIB) is a rare and potentially life threatening condition in childhood. In adults with AUGIB validated scoring systems exist but these are not applicable to children. The aim of this study was to construct a clinical scoring system to accurately predict the need for endoscopic haemostatic intervention.

Methods: A retrospective data collection occurred over a three year period at a tertiary children's hospital. A total of 69 patients who had had endoscopic assessment were divided into Group 1 (no endoscopic haemostasis required) and Group 2 (endoscopic haemostasis required). A wide range of clinical parameters were collated including: pre-existing conditions; melaena; haematemesis and degree; transfusion requirement; parameters of hypovolaemia; presenting haemoglobin (Hb); Hb drop over 24 hours; platelet count; coagulation indices; liver function tests; and urea/electrolytes.

Results: Parameters which reached statistically significance for endoscopic intervention (Group 1 v 2) were: presence of significant pre-existing condition; melaena; large haematemesis; heart rate (HR) >20 mean HR for age; prolonged capillary refill time; Hb drop of more than 20 g/l; need for fluid bolus; need for blood transfusion (Hb<80g/l); and need for other blood products. Using these parameters a number of scoring models were tested with multiple regression, and the most predictive resulted in a scoring system constructed with a total=24 and a cut off for intervention of 8.

The scoring system consists of the following: significant pre-existing condition: 1; presence of melaena: 1; history of large amount of hematemesis: 1; heart rate more > 20 from the mean heart rate for age: 1; prolonged capillary refill: 4; haemoglobin drop of more than 20 g/l: 3; need for a fluid bolus: 3; need for blood transfusion (haemoglobin < 80g/l): 6, need for other blood product: 4. Using this model would have resulted in 4 false negatives in the interventional group and 3 false positives in the non-interventional group. Hence: PPV of 91.18% (95% CI: 76.3% to 98.04%); NPV of 88.57% (95% CI of 73.24% to 96.73%); sensitivity of 88.7% (95% CI: 73.24% to 96.73%); and specificity of 91.18% (95% CI of 76.3% to 98.04 %).

Conclusion: In our study population, we were able to formulate a scoring system with good positive and negative predictive value for endoscopic haemostatic intervention in AUGIB in children. This may prospectively be studied and potentially lead to appropriate endoscopic intervention in this paediatric emergency.

Disclosure of Interest: None Declared
PROCTITIS IS A FREQUENT LOCATION OF PAEDIATRIC-ONSET ULCERATIVE COLITIS AND IS NOT A MINOR DISEASE: A POPULATION-BASED STUDY

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Objectives and Study: Natural history of paediatric-onset proctitis is poorly described. Our aim was to study the phenotype and disease course of proctitis in a population-based paediatric-onset ulcerative colitis (UC) cohort.

Methods: We included all patients from a population-based cohort with a definite or probable UC diagnosis <17 y between January 1988 and December 2004, and a follow-up >2 y. UC location was defined according to the Paris classification (1). Cumulative risks of colonic extension, treatment with immunosuppressants (IS) (azathioprine, methotrexate) and/or anti TNF, and colectomy were estimated using Kaplan-Meier method and compared between groups by log-rank tests. Risk factors for colonic extension were assessed using Cox hazards proportional models.

Results: 158 paediatric-onset UC patients (91 females) with a median follow-up of 11.4 y (Q1: 8.2-Q3: 15.8) were recorded; 40 (25%) of them had proctitis (E1) with a median age at diagnosis of 14 y (Q1=11-Q3=16). There was no difference between the E1 group and the more extensive UC group (E2-E3-E4) with respect to gender, age at diagnosis, family history of IBD, delay in diagnosis, and presence of extra-intestinal manifestations. At maximal follow-up, colonic extension occurred in 48% of patients with E1 (33% progressed to E2; 3% to E3; 13% to E4). Cumulative risk of colonic extension was 10% at 1 y 45% at 5 y, 52% at 10 y, and 52% at 15 y. No factor was associated with colonic extension in the E1 group, including gender, presence of mucus, abdominal pain and diarrhoea. Only corticosteroid treatment seemed to be associated with colonic extension (HR=2.37, p=0.06 (CI: 0.96-5.84). Patients with E1 received significantly less IS than those of the E2-E3-E4 group (10% vs 39% at 10 y; p=0.049). Cumulative risk for colectomy was 3% at 1 y, 10% at 5 y, 13% at 10 y, and 13% at 15 y. There was no difference between the E1 group and the E2-E3-E4 group with respect to risk for colonic extension, treatment with anti TNF, and risk for surgery.

Conclusion: Ulcerative proctitis is frequent in paediatric-onset ulcerative colitis and should not be considered as a minor disease. Compared to more extensive forms (E2-E3-E4), characteristics at diagnosis, risk for colonic extension, risk for anti TNF treatment, and risk for colectomy were similar, while the risk for treatment with immunosuppressants was low.

Disclosure of Interest: None Declared
**Hepatology**

**Transplantation**

CP-H-0017

**OUTCOME OF 250 PEDIATRIC LIVING DONOR LIVER TRANSPLANT RECIPIENTS: VASCULAR RECONSTRUCTION, ABO INCOMPATIBILITY AND RISK FACTORS OF REJECTION**

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**Objectives and Study:** Pediatric living donor liver transplantation (LDLT) including ABO-mismatched transplants alleviate organ shortage in children. Vascular complications of portal vein (PV) hypoplasia in biliary atresia (BA), and acute rejection (AR) are still major concerns in this field. The aim of this work was to review our experience in our first 250 LDLT cases.

**Methods:** Data, from 250 pediatric LDLT recipients, performed at Cliniques universitaires Saint-Luc between July 1993 and June 2012, were reviewed retrospectively, with a special insight into ABO matching and PV complications. Patient-, graft- and acute rejection-free-survivals were calculated with the Kaplan-Meier method. Uni- and multi-variate analysis was used to study the impact of immunosuppression, gender match and maternal donation on AR rate.

**Results:** One-year, 5-year, and 10-year post-transplant, patient survival rates were 96.0%, 93.9%, and 93.2%, and graft survival rates were 95.0%, 91.5%, and 90.0%, respectively. In the ABO non-identical patients (compatible, n=47; incompatible, n=11), neither patient or graft loss, nor vascular rejection, nor hemolysis were encountered, provided pre-transplant relevant isoagglutinin levels were below 1/16. In BA recipients, the rate of PV complications was lower after portoplasty (4.6%), when compared to truncal PV anastomosis (9.8%) and to jump graft interposition (26.9%, p=0.027). Regarding immunological results, the overall 1-year AR-free survival rate was 48.0%. In parental donation, maternal grafts were associated with higher 1-year AR-free survival (55.2%), when compared to paternal grafts (39.8%, p=0.041), but only in BA patients.

**Conclusion:** LDLT, including ABO-mismatched transplants, constitutes a safe and efficient therapy for liver failure in children. In BA patients with PV hypoplasia, portoplasty seems to constitute the best technique for PV reconstruction and maternal donation might be a protective factor for AR.

**Disclosure of Interest:** None Declared
Objectives and Study: In a previous study we have shown that the Role Reversal method for treating Infantile Feeding Disorders (IFD), focuses on maternal feeding behavior modification without any direct intervention in the child's eating habits or his caloric intake, significantly affected maternal feeding patterns and reduced the incidence of child's food refusal (1). In the present study, we examined prospectively the influence of this method on child's growth parameters and the relation to mother's perception and occupation regarding the child's IFD.

Methods: Mothers of infants and toddlers diagnosed with IFD were invited to participate in the study. Mothers filled out a questionnaire recording patient and parents' behaviors, attitudes and perceptions, at initiation and at the end of treatment (after 3-6 months). Anthropometric data of patients was collected and age- and gender-specific z-scores (SDSs) were determined according to Centers for Disease Control and Prevention (CDC) growth charts.

Results: Twenty-nine pairs of IFD patients, 23.1±15.7 months, and their mothers, participated in the study. Mean patients' weight for age was -1.48±1.45 SDS and 18 (60%) of them were diagnosed with Failure to Thrive (FTT) after crossing two major lines of the CDC growth charts. Following treatment, an increase or stabilization of weight gain (\(\Delta\text{Weight-Z Score}\geq 0\)) was found in 15 (52%) patients, 11 (73%) of them had had FTT. Weight gain was inversely correlated with patient's age (\(p<0.05\)) and maternal extent of occupation regarding patient's IFD (\(p<0.05\)). \(\Delta\text{Height-Z Score}\geq 0\) were found in 12 of 21 patients (57%). Higher levels of maternal education was associated with greater success in the program.

Conclusion: Modification of maternal feeding patterns alone, using the Role Reversal method, can improve growth parameters of patients with food refusal and FTT. This method was found to be more effective when applied in younger children.


Disclosure of Interest: None Declared
CRITICAL THINKING DURING LEARNING NEW TECHNIQUE PREMATURES ORAL FEEDING

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Objectives and Study: Prematures is a group of patients requiring special support to develop oral feeding function. Due to their developmental immaturity they are in higher risk of feeding disorders. Appropriate technique of feeding increases its efficacy and safety, as well as prevents deterioration of feeding disorder symptoms. Nurses are responsible for feeding preterm newborns during their hospitalization as well as for giving parents the instructions how properly feed their child. Hence, nurses should be highly qualified in feeding techniques. Although it is commonly believed that the preterm newborns feeding: do not require special skills, is similar to the healthy and term newborns feeding, do not require any mental predispositions, such as critical thinking about feeding techniques, none of above statements are true.

Aim: Examining changes in nurses’ critical thinking level during training concerning acquisition of new skills in oral feeding technique of preterm infants.

Methods: Trainings for nurses (N = 31) were performed in 5 different Neonatal Intensive Care Units in Poland. The trainings were focused on developing such skills of feeding preterm newborns as: working with the body of the child, selecting accessories for feeding, a selection of oral control and dynamic stabilization and recognizing the signs of baby’s readiness for start and for end of feeding. Training was divided into 4 stages: a lecture about feeding disorders of preterm infants (1), an assessment of participants feeding skills before the beginning of practical work (2), workshops (3), the assessment of feeding skills after training (4). At the end of each stage the level of critical thinking about feeding techniques was examined. Results were analyzed with ANOVA with repeated measures.

Results: The analysis showed significant changes: $F(3,90) = 13.962; p = .0001; \text{eta}^2 = .318$ in level of nurse’s critical thinking. Comparison post-hoc with Sidak’s correction showed positive changes between the measurements (1) and (3) ($p = .001$) and (1) and (4) ($p = .0001$), respectively. Significant changes were also observed between the measurements (2) and (4) ($p = .002$). There were no statistically significant differences between the measurements (1) and (2), (2) and (3) and (3) and (4).

Conclusion: Critical thinking is involved during acquisition of new feeding skills. Mental predisposition to critical thinking about the technique of feeding may change during the proper training.

Disclosure of Interest: None Declared
Allied Health Professionals
Allied Health Professionals (including Nurses and Dieticians)
PO-AHP-0002

Dietary Fibre Intake in Children with Inflammatory Bowel Disease.
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Objectives and Study: High-fiber diet may play a potential anti-inflammatory role in inflammatory bowel disease (IBD), since it has been shown to maintain remission and reduce colonic damage. The aim of the study was to assess the quantity of dietary fiber intake in children with IBD.

Methods: The study group consisted of children who were in clinical remission or with mild ulcerative colitis (UC) or Crohn’s disease (CD), assessed according to PUCAI (Pediatric Ulcerative Colitis Activity Index) or PCDAI (Pediatric Crohn Disease Activity Index), respectively. For the nutritional assessment, a 3-day dietary record method was used. Mean values of dietary fiber and its fractions were calculated based on literature data. Results were compared with adequate intake (AI) for age.

Results: 50 patients were evaluated: 27 with CD and 23 with UC. There were no statistically significant differences in age, weight and height between the CD and UC patients. The average intake of dietary fiber was 15.9 g per person/day, 8.7 g per 1000 kcal and 0.37 g per kg of body weight. Insoluble fiber accounted for 66% (10.5 g/day) and soluble fiber 34% (5.4 g/day). There were statistically significant correlations between fiber intake and age (r=0.32) and between fiber and energy intake (r=0.51). CD patients had higher fiber intake values than UC patients but the differences were not statistically significant. 78% of patients didn’t meet the AI recommendations.

Conclusion: Majority of IBD children with no or mild disease activity had low dietary fiber intake. The results of the study indicate the need for the routine dietary assessment in these patients.

Disclosure of Interest: None Declared
Allied Health Professionals
Allied Health Professionals (including Nurses and Dieticians)
PO-AHP-0003

SUPPLEMENTATION OF PARENTAL NUTRITION IN INFANTS WITH END STAGE LIVER DISEASE TO OPTIMISE NUTRITION STATUS

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Objectives and Study: Optimal nutrition has been increasingly recognized to optimize both short and long-term outcomes for infants waiting for a liver transplantation. A number of infants diagnosed with end-stage liver disease (ESLD) had poor growth with enteral nutrition (EN) support alone due to severe malabsorption and/or poor volume tolerance related to ascites. It is hypothesized using parental nutrition (PN) to supplement EN will optimize nutritional intake of infants with ESLD and improve growth outcomes. Aim: To determine whether supplementation of PN support improves dry weight gain and growth outcomes in infants with ESLD that had poor growth on EN support alone.

Methods: Anthropometric data including weight, tricep skinfold, mid upper arm circumference (MUAC) and thigh circumference was measured on 4 patients with ESLD monthly whilst receiving similar energy and protein intake either by EN only or a combination of EN and PN support. Z scores for all anthropometric measurements were determined through WHO growth charts. Results are expressed as mean ± standard deviation.

Results: All patients in the sample were diagnosed with Biliary Atresia, of which 3 had partial draining Kasai. The age range was between 3 months to 18 months and even distribution of male and females subjects. The mean energy and protein provided with EN support only was 559 ± 55KJ/kg/d and 3.37 ± 0.25g/kg/d respectively. The mean energy and protein provided with a combination of EN and PN support was 536 ± 54KJ/kg/d and 3.44g ± 0.5g/kg/d respectively with an average of 55% of energy from PN. All 4 patients had increase z scores in anthropometric measurements with a combination of PN and EN support compared to EN support only (Table 1).

Table 1: Average Monthly Changes in Anthropometrical Measurement

<table>
<thead>
<tr>
<th>Anthropometric Data</th>
<th>Average monthly change in Z score</th>
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<tbody>
<tr>
<td></td>
<td>EN support</td>
</tr>
<tr>
<td>Weight</td>
<td>0.02 ± 0.96</td>
</tr>
<tr>
<td>MUAC</td>
<td>0.08 ± 0.58</td>
</tr>
<tr>
<td>Tricep skin fold</td>
<td>0.16 ± 0.52</td>
</tr>
<tr>
<td>Thigh circumference</td>
<td>-0.75 ± 0.68</td>
</tr>
</tbody>
</table>

Results suggest that supplementation of PN to EN support can optimize nutritional status in ESLD patients that had poor weight gain on EN support alone, resulting in reduced morbidity. Despite the
associated risk factors of long term PN such as sepsis, supplementing with PN should be considered to optimize nutritional status.

**Conclusion:** Supplementation of PN can lead to dry weight gain and improve growth outcome measures in patients with ESLD that had poor growth on EN support alone despite similar energy and protein intake.

**Disclosure of Interest:** None Declared
Allied Health Professionals

Allied Health Professionals (including Nurses and Dieticians)

PO-AHP-0004

OVERWEIGHT AND OBESITY IN CHILDREN WITH NEWLY DIAGNOSED INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Overweight and obesity rates have been rising in the general pediatric population in Poland, this problem may also refer to children with inflammatory bowel disease (IBD). The aim of the study was to determine the prevalence of overweight and obesity in children with IBD at the time of diagnosis.

Methods: This was a multicenter retrospective study. The study group consisted of children with new cases of IBD diagnosed in 2005-2013 according to the Porto criteria. Hospital admission records were reviewed for demographic and clinical characteristics. BMI-for-age and gender percentile charts were used to define overweight as ≥85th BMI percentile and obesity as ≥95th BMI percentile.

Results: 675 patients were evaluated: 368 with Crohn’s disease (CD) and 307 with ulcerative colitis (UC). Of these, 54.8% were boys and 45.2% were girls. There were no statistically significant differences in age, weight, height and disease activity between the CD and UC patients. The UC patients had higher BMI values than the CD patients. The prevalence of overweight and obesity was higher in the UC than the CD patients (4.89% CI95 2.76-7.93 vs. 2.45% CI95 1.12-4.59 and 8.47% CI95 5.61-12.16 vs. 1.9% CI95 0.77-3.88, respectively); the differences were statistically significant (-2.44% CI95 -5.45-0.49 and -6.57% CI95 -10.5-3.1, respectively). The risk of overweight/obesity was 3.5 times higher for patients with UC (OR=0.272, CI95 0.14-0.49, p=0.0004).

Conclusion: The prevalence of overweight and obesity in newly diagnosed children with IBD was 8.4% and was higher in patients with UC than in patients with CD. The results of this study have shown that not only malnourished children may suffer from IBD but also children who are overweight or obese at the time of diagnosis.

Disclosure of Interest: None Declared
GLUTEN-FREE PRODUCTS FOR COELIAC DISEASE PATIENTS: CAN BE CONSIDERED AS SUBSTITUTES OF THEIR GLUTEN-CONTAINING COUNTERPARTS?

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Objectives and Study: Up-to-date the only available therapy in the treatment of Coeliac Disease (CD) is to follow a lifelong and strict gluten-free diet. A range of special gluten-free products (GFP) is currently available in the market, offering to CD patients a huge variety of brands and options. GFP are included in the CD patients’ diets as substitutes of the cereal-based foods, such as bread or pasta, which are a main pillar in a healthy diet and should ingested in all the meals of the day. However, we have observed nutrient unbalanced diets in our CD patients, and some clinical conditions such as high-blood cholesterol or iron deficiency, having been these disorders already identified by other authors. We have hypothesised that the above-mentioned conditions found in our CD population could be related to the regular consumption of GFP. The aim of this study was to assess the GFP nutritional composition as compared to the GCP.

Methods: Parents of 71 CD patients pertaining to our unit completed a food frequency questionnaire by indicating frequency of GFP consumption and brands. With the data obtained, nutritional information was collected from the package of a series of GFP of different brands, and also from an equal number of brands of each GCP counterpart.

Results: 16 different kinds of products were selected, from each 5 brands were studied, both in the case of GFP and their GCP counterparts. It was obtained for that GFP presented an overall statistically significant lower protein content than their counterparts, and statistically significant higher carbohydrates, saturated fatty acids and fibre (table). A tendency of a higher content in sugars and fat was also found in GFP. Additionally it was obtained a high variability in the nutritional composition for each GFP among the different brands.

Image:

<table>
<thead>
<tr>
<th></th>
<th>Mean values (GFP)</th>
<th>Mean values (GCP)</th>
<th>Est. Diff</th>
<th>Confidence Interval 95%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy (kcal)</td>
<td>375.13</td>
<td>378.21</td>
<td>-0.62</td>
<td>0.05 - 7.71</td>
<td>0.82</td>
</tr>
<tr>
<td>Protein (g)</td>
<td>3.36</td>
<td>3.94</td>
<td>-0.58</td>
<td>[3.94 - 4.2]</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Carbohydrates (g)</td>
<td>61.99</td>
<td>68.01</td>
<td>6.02</td>
<td>[5.24 - 6.78]</td>
<td>0.003</td>
</tr>
<tr>
<td>Sugars (g)</td>
<td>15.55</td>
<td>14.08</td>
<td>1.47</td>
<td>[1.04 - 1.9]</td>
<td>0.70</td>
</tr>
<tr>
<td>Fat (g)</td>
<td>10.39</td>
<td>16.51</td>
<td>6.12</td>
<td>[5.94 - 6.4]</td>
<td>0.073</td>
</tr>
<tr>
<td>Saturated Fatty Acids (g)</td>
<td>3.99</td>
<td>4.73</td>
<td>0.74</td>
<td>[0.04 - 1.44]</td>
<td>0.026</td>
</tr>
<tr>
<td>Fibre (g)</td>
<td>3.32</td>
<td>3.95</td>
<td>0.63</td>
<td>[0.35 - 1.23]</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

* Table: statistical analysis results

Conclusion: The range of GFP currently available in the market, although present a high fibre content, have an unbalanced nutritional profile because of the low protein content and high saturated fatty acids as compared to their GCP counterparts, thus cannot be considered as substitutes. The differences obtained evidence the lack of adequacy of the rough materials used in the elaboration of
GFP. All these plus the variability obtained among different brands leads to the need of implementing nutritional education to CD patients so as to enable them to successfully self-manage the products choice at the best nutritional composition profile. We finally encourage the GFP industry to apply the recent advances in the formulation of healthy and nutritionally rich GFP already developed by several investigation groups.

**Disclosure of Interest:** None Declared
OUTCOMES OF THE NUTRITIONAL INTERVENTION ON A PAEDIATRIC CYSTIC FIBROSIS POPULATION: QUALITY OF THE DIET, WEIGHT AND HEIGHT GAIN AND FAT REABSORPTION COEFFICIENT

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Objectives and Study: Cystic Fibrosis (CF) patients suffer from lifelong pancreatic insufficiency leading to maldigestion of foods and malabsorption. Pulmonary infection and inflammation lead to increased energy requirements so as to maintain the respiratory function. Following an hyper-caloric diet is a key pillar to allow for the avoidance of growth stunting and malnutrition. The present study aims at assessing the impact of a nutritional intervention on diet in terms of energy intake and macronutrients distribution, on the progress of weight and height gain, and on the fat absorption in terms of Fat Absorption Coefficient (FRC).

Methods: We conducted a prospective study during 3 years with 69 CF patients aged 1-16 years. Follow-up visits were scheduled at least annually and included a 4-days FR dietetic assessment coinciding with a 3-days stool collection, and weight-height measurement and FRC calculation. Along the duration of the study patients were provided with personalised nutritional recommendations when came to the hospital for a regular visit. 1st visit was considered as the baseline. Evolution of the energy intake, macronutrients %, FRC and weight-height percentiles were analysed.

Results: It was found that FRC is higher and constant in patients aged between 1-4 years because of the stable dietary pattern. However, from 4 years on diet is diversified and it becomes difficult to maintain the FRC > 90%; enzyme replacement dosage becomes extremely relevant at this point to ensure in each meal the maximum fat digestion and the minimum loss in stools. Percentage of dietary fat increases with age at expenses of a decrease in carbohydrates, which leads to a higher energy intake (figure), what even more stresses the need of a correctly adjusted enzyme dosage. Finally it was not found that nor weight or height percentiles increased with age, but were kept maintained.

Image:
**Conclusion:** Through a nutritional support plan it is possible to achieve a nutrient-balanced diet according to the CF needs, but we need to be very cautious when recommending patients to increase dietary fat intake, since the enzyme replacement dosage must be re-adjusted accordingly so as to achieve and maintain high values of FRC over time: a close nutritional follow-up is crucial. Current recommendations on enzyme dosage adjustment are not sufficiently evidence-based and that a new criterion should be applied taking into account fat content of meals instead of patients' body weight and age.

**Disclosure of Interest:** None Declared
VALIDATION OF A QUESTIONNAIRE OF SUBJECTIVE GLOBAL NUTRITIONAL ASSESSMENT FOR BRAZILIAN CHILDREN AND ADOLESCENTS

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Objectives and Study: To validate the SGNA for Brazilian children and adolescents

Methods: A prospective cross-sectional study with 242 patients, aged 30 days to 13 years, treated in paediatric units of a tertiary hospital with acute illness and minimum hospitalized length of stay of 24 hours. After authorization of the authors and performing the translation of questionnaires SGNA, through the method of backtranslation, subjects were consecutively selected considering the following exclusion criteria: developmental delay, chronic use of medication except for sulfate ferrous and multivitamin in prophylactic doses, previous hospitalization less than 30 days ago, patients with less than a month old, infectious process in the last seven days, impossibility of an anthropometric assessment, patients and carers who did not speak Portuguese. The variables studied were: age, sex, weight and length at birth, prematurity and anthropometry (weight, height, body mass index, arm circumference, triceps skinfold and subscapular skinfold). Patients were classified according to the SGNA: well nourished, moderately malnourished or severely malnourished. The primary outcome was the need for admission/readmission within 30 days after hospital discharge

Results: The median (P25-75) age of the sample was 10.4 (4.3 to 33.4) months. Most children aged below two years old (67.8%) and were male (61.6%). According to the classification of SGNA 80% of patients were classified as well nourished, 14.5% as moderately malnourished and 5.4% severely malnourished as. In the assessment of concurrent validity, the SGNA showed good correlation with all anthropometric measures commonly used (P <0.05). Regarding predictive validity, the SGNA was associated with all outcomes studied (P <0.05). Finally, the analysis of interobserver reliability, the SGNA has obtained good agreement among evaluators (kappa = 0.76).

Conclusion: SGNA proved to be a valid method to assess the nutritional status of hospitalized Brazilian children and adolescents.


Disclosure of Interest: None Declared
**Objective and Study:** Intestinal T cells are important in both promoting and restraining inflammation. Type 1 Interferon (T1IFN), essential in anti-viral responses, ameliorates murine colitis. The role of T1IFN in the human gut’s adaptive immune system is not known. We therefore studied whether human intestinal T cells were responsive to T1IFN, and its effect on T cell phenotype.

**Methods:** Endoscopic biopsies or resection specimens were frozen for immunohistochemistry (IHC) or cultured in the presence of neutralising anti-IFNβ or isotype-matched control antibody. Cells were harvested, stimulated with anti-CD3/CD28 antibodies and analysed for cytokine production by intracellular staining and by multiplex ELISA of culture supernatants. Phosphorylated STAT1 was measured by flow cytometry with or without prior T1IFN stimulation. Frozen sections of colonic mucosa were stained with an IFNβ and analysed using fluorescent IHC. Finally, CD3+ T cells were FACS sorted and expression of Interferon Stimulated Genes (ISGs) and Suppressors of Cytokine Signalling (SOCS) 1 and 3 determined by quantitative real-time PCR.

**Results:** T1IFN (IFNβ) was detected in the lamina propria of both control and IBD tissue and ISGs (MxA and 2504S) were expressed by intestinal T cells sorted from tissue. In vitro, IFNβ neutralisation reduced the frequency of pSTAT1+ intestinal T cells (n=6, p=0.05) and, in healthy controls, decreased the proportion of IL10-producing intestinal T cells (n=8, p=0.01). There was a trend for more IFNγ-producers (p=0.059) and IFNγ concentrations in supernatants were increased (n=10, p=0.016). In IBD, intestinal T cells were more responsive to IFNb in vitro, as assessed by ISG induction, (n=10 for patients and controls, p<0.03) and constitutive pSTAT1 was increased in T-cells isolated from IBD patients compared with controls (n=30 IBD, 16 control, p=0.03). Concordantly, SOCS1 expression was decreased in IBD samples compared to controls (n=8 IBD, 6 control), p=0.047). In contrast to control tissue, neutralisation of IFNβ in IBD samples led to a generalised increase in cytokine production, with an increase in the frequency of T cells producing all cytokines examined (IL-10, IFNγ, IL-17 and TNFα, n=10).

**Conclusion:** T1IFN in the human intestine promotes a STAT1-mediated regulatory response from T cells, which may be important in maintaining mucosal integrity in health and in response to viral infections. There is increased responsiveness of the T1IFN pathway in T cells from IBD patients, associated with a generalised suppression of cytokine production. Thus, immunoregulatory effects of intestinal T1IFN are context dependent. This may help explain the varied clinical response to T1IFN as a therapeutic agent in IBD.
Disclosure of Interest: None Declared
Mitochondrial Dysfunction in Food Allergy: Evidences from a Mice Model of Peanut Allergy

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Objectives and Study: Immune function and mitochondrial activity are related. Mitochondrial dysfunction plays a role in the pathogenesis of asthma. We aimed to see whether these features are present also in food allergy, and if they could be modulated by a nutritional intervention with an extensively hydrolyzed casein formula containing the probiotic *L. rhamnosus* GG.

Methods: 4-week-old female C3H/HeOuJ mice were sensitized by oral route with five weekly doses of peanut extracts (6 mg) plus cholera toxin (10 μg) as adjuvant in the presence or absence of a 14-day pre-treatment with an extensively hydrolyzed casein formula containing the probiotic *L. rhamnosus* GG (EHCF+LGG). Liver mitochondrial respiration rates were evaluated polarographically in isolated mitochondria in the presence of succinate (substrate FAD dependent) or palmitoyl-L-carnitine (fatty acid oxidation) using the Clark electrode, soon after oral food challenge. The carnitine-palmitoyl-transferase (CPT) (rate limiting enzyme of the mitochondrial fatty acid oxidation) and aconitase (oxidative stress marker) activities were measured spectrophotometrically. H2O2 yield was assayed by following the linear increase in fluorescence (ex 312 nm and em 420 nm) due to the oxidation of homovanillic acid in the presence of horseradish peroxidase.

Results: We found in sensitized mice a lower state 3 respiration rate in presence of succinate and decreased fatty acid oxidation than controls (-36%, p<.05), although no difference in CPT activity was observed between these two groups. Moreover, an increased oxidative stress in sensitized group was proven by inactivation of aconitase activity (-25%, p<.05) and higher H2O2 yield (+52%, p<.05). Pre-treatment with EHCF+LGG exhibited an improvement of mitochondrial function (+85%, p<.05) and redox state (-57%,p<.05) if compared to sensitized group. No changes on CPT activity was observed in mice receiving EHCF+LGG.

Conclusion: Food sensitization induces mitochondrial dysfunction and increases oxidative stress at liver level. EHCF+LGG efficiently prevents these effects.

Disclosure of Interest: None Declared
**Nutrition**

**Basic Science**

PO-G-0003

**EARLY LIFE VITAMIN D DEFICIENCY AGGRAVATES FOOD ALLERGIC RESPONSE VIA INHIBITING TREG CELL POPULATION**

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**Objectives and Study:** Vitamin D deficiency in early life might be one of the risk factors contributing to the high prevalence of food allergy in modern society. The present study was to investigate whether vitamin D-deficiency in utero and during early life as well as vitamin D supplementation after weaning can affect the development of food allergy and the underlying mechanisms in BALB/c mice.

**Methods:** Female BALB/c mice were fed with control diet or vitamin D-deficient diet. After delivery, dams were maintained on the same control or vitamin D-deficient diet. After weaning, offspring from both control and vitamin deficient dams were further divided into control or vitamin D-deficient diet. At 6 weeks, food allergy model was induced in female offspring by injection of ovalbumin with aluminium hydroxide.

**Results:** Vitamin D-deficient model in both maternal and offspring mice was successfully established by vitamin D-deficient diet feeding. All OVA induction groups showed significantly increased serum OVA-IgE level compared with negative control. The level of OVA-IgE in the offspring who were exposed to vitamin D-deficient diet during the whole experiment or during early life (from utero to before weaning) was significantly higher than the control diet group, whereas, OVA-IgE concentration in the offspring who were fed with vitamin D-deficient diet only after weaning were not significantly different compared with control diet group. This result suggests that vitamin D deficiency during early life (in utero and postnatal period) may have the most significant influence on the susceptibility to food allergy. By comparing IFN-\(\gamma\) and IL-4 produced by lymphocytes of spleen and mesenteric lymph nodes and the ratio of IFN-\(\gamma\)/IL-4, no obvious difference was found among all the experimental groups, which suggests the imbalance of Th1/Th2 cytokines seems not involved in the OVA induced allergic response is this early life vitamin D deficient model. Compared with the negative control group, the percentage of CD4\(^+\)CD25\(^+\)Foxp3\(^+\) Treg cells from spleen and mesenteric lymph nodes in all the OVA induction groups was significantly decreased. When compared with the control diet group, only offspring who were exposed to vitamin D-deficient diet during early life (in utero and postnatal period) or the whole experiment was significantly decreased.

**Conclusion:** Vitamin D deficiency in early life may influence the differentiation of Foxp3\(^+\) Treg cells population, which will further increase the occurrence of OVA induced food allergy.

**Keywords:** early life vitamin D deficiency; food allergy; Treg cell; immune balance

**Disclosure of Interest:** None Declared
CROSSTALK BETWEEN WNT AND NOTCH SIGNALING IN INTESTINAL EPITHELIAL CELL FATE DECISION AFTER MASSIVE SMALL BOWEL RESECTION IN A RAT

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Objectives and Study: Various signaling cascades have been implicated in the control of intestinal stem cell activity. Wnt/β-catenin signaling plays a central role in regulating proliferation and differentiation of stem cells within the intestinal epithelium toward either enterocytes or one of three secretory cell lineages. The Notch pathway is a master regulator of cell fate decisions and has been shown to stimulate cell differentiation in the normal intestine. Several experiments have described the crosstalk between Wnt and Notch signaling in intestinal tissue. The purpose of the present study was to evaluate the crosstalk between Wnt/β-catenin and Notch signaling in the late stages of intestinal adaptation in a rat model of short bowel syndrome (SBS).

Methods:
Male rats were divided into two groups: Sham rats underwent bowel transection and SBS rats underwent a 75% bowel resection. Illumina’s Digital Gene Expression (DGE) analysis was used to determine Wnt/β-catenin and Notch signaling gene expression profiling. Twelve Wnt/β-catenin and five Notch-related gene and protein expression were determined using Real Time PCR, Western blotting and immunohistochemistry.

Results: From the total number of 20000 probes, 20 genes related to Wnt/β-catenin signaling and seven genes related to Notch 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. Six genes (from seven) related to Notch signaling were upregulated in SBS rats. 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. Four genes related to Notch signaling (from five genes) and Notch protein levels were upregulated in resected rats.

Conclusion: Two weeks following massive bowel resection in rats, Notch signaling was stimulated while Wnt/β-catenin signaling pathway is inhibited. It appears that cell differentiation rather than proliferation is most important in the late stages of intestinal adaptation.

Disclosure of Interest: None Declared
ORAL ANTIBIOTICS PREVENT NECROTISING ENTEROCOLITIS IN PRETERM PIGS
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Objectives and Study: Prematurity, enteral nutrition and gut colonization are dominating risk factors for necrotizing enterocolitis (NEC). Neonatal antibiotic (AB) treatment is common for preterm infants but it is not known whether oral vs. systemic AB provide different effects on gut colonization and NEC sensitivity. We hypothesized that prophylactic oral AB would be superior to systemic AB in suppressing gut colonization and NEC development.

Methods: Preterm caesarean-delivered pigs were fed increasing doses of infant formula after birth. The pigs were given either oral broad-spectrum AB (metronidazole/ampicillin/gentamycin) (PO, n=16), an equivalent dose of systemic AB (SYS, n=17) or saline (CON, n=16). Pigs were euthanized on d 5 and scored for macroscopic NEC lesions (range 1-6). Intestinal samples were collected for analyses of digestive enzyme activity. Bacterial abundance in the small intestine was evaluated with fluorescence in situ hybridization (FISH) on tissue sections using a semi-quantitative score (range 1-7) and by qPCR on luminal colon content. Short-chain fatty acids (SCFA) in colon content were analysed by gas chromatography. A sugar absorptive capacity test was done on d 4 and intestinal permeability was estimated as urine lactulose/mannitol ratios following oral administration 4 h before euthanasia.

Results: The NEC incidence was lower (0%) for PO than for SYS and CON pigs (59-63%, P<0.001), with the most severe lesions in CON pigs. PO showed reduced small intestinal bacterial abundance, relative to the other groups (1.1 vs. 1.9-2.4 FISH scores, P<0.05). SYS showed reduced bacterial abundance relative to CON only in the proximal part (1.7 vs. 2.9, P<0.05). Bacterial translocation into the intestinal wall was only seen in CON and SYS. Relative to SYS and CON pigs, PO pigs had lower numbers of 16S rRNA gene copies in colon contents (log_{10}(16S rRNA gene copies/g) 6.05 vs. 7.88-7.94, P<0.001). Total SCFA concentration was lower in AB treated pigs compared to CON (13.4±17.5 vs. 61.1±25.6 μmol/g, P<0.001) and lower in PO compared to SYS (4.3±6.9 vs. 21.5±20, P<0.05). Total SCFA was higher in NEC pigs compared to healthy pigs (38.0±28.3 vs. 21.4±29.5, P<0.01). No differences were found for digestive enzyme activities, galactose absorptive capacity and intestinal permeability.

Conclusion: Oral AB is superior to systemic AB treatment with regard to NEC prevention. Oral AB more profoundly suppressed bacterial colonization and fermentation in the intestine and colon, without marked effects on small intestinal function. Further studies are required to elucidate the possible long term effect of oral AB on gut function and NEC, and the development of antibiotics-associated microbial resistance.
Disclosure of Interest: None Declared
**Gastroenterology**  
**Basic Science**  
PO-G-0006

**FETAL GUT MICROBIOME DIVERSITY IS MODULATED BY SUBCLINICAL ILEUM INFLAMMATION DUE TO SYSTEMIC ENDOTOXIN EXPOSURE AND BY VAGAL DENERVATION**

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**Objectives and Study:** The recent discovery of the placental microbiome has challenged the notion that the fetus develops in a sterile environment. Intestinal microbiota are an integral part of the gut-brain axis essential for proper intestinal development and the inflammatory response. The gut is the most extensive vagus-innervated organ. We aimed to determine if a microbiome is present in the fetal gut near-term and to test how brain-gut communication via the vagus nerve influences this microbiome. We hypothesized that ileal inflammation will result in reduced α-diversity in the fetal ileal microbiome.

**Methods:** Near-term fetal sheep were surgically prepared with vascular catheters. Arterial blood samples were drawn at baseline and seven selected time points to profile lipopolysaccharide (LPS)-induced inflammation. At 54h post LPS, necropsy was performed. The plasma levels of IL-6 (ELISA, pg/ml) and the Iba1+ cell intensity in terminal ileum were used to quantify the degree of inflammation and macrophage activation, respectively. The microbiome composition was characterized by high-throughput sequencing of the V6 hyper-variable region of the 16S rRNA gene. Results are reported for P<0.05 as mean±SD.

**Results:** In the LPS group, but not in the control and Vx+LPS groups, at 3h post LPS, IL-6, but not TNF-α, was elevated compared to baseline: 0.6 ± 1.5; 261.7 ± 228.7; 155 ± 200.5; 1.3 ± 3.9 (Controls; LPS; Vx+LPS; mean baseline across all groups, respectively). IL-6 values were higher at 3h in the LPS group vs. control, but not vs. Vx+LPS group; Vx+LPS did not differ from controls. In line with Vx effect on systemic inflammation, Iba1+ cell intensity was lower in Vx+LPS vs. LPS group but not different from controls. The presence of a fetal ileum microbiome was validated and its dependence on intact vagal innervation revealed: α-diversity decreased in response to LPS, but was higher in more inflamed ilea after vagal denervation (Spearman R=0.75).

**Conclusion:** Late gestation sheep’s fetal gut contains a full complement of intestinal bacteria whose diversity is influenced by the exposure to low doses of endotoxin if brain-gut communication is interrupted.

**Disclosure of Interest:** None Declared
ORAL ANTIBIOTICS MODULATE IMMUNE CELL DEVELOPMENT AND PREVENT NECROTISING ENTEROCOLITIS IN NEONATAL PRETERM PIGS

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Objectives and Study: The systemic and mucosal immune systems are immature in newborns, particularly those born preterm, leading to higher susceptibility to infections and necrotizing enterocolitis (NEC). Following birth, a few days of systemic treatment with antibiotics is often applied for preterm infants to prevent sepsis and infections but the effects on immune system development and NEC are not clear. Likewise, it is not clear whether the route of administration, oral or systemic, is important.

Methods: Preterm pigs received increasing amounts of infant formula for 5 days after birth (0-120 mL/kg/day). During this period, groups of pigs (n = 17-18) were administered saline (CON) or broad spectrum antibiotics orally (ORA) or systemically (SYS). Temporal changes of blood cell parameters were analyzed by flow cytometry. Bacteria in the intestine and the blood were characterized by sequencing and mass spectrometry, and quantified by quantitative PCR and culturing.

Results: At birth, preterm pigs were immunologically immature as evidenced by lower counts of neutrophils, thrombocytes and erythrocytes, and higher frequency of progenitor cells, relative to term pigs. Regardless of treatment, blood neutrophils and monocytes gradually matured postnatally with increased CD14 expression and decreased CD172a expression, whereas TLR2 expression was unchanged. ORA pigs had more mature neutrophils with lower cell size and CD172a expression whereas monocytes in CON pigs were activated to higher degree with greater CD14 expression and cell granularity. None of the ORA pigs developed NEC within the first 5 days after birth and on day 5 they had lower number and granularity of monocytes, and negligible amount of bacteria in the blood and intestinal lumen. In contrast, CON and SYS pigs showed high NEC incidence (59-63%), abundant Gram-positive bacteria in the blood and the gut lumen. NEC was associated with low counts of total leukocytes and lymphocytes, high monocyte granularity, and excessive intensity of CD14 in monocytes and neutrophils.

Conclusion: Oral antibiotics induce maturation of neutrophils and maintain the gut microbiota at low density, thereby preventing bacterial translocation and NEC in preterm pigs. The impaired TLR2 development in neutrophils and monocytes suggests a low clearance capability for blood Gram-positive bacteria. This may justify the use of prophylactic oral antibiotics during the first few days after preterm birth. However, the risk of selection of microbial resistance remains to be explored.
Disclosure of Interest: None Declared
COMBINED EXPOSURE TO BETA-LACTOGLOBULIN-DERIVED TOLERGENIC PEPTIDES AND SYNBIOTICS ALLEVIATES FOOD ALLERGY RESPONSE IN VIVO

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Objectives and Study: At-risk infants can be prevented from developing food allergy symptoms by feeding them hypoallergenic formulas containing cow’s milk protein hydrolysates. This preventive effect might be a result of oral tolerance induction by immunogenic peptide fractions in the hydrolysates. Early exposure to tolerance-inducing peptides could prevent the development of allergic symptoms. It is hypothesised that synbiotics (pre- and probiotics) can further enhance tolerance induction.

Methods: Three-week-old female C3H/HeOuJ mice (N=6-8) were exposed orally to (1) PBS (positive control for allergy), to (2) whey protein (positive control for tolerance induction), or (3) a low dose mixture of beta-lactoglobulin-derived peptides (18 amino acids) with a synbiotics-enriched diet prior to sensitization. Thereafter, the mice were fed a control cow’s milk protein-free diet and sensitized to whey protein using cholera toxin as an adjuvant. Mice were intradermally challenged with whey protein, and clinical symptoms, such as acute allergic skin response and anaphylactic shock, were measured.

Results: The combination of the peptide intervention with a synbiotics-enriched diet resulted in a significant reduction in the acute allergic skin response compared to the allergic positive control. Furthermore, the combined peptides-synbiotics exposure prevented from developing significantly higher anaphylactic shock symptoms when compared to the sham-sensitized controls.

Conclusion: Oral exposure to specific beta-lactoglobulin-derived peptides with synbiotics leads to protection against acute allergic responses. The beta-lactoglobulin-derived peptides were administered at a dosage 100-fold lower than previously described by Meulenbroek et al. [1], therefore a combined approach like this might reduce the peptide dose needed to prevent allergy. Future research is needed for unravelling the underlying mechanisms of the preventive effect of this combined exposure.


Disclosure of Interest: None Declared
**Objectives and Study:** The rat is a suitable model for studying gut maturation since it is an altricial species and vast gut changes occur postnatally until weaning (from day 21). Recently reported data showed that the transcription factor, B lymphocyte-induced maturation-protein-1 (Blimp-1), is highly expressed in the small intestine (SI) epithelium during the embryonic and neonatal periods with an abrupt decrease at weaning in mice [1, 2]. Hence the objective of the study was to investigate Blimp-1 expression during postnatal development and its correlation with two markers of SI maturation: the expression of the immunoglobulin G receptor of the neonate, FcRn, in the proximal SI and the presence of cells with large digestive vacuoles in the distal SI.

**Methods:** Sprague Dawley rats were studied during their natural development (7, 14, 21, 28, 35 days of age) and after precociously induced maturation at 17 days of age by 3 days of gavage with a lectin (PHA), microbial protease or water as control. SI samples from the proximal and distal portions were formalin-fixed, paraffin-embedded and proceeded for immunohistochemistry of Blimp-1 and FcRn, and for analyses of vacuolated enterocytes.

**Results:** Blimp-1 appeared highly expressed in both nuclei and cytoplasm of the SI epithelial cells from crypts to the top of villi in the suckling 7d old group. In post-weaning rats (28 and 35d old) maturation was completed and there was a redistribution of Blimp-1 expression, nuclei lost intensity and disperse epithelial cells appeared negative. The distal SI appeared more strongly stained than the proximal SI at all ages. The loss of Blimp-1 from nuclei correlated with the appearance of mature-type enterocytes, lacking FcRn in the proximal SI and vacuolated enterocytes in the distal SI.

**Conclusion:** Using the model of precocious induced gut maturation, we have demonstrated that the genetically programmed SI maturation process can be modified, contributing to a better understanding of the regulating mechanisms. The changes in SI expression of Blimp-1 during precociously induced maturation were similar to those occurring during natural rat development. The correlation between the expression changes of Blimp-1 and that of FcRn and the disappearance of vacuolated cells, indicate that Blimp-1 might be involved in regulation of the SI maturation in neonatal rats.

Objectives and Study: Introduction: Due to their ability to cross-link proteins, there has been great interest in transglutaminases and they have multiple applications. In the food industry, microbial transglutaminase (mTg) is used to modulate texture and improve the properties of food products, acting as a universal food glue. Due to their common enzymatic functions, the question has arisen whether complexes of mTg formed by transamidation reactions could be relevant for celiac patients.

Aim: To compare the linear and three dimensional structure of the complexes formed by tTg or mTg and gliadin, and look for potential immunopotency.

Methods: Material and Methods: Complexes of mTg or tTg and gliadin were formed, resulting in mTg neo-epitopes or tTg neo-epitopes. These complexes were separated by asymmetric field flow field fractionation (AF4) and confirmed by SDS-PAGE and multi angle light scattering (MALS). For the structural alignment and docking experiment, the molecular-graphics-modelling and -simulation program YASARA was used. Structural alignment was performed with the primary structures of mTg (PDB-ID: 1IU4) and tTg (PDB-ID: 2Q3Z) by using the MUSTANG-algorithm in a way such that the amino acids of the catalytical triade have maximum alignment.

Results: Results: No alignment on the α-C atoms of the protein backbones and the 3D structure between mTg and tTg were observed. Glutamine or other positive residues are directed to the active centre due to a mainly negatively charged surface. After docking of the gliadin peptide (PDB-ID: 1NNA) to mTg and tTg, both enzymes show adjacent partial-positive charges. Moreover, both neo-epitope complexes show a superimposed epitope similarity, even though the homology at the entrance to the active centre is still low.

Conclusion: Discussion: Analogous to the neo-epitope described in the literature, it is hypothesized that mTg neo-epitopes are formed by stochastic cross-linking between mTg and gliadin peptides. It is only after docking of the gliadin peptides to both Tgs that charges and structure of the epitopes’ similarities appear. If molecular mimicry leads from mTg neo-epitopes to tTg-neo-epitopes there must exist a similarity between these enzymes. If an antibody-paratope exists, there is a possibility that an anti-mTg neo-epitope antibody shows cross reactivity and binds to a tTg neo-epitope.

Disclosure of Interest: None Declared
INTESTINAL EPITHELIUM SENSITIVITY TO ACETYLCHOLINE VARIES WITH AGE AND INTESTINAL LOCATION IN PIGLETS

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Objectives and Study: Defaults in intestinal barrier function, including altered tight junction permeability and electrolyte secretion, are involved in various diseases in children but little is known about its nervous regulation and its postnatal maturation. The aim of our study was to describe the evolution of intestinal barrier permeability and electrolyte secretion within the first month of life and its regulation by the cholinergic system in piglets.

Methods: 28 suckling piglets were sacrificed at age 0, 2, 14 and 28 days. Jejunum, ileum and colon were sampled to study intestinal barrier function in Ussing chamber. Short-circuit current (Isc) and flux of FITC-dextran 4000 (FD4) were used to evaluate electrolyte secretion and paracellular permeability, respectively. Cholinergic modulation was investigated by the use of carbachol, a cholinergic agonist. Acetylcholine esterase (AChE) assay was performed on each level of the bowel at each age to describe acetylcholine catabolism.

Results: An age effect was identified for most of the parameters studied, yet with different patterns depending on the location and the parameter considered. In the jejunum, FD4 flux increased with age (+420%, P<0.05) while Isc decreased sharply after birth (-64%, P<0.05). Cholinergic stimulation tended to reduce FD4 flux (-50%, P=0.11) at birth with no further effect on jejunal permeability in older piglets. In contrast, carbachol-induced electrolyte secretion increased with age (+317%, P<0.05). A similar pattern was observed in the ileum, although basal Isc decrease with age occurred later, between d14 and d28 (-830%, P<0.05). Conversely, in the colon although basal FD4 flux and Isc post-natal evolution trend was similar than in the small intestine, the changes were more progressive and with less amplitude within the first month of life (difference between d0 and d28: FD4 flux +162%, P<0.05 and Isc -70%, P=0.08). Opposite to the small intestine, carbachol had no effect on colonic FD4 flux at any age and induced electrolyte secretion at birth but not in older piglets. AChE activity decreased sharply (-50%, P<0.05) between birth and day 2 in the jejunum with no further changes with age and was stable with time in the ileum. In the colon, AChE activity was nearly 10 times higher and decreased progressively with age (-22% between d0 and d28, P<0.05).

Conclusion: Our study demonstrates that intestinal epithelial cell sensitivity to acetylcholine differs with post-natal age in piglet small and large intestine. It also emphasizes the need for more studies to understand how, where and when cholinergic system modulates the intestinal barrier.

Disclosure of Interest: None Declared
**Objective and Study:** Since 1960s, the total parenteral nutrition (TPN) has been widely used for nutritional support of premature infants and other neonates with functional disorders of the gastrointestinal tract who cannot be fed orally(1, 2). The infants are frequently at greater risk of TPN-mediated oxidative stress because of their immature antioxidant defenses (3). miRNAs, small non-coding RNAs (about 21-23 nucleotides), can regulate the stability of their target messenger RNAs (mRNAs) and/or by down-regulating their translation (4). In 47th Annual Meeting of ESPGHAN, we reported that the expression of miR-200 family could be altered by oxidative stress. In this regard, miR-200 may be essential regulators of the oxidative stress response. We here sought to investigate the potential role of miR-200 in response to oxidative stress. Additionally, we also explored the underlying mechanisms of miR-200s induction by H\(_2\)O\(_2\) treatment.

**Methods:** Intracellular reactive oxidative species (ROS) production was analyzed using the CM-H2DCF-DA. Whether p38\(\alpha\) was able to interact with p53 by using immunoprecipitation (IP) assay in extracts from L02 cells expressing Flag-tagged p38\(\alpha\) and HA-tagged p53. To validate physically associated association of p53 with miR-200 promoters, we performed chromatin immunoprecipitation (ChIP) analysis using p53-specific antibody.

**Results:** The unregulated miR-200-3p modulates the H\(_2\)O\(_2\)-mediated oxidative stress response by targeting p38\(\alpha\). Members of the miR-200 family are induced by the tumor suppressor p53 and are known to inhibit epithelial to mesenchymal transition (EMT). We here show that p53 phosphorylation at Ser33 contributes to H\(_2\)O\(_2\)-induced miR-200s transcription. In addition, we also show that p38\(\alpha\) can directly phosphorylated p53 on serine 33 upon H\(_2\)O\(_2\) exposure. Thus, we suggest oxidative stress-induced p53 Ser33 phosphorylation via p38\(\alpha\) is essential for its functional regulation of oxidative stress-inducible miR-200 transcription in liver cells.

**Conclusion:** Collectively, our data indicate that p53-dependent expression of miR-200a-3p controls oxidative stress in liver cells by inhibiting a p38/p53/miR-200s feedback loop.

**References:**
Disclosure of Interest: None Declared
PREVALENCE OF RS1801197 POLYMORPHISM OF A CALCITONIN RECEPTOR (CALCR) GENE IN PREGNANT AND BREASTFEEDING MOSCOW WOMEN AND ITS CONNECTION TO THEIR LEVEL OF MINERAL BONE DENSITY AND EXCRETION OF BIOMARKERS OF BONE RESORPTION

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Objective and Study: Pregnancy and breastfeeding could lead to the increase of risk of mineral bone density (MBD) reduction and development of osteoporosis. MBD is under the influence of genetic factors. Despite intensive studying of their influence on MBD, results of these researches are indefinite and vary in different populations, that is especially important for such multiethnic state as the Russian Federation.

Methods: Research of rs1801197 genetic polymorphism of CALCR gene by real time polymerase chain reaction was carried out in 96 pregnant, 29 breastfeeding and 28 non-pregnant Moscow women of reproductive age (n=153). Examination of women was conducted on the basis of the Moscow outpatient clinics from October, 2012 to March, 2013 after receiving their informed consent. MBD measurement in women was carried out with the ultrasonic densitometer Omnisense 7000 (Sunlight Medical Ltd., Israel), considering z-score > -1 SD as normal MBD, z-score from -1 to -2,0 SD as reduced MBD, z-score ≤ -2,0 SD as considerably reduced MBD. Determination of the excretion level of piridinolin (Pid) and dezoksipiridinolin (Dpid) biomarkers in pregnant and breastfeeding women was carried out in portions of morning urine by HPLC method with fluorescent detection at λ1 = 290 nm and λ2= 395 nm, the results were expressed as nmol/mmol creatinine.

Results: Genotypes CC, CT and TT frequency of rs1801197 polymorphism of CALCR gene in examined women with a normal MBD were represented at approximately equal rates (29%, 35%, 35%, respectively), frequency of allele C – 47%, of allele T – 53%. During MBD reduction the progressive increase in frequency of CC genotype in all examined women was observed. Existence of reliable connection between allele C and genotype CC of rs1801197 polymorphism of CALCR gene (OR = 1,774, p = 0,037, n = 153) and MBD reduction in examined women was established. There were no significant changes in Pid and Dpid excretion during MBD reduction in pregnant and breastfeeding women. However, the excretion level of these markers at its highest tertile was connected to high frequency of allele C of rs1801197 polymorphismon CALCR gene in pregnant women.

Conclusion: It is possible to consider MBD reduction at the presence of risk allele C rs1801197 polymorphism of CALCR gene in pregnant women to be caused by enhanced resorption of bone tissue the indicator of which is increased excretion of resorption biomarkers Pid and Dpid.
Disclosure of Interest: None Declared
Objectives and Study: Changes of the exocrine pancreatic function coincides with the dietary change from milk to solid food during postnatal development. Recently, we have shown that feeding serine proteases can induce precocious maturation of the small intestine (SI) in neonatal rats. Since, the proteinase-activated-receptor (PAR-2) might be a potential target for luminal proteases, the present study investigated changes in pancreatic proteolytic activity and PAR-2 receptor expression during SI maturation.

Methods: Rats were studied during the suckling period (7 and 14 days of age), at weaning (21 days) and after weaning (28 and 35 days). Pancreatic homogenates were analyzed for protein content (Lowry method) and trypsin activity using Bz-Arg-p-nitroanilide as the substrate. In addition, homogenates were analyzed after electrophoretic separation in agarose gel using the substrates, N-Bz-DL-Phe-β-naphtyl-ester for trypsin/chymotrypsin-like activity and N-CBZ-L-Ala-β-naphthyl-ester for elastase-like activities. Paraffin-embedded SI samples from the proximal and distal portions were proceeded for immunohistochemistry of PAR-2.

Results: Pancreatic weight, protein content and trypsin-like activity were low during the suckling period but markedly increased at weaning. A major difference in the electrophoretic enzyme pattern was observed, since an anodal elastase activity band was only observed in 7d old rats. PAR-2 receptors were highly expressed in both proximal and distal SI in all age groups of rats.

Conclusion: The high PAR-2 receptor expression in immature SI epithelium and the increasing pancreas enzyme production during the suckling period indicate that PAR-2 may play an essential role initiating the maturational process in the SI after being activated by luminal proteinases at weaning. Since elastase activity has been shown to have a diminishing effect on PAR-2 receptors, i.e., disarming them by enzymatic cleavage in respiratory epithelium, the high activity of pancreatic elastase found during the early suckling period might play a similar role, inactivating PAR-2 and postponing SI maturation, to keep it immature and well-adapted for absorption of maternal milk. Although more studies are needed, our results indicate that pancreatic proteases might have an important role in the regulation of SI maturation in the suckling to weaning transition period.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: High mobility group box 1 (HMGB1) protein is a highly conserved nuclear protein with important functions in the regulation of transcription. In inflammatory conditions, HMGB1 is actively secreted from immune cells in the extracellular matrix, where it behaves as a pro-inflammatory cytokine. Dipotassium glycyrrhizate (DPG) is a glycyrrhizin-derived compound that is known to inhibit the pro-inflammatory activity of extracellular HMGB1. We previously showed that DPG significantly reduces, without adverse side effects, the DSS-induced colitis in mice. Since a known relationship exists between HMGB1 and oxidative stress as well as between the latter and inflammation, the aim of the present study is to investigate whether DPG acts on the oxidative stress mechanisms to reduce inflammation.

METHODS: In vivo: DPG (8mg/Kg) was administered to DSS-treated C57BL/6 mice. After 7 days, mice were sacrificed and inflamed colon removed. Expression levels of iNOS and COX2, involved in oxidative stress, were analysed by RT-PCR. In vitro: RAW267.4 cells were treated with LPS, DPG, LPS+DPG, HMGB1-B-Box, HMGB1-B-Box+DPG at an earlier (4-8h) or later (24-48h) time. Expression levels of iNOS and COX2 were analysed by RT-PCR and AMPK phosphorylation was analysed by western blot.

RESULTS: In vivo: mice treated with DPG+DSS showed a significant decrease of iNOS and COX2 mRNA expression, compared to DSS-treated mice. In vitro: DPG reduced iNOS and COX2 expression induced by LPS at the later time and COX2 expression at the earlier time. Besides, HMGB1-B-Box increased iNOS expression at the earlier time, but this effect was counteracted by DPG. Finally, DPG induced AMPK phosphorylation, that is known to inhibit COX2, after LPS treatment.

CONCLUSION: Our data show that DPG affects oxidative stress reducing iNOS and COX2 expression during inflammation. It is likely that DPG reduces iNOS through a mechanism HMGB1-dependent and COX2 through a mechanism AMPK phosphorylation-mediated.

DISCLOSURE OF INTEREST: R. Vitali: None Declared, F. Palone: None Declared, L. Stronati: None Declared, A. Negroni: None Declared, M. Pierdomenico: None Declared, S. Oliva: None Declared, F. Nuti: None Declared, A. Dilillo: None Declared, S. Cucchiara Conflict with: Develop Registry, Johnson & Johnson
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MICROBIAL CHANGES AND TLR4 EXPRESSION DURING NATURAL AND INDUCED INTESTINAL MATURATION IN NEONATAL RATS

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Objectives and Study: In young mammals, changes in the gastrointestinal (GI) function at weaning is coinciding with a changed composition of the bacterial flora, i.e., an increased gram-negative, (G-) flora. It is known that G- bacteria can interfere with the host via Toll-like receptor 4 (TLR4). Thus, using the neonatal rat as a model, we aimed to elucidate the correlation of G- bacteria with TLR4 expression during natural and precociously induced intestinal maturation.

Methods: Rats were studied during suckling period (7 and 14 d of age), at weaning day (21 d of age) and after weaning (28 and 35 d of age). To induce precocious GI maturation, 14 days old rats were fed with a microbial protease (0.4 mg/g. bwt), phytohaemagglutinin (PHA, 0.05 mg/g. bwt), and water (controls) during three days and then studied at 17 days of age. The small intestine (proximal and distal parts) was collected for TLR4 immunohistochemistry and the cecum content was collected for bacterial culture (e.g. G- Enterobacteriaceae, and G+ Lactobacillales) and microscopy (Gram staining).

Results: Microscopy of the cecum content showed significant change in the ratio between G+ and G- bacteria with prevalence of G- after natural weaning. In contrast, both PHA and protease treatments diminished the proportion of G- bacteria, resulting in increased number of cultivable lactobacilli. Generally, a high expression of TLR4 was observed in intestinal villi of all studied rats but with a higher expression in the proximal than in the distal part. No major change in the expression of TLR4 was observed in the villi during neither natural nor induced development. However, the TLR4 expression in the intestinal crypts appeared at 21 days of age under natural conditions and after induction with PHA and protease already at 17 days of age.

Conclusion: TLR4 is highly expressed already during the suckling period, without any marked changes during intestinal development, indicating that there is no obvious correlation between the expression of this receptor and functional changes in the GI tract. However, since a changed bacterial ratio, with increased number of cultivable lactobacilli was found after PHA and protease treatments, we speculate that species of G+ bacteria might influence the GI maturation in neonatal rats.

Disclosure of Interest: None Declared
CLOSTRIDIUM NEONATALE AND GUT MICROBIOTA IN PRETERM NEONATES

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Objectives and Study: In 2002, an outbreak of necrotizing enterocolitis (NEC) in a Canadian neonatal intensive care unit was associated with a proposed novel species of Clostridium "Clostridium neonatale". To date there is no data about this species isolation, identification, and clinical significance. Additionally, “C. neonatale” has not been formally classified as a new species rendering its identification challenging. Indeed, “C. neonatale” 16S rRNA gene sequence shows high similarities with another Clostridium species involved in neonatal necrotizing enterocolitis, Clostridium butyricum.

Methods: We performed polyphasic study combining phylogenetic analysis (16S rRNA gene sequencing and multilocus sequence analysis) and phenotypic characterization with mass spectrometry to characterize Clostridium neonatale clinical isolates from preterm neonates.

Results: We demonstrated that “C. neonatale” is a new species within the Clostridium genus sensu stricto for which we propose the name Clostridium neonatale sp. nov.. The use of MALDI-TOF MS has been demonstrated useful to the better differential identification of “C. neonatale” and C. butyricum clinical isolates.

Conclusion: Now that C. neonatale status has been clarified the use of MALDI-TOF MS will participate to the better differential identification of C. neonatale and C. butyricum clinical isolates. Consequently, it will allow the characterization of C. neonatale at the clinical level, particularly when considering NEC studies.

Disclosure of Interest: None Declared
LONGITUDINAL GENE EXPRESSION ANALYSIS OF CANDIDATE GENES IN COELIAC DISEASE

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Objectives and Study: Despite numerous studies, the diagnosis of coeliac disease (CD) before clinical and serological manifestations still remains a promise. The chance to diagnose an asymptomatic patient, without a duodenal biopsy, would represent a major step forward in the management of these patients, preventing the rise of symptoms. Aim of this study is to evaluate how gene expression on peripheral blood could help to diagnose CD before clinical manifestations.

Methods: We identify, among a cohort of 300 newborns from at risk families (with a proband), followed up for 6 years, 10 children who developed CD and 12 who did not. PBL were obtained every 6 months since birth. We examined candidate gene haplotypes and gene expression at 6 months, at the time of small bowel biopsy (18 months) and 6 months after (24 months).

Results: Although they belong to families at risk (with HLA DQ2/DQ8 +), the children who developed CD showed different haplotypes on 3/9 candidate genes (SH2B3, TNFSF14, c-REL) compared to the unaffected. The expression of 9 candidate genes showed that KIAA1109, TAGAP and SH2B3 were over-expressed, whereas RGS1 was down-regulated in CD children compared to those who did not developed CD, long before clinical and serological diagnosis. Since all gene expression are multi-correlated it was mandatory to develop a multivariate model to estimate the variables able to predict the development of CD. By using a stepwise discriminant analysis, the expression of 4 genes (SH2B3, RGS1, TAGAP and TNFS14) was selected for significant discriminating capacity between CD and not-CD before the diagnosis, predicting correctly 10/10 of CD and 11/12 not-CD (overall 95.5% correct prediction).

In order to avoid an over-enthusiastic estimation of the predicting capacity, since we classified the same cohort from which the discriminant function was derived, we adopted an auto-exclusion strategy to get an unbiased estimate of the predicting capacity of the discriminant function: indeed still 87% of CD and not-CD are correctly predicted, confirming the robustness of the model.

Conclusion: Within families with a confirmed risk of CD it is now possible, for the DQ2 or DQ8 positive newborns, to estimate the risk to develop CD at birth on a drop of cord blood by candidate genes genotypes, and more accurately at 6 months on a drop of blood by estimating the expression of a small set of genes, much before the appearance of any antibody or clinical symptoms.

This work opens for the first time the chance to anticipate the diagnosis of CD much before the appearance of any antibody as well as any clinical sign: on a drop of blood is now possible to estimate the predictors to develop CD.
Disclosure of Interest: None Declared
**Objectives and Study:** The major environmental factor that triggers CD is gluten. Some undigested gliadin peptides, in particular P31-43, have been shown to impair the endocytic traffic (Barone MV, PloS One 2010) and to enhance interleukin-15 (IL-15) expression, a key innate cytokine involved in the activation of IELs in the CD mucosa (Nanayakkara, AJCN and PloS One 2011). Viral infections, in particular entroviral infections, such as rotavirus, have been suggested to trigger CD and other autoimmune disorders through the induction of type-1 IFN. An increase of type-1 IFN has in fact been reported in the small gut of CD patients. Recent studies suggest the possibility that Toll-like receptors (TLRs) play a pathogenic role in CD. Our hypothesis is that undigested gliadin peptides could activate the same pathways as viruses, particularly those leading to innate immune activation. We investigated whether gliadin peptide P31-43 may activate Toll-like receptor 7 (TLR7) pathway by comparing its activity with viral ligand loxoribine (LOX).

**Methods:** Caco-2 cells were incubated for 30min, 3h and 6h with 100µg/ml of P31-43 or with 1mM LOX. Total lysates were analyzed by western blotting with anti-phosphorylated pERK, pJNK, pp38, pNF-kB and with anti-TLR7, anti-MxA.

**Results:** The stimulation with P31-43 resulted in an increase of the expression of TLR7 and MyD88 at all times analyzed; the same was observed after stimulation with LOX. We then analyzed the levels of the phosphorylation of three MAPK involved in our pathway, JNK, ERK and p38, pNF-kB p65. We found that they have the same trend at all times investigated, both after LOX and P31-43 stimulation. Finally, we analyzed MxA that resulted increased at all times after stimulation both with P31-43 and LOX.

**Conclusion:** Our data show that in Caco-2 cells P31-43 is able to activate the whole TLR7 pathway similarly to LOX. This confirms the hypothesis that gliadin is capable of activating innate immunity as a result of mechanisms typically induced by viral infections.

**References:** Barone MV and et al; PloS One 2010
Nanayakkara and et al; AJCN 2013
Nanayakkara and et al; PloS One 2011

**Disclosure of Interest:** None Declared
Objectives and Study: To analyze the presence of total IgA and anti-gliadin antibodies (AGA) in breast milk (BM) from coeliac mothers who follow a gluten free diet (GFD).

Methods: 224 samples of mature milk were obtained at different months of lactation (1-9) from 82 mothers from Italy (Naples), The Netherlands (Leiden) and Spain (Madrid, Valencia and Reus): 42 coeliac disease (CD) mothers on a GFD and 40 non-CD mothers on a normal diet (ND). Whey samples were analyzed for Secretory AGA-IgA (S-AGA) and AGA-IgA by an indirect homemade ELISA and for total IgA (g/L) by a commercial ELISA kit (Bethyl Laboratories).

Results: S-AGA and AGA-IgA were detected in BM, both in mothers on a GFD and mothers on a ND. AGA levels vary from one mother to another, but for each mother values at different months of lactation remain relatively stable.

For AGA-IgA and S-AGA, no differences were found between CD and non-CD mothers from Italy (p=0.64 and 0.92 respectively), The Netherlands (p=0.78 and 0.96), Madrid (p=0.90 and 0.78) Valencia (p=0.11 and 0.19) and Reus (p=0.55).

Total IgA values varied between 0.1 and 1 g/L for the majority of samples (median IgA:0.668 g/L). We observed a great variability among mothers, some cases showing uncommonly high values. In Italy women on a ND showed statistically significant higher values of IgA as compared to those following a GFD (p=0.035). This difference was not observed in samples from other countries.

Total IgA, AGA-IgA and S-AGA follow a similar longitudinal pattern in each mother. A statistically significant association was found between the means of total IgA and AGA-IgA (p<0.001) and of IgA and S-AGA (p=0.003); this is also true for the two groups of mothers when analyzed separately.

Conclusion: Since the great majority of BM samples, both from mothers on a GFD and on a ND, contain AGA, the diet is not a key factor influencing the presence of AGA in BM. Moreover, presence of AGA in breast milk samples from mothers on a GFD for years reflects the existence of a long-lasting immunological memory, independent of the mother’s diet. On the other hand, the association between total IgA and AGA levels in the two groups of mothers suggests that AGA production in BM depends on the same humoral mechanism that regulates total IgA production by the mammary gland.
Disclosure of Interest: None Declared
THE EPITOPES OF HUMAN AND MICROBIAL TRANSGLUTAMINASES ARE SIMILARLY RECOGNISED BY COELIAC DISEASE SERA

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Objectives and Study: The use of microbial transglutaminase (mTg) from Streptovercillium mobaraense in the food industry is expanding rapidly and mTg is ingested in large amounts in the common Western diet, including by celiac patients. Being related to human endogenous tTg, mTg shares multiple functional similarities, although immunogenic comparison of the two enzymes in celiac disease (CD) is lacking.

Methods: Complexing mTg and gliadin results in mTg neo-epitope (mTg neo). These complexes were purified by asymmetric field flow field fractionation and confirmed by multi angle light scattering and SDS-PAGE. Sera from an in house cohort of 81 CD patients (mean age 30±17) and 81 healthy blood donors (mean age 29±21) were analysed using the following ELISAs: AESKULISA® tTg New generation (tTg neo-epitopes) IgA and IgG, AESKULISA® Gliadin IgA and IgG, AESKULISA® DGP IgA and IgG and AESKULISA® Research use only (RUO, IgA and IgG) kits against mTg and mTg neo-epitopes.

Results: Purified mTg-neo IgG and IgA (AUC = 0.92, 0.93 respectively) showed a statistically significant increase in immunoreactivity compared to mTg or gliadin (p<0.001) alone, but similar immunoreactivity in the tTg-neo IgG and IgA ELISA (p<0.0003) (AUC=0.94, 0.95, respectively). In competition ELISA, the mTg- and tTg-neo-epitopes have identical outcomes with regard to CD sera, both showing a decrease in optical density of 55±6%, p<0.0002. Comparing antibody levels in individual CD patients, sera with high antibody titre [U/ml] against the tTg neo-epitope also show high antibody activities to the mTg neo-epitope and vice versa indicating the presence of similar epitopes within the Tg-gliadin complexes.

Conclusion: Even without overall homology, mTg and tTg display a comparable immunopotent epitope. mTg neo-epitope IgA and IgG antibodies are immunogenic in CD. If substantiated this will impact on food industry policy for additives, food products labelling, consumer awareness and public health implementation.

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LESS HERPES VIRUS INFECTIONS IN ANTI-TISSUE TRANSGLUTAMINASE ANTIBODY POSITIVE CHILDREN: THE GENERATION R STUDY

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Objectives and Study: Persistent viral infections have been implicated in the aetiology of autoimmune diseases in adulthood, but it is not known whether herpes viruses are associated with the development of celiac disease autoimmunity (CDA) in children. We assessed whether herpes virus infections are associated with tTG-IgA levels in children at 6 years of age.

Methods: This study was embedded within a population-based prospective cohort study. Serum IgG levels against EBV (epstein-barrvirus), CMV (cytomegalovirus) and HSV-1 (herpes simplex virus type 1) were measured by ELISA and tTG-IgA levels with fluorescence enzyme immunoassay (FEIA) in 4,420 children at 6 years of age. Children were categorized based on tTG-IgA levels into negative (<7 U/ml), positive (>7-70 U/ml) and strongly positive (>70 U/ml), i.e. 10 times upper limit normal (ULN). Multivariable logistic regression analyses were performed.

Results: 59 children (1.3%) were found to carry positive anti-tTG antibodies, and of these n=31 (53%) had levels >70 U/ml. Fewer children with anti-tTG levels >70 U/ml were infected with CMV (aOR 0.38; 95% CI 0.14, 0.98; p=0.04) and with any of the three viruses (aOR 0.38; 95% CI 0.18, 0.78; p=0.008) than children with negative anti-tTG antibodies. In addition to single herpes virus infections, infections with >2 viruses were less frequent in anti-tTG positive children, than in children without anti-tTG antibodies (aOR 0.44; 95% CI 0.21, 0.90; p=0.02)

Conclusion: Both CMV single infection and combined CMV, EBV and/or HSV-1 infections are inversely associated with anti-tTG IgA positivity. This might indicate a protective effect of herpes virus infections in the pathogenesis of CDA.

Disclosure of Interest: None Declared
**Objectives and Study:** Microbial transglutaminase (mTg) is an enzyme capable of cross-linking numerous molecules thereby revolutionizing industrial food product qualities. It belongs to the family of transglutaminases where human tissue transglutaminase (tTg) is an autoantigen and anti-tTg antibodies are specific serological markers in CD. Both enzymes de/transamidate gluten, dependent on the surrounding conditions. Despite declarations of the safety and non-allergenicity of mTg usage, direct evidence for immune pathogenicity of the enzyme in celiac patients is lacking.

**Methods:** In order to explore the immunogenicity of mTg, the serological activity of mTg, tTg, gliadin complexed mTg (mTg neo-epitope) and gliadin complexed tTg (tTg neo-epitope) were studied in the sera of 3 groups: 95 pediatric celiac patients (CD) mean age 8, 99 normal children (NC) mean age 8.5 and 79 normal adults (NA) mean age 28.1. All sera were tested using the following ELISAs, detecting IgA, IgG or both IgA and IgG: *AESKULISA® tTg (tTg), AESKULISA® tTg New Generation (tTg neo-epitope (tTg-neo)), microbial transglutaminase (mTg) and mTg neo-epitope (mTg-neo). The results were correlated to the degree of intestinal injury, using revised Marsh criteria.

**Results:** Comparing pediatric CD patients with the 2 normal groups: mTg-neo IgA, IgG and IgA+IgG antibody activities exceed significantly the comparable mTg ones (p<0.0001). All mTg-neo and tTg-neo levels were significantly higher (p<0.001). tTg IgA and IgG+IgA were higher than mTg IgA and IgA+IgG (p<0.0001). The levels of tTg-neo IgA/IgG were higher than tTg IgA/IgG (p<0.0001).

The sequential antibody activities, reflecting best the increased intestinal damage, going from M0 to M3c were: tTg-neo IgG ≥ mTg-neo IgG > mTg-neo IgA+IgG > tTg-neo IgA > tTg IgA > mTg-neo IgA > tTg IgA+IgG > tTg IgG > tTg IgA+IgG. Taken together, mTg-neo IgG and tTg-neo IgG correlated best with intestinal pathology (r²=0.989, r²=0.989, P<0.0001, p<0.0001, respectively). mTg-neo IgG had higher sensitivity than tTg-neo IgG, with lower specificity (98.95, 89.47 and 92.93, 97.98%, respectively).

**Conclusion:** It is concluded that mTg is immunogenic in children with CD and by complexing to gliadin its immunogenicity is enhanced. Anti-neo-epitope mTg antibodies correlate with intestinal damage to the same degree as anti-tTg. mTg-neo IgG is more sensitive and tTg IgG more specific for CD diagnosis. mTg-neo IgG can be considered a new marker for CD. In view of the pathogenic role allocated to tTg antibodies, further studies are needed to explore the pathogenic potential of immunogenic mTg and anti-mTg antibodies in CD.
Disclosure of Interest:  A. Lerner: None Declared, T. Matthias Conflict with: Shareholder of AESKU.DIAGNOSTICS, P. Jeremias: None Declared, S. Neidhoefer: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0024

**SPECIFIC DEVELOPMENTAL DEFECTS OF ENAMEL IN CHILDREN WITH ELEVATED ANTI-TISSUE TRANSGLUTAMINASE CONCENTRATIONS**

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**Objectives and Study:** Coeliac Disease (CD) has occurred as one of the most prevalent autoimmune-mediated diseases among Western people, but it often remains undiagnosed because of its broad variance of nonspecific symptoms. Little is known about the effects of increased concentrations of anti-tissue transglutaminase (tTG) in this undiagnosed population. Recently, in our group Jansen et al found a significant association between anti-tTG positive children, a lower bone mineral density and reduced growth trajectories. CD might induce specific dental enamel defects, the aim of this study is to investigate whether increased levels of anti-tTG are associated with specific developmental defects of enamel in the deciduous dentition.

**Methods:** This study was embedded in the Generation R Study, a population-based prospective cohort study from fetal life until young adulthood. Serum samples were collected and clinical photographs of clean, moist teeth were taken with an intra-oral camera from 4233 children with a median age of 6 years. All children were born between April 2002 and January 2006. We excluded those with previous diagnosed CD and/or a gluten free diet. Children were divided in an anti-tTG negative (<7 U/ml, n=4174) and anti-tTG positive (≥7 U/ml, n=59) group. Children's levels of anti-tTG were further categorized in a group based on ≥10 times upper limit of normal (70 U/ml, n=31). Our definition of developmental defects of enamel was based on Aine’s criteria. Non-specific defects were defined by dmft-scores. Univariate analysis was performed.

**Results:** tTG-IgA positive children tended to have more developmental defects of enamel (OR 1.72; 95% CI 0.84-3.53). Results were more prominent in the ≥10 times upper-limit group (OR 2.29; 95% CI 0.94-5.63). No differences were found in the occurrence of non-specific dental enamel defects between groups (OR 0.93; 95% CI 0.58-1.64).

**Conclusion:** Our study shows that screening identified tTG-IgA positive children tended to have more specific enamel defects in the deciduous dentition, although effects were not significant. This suggests that elevated tTG-IgA concentrations might be harmful for enamel development.

**Disclosure of Interest:** None Declared
USEFULNESS OF HLA-DQ GENOTYPING FOR THE DIAGNOSIS OF COELIAC DISEASE IN A SELECTED POPULATION OF PATIENTS WITH CLINICAL SYMPTOMS AND POSITIVE SEROLOGICAL TESTS

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Objectives and Study: to investigate the accuracy of coeliac disease (CD) diagnosis without HLA-DQ genotyping in a selected population of patients with a combination of clinical symptoms and positive serological tests.

Methods: retrospective review of 155 patients aged 1 to 17.4 years (median age 6 years) who underwent intestinal biopsy for suspicion of CD between 2010 and 2011 at our Institution. Children were classified in 2 groups according to their triple test (TT) positivity or negativity. TT was considered positive if symptoms and/or signs suggestive of CD occurred, anti-tissue-transglutaminase (anti-TTG-IgA) levels were > 10 times upper limit of normal (ULN), and anti-endomysial antibodies (EMA-IgA) were present. TT was considered negative whenever 1 or more of these criteria was not fulfilled. Positive predictive value (PPV), negative predictive value (NPV), sensitivity and specificity of the TT were calculated using histology where Marsh II and III lesions were considered diagnostic of CD.

Results: of 155 patients, 69 were classified as TT positive and 86 as TT negative. All the TT positive patients had an intestinal biopsy diagnostic for CD, yielding a PPV for TT of 100% and a corresponding specificity of 100%. Among the 86 TT negative patients: 63 had a histologically proven CD. Therefore NPV for TT was 26.7% with a 52.3% sensitivity. (Table)

<table>
<thead>
<tr>
<th>Group 1 (CD-positive biopsy)</th>
<th>Group 2 (CD-negative biopsy)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive triple test</td>
<td>True positive 69</td>
</tr>
<tr>
<td>Negative triple test</td>
<td>False positive 0</td>
</tr>
<tr>
<td></td>
<td>Positive predictive value 100%</td>
</tr>
<tr>
<td>Sensitivity 52.3%</td>
<td>Specification 100%</td>
</tr>
</tbody>
</table>

Conclusion: our results suggests that due to the high accuracy of a positive TT, HLA-DQ genotyping is not necessary for CD diagnosis in symptomatic patients with anti-TG-IgA levels > 10 times ULN and EMA-IgA positivity.

Disclosure of Interest: None Declared
EPITHELIAL STRESS AND ADOPTIVE IMMUNE RESPONSE SYNERGYSE TO LICENSE CYTOTOXIC T CELL TO KILL INTESTINAL EPITHELIAL CELLS IN COELIAC DISEASE

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Objectives and Study: Innate immune activation of epithelial cells, anti-gluten CD4 T cell responses, and upregulation of natural killer activity in cytotoxic intraepithelial CD8 T cells (IE-CTL) are central to CD pathogenesis. In this study we aim to dissect the distinct contributions of adaptive and innate immune pathways to small bowel mucosal atrophy and how they relate to each other.

Methods: To address this question we analyzed NK receptor status by flow cytometry and epithelial stress markers expression by IHC in patients with normal intestinal mucosa with a family history of CD or potential CD patients (with anti-TG2 antibodies, but normal intestinal architecture). We also investigated by electron microscopy the presence of ultrastructural alterations in intestinal epithelial cells of these patients compared to controls and celiac subjects.

Results: We observed that TG2 negative family members showed an up-regulation, while potential CD patients showed a down-regulation, of both activating and inhibitory NK receptors. Furthermore we observed that TG2 negative family members, but not potential CD patients, show high levels of epithelial stress markers (Heat shock proteins and IL-15 expression) and ultrastructural impairment of intestinal epithelial cells, closely resembling the alterations observed in celiac patients.

Conclusion: Our results suggest that adaptive anti-gluten immunity (as assessed by the presence of anti-TG2 antibodies) and epithelial distress (as assessed by heat shock protein and IL-15 expression in the epithelium) can be dissociated. This dissociation is clearly represented by family relatives of CD vs potential CD patients. Furthermore, we have evidence that neither the innate nor the adaptive response alone is sufficient to license IE-CTL to kill and induce villous atrophy, however they are both required. The ability to identify isolated epithelial distress in subjects with normal histology will allow establish which subjects, among at risk individuals, are more prone to develop tissue damage even in those lacking adoptive immune response.

Disclosure of Interest: None Declared
Objectives and Study: Gluten-free diet (GFD) is characterized by a higher consumption of corn that may undergo some xenobiotic contamination. Mycotoxins are secondary metabolites produced by several microscopic fungi genera such as Aspergillus, Fusarium and Penicillium. The aim of our study was to assess the risk of mycotoxin exposure ( aflatoxin M1, ochratoxin A and zearalenone) in woman with coeliac disease (CD) and healthy control breastfeeding mothers (as well as in their offsprings) by quantifying these contaminants in breast milk.

Methods: From January 2011 to December 2013, 33 women with CD and 22 healthy breastfeeding controls completed the study. Human milk was collected throughout three days, during a complete 24h period, as following: one milk sample after overnight fasting, one 4 hours after lunch, and one 2 hours after dinner. Mycotoxin content in breast milk was investigated by a high-performance liquid chromatography (HPLC) method with fluorimetric detection. Dietary history on cereal consumption was recorded during the three days of breast milk collection.

Results: Aflatoxin M1 (AFM1) was detected in 37% (n=96) of samples belonging to women with CD [mean ± SD = 0.012 ± 0.011 ng/mL; range = 0.0035 ÷0.340 ng/mL]. The slightly higher concentration in those samples collected during fasting [0.017 ± 0.028 ng/mL] resulted statistically significant when compared to those collected 4 hours after lunch and 2 hours after dinner [0.011 ± 0.010 ng/mL and 0.009 ± 0.006 ng/mL respectively] (ANOVA, p-value< 0.001, significance level 0.05). When comparing to mothers with CD, the control group showed lower AFM1 concentration level in 22% of samples [mean 0.008 ± 0.007 ng/mL; range = 0.0035 ÷0.0370 ng/mL] resulting statistically significant with a p-value 0.004 (significance level 0.05). Estimating a daily average milk consumption of 530g for a hypothetical body weight of 3.4 kg, the exposure of newborns from mother with CD and from healthy control mothers resulted 1.87 and 1.24 ng/kg bw/d, respectively. No statistical significant difference was found as regards breast milk zearalenone (ZEA) content in both groups. Ochratoxin A was not significantly present in the investigated human milk samples of both groups.

Conclusion: The presence of AFM1 in breast milk is a marker both for infant and mother exposure. In our assessment, the AFM1 breast milk content was higher among mother with CD than among healthy breastfeeding controls. However, the maximum tolerable level
set by the EU Regulation 1881/2006 (0.11 ng/kg bw/d) was exceeded in both groups and this warrants further investigations.

Disclosure of Interest: None Declared
SHOULD THE NEW ESPGHAN GUIDELINES ON DIAGNOSING COELIAC DISEASE ALSO APPLY TO ASYMPTOMATIC CHILDREN?

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Objectives and Study: In 2012 ESPGHAN guidelines for diagnosing Coeliac Disease (CD) were modified1 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 (>10xULN) and HLA-DQ2 and/or DQ8 is positive. The aim of this study is to examine the relationship between TTG levels and histological grading in asymptomatic patients with newly diagnosed CD to establish whether the recent CD guidelines could be reliably applied to these patients.

Methods: Prospective data was collected at diagnosis on all asymptomatic children diagnosed with CD during March 2007 – September 2014. Our laboratory’s ULN is 10U/ml. The relationship between the modified Marsh criteria histological grading and contemporaneous TTG levels was analysed. Data was also collected on the age of children and reason for initial serological screening. Cost benefit of extending the new diagnostic criteria to asymptomatic children with suspected CD was estimated based on biopsy costing £1340.00 and TTG and HLA-DQ2 costing £65.00 per patient.

Results: 95 asymptomatic children were diagnosed with CD. 64/95 children (67%) had TTG titres >10xULN and all these had small bowel enteropathy (sensitivity 100%). Table below shows the histological grading with contemporaneous TTG titres. 45/64 (70%) had TTG >200U/l and this was associated with greater likelihood of total villous atrophy (Marsh 3c)

The mean age at diagnosis was 9.1 years (1.75 years – 17.25 years). Reasons for serological screening were: Diabetes Mellitus (n=32), family history of CD (n=22) and Down’s syndrome (n=5).

Estimated cost saving to the Health Service for each child = £1,275.

<table>
<thead>
<tr>
<th>TTG titres (U/ml)</th>
<th>Modified Marsh Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3a</td>
</tr>
<tr>
<td>100 – 150 (n=13)</td>
<td>3</td>
</tr>
<tr>
<td>151 – 200 (n=5)</td>
<td>0</td>
</tr>
<tr>
<td>&gt;200 (n=45)</td>
<td>7</td>
</tr>
</tbody>
</table>

Estimated cost saving to the Health Service for each child = £1,275.
Conclusion: All 64 asymptomatic children with TTG>10xULN had biopsy proven CD. 45/64 (70%) had TTG titres >200U/ml and were more likely to have total villous atrophy (Marsh 3c). Our study suggests that the ESPGHAN criteria for diagnosing CD via the serological pathway should be extended to asymptomatic children with resultant cost benefit to the health service and convenience for the family.


Disclosure of Interest: None Declared
**Gastroenterology**

**Coeliac Disease**

PO-G-0029

**BUCCAL SWABS AS NON-INVASIVE SOURCE FOR HUMAN LEUKOCYTE ANTIGEN TYPING IN COELIAC DISEASE DIAGNOSTICS**

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1 Maastricht University Medical Center, Maastricht, 2 Atrium Medical Center, Heerlen, Netherlands

**Objectives and Study:** Human leukocyte antigen (HLA) typing is an essential step in the diagnostic algorithm for celiac disease (CD) and is also frequently used for screening purposes. Collection of blood for HLA typing is invasive and accompanied with emotional impact especially in children. Genetic technological progress now enables HLA typing from buccal cell samples. This study evaluated the reliability and feasibility of HLA typing for CD-associated HLA polymorphisms in high-risk children using buccal swabs.

**Methods:** Blood and buccal swabs of 79 children with high risk for CD, were collected in this cohort study. Buccal swab tests were collected either by the investigator at the outward clinic or by the patient or its parent at home. To evaluate the possibility of self-administration, four families performed the test at home. DNA was extracted using an adapted QIAamp method. Quantity, quality and purity of DNA were recorded. HLA-DRB1, -DQA1, and -DQB1 typing was examined on buccal cell-derived and blood-derived DNA at low and, if necessary, at high-resolution level, using Sequence Specific Oligonucleotide (SSO) and Sequence Based Typing (SBT), respectively.

**Results:** DNA isolation using buccal swabs yielded a good quality and sufficient quantity of DNA to perform HLA-DQ typing in all individuals. HLA typing results on buccal-cell-derived DNA was identical to typing on blood-derived DNA, also for the self-administered samples.

**Conclusion:** Buccal swabs are minimal-invasive and an accurate DNA source for HLA typing of CD-associated risk genes for both diagnostic and screening purposes, and can be performed as a self-administrated test at home.

**Disclosure of Interest:** None Declared
ANTIBODIES AGAINST NEO-EPITOPE TTG COMPLEXED TO GLIADIN ARE MORE RELIABLE THAN ANTI-TTG FOR THE DIAGNOSIS OF PAEDIATRIC COELIAC DISEASE

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Objectives and Study: The new guidelines of ESPGHAN for the diagnosis of pediatric celiac disease (PCD) rely on anti-human tissue transglutaminase (tTg) as the prime and unique antibody for screening of the suspected PCD population. Despite the extended CD associated serological repertoire, none of them has challenged tTg premiership. tTg complexed to gliadin presents neo-epitopes resulting from the enzyme-substrate interaction and antibodies against the complex are called tTg neo-epitope (tTg-neo).

Aim: To compare reliability of anti-tTg and tTg-neo antibodies in diagnosis of PCD.

Methods: Materials and methods: 95 pediatric CD patients (mean age 8.3), 99 normal children (NC) (mean age 8.5) and 79 normal adults (NA) (mean age 28) were tested using the following ELISAs detecting IgA, IgG or both IgA and IgG: Aeskulisa® tTg (tTg; RUO) and Aeskulisa® tTg New Generation (Neo-epitope tTg complexed to gliadin). The results were compared to the degree of intestinal injury, using revised Marsh criteria. Sensitivity, specificity, positive and negative predicted values were calculated.

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

<table>
<thead>
<tr>
<th>Antibody</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predicted value</th>
<th>Negative predicted value</th>
<th>AUC</th>
</tr>
</thead>
<tbody>
<tr>
<td>tTg neo IgA+IgG</td>
<td>95.79</td>
<td>98.99</td>
<td>98.91</td>
<td>96.08</td>
<td>0.984</td>
</tr>
<tr>
<td>tTg IgA+IgG</td>
<td>83.16</td>
<td>100</td>
<td>100</td>
<td>86.09</td>
<td>0.961</td>
</tr>
<tr>
<td>Significance p&lt;</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.0001</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Conclusion: Conclusions: The tTg-neo IgA, IgG and IgA+IgG isotypes exhibited a higher OD activity and better reflected intestinal damage in PCD, compared to tTg isotypes. The tTg-neo combined IgA+IgG ELISA kit had higher sensitivity and a comparable specificity for the diagnosis of childhood CD. It is suggested that the revised ESPGHAN criteria should include tTg neo in the diagnostic flow chart.
Disclosure of Interest: T. Matthias Conflict with: Shareholder of AESKU.DIAGNOSTICS, P. Jeremias: None Declared, S. Neidhoefer Conflict with: Employed by AESKU.DIAGNOSTICS, A. Lerner: None Declared
Objectives and Study: Among patients with positive celiac disease (CD) serology, studies comparing differences between patients with and without type I diabetes mellitus (T1DM) are lacking. Our aims were to study, among children with positive CD-specific serology who undergo upper gastrointestinal endoscopy, the clinical and histopathological differences between children with and without established T1DM diagnosis.

Methods: We performed a structured medical record review of children aged 2-18 years without prior CD diagnosis who underwent an initial CD evaluation (ICD-9-CM 579.0) between 2000 and 2010 at a large teaching hospital. All children who had positive CD-specific serology (tissue transglutaminase antibody and/or endomysial antibody) and underwent upper gastrointestinal endoscopy were included. Modified Marsh classification was applied for duodenal biopsy interpretation to determine CD.

Results: Among 400 children with positive CD-specific serology who underwent endoscopy, we found 26 children (6.5%) with diagnosed T1DM. Overall, mean age at time of positive CD-specific serology was 9.5 (SD 4.6) years, most were female and white (see Table). In children with T1DM, we found significant higher proportions of children with an absence of gastrointestinal symptoms, and with a positive family history of T1DM and/or hypothyroidism. We found that chronic antral gastritis and reflux esophagitis were more common in children with T1DM.

Table. Characteristics of 400 children with positive celiac disease serology, by type I diabetes mellitus status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>With T1DM (n=26)</th>
<th>Without 1DM (n=374)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>% (95% Confidence Interval)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age of celiac disease diagnosis, median, years</td>
<td>9.2 (6.5-12.9)</td>
<td>9.2 (5.5-13.3)</td>
<td>.83</td>
</tr>
<tr>
<td>Female, %</td>
<td>58 (37-75)</td>
<td>63 (58-68)</td>
<td>.58</td>
</tr>
<tr>
<td>Absence of gastrointestinal symptoms*, %</td>
<td>31 (14-52)</td>
<td>14 (11-18)</td>
<td>.03</td>
</tr>
<tr>
<td>Family history of celiac disease, %</td>
<td>8 (1-25)</td>
<td>23 (19-28)</td>
<td>.09</td>
</tr>
<tr>
<td>Family history of T1DM and/or hypothyroidism, %</td>
<td>27 (12-48)</td>
<td>9 (6-12)</td>
<td>.001</td>
</tr>
<tr>
<td>Marsh III on biopsy, %</td>
<td>73 (52-88)</td>
<td>71 (66-75)</td>
<td>.79</td>
</tr>
<tr>
<td>Chronic antral gastritis on biopsy, %</td>
<td>54 (33-74)</td>
<td>29 (25-34)</td>
<td>.01</td>
</tr>
<tr>
<td>Reflux esophagitis on biopsy, %</td>
<td>20 (6-44)</td>
<td>5 (3-7)</td>
<td>.02</td>
</tr>
</tbody>
</table>

Abbreviation: T1DM, type I diabetes mellitus.

* Absence of subjective abdominal complaints, nausea, vomiting or bowel movement changes

**Conclusion:** In children with positive CD serology, children with T1DM had different clinical and histological features when compared to children without T1DM diagnosis. The histological differences merit further study.

**Disclosure of Interest:** None Declared
AMINO ACIDS LEVELS IN CHILDREN WITH COELIAC DISEASE

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Objectives and Study: The aim of the study is to measure the amino acid levels in children with Coeliac Disease and to investigate the relation between the amino acid levels and the course of the disease.

Methods: 124 children (62 patients with the history of coeliac disease of at least 6 months and 62 healthy children as control) aged between 1-18 years were included the study. Plasma amino acid levels of the children were measured by using Tandem mass spectrometry.

Results: The mean plasma citrulline (25.53 ± 9.39 nmol/ml), glutamine (848.47 ± 201.23 nmol/ml), cystine (28.95 ± 18.29 nmol/ml) and aspartic acid (40.09 ± 21.84 nmol/ml) levels were significantly lower in patients with coeliac disease than the healthy controls (71.58 ± 58.33, 986.43 ± 351.27 nmol/ml, 74.32 ± 53.04 nmol/ml and 102.60 ± 145.00 nmol/ml respectively). The mean plasma alanine (671.82 ± 224.76 nmol/ml), asparagine (92.62 ± 28.35 nmol/ml), glutamic acid (81.03 ± 37.49 nmol/ml), hydroxyproline (26.72 ± 12.91 nmol/ml), isoleucine (111.26 ± 38.15 nmol/ml), leucine (185.16 ± 63.12 nmol/ml), phenylalanine (101.39 ± 28.11 nmol/ml), proline (429.35 ± 148.95 nmol/ml), serine (239.97 ± 66.05 nmol/ml), threonine (188.22 ± 63.51 nmol/ml), valine (484.19 ± 164.54 nmol/ml) levels were significantly higher in patients with coeliac disease than the healthy controls.

Endomysial antibody was negative in eight (12.9%) of patients with coeliac disease and was positive in 54 of them (87.1 %) while it was negative in all (100%) of the control group.

Conclusion: This study indicates that plasma citrulline, glutamine, aspartic acid and cystine levels might also be regarded as a simple and reliable method for the diagnosis and the monitoring of the coeliac disease. Although this is the first study in children further studies with large groups are needed.

Key Words: Amino acids, children, coeliac disease.

Disclosure of Interest: None Declared
**Gastroenterology**  
**Coeliac Disease**  
PO-G-0033  

**PREVALENCE OF ABDOMINAL PAIN RELATED-FUNCTIONAL GASTROINTESTINAL DISORDERS IS INCREASED IN COELIAC PATIENT DESPITE STRICT GLUTEN FREE DIET.**

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**Objectives and Study:** A meta-analysis suggested that a high proportion of adult patients with celiac disease (CD) experience symptoms compatible with irritable bowel syndrome (IBS). These symptoms may improve with gluten avoidance, but sometimes they persist despite an apparently strict GFD. Few data are available in children.

Aim of our study was to assess the prevalence of abdominal pain related-functional gastrointestinal disorders (AP-FGIDs) in a cohort of paediatric patients with CD after a long period of strict gluten free diet (GFD).

**Methods:** We studied 401 (61.8% F; Mean age 11.2y; range 4.7-17.9) patients during the follow-up visit. All patients had previous diagnosis of CD according to ESPGHAN criteria, were on strict GFD since at least one year, and reverted positive serological test to negative after treatment.

To assess the prevalence of AP-FGIDs, the Questionnaire on Paediatric Gastrointestinal Symptoms-Rome III Version (QPGS-RIII) was used.

The closest, non celiac, sibling of the patient or if no siblings available, the next child in kinship was enrolled as control (389; 59% F; Mean age 11.3y, range 4.3-18).

**Results:** 41 children in the CD group (10.2%) and 16 children in the control group (4.1%) met criteria for an AP-FGIDs according to the QPGS-RIII [(10.2 vs 4.1% p<0.001) RR 2.5 (95% CI 1.42-4.35)].

When classified according to the Rome III criteria, we found a significantly higher prevalence of IBS and FAP in children with CD as compared to controls (6.7% vs. 3.1; p<0.03 and 1.5 vs. nil; p<0.03 respectively). In particular, the prevalence of IBS was significantly higher in CD children compared to controls [RR 2.2 (95% CI 1.12-4.25)]

**Conclusion:** Patients with CD have an increased risk of developing FGIDs, and in particular IBS. Our results suggest that new strategies aiming at the management of IBS in celiac patients should be planned.


Disclosure of Interest: None Declared
NO SIGN OF GLIADIN IMMUNOREACTIVITY INDUCED BY HYDROLYSED WHEAT FLOUR IN COELIAC DISEASE CHILDREN AFTER A SHORT ORAL CHALLENGE.

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Objectives and Study: Many efforts are going on to find new strategies to detoxify wheat flour suitable for the diet of celiac disease (CD) patients. Fermentation of wheat flour with sourdough lactobacilli and fungal proteases has already been demonstrated to reduce gluten-induced inflammatory effects in celiac patients.

Aim: In this study, we evaluated the effect of detoxified flour on peripheral blood immune response after a brief oral challenge in subjects with treated CD.

Methods: Four CD patients on a gluten-free diet from at least 2 years were voluntarily enrolled in the study. They ate for 3 days bread obtained with fermented flour (12 gr gluten/die). Immune reactivity to gliadin, either from detoxified or toxic wheat, was analyzed on peripheral blood cells by detecting INF-γ releasing cells before and 6 days after the challenge.

Results: No INF-γ secreting CD4+ T cells reactive to hydrolyzed gliadin with sourdough lactobacilli and fungal proteases were detected on day 6 of the challenge in any of 4 patients tested, instead of a consistent mobilization of T cells reactive to a pepsin-trypsin gliadin observed in celiac patients on a gluten-free diet consuming toxic wheat flour.

Conclusion: This in vivo challenge confirm that fermentation of wheat with sourdough lactobacilli and fungal proteases reduce the gluten-specific immunoreactivity in PBMCs. Our data demonstrated also that the in vivo procedure can be a good method to test new therapeutics approach in the future.

Disclosure of Interest: None Declared
HEALTH RELATED QUALITY OF LIFE IN SPANISH COELIAC CHILDREN AGED 8-18 YEARS

Josefa Barrio 1 Mª Luz Cilleruelo 2 Enriqueta Roman 2 Manuela Marquez 3 Mª Luisa Mearín 4 Cristina Fernandez 5
1 Paediatrics. H.U. Fuenlabrada, 2 H.U. Puerta Hierro, 3 Madrid Coeliac Association, Madrid, Spain, 4 Leiden University Medical Center, Leiden, Netherlands, 5 H.U. Clínico, Madrid, Spain

Objectives and Study: To evaluate the Health Related Quality of life (HRQOL) in a big group of Spanish coeliac patients aged 8-18 years, using both a generic and a specific questionnaire and also to estimate the correlation between both questionnaires.

Methods: A cross-sectional study HRQOL was assessed both by coeliac patients on a gluten-free diet and by their parents. The Madrid Celiac Association invited by e-mail the members in the target age-category to participate in the study. After informed consent, 2 questionnaires were sent, one coeliac disease specific (CDDUX) and one generic (kidscreen) with 3 and 10 dimensions, respectively. Scores were expressed as mean and standard deviation (DS) and recorded into a scale from 1 to 100. A 5-point Lickert scale was used, a score of 1–20 was considered very bad, 21–40 bad, 41–60 neutral, 61–80 good, and 81 to 100 very good. Demographic and clinical variables associated with HRQOL were also assessed. The correlation between the two questionnaires was taken into account. The project was approved by the Ethics Committee of the H.U. Fuenlabrada.

Results: The questionnaires were filled in by 434 out of 1602 coeliac patients. By CDDUX the mean (DS) HRQOL overall scores were similar in children and parents: 55.5 (12.7) and 53.89 (12.19), respectively. There were no significant differences in the paired comparison between children and parents in the different HRQOL domain. Factors related to HRQOL were age at diagnosis, years since diagnosis, disease manifestations at onset, having difficulties with the diet and adherence to the diet. When Kidscreen showed significant differences in 7 out of 10 HRQOL dimensions. Scores in children were significantly higher in each dimension, indicating a better HRQOL. Factors related to QOL were age at questionnaire completion, gender, adherence to the diet and having difficulties with the diet.

The maximal correlation between the results of both questionnaires was -0.254 and the minimal 0.009.

Conclusion: 1. In general the HRQOL among Spanish coeliac children is neutral to good, both assessed by the children as by their parents. 2. Disease specific and generic HRQOL questionnaires give different data about several aspects of QOL, so, both should be used to get complete information. 2. However both questionnaires revealed that the two factors affecting negatively the HRQOL were non-adherence to the diet and having difficulties to keep the gluten-free diet, indicating the need for alternative treatments for coeliac disease.

Disclosure of Interest: None Declared
Objectives and Study: Coeliac disease is an immune-mediated enteropathy triggered by exposure to gluten in genetically susceptible individuals. An antibody level to tissue transglutaminase enzyme (IgA tTG antibody) >10 times the upper limit of normal together with positive anti-endomysial antibodies in symptomatic, HLA DQ2/8 positive patients is now diagnostic of coeliac disease (ESPGHAN guidelines and 2013 BSPGHAN/Coeliac UK Guidelines). This combination of findings negates the need for intestinal biopsies in children suspected of having coeliac disease. The patchiness of coeliac disease has been well documented. More recently, a growing number of reports have shown that the histological changes of coeliac disease are more severe in the duodenal bulb (D1) when compared to the distal duodenum (D2 and beyond). Changes restricted to the duodenal bulb have also been reported, highlighting the need for both duodenal bulb and distal duodenal biopsies in the diagnosis of coeliac disease. However, the relationship between location of histological changes in the duodenum and the levels of IgA tTG antibodies has not previously been studied. Methods: A retrospective audit was carried out on 96 children diagnosed with coeliac disease at a tertiary paediatric gastroenterology centre between January 2011 – when a two-site biopsy policy (D1 and D2) was introduced for suspected coeliac disease – and June 2014. 85 were investigated because of symptoms. Biopsies were reported by a single histopathologist and graded using the Marsh criteria. IgA tTG antibody levels separated the symptomatic children into two groups: a “low” group with raised levels of IgA tTG antibodies <10 times the upper limit of normal as per the laboratory assay; and a “high” group with levels of IgA tTG antibodies of >10 times the upper limit of normal. Results: 66 of the 85 symptomatic children had both D1 and D2 biopsies. Children in the “low” tTG group were more likely to have greater histological changes in D1 than D2 (changes restricted to D1 in 35.7% of children in the “low” group compared to 7.7% in the “high” group), whereas children in the “high” tTG group were more likely to have similar histological changes in D1 and D2 (76.9% in the “high” group compared to 21.4% in the “low” group) Conclusion: Children undergoing biopsy for the diagnosis of coeliac disease based on a tTG between the upper limit and 10 times the upper limit of normal, require biopsy of D1 in addition to D2. Our findings suggest that IgA tTG levels increase with more extensive duodenal involvement.

Disclosure of Interest: None Declared
Objectives and Study: Maternal use of paracetamol during pregnancy is common and has been suggested to increase the risk of asthma in the offspring. In this first study, we aimed to investigate the association between maternal paracetamol use in pregnancy and the risk for coeliac disease in children. To contrast the association between maternal use of paracetamol, we also performed a secondary analysis estimating the effect of maternal use of non-steroid anti-inflammatory drugs (NSAIDs) as well as the use of paracetamol in the child’s first 18 months of life and subsequent coeliac disease.

Methods: Prospective questionnaire data on paracetamol use in pregnancy was available in 82,843 children participating in the Norwegian Mother and Child Cohort Study. With a mean age of the cohort of 8.4 years by end 2013, 636 children had developed coeliac disease. Coeliac disease was identified by a combination of questionnaires data and linkage to the Norwegian Patient Register. We used logistic regression to estimate odds ratios (ORs) for coeliac disease in offspring among mothers who used paracetamol in pregnancy, with adjustment for children’s age, sex and maternal coeliac disease.

Results: Coeliac disease was diagnosed in 8.0 of 1000 children whose mothers took paracetamol while they were pregnant, compared with 7.6 of 1000 children whose mothers did not (adjusted odds ratio (aOR) 1.04, 95% confidence interval (CI) 0.88 - 1.22). The children were then divided into quartiles based on paracetamol exposure duration in days in utero, with no use as the reference category; 1) 1 – 2 days (aOR 1.17, CI 0.94 – 1.97), 2) 3 – 4 days (aOR 0.92, CI 0.67 – 1.27), 3) 5 – 8 days, (aOR 0.83, CI 0.58 – 1.19) 4) > 9 days (aOR 1.09, CI 0.81 – 1.46). We also did a separate analysis of long-term exposure for the upper 5th centile (more than 24 days) with no significant difference compared to non-use (aOR 1.09, CI 0.61 – 1.95). In additional analysis we found that paracetamol use in the child’s first 18 months of life was not associated with later risk of coeliac disease (from 0-6 months aOR 1.07, CI 0.91 - 1.25 and from 6-18 months aOR 1.05, CI 0.82 – 1.24). Use of NSAIDs during pregnancy was infrequent (2.3%) and not associated to coeliac disease in the child (aOR 1.15, CI 0.71-1.87).

Conclusion: We did not detect a significant association between maternal use of paracetamol during pregnancy and coeliac disease in the offspring.

Disclosure of Interest: None Declared
Objectives and Study: Active screening of coeliac disease in at-risk children is still an issue of controversy. We compared the baseline and follow-up characteristics between large cohorts of screen- and clinically-detected coeliac disease children.

Methods: Altogether 458 children with biopsy-proven coeliac disease diagnosed in 2000–2013 were included and the following data were analysed: demographic and clinical characteristics, coeliac disease serology and various laboratory parameters, degree of small-bowel mucosal damage, presence of coeliac disease-associated complications, adherence to the gluten-free diet, and clinical and serological response to the diet. All study variables were compared between children diagnosed by screening in at-risk groups and those diagnosed due to clinical suspicion.

Results: 133 children were screen-detected and 325 clinically-detected. The groups did not differ in gender distribution (girls 60% vs. 66%, p=0.276) or median age (7.0 years vs. 8.0 years, p=0.366). Also 59% of screen-detected patients had clinical symptoms at diagnosis, although these were milder than in clinically-detected patients (p<0.001). Anaemia (7% vs. 22%, p<0.001) and poor growth (16% vs. 38%, p<0.001) were rarer in screen-detected children, whereas the levels of coeliac antibodies (p=0.757) and severity of small-bowel mucosal atrophy (p=0.399) were comparable in both groups. Also haemoglobin (126 g/l vs. 124 g/l, p=0.008) and albumin (41 g/l vs. 38 g/l, p=0.002) values were somewhat higher in screen- than clinically-detected children at diagnosis, while there were no significant differences in liver enzymes, thyroid hormones or iron status. The groups had equal adherence to the gluten-free diet (91% vs. 85%, p=0.091) and 96% of children in both groups had a good clinical and serological response to the treatment.

Conclusion: More than half of the screen-detected children had symptoms at diagnosis. Although the clinically-detected children had more symptoms and signs of some complications there were no differences in the levels of coeliac antibodies or severity of histological damage. Moreover, both study groups showed excellent adherence and response to the gluten-free diet. Our results give further support for active screening of coeliac disease among at-risk children.

Disclosure of Interest: None Declared
**Objectives and Study:** A specific, non-invasive and standardized method method to evaluate the
compliance to the gluten free diet (GFD) is current lacking. Recently a G12 competitive ELISA test
has been shown to easily quantify traces of gluten in feces and has been proposed as new method to
monitor the compliance. We aimed to investigate the performance of the new test in children with
celiac disease (CD) and to compare this method with traditional methods of evaluating the adherence
to the GFD.

**Methods:** CD children on a GFD for at least 6-months, healthy children on a normal diet and healthy
controls on a GFD for one week were enrolled. A 3-day food diary was used to monitor the diet before
the enrollment. The global adherence to the standards suggested by the Italian Celiac Society on the
supply, preparation and consumption of the GF foods was evaluated using a 16 points questionnaire.
Gastrointestinal symptoms were evaluated through the GSRS scale and celiac serology (TTG IgA and
DGP IgG antibodies) was collected within 1 month from the enrollment. The competitive ELISA
iVYLISA GIP (Biomedal Diagnostic, Sevilla) designed to detect and quantify gluten immunogenic
peptides was used to analyze the stool samples, collected after 3 days of food-record.

**Results:** Seventy-two CD children (mean age: 10.63 ys), 16 controls on a normal diet (mean age: 7.97 ys, SD) and 4 healthy volunteers (medical doctors trained on the
GFD) following a GFD for at least one week were enrolled. Overall 47% of CD children were found to have detectable amount of gluten in stools compared to 100%
of controls on a normal diet. Mean GIP values in CD group were significantly lower
compared to controls (p < 0.0001). No significant correlation was found between GIP
levels and adherence to the diet (measured by the diary and the questionnaire). Both
the GSRS score and levels of “celiac autoantibodies” were found to be positively
correlated with GIP values.

**Conclusion:** The iVYLISA GIP test is a non-invasive, very sensitive and promising test
to assess the compliance to the GFD, especially in children. Our results show that an
high percentage of CD children have detectable traces of gluten in faeces. This may
indicate incomplete adherence to the GFD and furthermore we found a significant
correlation with both clinical and serological data. Our preliminary findings need to be
replicated in other centres and possibly compared to a larger group of healthy
controls.

**References:** 1. Comino I, Real A, Vivas S et al. Monitoring of the gluten free diet in celiac patients by

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

**Coeliac Disease**

PO-G-0040

**PREVALENCE OF COELIAC DISEASE AMONG ASYMPTOMATIC CHILDREN WITH AUTOIMMUNE DISORDERS**

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**Objectives and Study: Introduction:** Many studies proved that classical definition of coeliac disease (CD) comprises only 30% of cases, the vast majority of patients being pauci-symptomatic. Active-case finding in groups at risk is considered a cost/effective strategy. **Objectives:** To determine the prevalence of CD in a paediatric population from the Western part of Romania with autoimmune thyroid disorders (AITD) and insulin-depended mellitus diabetes (IDDM) and in a control lot and to assess the clinical forms of presentation and HLA polymorphism.

**Methods:** The authors screened for CD 74 consecutive children with AITD (lot 1), 98 children with IDDM (lot 2) and 80 healthy children (control lot). In patients with at least one positive serologic test, intestinal biopsy was performed. All children underwent HLA typing for DQ2/DQ8.

**Results:** CD prevalence after screening in lot 1 was 7% (5 patients), in lot 2 it was 6% (6 patients). In the control lot, the prevalence was 0%. There were not significant differences between the frequency of CD among children with AITD versus children with IDDM (p>0.05). Most of the cases (82%) presented as silent CD. All children diagnosed with CD presented DQ2 or DQ8 haplotype. 20% of the control subjects associated heterozygous DQ2 alleles. From 69 children with AITD/without CD, only 3 patients (4%) presented predisposing haplotype for CD-heterozygous DQ2. The rest of 66 patients (96%) associated non-DQ2/DQ8 alleles. From 92 children with IDDM and negative results for CD, 25 patients (27%) associated homo or heterozygous DQ2 and DQ8 alleles. The rest of 67 patients (73%) had non-DQ2/DQ8 alleles. There were significantly more cases with IDDM/without CD with predisposing haplotype for CD (27%) compared to the number of patients with AITD seronegative for CD with DQ2/DQ8 alleles (4%), p<0.05.

**Conclusion:** Recommending AITD and IDDM as selection parameters for CD screening in asymptomatic children is justified by the high frequency of gluten enteropathy obtained in this study (7% and 6% respectively). HLA assessment alone cannot highlight a significant role of a certain allele in the pathogenesis of autoimmune comorbidity AITD/CD or IDDM/CD. Except the haplotype, genetic non-HLA and environmental factors play a major role in a child with an autoimmune condition for the initiation and maintenance of the immune response to gluten. Performing as first line approaching HLA typing in asymptomatic at risk children may be a valuable proposal. A negative result for DQ2/DQ8 alleles will render CD highly improbable and there will be no need for subsequent CD antibodies testing or repeated biopsies.

**References:**

**Disclosure of Interest:** None Declared
Objectives and Study: Studies have suggested a correlation between coeliac disease and other autoimmune diseases, of them thyroid autoimmunity being one of the most common. However, data are conflicting regarding the effect of coeliac disease treatment on the incidence of other autoimmune diseases. We investigated the association of thyroid autoimmunity and thyroid function in 12-year-old children with coeliac disease (treated and untreated) compared to their healthy peers.

Methods: Blood samples from 12632 children were collected. In total, 335 children with screening-detected (i.e. untreated) and previously diagnosed (i.e. treated) coeliac disease were identified. A case-control study was designed. Among those free of coeliac disease, 1695 controls were randomly selected. Thyroid autoimmunity was assessed with antibodies against thyroid peroxidase (TPO Abs), and thyroid function was assessed with thyroid stimulating hormone (TSH) and free thyroxine (fT4).

Results: Hypothyroidism was more common in children with coeliac disease and TPO Abs positivity (10/19, 52.6%) than in children without coeliac disease but with TPO Abs (12/46, 26.1%) with an odds ratio of 3.1 (95% CI 1.03–9.6). Positive TPO Abs titre increased the risk of developing hypothyroidism in all groups. The odds ratios (with 95% confidence intervals) were: (a) 5.3 (2.7-11) in healthy 12-year olds; (b) 10 (3.2-32) in screening-detected coeliac disease cases; (c) 19 (2.6-135) in previously diagnosed coeliac disease cases and (d) 12 (4.4-32) in all coeliac disease cases together.

Conclusion: Children with coeliac disease, even if well treated, have a higher prevalence of thyroid autoimmunity than their healthy peers. Having TPO Abs in addition to coeliac disease, increase the risk of thyroid dysfunction.

Disclosure of Interest: None Declared
Gastroenterology

Coeliac Disease

PO-G-0042

THE FREQUENCY OF OBESITY IN CHILDREN WITH COELIAC DISEASE AND THE EFFECT OF GLUTEN-FREE DIET

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Objectives and Study: Several studies in adults and children with coeliac disease (CD) indicate that obesity and overweight at the disease onset is not unusual. The aim of this study was to investigate the frequency of obesity in children with CD at presentation and the effect of gluten-free diet on body mass index (BMI).

Methods: Medical records of patients diagnosed with CD based on ESPGHAN criteria between 1999-2010 were reviewed retrospectively both at diagnosis and after at least one year of gluten free diet (GFD). Patient demographics, clinical type, weight, height, BMI and compliance to GFD were recorded. Nutritional status was stated based on BMI charts from CDC. BMI percentile was evaluated according to the CDC’s classification criteria.

Results: 58 coeliac patients (mean age 7.8 ± 4.6 year, 39 female) were included. Of 58 patients with CD, 27 (42.86%) were classical type, 26 (41.2%) were atypical type and 5 (7.6%) were silent type. At the diagnosis, weight and height were below 3rd percentile in 39.6% and 43.1% of patients, respectively. The mean BMI was 15.7±1.94. Among our patients, 51 (87.9%) children were underweight, 7 (12.1%) children were normal, however, there was no patient with overweight or obesity at the diagnosis. At the first year of GFD, the compliance to GFD was determined verbally and serologically in 51 and 47 patients, respectively. At the first year of GFD, of 58 patients, 60.3% gained weight, 18.9% lost weight while there was no change in weight in 18.9% of 58 patients and the mean BMI was increased from 15.7±1.94 to 18.7±2.48 (p< 0.001). After 1 year of GFD, an increase in BMI percentile was observed in 20 of 58 patients (34.4%), (p= 0.001), but there was no patient with BMI higher than 85th percentile. After 1 year of GFD Ratio of underweight children were significantly lower than baseline (p=0.001).

Conclusion: In our study, 87.9% of the patients with CD were underweight at presentation. None of the patients were obese or overweight at diagnosis. This result may be due to the fact that this study was conducted retrospectively, therefore, obese children might not have been suspected of having CD and therefore were not tested for the disease. Although there was significant increase in BMI percentile after GFD, unlike previous reports, there were no patients who have developed obesity. It may be due to the differences in socio-economic status or nutritional habits.

Disclosure of Interest: None Declared
SERUM ANTI-TRANSGLUTAMINASE CONCENTRATIONS AND DUODENUM MUCOSAL INFLAMMATION FOR COELIAC DISEASE DIAGNOSIS.

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Objectives and Study: The intestinal histologic pattern of celiac disease (CD) is often patchy and it has been reported that histologic damage may be limited to the duodenal bulb with normal mucosa in the distal duodenum. The aim of the present study was to evaluate the variability and distribution pattern of histological lesions and mucosal deposits of anti-transglutaminase antibodies (mucosal-tTG) in both proximal and distal parts of duodenum.

Methods: In seventy paediatric patients with suspected CD (presence of both pathological concentration of anti-tTG antibodies and CD-related HLA DQ2) and in ten paediatric patients with other gastrointestinal diseases (5 gastritis, 3 eosinophilic esophagitis, 2 Crohn disease) (control patients) endoscopic biopsies were taken from the distal duodenum and from the duodenal bulb. Histologic pattern and mucosal-tTG were evaluated in bulb and distal duodenal biopsies.

Results: Sixty-three/70 patients with suspected CD showed high serum anti-tTG concentrations (85±40 U/ml, normal values <7 U/ml), villous atrophy, increased intraepithelial lymphocytes (IEL 60±25/100 epithelial cells, normal values <25/100 epithelial cells) and mucosal-tTG only in the bulb intestinal specimens. Seven/70 (10%) patients showed low serum anti-tTG concentrations (10±11 U/ml), villous atrophy, pathological IEL concentration and mucosal-tTG only in the bulb intestinal specimens. In 10/10 control patients serum anti-tTG concentrations were negative (1.5±3 U/ml), no villous atrophy and no mucosal-tTG were found neither in the bulb nor in the distal duodenal samples.

Conclusion: Our observation, by using both immunological and histological assays, confirms that the gluten-dependent intestinal lesions have a proximal-to-distal gradient in untreated CD patients at diagnosis time. In patients with very low positive serum anti-tTG concentrations the villous atrophy and mucosal-tTG were confined to the duodenal bulb. From a clinical point of view, proximal and distal parts of the duodenum should be analysed in the presence of low serum anti-tTG concentrations for the CD diagnosis.

Disclosure of Interest: None Declared
**Objectives and Study:** Impaired growth is a well-known complication in childhood celiac disease but its prevalence and associated factors in the modern diagnostic era are poorly known. We investigated these issues in a large cohort of children with celiac disease.

**Methods:** The following data at diagnosis was gathered from 530 patients with celiac disease: age, gender, anthropometric parameters, type and severity of the symptoms, degree of mucosal damage, celiac disease serology and various laboratory values, and prevalence of concomitant diseases and celiac disease in the family. Next, these parameters were compared between children with growth failure and those with normal growth.

**Results:** Altogether 182 (34%) children had abnormal and 348 normal growth at diagnosis. Growth failure group had lower median age (6.3 vs. 8.0 yr, p <0.001) and hemoglobin (122 vs 126 g/l, p=0.016) and higher levels of endomysial antibodies (titer 1:500 vs. 1:200, p <0.001) and thyroid stimulating hormone (2.8 vs. 2.4 mU/l, p=0.013). There were no differences between the groups in other laboratory values. Significantly associated with growth failure at diagnosis were age <3 years (OR 4.3, 95% CI 2.5-7.5 vs older children), diagnosis before the year 2000 and in years 2000-09 (OR 3.1 (1.8-5.4) and OR 1.8 (1.1-2.8) vs diagnosis in 2010-13, respectively), presence of total and subtotal villous atrophy (OR 4.2 (2.5-7.0) and OR 2.0 (1.3-3.2) vs partial atrophy), severe symptoms (OR 3.4 (1.8-6.7) vs mild symptoms) and vomiting (OR 3.1 (1.5-6.3)). Abdominal pain reduced the risk for growth failure (OR 0.5 (0.3-0.7)), while there was no effect of gender, anemia, diarrhea, constipation, concomitant diseases and celiac disease in the family.

**Conclusion:** In particular young age and severe clinical, serological and histological presentation at diagnosis were associated with growth disturbance in celiac disease. The risk for growth failure has been reduced during the 2000s.

**References:**

**Disclosure of Interest:** None Declared
**Objectives and Study:** The ESPGHAN recently put forward new criteria for diagnosis of celiac disease (CD), in which it is stated that if IgA anti-tTG exceeds 10 times the upper limit of normal (ULN), there is a possibility to diagnose CD without duodenal biopsy, if supported by anti-EMA and HLA typing. We aimed to investigate the added value of taking into account the combination of IgA anti-tTG and IgG anti-DGP as well as the antibody level in the diagnosis of CD.

**Methods:** IgA anti-tTG and IgG anti-DGP levels were measured in 156 patients diagnosed with CD (49 males; 107 females) and 974 disease controls (436 males; 538 females). All patients and controls underwent intestinal biopsy. Assays from Thermo Fisher (EliA) and INOVA (QUANTA Flash) were used. Sensitivity, specificity and test result interval-specific [i.e. 1-3 ULN, 3-10 ULN, >10 ULN] likelihood ratios (LR) were calculated for IgA anti-tTG, IgG anti-DGP and combination of both tests. A sub-analysis was performed for children (<16 years old) (58 patients and 410 controls) and adults (≥16 years old) (98 patients and 564 controls).

**Results:** Double positivity for IgA anti-tTG and IgG anti-DGP was found in 78.2 and 81.4% of CD patients with EliA and QUANTA Flash, respectively, and in <1.0% of the controls. The LR for CD markedly increased with increasing levels of IgA anti-tTG and IgG anti-DGP for both assays and independently of the age group. Sensitivity of IgA anti-tTG and IgG anti-DGP for CD was significantly higher in children compared to adults. Patients with double positivity and/or high antibody levels had a high probability of having CD (table 1).

IgA anti-tTG (EliA and QUANTA Flash) and IgG anti-DGP (EliA) levels correlated significantly with the Marsh scores (p < 0.05).
Conclusion: In conclusion, our data suggest that combining IgG anti-DGP with IgA anti-tTG and defining thresholds for antibody levels improves the serologic diagnosis of CD.

Disclosure of Interest: None Declared
**WEANING IN THE MEDITERRANEAN AREA: DATA FROM THE MEDICEL COLLABORATION**

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**Objectives and Study:** WHO guidelines recommend to start weaning from the 6 month of life, introducing semi-solid and solid food according to their availability and to the cultural tradition, limiting the intake of protein (especially from animal product), salt and sugar. Within the framework of the MEDICEL collaboration, a network of Mediterranean countries devoted to the research and management of diseases induced by food, several information sources have been consulted to compare prevalence rates of exclusive breast feeding at the age of 6 months among the Mediterranean populations.

**Methods:** Then, a survey has been carried out among the MEDICEL collaborative centers using a mailed questionnaire to obtain information on some features of weaning in those countries.

**Results:** The analysis of data provided by International Agencies indicates that in the MEDICEL Mediterranean countries, involved also in the survey (France, Slovenia, Greece, Spain, Morocco, Tunisia, Croatia, Israel, Montenegro, Italy, Malta, Egypt, Turkey, Albania) the duration of exclusive breastfeeding reaches 6 months in less than 50% of the countries. Consequently, the starting of weaning is earlier than recommended in more than 50% of the countries. Italy and France are the less compliant with the WHO recommendations, but most of the Northern African countries are also little compliant. In the ad hoc survey carried out among the collaborative centers it has been possible to have information on the referent communities. The results indicate that: only in Morocco and Slovenia habitually the weaning starts from the age of 6 months. In Montenegro, Turkey, Israel, France, Malta, Spain, Albania, Algeria and Italy weaning starts habitually between the age of 4 to 5 months. In Egypt, Tunisia, Croatia and Greece a relevant part of the infants start weaning at 6 months. Cereals and fruit appears to be the most frequent early introduced food.

**Conclusion:** These data indicate how difficult is to achieve the goal proposed by WHO for weaning. Independently from the cultural differences in the Mediterranean countries, which refer to three different religions, the current trend is to introduce food other than breast milk earlier than what is recommended for the good health of individuals.

**Disclosure of Interest:** None Declared
GLUTEN FREE DIET OR ALTERNATIVE THERAPY: A SURVEY ON WHAT PARENTS OF COELIAC CHILDREN WANT

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Objectives and Study: The treatment of celiac disease (CD) is by means of a strict life-long gluten-free diet (GFD) and usually leads to remission. Novel therapeutic approaches are under development. Our study evaluated the willingness of CD children’s parents to alternative therapy and the GFD impact.

Methods: Parents of celiac children on GFD were surveyed by a questionnaire investigating both the need and preference for novel CD therapies, their children’s enrolment in clinical trials, the overall levels of compliance to and personal judgment on GFD, health status (HS) and quality of life (QOL).

Results: 116 completed questionnaires were collected: 59.5% surveyed parents expressed the need for an alternative therapy. The preferred choice was a vaccine-based strategy (39.9%) followed by the on-demand use of drugs (27.5%). 37.7% total parents would accept to enroll their child in an ad-hoc clinical trial but only 20.3% would agree to perform endoscopy during the trial. GFD compliance was 97.4% and was well accepted by 93.8% of the parents. HS and QOL significantly improved during GFD (p < 0.001).

Conclusion: 116 completed questionnaires were collected: 59.5% surveyed parents expressed the need for an alternative therapy. The preferred choice was a vaccine-based strategy (39.9%) followed by the on-demand use of drugs (27.5%). 37.7% total parents would accept to enroll their child in an ad-hoc clinical trial but only 20.3% would agree to perform endoscopy during the trial. GFD compliance was 97.4% and was well accepted by 93.8% of the parents. HS and QOL significantly improved during GFD (p < 0.001).

Disclosure of Interest: None Declared
ANAEMIA AND IRON DEFICIENCY IN CHILDREN WITH POTENTIAL COELIAC DISEASE

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Objectives and Study: Anaemia and iron deficiency are common in advanced coeliac disease (CD) with mucosal atrophy. Nowadays active case-finding and screening frequently detects children with positive coeliac antibodies but normal villous morphology (potential CD). Currently it is unclear whether these subjects already have clinical signs and thus should be treated. We investigated the prevalence of anaemia and iron parameters in children with potential and advanced CD.

Methods: The prospective study comprised 57 untreated children with advanced CD and 11 with potential CD. Coeliac patients were further categorized to those with partial or subtotal villous atrophy (Corazza B1, n=43) and those with total atrophy (Corazza B2, n=14). The groups were compared for the prevalence of anaemia and blood levels of haemoglobin, total iron, ferritin, transferrin receptor 1 (TfR1), transferrin iron saturation, and hepcidin. Eleven healthy controls were chosen for comparisons of haemoglobin and hepcidin levels.

Results: The groups did not differ in gender or median age at diagnosis. The prevalence of anaemia was 0% in controls, 18% in potential CD, 30% in B1 and 64% in B2 group. The mean haemoglobin was significantly lower in B2 (107.7 g/l) compared with the controls (123.8 g/l, p=0.003), potential CD (123.8 g/l, p=0.008) and B1 (120.0 g/l, p=0.003). Total iron below reference was seen in none in potential CD, 12% in B1 and 50% in B2 and the median value was lower in B2 (8.1 µmol/l) compared with the potential CD (13.9 µmol/l, p=0.009) and B1 (13.5 µmol/l, p=0.013). Increased TfR1 value was present in 9% in potential CD, 21% in B1 and 36% in B2 and the median value was higher in B2 (5.9 mg/l) than in potential CD (3.7 mg/l, p=0.016) and in B1 (4.3 mg/l, p=0.008). Low ferritin was found in 18% in potential CD, 30% in B1 and 78% in B2 and the median value was lower in B2 (6 µg/l) compared with potential CD (19 µg/l, p=0.001) and B1 (14 µg/l, p<0.001). Prevalence of low transferrin saturation was 18% in potential CD, 40% in B1 and 71% in B2 and the median saturation was lower in B2 (8%) compared with potential CD (21%, p=0.003) and B1 (18%, p=0.004). There were no differences in the median hepcidin levels between the groups.

Conclusion: Development of anaemia and/or iron deficiency in CD is a continuum and may be present already in potential CD with normal villous morphology. The results support active follow-up and individualized decision-making in dietary treatment of these children.

Disclosure of Interest: None Declared
HOW VALUABLE IS “10-TIME ULN THRESHOLD” FOR IDENTIFYING VILLOUS ATROPHY IN SCREENING-DETected PATIENTS?

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Objectives and Study: In 2011, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) has released its updated guidelines on coeliac disease (CD) diagnosis. According to these new guidelines, symptomatic children with anti-transglutaminase (anti-tTG) 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 “multiple” duodenal biopsies to confirm a suspected CD. The aim of the study was to calculate the positive predictive value (PPV) of anti-tTG levels ≥ 10 ULN in discovering a severe mucosal damage in asymptomatic children, identified by salivary screening.

Methods: From March 2007 to February 2014, 11698 children (age range: 5-10-years) were enrolled in Rome and Civitavecchia. A total of 8871 salivary samples were collected and tested for anti-tTG, using a fluid-phase radioimmunoassay (RIA). Salivary anti-tTG-positive children were analyzed for serum antibodies (EMA and enzyme-linked immunosorbent assay (ELISA) anti-tTG). Positive children underwent upper gastrointestinal endoscopy; histological lesions were graded according to the Marsh-Oberhuber (MO) criteria.

Results: Among the 8871 screened children, 68 (0.76%) had positive anti-tTG antibodies both in serum and salivary samples. Among them, 57 (83.82%) had anti-tTG titers ≥ 10 times ULN; of these, 56 (98.24%) showed severe lesion degree (3a, 3b, 3c MO) and 1 (1.75%) received a diagnosis of potential CD (MO1). On the contrary, 11 out of 68 (16.17%) children had anti-tTG titers < 10 times ULN; 10 (90.90%) of them had severe mucosal damage (3a,3b, 3c MO) and 1 (9.09%) was classified as potential CD patient (MO 0). These results suggest that anti-tTG ≥ 10 times ULN are remarkably reliable of severe histological damage in asymptomatic children (PPV= 98.2% CI: 90.0%>100%)

Conclusion: If proved in larger and multi center studies, our results suggest the possibility to apply the “biopsy-sparing” protocol also in asymptomatic patients with anti-tTG titer ≥10 times ULN.

Disclosure of Interest: None Declared
**Objectives and Study:** The clinical spectrum of Coeliac disease (CD) in children is wide. Recently, atypical or asymptomatic manifestations are becoming more commonly described in older children and adolescents. Typical forms of CD usually present in young children with failure to thrive, chronic diarrhea, abdominal distention, muscle wasting and hypotonia, poor appetite, and unhappy behavior. Atypical CD is characterized by unusual intestinal complaints (vomiting) or by extra-intestinal manifestations (e.g., pubertal delay, iron deficiency, aphthosis, dental enamel defects, and abnormalities in liver function test). Asymptomatic patients are usually screened for associated conditions such as diabetes mellitus type 1, autoimmune thyroiditis, epilepsy, Down’s Syndrome or a family history of CD. The aim of our retrospective study was to describe the presenting features of CD in a large court of children with coeliac disease diagnosed between January 2007 and December 2013.

**Methods:** We retrospectively assessed the clinical charts of 783 children (mean age: 8.3 years, age range: 10 months-17 years) who had received a CD diagnosis based on elevated titer of antibodies and histology. Patients were distinguished between symptomatic (with typical or atypical CD manifestations) and asymptomatic.

**Results:** Among 783 children with biopsy-proven CD, a group of 516 (65.90%) had symptoms of typical CD; recurring abdominal pain was present in 228 (44.18%) of them; 123 (23.83%) patients showed failure to thrive and 89 (17.24%) diarrhea; 56 (10.85%) showed constipation, and bloating was present in 19 (3.68%). Coeliac crisis occurred in only 1 (0.19%) child. Many patients showed more than one symptom. Atypical presentation was present in 107 (13.66%) children; anemia was the most common symptom in this group (45, 42.05%); 14 (13.08%) children showed vomiting, whereas alopecia and urticaria appeared in 3 (2.80%) and 2 (1.86%) patients respectively; 10 (9.34%) children had headache and only 1 (0.93%) child was screened for recurrent respiratory infections. No symptoms were found in 160 (20.43%) children; among these, 54 (33.75%) were screened for a family history of CD and 5 (3.12%) were screened for associated disorders (3 diabetes mellitus type, 1 Down’s Syndrome, 1 autoimmune thyroiditis).

**Conclusion:** Abdominal pain and failure to thrive are the clinical features of CD most frequently observed in childhood; anyway, symptoms such as anemia, headache, alopecia and urticaria should become more and more wake up-calls for CD.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Chronic diseases such as celiac disease (CD), involving a restrictive and specific diet, have been associated with problems of eating behavior and psychopathology. The objective of this study was to evaluate the frequency of dysfunctional eating behaviors, evaluate the perception of illness and psychological well-being in young people with CD.

**Methods:** The participants were celiac patients, diabetes type 1 and healthy subjects. They were evaluated by anonymous questionnaires send by mail with the Questionnaire of Beliefs about Illness, the Eating Disorders Questionnaire (EDE-Q5.2) and the Scale of Psychological Well-Being for Teens.

**Results:** The population was 47 celiac patients, 248 healthy subjects and 79 diabetes type 1 patients. The evaluation started in 2014 and 36 CD patients accepted to participate (76.6%), 21 (58.3%) were girls, aged between 11 and 28 years. The celiac diagnosis was at mean(M)±standard deviation(SD):3.26±3.21 years of age. CD was not an isolated disease in 16.7%. The body mass index was M:20.8±SD:3.1 kg/m², 72.2% reported being satisfied with their weight and 38.9% reported episodes of binge eating. Healthy subjects, aged between 13 and 18 years, reported more episodes of binge eating, \[U = 2774.00, p = .02\]; less satisfied with their weight \[U = 3134.00, p = .009\] and their body image \[U = 2764.00, p = .004\] than celiac patients. Diabetics type 1 patients, aged between 12 and 19 years, had a more eating psychopathology \[U = 490.50, p < .001\] than healthy subjects and celiac patients. Lower levels of psychological well-being and a more threatening perception of the disease were associated with higher levels of eating psychopathology in celiac patients. A more threatening illness perception has emerged associated with lower psychological well-being. The celiac patients had the lowest degree of eating psychopathology of the three studies groups.

**Conclusion:** Celiac patients had a lower degree of eating psychopathology. The management of CD in adolescence, can be a challenge for teenagers and young adults, and may be reflected in the level of feeding behavior and psychological well-being.
**Gastroenterology**

**Coeliac Disease**

PO-G-0052

**A CLINICAL AUDIT ON COMPLIANCE OF THE NEW EUROPEAN SOCIETY FOR PAEDIATRIC GASTROENTEROLOGY, HEPATOLOGY AND NUTRITION (ESPGHAN) GUIDELINES FOR DIAGNOSIS OF COELIAC DISEASE**

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**Objectives and Study:** A retrospective audit was carried out at a busy NHS Hospital that looked at all cases with a diagnosis of coeliac disease (CD) between January 2012 to November 2014 in order to analyse if the management was compliant with the current ESPGHAN CD guideline. The main conclusion of the guideline was that in the presence of high antibody levels the diagnosis of CD may be based on a combination of symptoms, antibodies, and HLA, thus omitting the duodenal biopsy.

**Methods:** The case notes and clinic letters for all potential patients (identified from clinic lists and clinical coding) were analysed to select patients who had a diagnosis of CD after January 2012, and were aged 16 or below at time of diagnosis.

**Results:** 14 cases were identified which met the inclusion criteria. Results showed a male to female ratio of 1:3. Mean age of diagnosis was ten years. All cases were of white Caucasian ethnicity with varied abdominal symptoms. 2 patients (14%) had type 1 diabetes and 1 patient (7%) had autoimmune hypothyroidism as co-morbidities. 8 patients (57%) had a family history of CD. All patients had measurement of IgA tissue transglutaminase type 2 antibody (TG2 antibody). However, only 4 patients (28%) had total IgA levels measured. 10 patients (71%) had TG2 levels greater than ten times the upper limit of normal. But all of them went on to have endoscopy and biopsy with no evidence in the notes of any discussion with the family about the current guideline. Only 2 patients (14%) had HLA testing. 10 patients had also measurement of IgA Endomysial antibodies (EMA). 12 out of 14 patients (86%) had endoscopy and biopsy to confirm the diagnosis. 2 patients did not have biopsy as their symptoms got better with gluten free diet and family was not keen to have gluten challenge. These 2 patients had positive HLA for CD. All patients who underwent biopsy had a four-quadrant biopsy but none of them were reported as per the modified MARSH criteria.

**Conclusion:** Despite clear guideline on the new diagnostic pathway of CD, a large variability of the clinical practice was observed. Most importantly biopsy could have been avoided in some of these patients with a high positive serology and a positive HLA test. Apart from early diagnosis, there might be a significant cost implication by avoidance of invasive procedures. Education and training of health professionals to make them aware of the current guideline is therefore recommended to achieve a better outcome in this multisystem disorder.


**Disclosure of Interest:** None Declared

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PREVALENCE OF COELIAC DISEASE AMONG SCHOOLCHILDREN WITHOUT THE CLASSICAL SYMPTOMS

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Objectives and Study: Estimate the prevalence of celiac disease among schoolchildren without the classical symptoms.

Methods: After random selection, 1606 apparently healthy children enrolled in 5th to 8th grade of municipal and state schools in the city of São José do Rio Preto were submitted to blood collection for a blood count and for the determination of the anti-transglutaminase IgA antibody (anti-tTG IgA). Samples with positive or indeterminate results for the anti-tTG IgA antibody were also tested for the presence of antiendomysium IgA antibody (AEM IgA). A total of 101 samples from children with laboratory anemia, chronic diarrhea, a family history of celiac disease, diabetes or with indeterminate anti-tTG IgA and negative AEM IgA were also tested for the presence of anti-tTG IgA by other kit, anti-tTG IgG antibody and for serum IgA determination. Children with positive anti-tTG IgA and AEM IgA antibodies or positive anti-tTG IgG associated with IgA deficiency were submitted to a duodenal biopsy.

Results: The diagnosis of celiac disease was confirmed in only one child. Thus, the prevalence of celiac disease in the study population was 1:1606 (0.062%; 95% CI, 0.003%>0.36%).

Conclusion: This is the first study of the prevalence of celiac disease among healthy schoolchildren in Brazil, and unexpectedly found a very low prevalence. We believe that further studies are needed to determine the true prevalence of celiac disease in Brazil, considering that studies on blood donors and on serum samples from a clinical laboratory, such as those previously conducted in our country, are not representative of the general population.

References:

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Disclosure of Interest: None Declared
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**Coeliac Disease**

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**COMPARISON OF THE RELIABILITY OF COELIAC DISEASE SEROLOGY TO REFLECT INTESTINAL DAMAGE**

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**Objectives and Study:** In view of the increasing importance of the serological biomarkers for the screening and diagnosis of CD, their differential performance, and the lack of head to head comparison, we undertook the task to evaluate the reliability of those isolated or combined antibodies to reflect the intestinal damage in children with CD.

**Methods:**

**Methods:** 95 pediatric CD patients (mean age 8.3±4.4), 45 nonspecific abdominal pain children (AP) (mean age 7.3±5.1), 99 normal children (NC) (mean age 8.5±4.2) and 79 normal adults (NA) (mean age 28±5.1) were tested by the following ELISAs, detecting IgA, IgG or both, IgA and IgG: Aeskulisa® Gliadin (AGA), Aeskulisa® tTg (tTG; RUO), Aeskulisa® DGP (DGP) and Aeskulisa® tTg New Generation (Neo-epitope tTg complexed to gliadin=tTg-neo). The results were compared to the degree of intestinal injury, using revised Marsh criteria.

Scatter diagrams and regression analysis comparing the 12 antibodies’ OD activities to the degree of the intestinal damage were correlated.

**Results:** In general, the comparison showed that most of the assays are able to differentiate patients with low and high degree of intestinal damage. Comparing the different correlations between CD associated IgA and IgG antibodies’ isotypes, the tTg neo IgA (r²=0.968, p<0.0025) and tTg-neo/DGP IgGs (r²=0.989, p<0.0001/ r²=0.985, p<0.0001, respectively) stood out, significantly, as the best indicators of the intestinal damage in CD.

The highest optical density (OD) values (medium OD 2.94±1.2, p<0.0001) were achieved by using the tTg-neo IgA ELISA in patients with Marsh 3c.

**Conclusion:** Therefore, it is suggested that tTg-neo IgA/IgG antibodies should be preferably used to reflect intestinal damage during screening, diagnosing and monitoring compliance in childhood CD.

**Disclosure of Interest:** T. Matthias Conflict with: All the ELISA kits used are Aaskulisa, produced in Aesku.diagnostics, P. Jeremias Conflict with: employed by Aesku.Kipp Institute, A. Lerner: None Declared, S. Neidhofer Conflict with: Employed by Aesku.Kipp Institute
THE CHANGING FACE OF COELIAC DISEASE IN NEW ZEALAND CHILDREN 1999-2014

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Objectives and Study: The classical presentation of coeliac disease with profound malabsorption in infancy is increasingly uncommon. With increasing awareness by the public and primary and secondary care, improved serological investigations and increased screening of at risk groups, the spectrum of disease presentation has become wider. We compare the prevalence and presenting clinical features of two cohorts of children diagnosed with coeliac disease over a 15 year period in one of two tertiary paediatric gastroenterology units in New Zealand.

Methods: Data were prospectively collected by questionnaire on children diagnosed with coeliac disease at Starship Children's Hospital, Auckland between April 2013 and October 2014. This included data on epidemiology (gender, age, ethnicity) and presenting symptoms. Results were compared with results of a retrospective study performed in the same institution between January 1999 and December 2002. (1)

Results: 79 children (F =50) were diagnosed with coeliac disease over an 18 month period. This compares with 48 children diagnosed between 1999 and 2002. The median age at presentation in the current study was 7.3 years, compared with 6.7 years in the historical cohort, with an overall trend to older age. Data on ethnicity are not presented in the 1999-2002 study. In our study, 84% of children were of Caucasian ethnicity. Although individuals of Maori and Pacific Island descent comprise 25-30% of the local population, no children were identified as belonging solely to either of these groups, though five children claimed mixed ethnicity incorporating Maori or Pacific Island heritage (in conjunction with New Zealand European heritage in all cases).

Nine children (11%) in our recent study were identified as a result of screening of at risk groups, compared with 9 children (19%) from the 1999-2002 study. These included 7 children with affected first degree relatives, two children with Type 1 diabetes mellitus and one child with Down syndrome. 49% of children in the recent study presented with symptoms suggestive of malabsorption, with a greater proportion presenting with non-specific gastroenterological symptomatology.

Conclusion: Over the past 15 years, there has been a greater than fourfold increase in incidence of coeliac disease presenting to our institution. There is a trend towards increasing age. Although some children still present with malabsorptive symptoms, the majority present with more non-specific symptomatology, though this has not changed significantly between the two studies. The lack of coeliac disease in the Maori and Pacific Island population is of note and is likely to reflect the low prevalence of coeliac-susceptible HLA phenotypes in these ethnic groups.

Disclosure of Interest: None Declared
DIFFERENCES IN CLINICAL AND HISTOLOGIC CHARACTERISTICS AMONG COELIAC PATIENTS FROM DIFFERENT ETHNIC ORIGINS IN ISRAEL.

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Objectives and Study:
Background: While the incidence of Celiac Disease (CD) is increasing, there is limited understanding of phenotypic differences and outcomes by ethnicity.

Aims: To investigate the possible association between the ethnicity, clinical presentation and severity of the disease

Methods: Patients and methods: Data were retrieved from the database of Assaf Harofeh Medical Center, Israel, and from a questionnaire filled out by CD patients that sent by the mail via the Israeli Celiac Foundation. Data included: demographic data, clinical presentation of disease, hemoglobin level, iron, parents’ country of birth, presence of CD among first or second degree relatives, presence of other autoimmune diseases and severity of disease by Marsh classification

Results: A total 1070 patients were included (median age of 9, range 1-82 years).
Distribution of ethnic origin was: North Africa 24%, North America 6%, Western Europe 19%, Eastern Europe 66%, Balkan 11%, Israel 16%, Central Asia 4% and Middle East 26% (alone or in combination). North Africa origin was less associated with anemia (p=0.018). Eastern Europe was associated with less severe CD according to Marsh classification, while North American origin has been associated with more severe CD, as well as Balkan origin (p=0.03). Compared to others, Israeli origin was associated more with classical presentation (intestinal). Elevated liver enzymes and thyroid disease were associated with West Europe origin (p=0.03).

Conclusion: Conclusions: We identified significant differences in clinical and histologic characteristics between different ethnicity groups in Israel. These results have implications for future genotype-phenotype studies

Disclosure of Interest: None Declared
EVALUATION OF SUBCLINICAL ATHEROSCLEROSIS AND ENDOTHEL DYSFUNCTION IN CHILDREN WITH COELIAC DISEASE

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Objectives and Study: Atherosclerosis and ischemic heart disease are increasingly diagnosed in adult coeliac patients owing to chronic inflammation in recent years. However, there is no data about paediatric coeliac disease (CD). In this study, we aimed to investigate the frequency of endothelial dysfunction and subclinical atherosclerosis in children with CD by pulse wave velocity (PWV) and carotid intima-media thickness (cIMT) as compared with healthy controls.

Methods: The study included 40 coeliac patients (6-18 years old) and 40 healthy age and sex matched controls. Patients who had obesity, diabetes mellitus, smoking exposure and positive family history for dyslipidemia and early coronary arterial disease were excluded. After an overnight fast, endothelial function was assessed by arterial tonometry and cIMT was measured by high-resolution ultrasonography. Additionally, height, weight, body mass index (BMI), blood pressure (BP), fasting lipid profile, 25-OH vitamin D, glucose level, C reactive protein (CRP), erythrocyte sedimentation rate (ESR), tissue transglutaminase antibody (tTG) IgA, serum IgA, and HbA1c were analysed in each child. PWV was assessed by sex-specific curves for height, and abnormal PWV was defined as PWV >90%.

Results: Five patients (1 CD, 4 control) were excluded from statistical analysis because of high HbA1c levels. Thirty-nine coeliac patients (%48.7 male, mean age 12.9±3.4 year) and 36 healthy children (%44.4 male, mean age 12.7±3.6 year) were enrolled. The median follow-up was 35 months (range 1-102 months). tTG antibody was negative in the control group, however, it was positive in 18 coeliac patients. Of 39 patients with CD, 61.5% were classical type, 28.2% were atypical type and 10.2% were silent type. Histopathologically, 73.7% of patients had Marsh 3c. There was no difference for age, gender, body mass index, blood pressure, HbA1c, lipid profile, 25-OH vitamin D, ESR, CRP, PWV and cIMT between groups. Frequency of abnormal PWV was higher in coeliac patients (43.6%) than control groups (26.4%), however, there was no statistical significance (p=0.201). No difference was found in PWV and cIMT between in coeliac patients with tTg positive and tTg negative. Moreover, an 11 year-old male with CD had both abnormal PWV and increased cIMT and atherosclerotic plaques.

Conclusion: Our study showed no significant increase regarding endothelial dysfunction and subclinical atherosclerosis in children with CD compared to controls. However, our results should be confirmed by other large studies.

This project was supported by the National Paediatric Society.
Disclosure of Interest: None Declared
RISK OF COELIAC DISEASE IN CHILDREN WITH TYPE 1 DIABETES MELLITUS AND POSITIVE ANTI-TISSUE TRANSGlutAMINASE TITRES

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Objectives and Study: Coeliac disease (CD) is one of the most frequent autoimmune disorder associated with type 1 diabetes mellitus (T1DM). According to American Diabetes Association (ADA) serological screening for CD should be performed in all T1DM patients using anti-tissue transglutaminase antibodies IgA (TTG-IgA) or IgG (TTG-IgG) if IgA-deficiency is present. In the presence of CD-related antibodies positivity it is mandatory to perform bowel biopsy to confirm diagnosis of CD. The aim of this study was to evaluate the correlation between positive TTG level and the clinical status of CD in children with T1DM. The second purpose was to determine the positive cut-off value of anti-TTG that best predicts histopathological diagnosis of CD in children with T1DM.

Methods: We enrolled 23 children (10 boys and 13 girls) aged 4-16.5 years (mean age was 9.68±2.98 years) with T1DM and positive serological screening for CD. In 7 children anti-TTG titres were slightly elevated (<3 x normal), in 9 moderately (3 to 10 x normal) and in 7 highly (>10 x normal). All these subjects underwent intestinal biopsy. CD was diagnosed based on Marsh score ≥ III. All subjects with intestinal biopsy proven CD had anti-TTG titres more than 10 times upper limit of normal (ULN) (3/7,43%). None of the T1DM subjects with anti-TTG titres elevated less than 10 times ULN was diagnosed with CD. 7 of 23 (30%) children had clinical symptoms of CD: 4 had abdominal pain (17%), 2 were diagnosed with growth failure (9%) and 1 with failure to thrive (4%). Symptoms were present in 2 of 3 (66%) children with biopsy proven CD (abdominal pain and growth failure). HLA DQ2 or/and HLA DQ8 haplotypes were found in 21 of 23 subjects (91%). Genetic predisposition was excluded in 2 patients with slightly and moderately elevated anti-TTG titres. 18 (78%) T1DM children with the CD-specific antibodies and compatible HLA but without histological abnormalities in duodenal biopsy were diagnosed with potential CD. In 2 (9%) T1DM patients with CD-specific antibodies but without compatible HLA and villous atrophy CD was excluded.

Conclusion: 1. There is positive correlation between level of anti-TTG antibodies and risk of villous atrophy. 2. It seems that T1DM children with slightly and moderately elevated anti-TTG titres could have been biopsied unnecessarily. 3. T1DM patients with anti-TTG titres more than 10 times ULN would have needed endoscopy to diagnose villous atrophy or to exclude histological abnormalities.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Incidence of coeliac disease (CD) is rising, but it is still underdiagnosed. The last decades brought considerable change in the presentation. Whom to test is an intriguing issue. The study aimed to establish the usefulness of active screening and identify symptoms or most common symptom associations that should now raise the awareness of physicians to test for CD.

METHODS: Patients presenting with CD symptoms admitted in Pediatrics Departments (Gastroenterology, Pneumology, Toxicology, General Pediatrics) from March 2013 until February 2014, were prospectively screened for CD. The inclusion criteria were gastrointestinal and/or non-gastrointestinal symptoms (ESPGHAN guideline). For each patient IgA antitransglutaminase antibodies (ATG) and seric IgA were determined. For patients with IgA deficiency, the level of IgG-ATG was used instead. Diagnosis of CD was established according to ESPGHAN criteria. Intestinal biopsy was performed using Marsh-Oberhuberand classification and indicated to all patients with positive ATG, with levels <10x normal. For patients with ATG >10x normal, anti-endomysial antibodies (EMA) and HLA DQ2/DQ8 were performed. A single/multivariate statistical analysis was used to identify risk symptoms and symptom associations.

RESULTS: We included 249 patients with symptoms at risk of CD. Mean age was 5.4 yr. IgA-ATG were positive in 11 patients. Eight had IgA deficiency and were tested for IgG-ATG, 3 testing positive. Out of 14 patients with positive ATG (IgA/IgG), 2 were lost from follow-up and for one HLA testing infirmed the diagnosis. In 6 cases the diagnosis of CD was confirmed through intestinal biopsy and in 5 with ATG >10x normal, through positive EMA and HLA. CD was diagnosed in 11 children (1:21 patients presenting at risk symptoms). Mean age at diagnosis was 4 yr. One in 12.6;16;18 children with chronic diarrhea, low stature, growth failure, but also 1 in 18.5 with recurrent abdominal pain and constipation respectively had CD. A number of symptom associations were demonstrated to have put the patient at high risk of CD: recurrent abdominal pain + weight loss (OR=29; p=0.001), chronic diarrhea + weight loss (OR=27; p=0.003), constipation + weight loss (OR=26; p=0.01), constipation + refractory anemia (OR=24; p=0.04).

CONCLUSION: A 4.4% prevalence of CD was observed in symptomatic patients. Classical symptom associations (chronic diarrhea + weight loss) as well as others (recurrent abdominal pain + weight loss, constipation + weight loss, constipation + refractory anemia) were demonstrated most oftenly in patients with CD. We consider that active screening among patients with symptoms and especially symptom associations at risk of CD according to ESPGHAN guideline would improve the diagnosis rates in paediatric CD.
Disclosure of Interest: None Declared
Gastroenterology
Coeliac Disease
PO-G-0060

DELAY IN DIAGNOSIS AND CLINICAL PATTERN OF CHILDHOOD COELIAC DISEASE HAVE CHANGED IN NE SLOVENIA IN LAST DECADE

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Objectives and Study: Burden of coeliac disease (CD) is increasing worldwide. Despite the wide availability of sophisticated diagnostic tools in many regions, long diagnostic delays still remain a major problem, and many patients remain undiagnosed for several years.

The aim of our study was to determine the changes in diagnostic delay and clinical presentation of childhood CD in NE Slovenia within the last decade.

Methods: Children diagnosed with CD in a single centre in NE Slovenia were divided into two groups based on the year of diagnosis. Patients diagnosed between 2002 and 2004 were included in the first group, and those diagnosed between 2012 and 2014 in the second. Diagnosis was based on the same ESPGHAN diagnostic criteria including positive serology, genetics and histology in all children. Demographic data, age at diagnosis, delay in diagnosis and presenting symptoms were documented.

Results: There were 32 patients in the first (68.8% females), and 49 (69.4% females) in the second group. Mean age at diagnosis has increased by 11m in the observed period (not significant). It was 5y 11m (range: 10m-17y 9m) in the first group, and 6y 10m (range: 1y 1m-16y 3m) in the second.

Diagnostic delay in symptomatic patients has decreased significantly, however (p<0.05), from being 2y 1m in the first group to 11m in the second. It was most pronounced in boys (from 1y 9m to just 6m). Significant difference was also observed in the mean age at the onset of symptoms (p<0.05). This increased from 3y 8m to 5y 11m respectively.

We also observed an important change in presenting clinical picture. The number of asymptomatic patients has doubled (from 9.4% to 18.4%), the number of patients with "typical" clinical picture (diarrhoea and failure to thrive) has decreased (from 43.8% to 26.5%), and predominant presenting symptom became unspecific abdominal pain (from 25% to 36.7%).

Conclusion: Diagnostic delay in children with CD has decreased significantly in our region despite the change of the clinical picture from "typical" to more diverse. Since the availability of diagnostic tests has not changed in the last decade this should be attributed to other causes.

Two major CD awareness projects funded by EU were implemented in the region during this period. This leads us to the conclusion that better awareness about the disease among both health care professionals and general public has the most important influence on the early recognition of CD and thus on avoiding unneeded burden of undiagnosed celiac disease. Such awareness activities should have high priority due to their important influence on general health of the population.
Disclosure of Interest: None Declared
Objectives and Study: The long-term evaluation of the final growth in height and weight of patients treated for coeliac disease (CD) under the gluten-free diet.

Methods: This study completed the enrolment of 34 patients, including 26 girls and 8 boys, suffering from CD, with a disease duration ranging from 11 to 15 years on a gluten-free diet, and benefiting from a regular monitoring in children's university hospital.

Results: At enrollment in the study, anthropometric data of patients showed that 70.6 per cent of children had a low weight-to-height ratio with severe energy deficit. Significant damage villous atrophy from grade IIIa (partial villous atrophy) to grade IIIc (total villous atrophy) according to the Marsh grading system were found on duodenal biopsies in 100 % of cases. We demonstrated a statistically significant association between good follow-up of a gluten-free diet and the clinical presentation and other laboratory markers at the medical check-up within one year of diagnosis (P = 0.004), and they have tested negative in a serological test for the specific antibody to the disease. (P = 0.003). There is a significant improvement of the height measured in standard deviations after 14 years of the gluten-free diet with an average increase of 1.48 standard deviations (P = 0.041) through proper observance of RSG and prolonged medical surveillance to check the patient's progress in diet.

Conclusion: Failure to thrive is a common manifestation in children of CD. Growth normalizes quickly after proper monitoring of the gluten-free diet and coeliacs who correctly followed the gluten-free diet during childhood have a normal adult height.

Disclosure of Interest: None Declared
Abstract Submission

Gastroenterology
Cystic Fibrosis and Pancreatic Disorders
PO-G-0062
EXTRACORPOREAL SHOCK WAVE LITHOTRIPSY IN TREATING CHILDREN WITH CHRONIC PANCREATITIS
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Objectives and Study: Extracorporeal shock wave lithotripsy (ESWL) of pancreatic stones is a treatment option for patients with chronic pancreatitis (CP), when pancreatic stones cannot be removed by endoscopic procedures during retrograde cholangiopancreatography (ERCP). To our knowledge there is only one report assessing the results of using ESWL in paediatric population with CP. The aim of our study was retrospective analysis of the efficacy and clinical outcome of ESWL in treating children with CP. We also evaluated the frequency of ESWL depending on the etiological factor of CP.

Methods: 208 children with CP were hospitalized in our centre between 1988 and 2014. In treatment of 12 (5,8%) children ESWL procedure associated with endoscopic drainage was administered (7 girls and 5 boys; mean age: 12 years, range: 5.5–17 years). ESWL was performed by electromagnetic lithotripter. 12 patients underwent 16 ESWL sessions. In 9 children was performed one ESWL procedure, four had undergone it twice.

Results: Pancreatic stones fragmentation was observed in 10 of 12 patients (83,3%). In 2 patients only the second ESWL session carried out in a short period of time was effective. ESWL treatment tolerance was good. There were no significant complications related to ESWL. One patient was excluded from further analysis because of no clinical observation after ESWL, due to the continuation of the treatment in another medical center. Early pain relief after therapeutic intervention was achieved in all 9 subjects with successfully conducted procedure. At a mean follow-up of 42.5 months (range: 7-108 months) 5 of 9 (55,5%) children had no pain, 3 (33,3%) patients had episodic severe pain, whereas 1 patient had mild episodes of pain. Recurrence of pancreatic stones was revealed in 8 cases (80 %), but among them only in two children calculi were endoscopically irretrievable and require another ESWL treatment. Acute episodes of CP after ESWL - were observed in 2 of 9 (22,2%) patients.

9 of 12 children, who undergone ESWL, had a mutation of the gene PRSS1, SPINK1 or CFTR predisposing to CP. ESWL was performed significantly more frequently in children with hereditary pancreatitis compared to the group of patients with other etiologies of CP (19.2% vs 3,85%; p <0.05)

Conclusion: Extracorporeal shock wave lithotripsy is a safe and fairly successful technique in children with large pancreatic stones. This method is, however, rather the type of palliative treatment to reduce pain and improve the quality of life and does not prevent or postpone disease progression.

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Disclosure of Interest: None Declared
LONGITUDINAL TRANSIENT ELASTOGRAPHY MEASUREMENTS (FIBROSCAN) USED IN FOLLOW-UP FOR PATIENTS WITH CYSTIC FIBROSIS.

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1 Ghent University Hospital, Ghent, Belgium

Objectives and Study: Insidious developing cystic fibrosis related liver disease (CFLD) is diagnosed using a combination of criteria (1). Transient elastography (TE), an ultrasonografic method to evaluate liver stiffness, differentiates cystic fibrosis patients with and without liver disease (CFnoLD) (2) and identifies patients with an increased risk for developing varices as result of portal hypertension (3).

Aim: Can consecutive TE measurements detect evolving CFLD?

Methods: Retrospective study (2007-2013) including all patients with TE measurements, performed by the same operator and correlating the measurement to the presence or development of CFLD based on the medical files.

Results: 150 CF patients (median age 17(9-24) years), were included. Twenty (14%) had CFLD at the first TE measurement, according to the criteria (debray et al 2001). Four (3%) developed CFLD during follow-up. The median TE value in CFLD was 14 (8.7 – 32.2) compared to 5.3 (4.9 – 5.7) in CF patients without CFLD (CFnoLD) (P=0.0001). The intra-individual differences between 2 consecutive measurements was 0.05 (-1 – 1.2) in the CFnoLD and 0.55 (- 1.68 – 1.53) in the CFLD patients. The AUROC for TE predicting CFLD was 0.985. TE measurements above 6.55 kPa predicted CFLD with a sensitivity of 94.7% and a specificity of 90.8%. In the age group below the age of 14 years a TE measurement above 6.55 kPa had a positive predictive value of 83%, decreasing to 60% for the total group and a negative predictive value of 100%. Flaring of liver enzymes caused temporary increase of TE measurement. Patients with developing CFLD had progressively increasing TE measurements.

Conclusion: TE measurements progressively increased in CF patients developing CFLD. A prospective study is needed to evaluate whether TE will be able to detect CFLD before it becomes clinically apparent.

References:
Disclosure of Interest: None Declared
MRCP VERUS ERCP IN DIAGNOSIS OF CHRONIC PANCREATITIS IN CHILDREN - WHICH BETTER TO CHOOSE?

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Objectives and Study: The present study was undertaken to evaluate the diagnostic accuracy of (MRCP - magnetic resonance cholangiopancreatography) in detecting changes characteristic for chronic pancreatitis (CP) in paediatric population. Furthermore, we aimed to assess the diagnostic value of MRCP in detecting pancreas divisum (PD) – the most common congenital anomaly of pancreas - as a potential cause of CP in children.

Methods: 48 children diagnosed with pancreatic disorders hospitalized at our center since 1988 to 2014 were enrolled into the study (22 girls and 26 boys; mean age: 12.1 years, range: 3.0-17.1 years). We reviewed patients who have both ERCP (endoscopic retrograde cholangiopancreatography) and MRCP with an interval 1 to 4 months between these two procedures. We compared the results of MRCP studies to those obtained during ERCP procedure for sensitivity, specificity, positive predictive value and negative predictive value.

Results: During ERCP, diagnostic pancreatograms were achieved in 41 patients (85.4%) and only them were enrolled to the further statistical analysis. In 7 patients it failed to perform ERCP due to the difficulties in cannulation of pancreatic ducts. MRCP was done in all 48 patients (100%) and in all diagnostic images were obtained. MRCP showed sensitivity (and positive predictive values) of 77.1 % (90%) and the specificity (and negative predictive value) of 50% (27.3%) for recognition of chronic pancreatic features. There was a significant difference between the group of patients with consistent results of MRCP and ERCP (true positives and true negatives) comparing to the patients with incompatible results of these two studies (false positives and false negatives) in terms of age of MRCP embodiment (14.2±3.6 years vs 10.5±4.2 years; p<0.05) and CP staging on the basis of Cambridge scale (median 4.0 vs 2.0).

In seven children, MRCP suggested pancreas divisum, which was then confirmed during ERCP only in four patients (66.7%). Among the 14 patients with PD demonstrated by ERCP procedure, MRCP revealed this anatomic anomaly only in 4 children (28.6%).

Conclusion: MRCP is useful in providing diagnostic information equivalent to ERCP in a large percentage of paediatric patients with CP and should be used as the image modality of first choice, especially if the likelihood of therapeutic intervention is small. Similarly to the meta-analysis of conducted to date studies among adults [1], it seems that MRCP is of little use if detection of pancreas divisum is desired.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Pancreatic disease is becoming recently more prevalent in children. A wide spectrum of underlying pathology is observed with diagnosis and treatment proving challenging for pediatricians. We present our recent experience and work up in children with pancreatitis.

METHODS: 92 children with pancreatitis were referred to our centre in 2004-2014. Demographic, clinical and laboratory data were collected.

RESULTS: 60 patients(26M), median age 10.15yrs were diagnosed with acute pancreatitis(AP). Three presented with necrotizing and 1 with hemorrhagic pancreatitis. Hereditary(HP) and autoimmune(AIP) pancreatitis was confirmed genetically and histologically in 5 and 2, respectively. Two were diagnosed with drug-induced pancreatitis. Radiological findings included pancreatic pseudocyst(9), peri/pancreatic collection(5), pancreatic atrophy(4), necrosis(1) and laceration(6), pancreas divisum(3), CBD stricture/dilatation(2/8), pancreatic duct(PD) stricture/dilatation(2/6), accessory pancreatic duct(1), long common channel(3), choledochal malformation(7), pancreatic mass(1), stones(2), gallstones(3) and NAFLD/NASH(3/3).

32 patients(17M), median age 10.2yrs were diagnosed with chronic pancreatitis(CP). The work up and findings are shown in Table 1. Seven and four children were diagnosed with HP and AIP, respectively. 34 surgical procedures were performed. Pancreatic insufficiency was confirmed only in 12%. Radiological findings included pseudocyst(3), peri/pancreatic collection(2), atrophy(5), necrosis(1), pancreas divisum(2), CBD stricture/dilatation(13), PD stricture/dilatation(6), long common channel(1), pancreatic mass(2), stones(5), and NAFLD(2).A pacreatoblastoma and a pancreatic solid pseudopapillary tumour were diagnosed. ERCP and endoscopic ultrasound(EUS) were utilized in 43% and 87% of AP and CP, respectively. Investigations and management are listed in Table 1. The etiology of AP and CP remained unknown in 12(20%) and 5(15%) children, respectively.

<table>
<thead>
<tr>
<th>Work up</th>
<th>AP</th>
<th>CP</th>
</tr>
</thead>
<tbody>
<tr>
<td>US/MRCP/MRI/CT</td>
<td>30/18/7/6</td>
<td>8/14/1/1</td>
</tr>
<tr>
<td>ERCP/Endoscopic US/biopsy</td>
<td>23/1/2</td>
<td>28/1/5</td>
</tr>
<tr>
<td>Secretin stimulation test</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>SPINK1+/PRSS1+/CPA1+/CFTR</td>
<td>2/3/0</td>
<td>5/3/0/1</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Procedure</th>
<th>Count 1</th>
<th>Count 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stent insertion/Sphincterotomy</td>
<td>17/1</td>
<td>18/3</td>
</tr>
<tr>
<td>Hepaticojejunostomy/plasty</td>
<td>5/1</td>
<td>3</td>
</tr>
<tr>
<td>Excision of choledochal malformation</td>
<td>7</td>
<td>0</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Whipple procedure/Puestow</td>
<td>1/1</td>
<td>0/5</td>
</tr>
<tr>
<td>Laparotomy and wash out/Collection drainage</td>
<td>1/4</td>
<td>0/3</td>
</tr>
<tr>
<td>Antibiotics/NG-NJ feeds/Parenteral nutrition</td>
<td>7/1/4</td>
<td>2/1/1</td>
</tr>
<tr>
<td>Pancreatic enzyme supplementation</td>
<td>0</td>
<td>4</td>
</tr>
</tbody>
</table>

**Conclusion:** The commonest causes of pancreatitis in our series were anatomical abnormalities, HP, AIP or indeterminate. Endoscopic investigations and pancreatic biopsy in children are safe procedures enhancing the diagnostic pathway.

**Disclosure of Interest:** None Declared
INCREASED VITAMIN D DOSE REDUCES PULMONARY EXACERBATIONS AND HOSPITALISATIONS IN PATIENTS WITH CYSTIC FIBROSIS

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Objectives and Study: Cystic Fibrosis (CF) is associated with vitamin D deficiency. The North American CF Foundation recently published new guidelines for the treatment of vitamin D deficiency in individuals with CF. The objective of our study was to assess the efficacy of the new guidelines, and to correlate vitamin D levels and pulmonary function and exacerbations.

Methods: Pulmonary function tests and serum concentrations of 25-hydroxyvitamin D [25(OH)D] were measured in CF patients in one CF Center for one year prior to increasing vitamin D dosage and at least one year of follow-up. In addition, Days Of Hospitalization (DOH) and Respiratory Exacerbations (RE) were counted and an average per year (DOHA and REA, respectively) were calculated.

Results: Of the 90 patients in the study, 49 were males (54.4%), 74 had pancreatic insufficiency (82.2%); mean age 18.17 years. The mean serum concentration of vitamin D at baseline was 20.97 ng/ml compared to 25.41 ng/ml at the end of follow-up (p<0.001). The mean DOHA at baseline was 20.00 days per year compared to 19.04 at the end of follow-up (correlation coefficient = -0.484, p=0.001). The mean REA at baseline was 2.79 exacerbations per year compared to 2.15 at the end of follow-up (correlation coefficient = -0.318, p=0.002).

Conclusion: The new guidelines for management of vitamin D deficiency improve vitamin D levels in patients with CF. The increase in vitamin D levels in individuals with CF decreases both respiratory exacerbations and number of days of hospitalization per year.

Disclosure of Interest: None Declared

Keywords: None
NEW GENETIC POLYMORPHISMS IN IDIOPATHIC RECURRENT PANCREATITIS: A CASE SERIES OF 13 CHILDREN

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Objectives and Study: Today, genetic risk factors are attributed a much more important role. A significant number of patients with idiopathic recurrent acute and chronic pancreatitis have an underlying genetic susceptibility. Genetic pancreatitis are associated with mutations in CFTR (Cystic Fibrosis Transmembrane Conductance Regulator), PRSS1 (Serine Protease 1), and SPINK1 (Serine Peptidase Inhibitor Kazal type 1) genes. Recent advances in cell biology, genetics and imaging technology provide hope that improved understanding of pancreatitis will facilitate novel therapeutic strategies.

Methods: We describe a case series of 13 children (8 boys and 5 girls, mean age at onset 7 years) affected by idiopathic recurrent pancreatitis (IRP). The diagnosis of pancreatitis was made by the presence of typical abdominal pain, serum amylase and/or lipase three times greater than the upper limit of normal and characteristic imaging findings. Sequence analysis of CFTR, PRSS1 and SPINK1 genes was performed.

Results: 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. A 3-years old girl with the most severe form of IRP showed 5T/7T-13TG/9TG. The 5T allele, in cis with 13TG, was associated in trans with F508del, a severe CFTR mutation. In two patients (sibs) sequence analysis of PRSS1 gene showed the presence of the known and causative mutation p.N29T (c.86A>C) in exon 2, inherited from the mother. In four patients was found a new variant V213I (c.637G>A) of PRSS1 gene, never described in literature before. By the analysis on PolyPhen-2 (Polymorphism Phenotyping v2), a tool which predicts possible impact of an amino acid substitution on the structure and function of a human protein, it would seem that the p.V213I variant appears to be benign, but it remains with unknown pathogenic significance.

Conclusion: CFTR, PRSS1 and SPINK1 genes play a crucial role in the etiopathogenesis of idiopathic recurrent pancreatitis. Sequence analysis of these genes is indicated in patients presenting the disease. In particular, we described the 5T variant, 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 12 or 13TG repeats are more likely to exhibit an abnormal phenotype (non-classic CF, recurrent pancreatitis) than those with 5T adjacent to <12TG. The high prevalence of 5T carriers makes the assessment of TG repeat number of great interest as a
reliable predictor of 5T penetrance. Further studies are needed to define the role of these new variants in pancreatic disease.

Disclosure of Interest: None Declared
VITAMIN K STATUS IN CYSTIC FIBROSIS PATIENTS WITH LIVER CIRRHOSIS

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Objectives and Study: The possible causes of vitamin K deficiency in cystic fibrosis (CF) may include cholestatic and non-cholestatic liver disease. However, the available data on the influence of liver cirrhosis on vitamin K status in CF patients are scarce. Therefore, the aim of the present study was to assess the frequency of vitamin K deficiency in this group of CF patients.

Methods: The study group comprised of 27 CF patients with liver cirrhosis aged 6.6-30.2 years (median age 15.7 years). Sixty-three non-cirrhotic CF subjects aged 7.9-26.9 years (median age 16.1 years) constituted the comparative group. Twenty-one (77.8%) cirrhotic and 56 (88.9%) non-cirrhotic subjects received vitamin K supplementation (median dose [1st-3rd quartile]: 10.0 mg/week [5.0-22.5] and 20.0 mg/week [8.4-20.0], respectively). Vitamin K status was estimated by prothrombin induced by vitamin K absence (PIVKA-II) and the percentage of undercarboxylated osteocalcin (u-OC). Values lower than 2 ng/ml and 20%, respectively, were considered to be normal.

Results: Elevated PIVKA-II concentrations were found in sera of 16 (59.2%) cirrhotic and 22 (34.9%) non-cirrhotic CF patients. Increased percentages of u-OC were observed in 15 (55.6%) subjects with and 25 (39.7%) without liver cirrhosis. The frequency of vitamin K deficiency defined as abnormal PIVKA-II and u-OC status did not differ between the groups (p=0.1559 and p=0.1649, respectively). PIVKA-II concentrations were higher in cirrhotic than in non-cirrhotic CF patients (median [1st-3rd quartile]: 3.2 ng/ml [1.0-10.0] vs. 1.3 ng/ml [0.2-2.6], p=0.0029). On the other hand, u-OC percentages did not differ between the studied groups (49.4% [7.0-73.8] vs. 8.0% [2.6-59.1], p=0.0501).

Conclusion: The prevalence of vitamin K deficiency in CF patients with liver cirrhosis is high. However, CF itself rather than liver cirrhosis seems to be the most important risk factor.

Disclosure of Interest: None Declared
**Objectives and Study:** Cystic Fibrosis Related Liver Disease (CFRLD) slowly progress to fibrosis and cirrhosis in about 10 to 15% of patients. Liver biopsy cannot be repeated, and data from non invasive markers of this evolution are lacking. The aim of this study is to evaluate CFRLD progression with repeated elastometry.

**Methods:** We studied 86 CF children, 49 boys and 37 girls, median age 6.9 years, with at last 2 elastometry measurements with Fibroscan® at a minimum of 2 year-interval. CFRLD was diagnosed according to classical criteria (hepatomegaly, increased ALT, hyperechogenicity on US examination).

**Results:** Median initial elastometry value was 3.7 kPa (IQR: 1.3) and final elastometry value was 4.8 kPa (IQR: 2.23). Mean increase of elastometry was 0.24 kPa/year (7%/year). 7 children developed CFRLD during the study period. Increased initial ALT value was the only factor found to be predictive of developing CFRLD (p=0.0001). Increased initial ALT value was correlated with the evolution slope of elastometry (r=0.38; p=0.0005). Percentage of increase of elastometry was higher in children developing CFRLD compared to who remained without CFRLD (94% vs 23%; p=0.002). Genotype, pancreatic insufficiency, severity of lung disease had non influence on evolution of elastometry.

**Conclusion:** Elastometry measured by Fibroscan® slowly worsens in CF children. An elevated ALT value and a rapid increase of elastometry value are predictive of a progression to CFRLD.

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

**Cystic Fibrosis and Pancreatic Disorders**

PO-G-0070

**CYSTIC FIBROSIS AND COELIAC DISEASE: A FREQUENT ASSOCIATION**

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**Objectives and Study:** Coeliac Disease (CD) is a gastrointestinal system's affection, prevalence being frequent (>1%) in the general population. Clinical symptoms include diarrhoea, malnutrition and ponderal stunning, all of them being common to Cystic Fibrosis (CF). Coexistence of both diseases has been described mainly in short series and in isolated cases. Our aim was to study the association of CD with CF in our CF population, and find out if this association is higher than in the general population.

**Methods:** We have followed a descriptive study consisting of data collection from our patients diagnosed with CF and then on with CD. CF diagnosis was performed by genetic study plus sweat test, and CD diagnosis by serological markers such as antitransglutaminase antibodies ($\text{TG}_2$), antigliadin antibodies and antiependymum antibodies, and HLA study plus small bowel biopsy (SBB) except from one case in which new ESPGHAN criteria was applied and therefore the SBB was omitted. Additionally, the incidence of CD in CF in our population was estimated.

**Results:** 6 patients aged between 1-9 years were included. 4 of the patients were diagnosed between 1-3 years of age. As shown in the table, the most frequent symptom in the CD debut was diarrhoea, which is also often present in CF. $\text{TG}_2$ values in our patients were found to be >10 times the cut-off value in all the cases except from one, aged 3 years when CD was diagnosed, who displayed high values of antigliadin antibodies. All patients showed a favourable evolution after adherence to the gluten-free diet. We found an incidence of 6 out of 110 patients in 11 years and current prevalence of 8.5% (6 out of 70 CF cases).

**Image:**

<table>
<thead>
<tr>
<th>HLA</th>
<th>DQ8</th>
<th>DQ2/DQ8</th>
<th>DQ8</th>
<th>DQ2</th>
<th>DQ2</th>
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</tr>
</thead>
<tbody>
<tr>
<td>$\text{FQ Genotype}$</td>
<td>$\text{M1101K/R1009C}$</td>
<td>$\text{F508del/F508del}$</td>
<td>$\text{F508del/F508del}$</td>
<td>$\text{F508del/F508del}$</td>
<td>$\text{F508del/F508del}$</td>
<td>$\text{F508del/F508del}$</td>
</tr>
<tr>
<td>$\text{TG}_2$ at debut</td>
<td>&gt;100</td>
<td>&gt;7</td>
<td>0.7</td>
<td>&gt;128</td>
<td>&gt;128</td>
<td>&gt;128</td>
</tr>
<tr>
<td>Antiependymum antibodies</td>
<td>ND</td>
<td>ND</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
<td>Positive</td>
</tr>
<tr>
<td>Biopsy - MARSH</td>
<td>3b</td>
<td>3b</td>
<td>3b-c</td>
<td>3a</td>
<td>ND</td>
<td>3b</td>
</tr>
<tr>
<td>Symptoms</td>
<td>Diarrhoea + weight loss</td>
<td>Chronic diarrhoea</td>
<td>Abdominal distension</td>
<td>Ponderal stunning</td>
<td>Generalised edemas + hipoprotenemia</td>
<td>Abdominal pain + liquid diarrhoea</td>
</tr>
<tr>
<td>Age at CF Dx</td>
<td>2.5m</td>
<td>18m</td>
<td>4m</td>
<td>8.5 m</td>
<td>4m</td>
<td>28d</td>
</tr>
<tr>
<td>Age at CD Dx</td>
<td>1y 7m</td>
<td>3y 6m</td>
<td>1y 11m</td>
<td>8y 10m</td>
<td>11m</td>
<td>8y 7m</td>
</tr>
</tbody>
</table>

**Conclusion:** There is a high incidence of coeliac disease in patients with cystic fibrosis. Although we cannot calculate the cumulative incidence as it is not a static cohort, our data support a higher prevalence than in general population. We consider that serological CD markers should be included in
routine CF evaluation, especially in toddlers, and whenever gastrointestinal and nutritional management do not respond as expected. Otherwise similarity of symptoms in both pathologies may unduly delay CD diagnosis.

**Disclosure of Interest:** None Declared
Gastroenterology

Cystic Fibrosis and Pancreatic Disorders

PO-G-0071

Cystic Fibrosis and Acute Gastrointestinal Complications: A 10-Year Retrospective Study at Strasbourg University Hospital.

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1Strasbourg University Hospital, Strasbourg, France

Objectives and Study: Cystic fibrosis (CF) leads to chronic respiratory and digestive complications, but acute gastrointestinal manifestations of the disease can also be very disabling, and strongly contribute to patient morbidity. Acute digestive complications remain poorly described and little is known about their incidence. The objective was to evaluate, among CF paediatric patients followed in Strasbourg, the incidence of acute gastrointestinal complications: constipation, occlusion and distal intestinal obstruction syndrome (DIOS), hepato-biliary and pancreatic complications. We also searched for risk factors for DIOS.

Methods: We retrospectively reviewed the medical charts of the 155 paediatric patients followed in Strasbourg University Hospital between 2002 and 2012. Patients between 1 month and 18 years old who presented with digestive symptoms in Strasbourg or in other emergency departments in the region were included and data management noted. Acute gastroenteritis and digestive symptoms attributed to respiratory exacerbation were excluded.

Results: Sixty-five episodes of acute gastrointestinal complications were diagnosed in 47 patients (30%) during this period, for a total incidence of 64.1 episodes per 1000 patient-years. The median age at first episode was 9.0 years [0.1-18.3]. Acute constipation (22/65), stercoral ileus (6/65) and DIOS (10/65) accounted for 58% of episodes and solely concerned pancreatic insufficient patients. Surgery was exceptional (only 1 case of DIOS), but patients were generally very symptomatic: 2/3rds of episodes required hospitalization for a median duration of 4 days. All patients with DIOS had exocrine pancreatic insufficiency and a severe genotype; 70% had a history of meconium ileus. Acute pancreatitis affected 2.5% of patients (12.5% of pancreatic sufficient patients), with a substantial risk of recurrence and possible progression to pancreatic insufficiency. Surgical complications were rare (7 episodes/65) and represented by acute appendicitis and mucocele of the appendix, adhesive small bowel obstruction and intussusception.

Conclusion: Constipation, stercoral ileus and DIOS represent the majority of acute gastrointestinal complications in patients with cystic fibrosis. These episodes seem to be related to pancreatic insufficiency and a history of meconium ileus. Pancreatitis mainly concerns pancreatic sufficient patients. A better description of these complications should help to optimize the diagnosis and management of such children in paediatric services.

Disclosure of Interest: None Declared
Objectives and Study: Artificial enteric nutritional support is vital in the management of patients who are unable to maintain oral nutrition. Gastric feeding may not be optimal due to severe GERD, delayed gastric emptying or antro pyloric dysmotility. In some circumstances, post pyloric feeding can be used and can avoid parenteral nutrition. For delivery of long term post pyloric feeding a jejunal feeding via a direct jejunostomy provides a more stable and secure jejunal access compared with the nasojejunal or gastrostomy with jejunal extension(1).

It has been suggested that direct percutaneous jejunostomy insertion is technically more difficult and associated with a higher risk of complications, therefore; its usage has not, to date, been widespread (2). The aim of this audit was to review the novel approach of laparoscopic assisted direct percutaneous jejunostomy(LAPEJ).

Methods: Case records of paediatric patients who underwent LAPEJ between January 2008 and September 2014 were reviewed.

With a 2 port laparoscopic technique, the DJ flexure and jejunum were identified. Simultaneously an endoscope was passed to the jejunum. Safe and optimal positioning of the jejunostomy site, close to the abdominal wall, was followed by insertion of a percutaneous needle and then guidewire is passed in to the jejunum as per standard PEG placement. The guidewire was retrieved and a 12Fr Corflo PEG Tube was then pulled in to position.

Results: 14 patients were identified (median age 6.5 years, range 2-17), 11 had significant neurological impairment and 9 had already had had a fundoplication. Current median follow up is 20 months (1-60).

All LAPEJ were sited successfully, feeds commenced within 6 hours with no evidence of of leak or peritonitis. Two patients developed gastrointestinal volvulus (3 months and 2 years post insertion). Both had abnormal gastrointestinal anatomy; one with a jejunal diverticulum which has been reported as a rare cause of midgut volvulus (3), and one with a complete small bowel malrotation which was evident only on laparotomy following LAPEJ. Barium meal is therefore a wise precaution before LAPEJ.

Conclusion: LAPEJ placement seems to be a relatively safe and successful approach for children requiring jejunal enteral feeding.


**Disclosure of Interest:** None Declared
**Objectives and Study:** Esophageal stenosis (ES) in children is a rare clinical condition caused by numerous etiologies. Conservative treatment consists of intraluminal dilation using balloon (endoscopic or radiology assisted) or Savary-Gilliard bougies.

**Methods:** The goal of this study is to report our twenty years experience (1994-2013) in the management of children with esophageal stenosis. We retrospectively reviewed the medical records of these children treated by either balloon (endoscopic or radiology assisted) or Savary-Gilliard bougies in regards to safety and their short and long term outcome.

**Results:** During last 20 years, 42 patients (22 males and 20 females) underwent 190 dilations. Mean age at diagnosis was 5.7 years ±3.9 years, with median age 1.3 years (range 1 day -20 years). The median treatment period was 5.5 months (range 0.1 ± 10 years); with median follow-up after the last dilation of 2.25 years. Average number of dilations per patient was 3 (range 1-22). On long term follow-up, comparing success rate according to etiology of stenosis demonstrated 75% success rate in children after caustic agents ingestion, and after surgical correction of esophageal atresia, 100% success rate in children with various etiologies (congenital esophageal stenosis, eosinophilic esophagitis, foreign body ingestion, post fundoplication) and no success at the motility disorder group (p<0.05). Comparing success rate to method of dilation revealed 87% success rate among the bougienage group and 67% in the balloon group (p=NS). There were 6 (3.1%) procedure-related complications treated conservatively.

**Conclusion:** Esophageal dilation in children is a safe procedure with high rate of long term success. We conclude that among children with esophageal stenosis, long term success of dilation depends primarily on etiology of stenosis and less by method of dilations.

**Disclosure of Interest:** None Declared
Objectives and Study: Recently the number of endoscopic procedures performed has increased considerably worldwide [1], raising questions about their appropriateness and cost-efficacy. The aim of this evaluation therefore was to determine diagnostic yield of endoscopy in a paediatric population in a large tertiary centre.

Methods: 147 randomly selected cases were assessed from April 2012 to October 2014. 3252 endoscopic procedures were performed on 2471 children during this period. Indications for endoscopy, endoscopic and histopathological findings were collated and the endoscopic diagnostic yield and contribution to the management was evaluated.

Results: The mean age was 9.58 (0.5-16.5) years, M:F ratio 1:1.42. Indications included: abdominal pain (66.6%); diarrhoea (42.4%); bleeding PR (27.4%); weight loss 19.6%; mucus PR 19.6% and urgency (9.6%) and nocturnal symptoms (9.8%) were also noted. Other indications included vomiting/suspected reflux (20.9%) and feed aversion (12%).

The positive diagnostic yield was 18.9% for oesophagogastroduodenoscopy (OGD) alone, 32.6% for ileocolonoscopy (IC) alone and 39.21% when both occurred.

The pre-test probability of making a positive diagnosis prior to endoscopy was 42.8% with likelihood ratio of a positive test of 2.49. Using Fagan’s likelihood ratio nomogram a post-test probability of 65 is calculated indicating a high degree of diagnostic contribution.

In 45% of the patients management was actively changed due to endoscopy and histopathology findings, and management contribution occurred in all patients.

<table>
<thead>
<tr>
<th>Endoscopy</th>
<th>Positive</th>
<th>Negative</th>
<th>PPV = 65.21</th>
<th>NPV = 76.9%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Positive</td>
<td>45</td>
<td>24</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Negative</td>
<td>18</td>
<td>60</td>
<td></td>
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</tr>
</tbody>
</table>

Discussion:
In children a positive diagnosis is important but so may significant negative findings in terms of patient management and reassurance. Hence the relatively low positive diagnostic yield of OGD (18.9%) and IC (32.6%) in this cohort must be interpreted in this clinical context.

Overall endoscopic procedures had good sensitivity (71.4%) and specificity (71.4%) with NPV of 76.9% and PPV of 65.2% in our Centre. Of course appropriate selection of patients is contributory to this. Various studies have suggested that the diagnostic yield of endoscopic procedures improve if indications and appropriateness are critically assessed with use of Guidelines.

**Conclusion:** To improve the diagnostic yield of endoscopic procedures we recommend adherence to well established Guidelines for appropriateness and indication of endoscopy in children but it should be noted that a significant negative finding may be as important as a positive diagnosis in the care of these families.

**Disclosure of Interest:** None Declared
ROLE OF ENDOSCOPIC ULTRASOUND IN PAEDIATRIC PANCREATICOBILIARY DISORDERS – FROM DIAGNOSIS TO TREATMENT

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Objectives and Study: The diagnostic and therapeutic role of endoscopic ultrasound (EUS) in children was demonstrated only recently and data on the technique's indications remain scarce. We therefore evaluated diagnostic and interventional EUS indications and safety in children with pancreaticobiliary disorders.

Methods: We retrospectively reviewed our single pediatric center experience covering a 15-year period.

Results: Between January 2000 and December 2014, 52 EUS procedures were performed on 48 children (mean age 12yrs; range 2-17yrs) with pancreaticobiliary disorders for the following indications: suspected biliary obstruction (n=20/52), acute/chronic pancreatitis (n=20), pancreatic mass (n=3), pancreatic trauma (n=7), and ampullary adenoma (n=2). EUS examination precluded endoscopic retrograde cholangiopancreatography (ERCP) (n=13 biliary; n=6 pancreatic), focusing on endotherapy (n=7 biliary; n=14 pancreatic), or reorienting therapy towards surgery (n=7). EUS-guided fine-needle aspiration was carried out on 12 patients for pancreatic tumor (n=4) or pancreatic cyst fluid analysis (n=4), autoimmune pancreatitis (n=2), and suspicion of biliary tumor (n=2). Thirteen therapeutic EUS procedures (11 children) were conducted, nine of which (7 children, mean age 8yrs, range 4-11yrs) were combined EUS-ERCP procedures, three (2 children) were EUS-guided pseudocyst drainage, and one was a EUS-guided transgastric biliary drainage. One child developed an haemorrhagic complication one week after the EUS procedure.

Conclusion: We report on a large pediatric EUS series for diagnostic and therapeutic pancreaticobiliary disorders, demonstrating the impact of diagnostic EUS and affording insights into novel EUS and combined EUS-ERCP therapeutic applications. We suggest considering EUS as a diagnostic and therapeutic tool in the management of pediatric pancreaticobiliary diseases.

Disclosure of Interest: None Declared
Objectives and Study: To determine terminal ileum intubation (TII) rate of paediatric ileocolonoscopy in an active training environment and compare with previously calculated rates before Training the Trainer (TTT) Courses had been attended by the trainers. Rates of TI completion in the paediatric literature were also used for comparison.

Methods: From April 2012 to October 2014 928 ICs occurred and 100 were randomly selected from the Centre’s endoscopy database. The cases were interrogated for initial presentation, indication for IC, endoscopic findings, histopathological findings and resultant change in management due to IC.

Results: TII occurred in 98/100 of this cohort – poor bowel preparation and technical difficulty accounted for failure in the 2 remaining cases.

The mean age at diagnosis overall was 9.58 (0.5-16.5) years, M:F ratio 1:1.42. Presenting symptoms included: abdominal pain (66.6%); diarrhoea (42.4%); bleeding PR (27.4%); weight loss 19.6%; mucus PR 19.6% and urgency (9.6%) and nocturnal symptoms (9.8%) were also noted.

Discussion: TII is considered mandatory in children and accounts for IBD differentiation in around 10-15% of cases. At our centre the TII rate for 2012-14 was 98%, which compares favourably to 89% between 2009-11. Historical data in other paediatric studies report a steady increase from 22% in 1994-96, 66% in 2000, 61% in 2004-05 and 79% in 2008-09. [3] Adult reports have suggested TII rate of around 95-96% [4-6] which equates to our present experience. We suggest that the evolution of a training centre with TTT Courses attended by trainers within an active training environment utilising Scope-guide 3-D imaging is beneficial to TII rate and therefore overall patient care.

Conclusion: As Porto criteria mandate TII in order to improve IBD diagnosis [4], TII is now integral to care in paediatric IBD. This evaluation suggests that a full endoscopic evaluation is more likely to be completed in an actively-training centre.

References:


**Disclosure of Interest:** None Declared
Objectives and Study: One-man method colonoscopy was adopted for pediatric GI fellow colonoscopy training in our hospital since July 2013. The aim of this study is to investigate the clinical indicators between one-man method and two-man method colonoscopy in children.

Methods: In this retrospective study, from July 2010 to June 2014, colonoscopy studies in children age less than 18 year old in our hospital were recruited. These colonoscopy examinations were performed by second-year pediatric GI fellows in our hospital with attending physician supervise. General characteristics and indicators such as age, gender, body weight, cecal intubation rate (CIR) and cecal intubation time (CIT) between one-man and two-man method group were assessed. The primary outcome is cecal intubation rate.

Results: Total 72 colonoscopy examinations used one-man method and 166 examinations used two-man method were enrolled. The baseline characteristics such as age, gender and bodyweight between one-man and two-man method group did not have significant difference. The cecal intubation rate (CIR) in one-man method group was 81.94% and CIR in two-man method group was 67.47%. One-man method colonoscopy had higher CIR than two-man method colonoscopy in children. (odds ratio, OR=2.18, 95% confidence interval, CI= 1.11 to 4.29, p=0.02) The mean cecal intubation time (CIT) did not have significant difference between one-man method and two-man method colonoscopy. The mean (±SEM) CIT was 25.0 ± 12.2 minutes in two-man method and 27.1 ± 1.6 minutes in one-man method.

Conclusion: The present study showed that one-man method colonoscopy had higher cecal intubation rate than two-man method colonoscopy in children.

Disclosure of Interest: None Declared
WIRE GUIDED CANNULATION VS. CONVENTIONAL CONTRAST GUIDED CANNULATION IN PAEDIATRIC ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY (ERCP)

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Objectives and Study: Objectives: Wire guided cannulation (WGC) of the common bile duct may be associated with fewer complications and higher success rate compared to contrast guided cannulation (CGC) in adults. Data in children are lacking. The aim of this study was to compare the outcome and complication rate of WGC and CGC in pediatric ERCP.

Methods: Patients and Methods: We report a retrospective cohort study comparing WGC to CGC in a pediatric cohort. We reviewed the medical records of 167 children who underwent ERCP over a 10 year time period (CGC; 1999-2003, WGC; 2003-2009). Indications, findings and outcome measures were analyzed.

Results: Results: A total of 93 patients (56%) underwent WGC and 74 (44%) CGC. Children in the WGC group were younger (9.5±4.7 vs. 11.5±4.6 years in CGC; p=0.006) and underwent more therapeutic ERCP interventions (70% vs. 40% in CGC), while diagnostic ERCP was more common in the CGC group (60%; P<0.005). The overall success (96%) and complication rate (8%) were identical in both groups but a trend towards a reduction in the complication rate over time was noted in the WGC group. Post ERCP pancreatitis (PEP) was documented in 1 patient in the WGC group (1.1%) and 3 patients (4.2%) in the CGC group (P-NS).

Conclusion: Conclusion: The success and complication rate in both CGC and WGC are comparable in children but considering the patient and procedure complexity and the trend toward lower PEP in the WGC group, WGC may be the preferable cannulation technique for ERCP in children.

References: References:

Disclosure of Interest: None Declared
Objectives and Study: Patency capsule (PC), a swallowable and dissolvable capsule, was developed to know the risk of retention of capsule endoscopy (CE), but the feasibility and usefulness of PC is not fully understood in children. We aimed to evaluate the feasibility and usefulness of PC prior to CE procedure in children.

Methods: Pediatric patients (6-18 yr) with suspected or confirmed small intestinal diseases were examined for PC prior to CE procedure. Success rate of capsule swallowing, swallowing time and outcome of PC and CE procedure were evaluated.

Results: A total of 44 patients (median 12.7 yr; range, 7.4-17.3; 31 male; 2 known CD, 2 known UC, 9 suspected CD, 3 suspected tumor, 4 OGIB, 21 recurrent abdominal pain, 2 chronic diarrhea, 1 growth failure) were included in the study. 35/44 (79.5%) patients were able to ingest PC at the initial trial. Receiver operating characteristic analysis demonstrated the cut-off age for the capsule swallowing success as 10.6 yr of age (odds ratio 10.6). Time for PC swallowing was 24.6±63.8 minutes (mean±SD). Time for PC excretion or passage to the colon was 30.1±14.7 hours. None of the ingested PC showed dissolved form. All of patients successfully ingested PC were able to swallow CE with 9.5±28.3 minutes. Among 9 patients who were unable to swallow PC, 4 patients could ingest CE, 1 patient had an endoscopic CE replacement after CE swallowing failure, and 1 patient ingested PC after rechallenge followed by CE procedure. All of patients who ingested CE after PC procedure told the swallowing easiness of CE compared to PC. Among 36 patients who successfully ingested PC, 1 patient took 71.3 hours for the PC excretion without PC dissolution, and CE showed multiple narrowing of small intestine without capsule retention.

Conclusion: PC is feasible in children but swallowing difficulty should be taken into consideration in children under 10 years of age. PC examination is useful for children not only to detect the risk of capsule retention but also to facilitate the following CE swallowing.

Disclosure of Interest: None Declared
PATIENT EXPERIENCE WITH ENDOSCOPY AT A SINGLE REGIONAL ENDOSCOPY UNIT

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Objectives and Study: A Global Rating Scale (GRS) is used in adult UK gastroenterology endoscopy services as a quality improvement and assessment tool 1. Within this quality of patient experience is measured and feedback is embedded. A paediatric endoscopy GRS in development will include evaluations of patient experience, an essential part of service evaluation. We piloted a survey to assess patient experience.

Methods: A patient/parent survey was developed with our PALS and clinical governance teams. It was distributed to all patients on elective and emergency lists prior to the procedure and collected the same day. The study periods ran from 10 December 2013 to 31 January 2014 and 25 June till 1 August 2014. Data was analysed with Excel.

Results: 229 (109 in winter) patients underwent endoscopy during the study periods. There was a 33% (n=36) response rate during the winter period and 49% (n=59) in summer. Sex distribution of the respondents mirrored those listed. There were significantly less (ANOVA p<0.003) responses from under 2s and more (ANOVA p<0.003) from 13-15yrs age groups. Main procedures performed included Upper GI endoscopy, ileocolonoscopy, pH, bravo pH and impedance studies and PEG procedures.

100% of respondents felt they had opportunities to ask questions prior to the procedure. 3% of respondents stated the procedure was not explained prior to consent. 2% felt they did not understand the procedure. Information leaflets were given to 80% of respondents. 25% of respondents in winter and 17% in summer stated they were not informed of waiting times. 73% of respondents in winter and 49% in summer felt waiting times were about right. 24% in winter and 46% in summer felt it was too long. 1 in winter and 3 in summer felt it was too short! Most felt prepared based on information given (94% acceptable or above).

46% of respondents stated complications, chiefly pain (35% winter and 40% summer).

<table>
<thead>
<tr>
<th>Domain: Care for</th>
<th>Winter(%)</th>
<th>Summer(%)</th>
<th>Domain: Care for</th>
<th>Winter(%)</th>
<th>Summer(%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Comfort</td>
<td>Good/excellent</td>
<td>97</td>
<td>92</td>
<td>Good/excellent</td>
<td>94/90</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td>0</td>
<td>4</td>
<td>Acceptable</td>
<td>7/10</td>
</tr>
<tr>
<td></td>
<td>Poor/terrible</td>
<td>3</td>
<td>4</td>
<td>Poor/terrible</td>
<td>0/0</td>
</tr>
<tr>
<td>Dr’s sensitivity &amp;</td>
<td>Good/excellent</td>
<td>97</td>
<td>94</td>
<td>Additional needs</td>
<td>Good/excellent</td>
</tr>
<tr>
<td></td>
<td>Acceptable</td>
<td>3</td>
<td>2</td>
<td>Acceptable</td>
<td>0</td>
</tr>
</tbody>
</table>

1 in winter and 3 in summer felt it was too short! Most felt prepared based on information given (94% acceptable or above).
| courtesy | Poor/terrible | 0 | 4 | | Poor/terrible | 14 | 10 |
| Dr's sensitivity explaining findings | Good/excellent | 92 | 87 | Overall feedback | Good/excellent | 97 | 94 |
| | Acceptable | 4 | 5 | Acceptable | 0 | 2 |
| | Poor/terrible | 4 | 8 | Poor/terrible | 3 | 4 |

**Conclusion:** Overall patients had a good experience of endoscopy in our unit. Areas identified to improve include analgesia and procedure and waiting time explanations.

**References:** 1. Global rating Scale Accessed 5/11/14

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

**Endoscopy**

PO-G-0082

**APPRAISAL OF THE USE OF BALLOON ENTEROSCOPY IN PAEDIATRIC PATIENTS**

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London, United Kingdom

**Objectives and Study:** The aim of this single-centre, retrospective study is to evaluate the use of balloon enteroscopy in paediatric gastroenterology; assessing the indication for, and efficacy of, balloon enteroscopy in the diagnosis and management of small bowel disease in children.

**Methods:** All paediatric single (SBE) and double (DBE) balloon enteroscopy cases for a tertiary paediatric gastroenterology centre were analysed against clinical indication, preceding investigations, procedure details, diagnostic or interventional findings and complications.

**Results:** 54 patients (27 males) with a median age at procedure of 12 years (range 2 to 20 years) underwent 65 enteroscopy procedures (39 SBE; 26 DBE). 9 patients underwent 2 enteroscopies at an average interval of 2.5 years, 1 patient underwent 3 enteroscopies. 44 patients had both antegrade (trans-oral) and retrograde (trans-anal) examinations, 1 patient underwent enteroscopy intraoperatively, 1 patient had retrograde examination only; the remainder had trans-oral examinations only. 9 patients underwent roux-en-y loop examination. 18 cases were scoped under fluoroscopy. The entire bowel was examined in 28 patients. In the remainder, distance of small bowel scoped ranged from 100 to 350cm; 80 to 300cm of small bowel distal to the pylorus, from antegrade approach and 20 to 60 cm of small bowel proximal to the ileo-caecal valve from retrograde approach. The average time of procedure was 120 minutes per case. 25 cases were inpatients. The most common indication for enteroscopy was reassessment of known Crohn's disease. 23 patients had been previously investigated with gastroscopy, 11 with capsule endoscopy and 16 with both. 7 enteroscopy cases were unremarkable. 11 scopes were macroscopically diagnostic. 58 cases were biopsied, of which a further 28 were diagnostic. 7 scopes were interventional, comprising of stricture dilation, clipping of anastomotic leak and removal of polyps. All procedures were conducted under general anaesthetic. Side effects of enteroscopy included bloating and vomiting, managed by nasogastric tube insertion whilst under anaesthetic. There were no reported complications of enteroscopy.

<table>
<thead>
<tr>
<th>Clinical indication for enteroscopy</th>
<th>Per rectum bleeding</th>
<th>Crohn's disease reassessment</th>
<th>Gastroenterological symptoms; consistent with inflammatory bowel disease</th>
<th>Unexplained</th>
<th>Post liver transplant</th>
<th>Post Kasai procedure</th>
<th>Post small bowel transplant</th>
<th>Other</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of</td>
<td>6</td>
<td>17</td>
<td>12</td>
<td>3</td>
<td>9</td>
<td>6</td>
<td>4</td>
<td>8</td>
<td>65</td>
</tr>
</tbody>
</table>
Conclusion: Balloon enteroscopy is both safe and effective in the diagnosis and therapeutic intervention of paediatric small bowel disease, not achievable with the conventional endoscope or current modalities which enable non-interventional imaging of the small bowel.

Disclosure of Interest: None Declared
Gastroenterology
Endoscopy
PO-G-0083

EFFICIENCY AND SAFETY OF LOW DOSE KETAMINE AND MIDAZOLAM COMBINATION FOR
UPPER GASTROINTESTINAL ENDOSCOPY IN CHILDREN

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Objectives and Study: To evaluate the effectiveness and safety of intravenous low dose ketamine-
midazolam sedation during pediatric endoscopy.

Methods: The study was performed prospectively in pediatric gastroenterology unit during 1 year
period. All children were > 1 year old and weighed > 10 kg with American Society of Anesthesiologists
class 1 or 2 (n=425, 184 male, 10.7±3.8 years). Patients received intravenously midazolam 0.1 mg/kg
(maximum 4 mg) and ketamine 0.5 mg/kg. Efficiency of the procedure and complications during and
after procedure were recorded.

Results: Endoscopy procedure was successfully completed in 414 patients (97.4%, 95 CI %: 95.8-
98.9). Median duration of procedure was 6.0 min (6.36±1.64 min). Minor complications occurred
during the procedure in 165 patients (38.8%). The most common complication was increased oral
secretion (139 patients, 32.7%). No major complications such as apnea, bradycardia or cardiac arrest
were observed in any patient. Mean recovery time was 22 min (25.00±12.32 min). Complications
developed in 249 patients (58.5%) during recovery. The most complication were transient double
vision (n=127, 30.6%). Emergence reaction was observed in 5 patients (0.9%).

Conclusion: The procedure was completed with a high level of success without any major
complications, despite the use of ketamine at the low dose of 0.5 mg/kg. Although, recovery
complications are high, the use of a combination of midazolam and ketamine in low doses
intravenously is effective and safe in endoscopy in children.

Disclosure of Interest: None Declared
**Objectives and Study:** Background – Esophageal foreign body and food bolus impaction (EFBFBI) are a common problem in children and adolescents requiring urgent evaluation and treatment, and may be the first sign of underlying esophageal pathology. Objective – To determine if there were any changes, over a 30-year period in 10-year frames, especially in respect to the nature of the foreign body (FB) ingested and esophageal pathology.

**Methods:** Design – Retrospective study. Setting – Tertiary care center. Cases of EFBFBI were identified by querying endoscopic reports from October 1984 to September 2014 for “foreign body” or “food impaction” in the esophagus. The variables examined were age, sex, FB type, FB location, presence of esophageal disease and esophageal pathology. Histological findings of esophageal biopsies were reviewed.

**Results:** During the period in study a total of 249 patients presented EFBFBI (81, 82 and 86 in each 10-year frame). Male/Female ratio and the mean age ± standard deviation (SD) were 1.11:1.0, and 4.8 ± 4.3 years, respectively. Endoscopic localization of the objects showed: 155 proximal, 40 middle and 54 in the distal esophagus. Considering FB nature, 191 (76.7%) were inorganic and 58 (23.3%) were organic, being coins (54.6%) and meat (13.3%) the main cause of impaction in each group. The esophageal mucosa showed non-specific changes in 203 (85.3%) patients. An underlying stricture was found in 33 (13.3%) children associated with esophageal atresia (16), peptic esophagitis (11) and caustic esophagitis (6). Eosinophilic esophagitis (EoE) and reflux esophagitis features was found in 9 and 4 patients, respectively. There were no significant differences in the number and type of FB over each 10-year period, exception for a slight decrease in the number of coins impaction and an increase in the number of button batteries (BB) and food meat bolus impaction in the last 10-years period. There were 33 meat bolus impaction, 15 in the first 20-year period and 18 in the last 10-year period, being 5 associated with esophageal stricture, 9 with EoE, 3 with reflux esophagitis and 1 with normal mucosa. There was esophageal damage in all 9 BB impactions with one esophageal stenosis as a delayed complication. All the diagnosis of EoE were made in the last 8 years. Esophageal biopsies were only performed in 12 patients with meat bolus impaction.

**Conclusion:** Inorganic FB ingestions remained stable over the last 30 years, but the number of BB ingestions increased with potentially fatal clinical implications. Public awareness is essential in preventing complications. The number of meat bolus impaction has increased with the increasing prevalence of EoE. Esophageal mucosal biopsy should be considered for all children with middle and distal EFBFBI not attributed to stricture, particularly those with meat bolus impaction.
Disclosure of Interest: None Declared
TRANS LUMINAL ENDOSCOPIC DIVISION OF DUODENAL WEB USING ENDO KNIFE - A NOVEL TECHNIQUE IN A CHILD

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Objectives and Study: Open surgery has been the traditional treatment for fenestrated duodenal web. Endoluminal web resection could resolve the duodenal obstruction without the need for open surgery. We describe a new endoscopic technique to divide the web transluminally using endoscopic technique.

Methods: Under General Anesthesia, a standard paediatric endoscope was passed to duodenum to visualize the web, any potential conditions which could contraindicate the procedure like ulcer and severe inflammation around the web were excluded. After initial examination, endo clip (Olympus) was applied on either side of the web as a precautionary action to avoid the potential bleeding. “SB endo knife” was connected to diathermy unit and passed via 2.8mm biopsy channel to the duodenum. Endo knife* was applied radially in the middle of the web between the endoclips until the web is divided. Endoknife was originally designed to use in ESD (endoscopic submucosal dissection) in adults, this knife has a curved tip that allows to keep the proper dissecting layer, and has an advantage of grasping cauterization which could be used to dissect tissue, as in our case. Endocut-Q, effect 3 (duration 1, interval 6) was used as diathermy* setting to facilitate this.

Results: We performed this procedure on a 3-year-old boy with history of intermittent vomiting, who also known to have short gut syndrome and dependent on TPN. Procedure was completed within 30 minutes successfully. Oozing of blood was observed as an immediate complication after the procedure (from the dividend end of the web) inspite of endo clips was still in place. Argon plasma coagulation was used successfully to stop this bleeding. There were no serious complications reported following this procedure. 4 months after the procedure, no further vomiting episodes were reported and enteral feeds were successfully reintroduced.

Conclusion: Transluminal endoscopic division of duodenal web is possible using endoknife, this will avoid the need for open surgery.

References: *SB Knife™, Sumitomo Bakelite Co, Tokyo, Japan.
*ERBE VIO 200D, ErbeMedezin, Germany

Disclosure of Interest: None Declared
Objectives and Study: Procedural sedation and analgesia has become standard of care for the safe and effective control of pain, anxiety and motion in pediatric age group. Procedural sedation and analgesia (PSA) refers to the pharmacologic technique of managing a child’s pain and anxiety in order to successfully perform a diagnostic or therapeutic procedure safely. To evaluate the safety and effectiveness of procedural sedation and analgesia with intravenous midazolam and ketamine during pediatric endoscopy.

Methods: A retrospective cohort study of all pediatric endoscopic procedures performed between Jan 2008- July 2014 at the Artemis Health Institute, Gurgaon, India was conducted. All children who underwent any endoscopic procedure were enrolled. Intravenous midazolam and intravenous ketamine were the drugs used for procedural sedation and analgesia. Evaluation was performed in terms of sedation-related complications (desaturation, respiratory distress, apnea, bradycardia, cardiac arrest, drug reactions), adequacy of sedation, need for sedation reversal, or failure to complete the procedure.

Results: Sedation is not a primary therapy but rather a treatment of procedural side effects such as pain, anxiety and dangerous movement. Inability to handle these side effects may mean the avoidance of sedative drugs and the occurrence of dangerous side effects. Thus, though no child may die of their pain or stress, physical restraint and anxiety. Psychological trauma to patient and parents, as well as loss of valuable time and less than optimal results will be the price to pay for not sedating them. Analysis of the data included demographic details (age, gender, weight, procedure(s)) performed, doses of each medication/kg body weight, effectiveness of sedation, need for other sedatives, side effects and complications. A total of 557 patients (363 males, 194 females) were enrolled. Patient had mean age of 5.26 years and 65% were from urban area. About 99.3% of patient had effective and uneventful sedation. Mean dose of 0.2mg/kg midazolam and 1.56 mg/kg of ketamine was used, respectively within the recommended dosage guidelines. Transient desaturation occurred in 51 (9.1%) patients which was reversible by supplemental oxygen. About 15 (2.6%) patients had respiratory distress and stridor, hic-cough. No patient required reversal and 4 (0.7%) patient failed to complete the procedure. No patient developed apnea, bradycardia, arrest, or allergic reactions.

Conclusion: Procedural sedation and analgesia in endoscopy using midazolam and ketamine is a safe and efficient method of limiting anxiety and procedure related pain and can be successfully administered by non-anaesthesiologists in developing country. The complication rate is low and can be easily managed.
Disclosure of Interest: None Declared
ESOPHAGEAL STENTS IN DIFFICULT CORROSIVE STRICTURES - FOOD FOR THOUGHT

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Objectives and Study: To evaluate the safety and efficacy of oesophageal stents in the management of difficult corrosive strictures

Methods: The management of pediatric corrosive oesophageal strictures poses a unique challenge owing to the small sized esophagus. The authors describe the successful use of oesophageal stents in the management of corrosive strictures that were resistant to standard endoscopic therapy (serial dilations).

Results: A 2.5 yr old boy had accidental ingestion of toilet cleaner (alkali) leading to severe corrosive injury. He presented to our hospital with marasmic kwashiorkor secondary to vomiting! He underwent a feeding jejunostomy and was nutritionally rehabilitated.

Barium studies revealed multiple level (three) esophageal strictures. The proximal stricture was the tightest and the longest (3.5cm) of them all and had an eccentrically placed pinhole meatus. The middle and distal strictures were both short in length as well as less tight than the proximal stricture. The boy underwent eight serial oesophageal balloon dilations upto 10/ 11mm with a through the scope CRE balloon followed by local application of Mitomycin C at 14 day intervals. Though the proximal stricture seemed easier (softer) to dilate with every sitting of dilation it seemed to promptly collapse back again – thus narrowing the lumen.

The authors successfully deployed a custom made biodegradable & self expandable (ELLA) stent – 12mm diameter & 80mm length across the oesophageal strictures. The boy improved and was able to eat solids but was lost for follow-up. He presented to us 10 months later with recurrence of dysphagia for solids. Upper GI contrast studies & UGI scopy confirmed the recurrence of strictures though less narrow than before. The biodegradable stent had completely degraded.

A case conference was held to discuss further management. Multiple expert opinions were sought. The merits of retaining the native esophagus with continued endoscopic therapy along with an excellent quality of life clearly won over the option of surgery (gastric conduit) and its attendant risks.

A 14mm diameter 80mm length self expandable and removable Niti-S (CONIO) stent was deployed and the boy was able to eat solids again!

There was no significant post procedural pain with both the stents. There were no significant complications like stent migration, perforation or bleeding.

Conclusion:
- Oesophageal stents represent a novel and viable alternative to serial endoscopic dilations/surgery of resistant corrosive strictures
- Oesophageal stents are safe to use in children with minimal complications
- Oesophageal stents offer an excellent quality of life and prolong the duration between sittings of oesophageal dilation in resistant strictures.

**Disclosure of Interest:** None Declared
HOW WELL TOLERATED IS COLONOSCOPY IN MINIMALLY SEDATED ADOLESCENTS?

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Objectives and Study: Colonoscopy is routinely performed in children and adolescents <16 under general anaesthetic (GA), with a low morbidity but high costs attendant to the GA. Our patient cohort expressed interest in avoiding a GA prior to transition into adult practice. Our unit specialises in IBD and polyposis and therefore all included patients only required lower GI endoscopy. We sought to audit prospectively patients who opted for sedation looking at tolerance, depth of sedation, safety and patient preference.

Methods: A questionnaire was completed by the paediatric nurse who was present throughout the procedure and reviewed the patient following recovery. Data collected included colonoscopy completion, patient tolerance, length of procedure and overall length of admission. Subsequently a questionnaire, based on recognised satisfaction tools was given to the patient to complete. Adolescents aged 14 to 17 years who elected to have their colonoscopy under sedation between June & October 2014 were included.

Results: 15 patients were recruited with a median age of 16 (14-17) years. 14/15 patient questionnaires were returned.

All procedures were undertaken by a single paediatric endoscopist, maximum sedation doses were 2.5mg midazalam and 50mg fentanyl as defined by NICE (2010). We achieved 100% caecal with minimal sedation. No adverse events were reported.

The mean duration of colonoscopy was 32 (10-55) minutes, and the mean time to full recovery was 56 mins (0-120mins). Time to full recovery was assessed on the ability of the adolescent to hold a conversation. There was wide variation in time to discharge due to different practices in paediatric day care and endoscopy suite.

100% (n=14) of patients felt that they had received enough information about having the colonoscopy under sedation. 78% (11/14) reported mild or very mild discomfort during the procedure and did not experience any discomfort post endoscopy. No patient reported pain during the procedure. 50%(7/14) of patients had been worried prior to the procedure but post procedure there was 100% agreement that they would now choose sedation endoscopy over GA.

Conclusion: Pan-Colonoscopy can be safely and painlessly performed under minimal sedation in selected adolescents. The procedure is uniformly well tolerated and preferred in our cohort. Sedation enables speedier discharge and reduced costs compared to GA.

Patient concerns regarding sedation endoscopy pre endoscopy may improve with increased use of written sedation endoscopy information, only received by 3/15 patients. Consistent discharge criteria
needs to be developed to ensure a uniform discharge process for patients attending paediatric day care and endoscopy suite.


Disclosure of Interest: None Declared
SHORT-TERM COMPLICATIONS OF PERCUTANEOUS ENDOSCOPIC GASTROSTOMY ACCORDING TO THE TYPE OF TECHNIQUE

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Objectives and Study: To compare short-term complications and prognosis between patients who underwent the pull technique and two other types of introducer techniques, the trocar introducer technique and T-fastener gastropexy technique.

Methods: Twenty-six patients who underwent PEG were enrolled in this study. We retrospectively investigated the age, sex, body weight, weight-for-age Z-score, underlying diseases, PEG indications, complications, duration of NPO, pain control frequency, and duration of antibiotic therapy. The patients were classified into three groups according to the PEG technique. The occurrence of complications was monitored for 10 weeks after the procedure.

Results: The age, sex, body weight, and weight-for-age Z-score were not significantly between the three groups. Most patients had cerebral palsy and seizure disorders. Dysphagia was the most common indication for PEG. Major complications occurred in 5 (50%), 4 (66.7%), and 0 (0%) patients in group I, II, and III, respectively (p=0.005). Further, peristomal infection requiring systemic antibiotic therapy occurred in 2 (20%), 3 (50%), and 0 (0%) patients in group I, II, and III, respectively (p=0.04). There was no significant difference between the groups with respect to minor complications, duration of NPO, pain control frequency, and duration of antibiotic therapy.

Conclusion: The results indicate that the T-fastener gastropexy technique was associated with the lowest rate of major complications.


Disclosure of Interest: None Declared
DOES PROPOFOL SEDATION ADMINISTRATION BY GASTROENTEROLOGISTS FOR PEDIATRIC ENDOSCOPIC PROCEDURES SAFE AND EFFICIENT?

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Objectives and Study: The number of gastrointestinal endoscopies (GE) performed in childhood has increased over the last two decades, improving both diagnosis and treatment of children’s gastrointestinal diseases. This has dramatically increased the demand for safe and effective procedural sedation. Propofol is an ultra-short acting sedative agent with amnestic effects. Its use in GE is favored since it has a rapid onset and offset of action. It is also associated with fast recovery times and there is reported high patient and physician satisfaction. There is a considerable literature on the administration of propofol by nonanesthesiologists for endoscopy in adults, but very few data are available on this issue in children. We aimed to assess the efficacy and safety of propofol sedation use by gastroenterologists for pediatric endoscopies.

Methods: A retrospective chart review of all pediatric endoscopies sedated by gastroenterologist in Elisha and later in Assuta hospitals since 2008 (introduction of propofol sedation) and Rambam hospital (since 2009). Data was collected until 2013.

Results: 1214 children received propofol sedation. Mean age 11.8±4.3 years, 47% males. A satisfactory level of sedation was achieved for all the procedures. The addition of fentanyl significantly decreased propofol dosage for optimal sedation. There is an inverse correlation between the child age and propofol dosage per kilogram. Girls required significantly less dosage of propofol than boys in order to reach an equivalent level of sedation. There were seven minor adverse outcomes (0.5%) all reported in Rambam: a child experienced laryngospasm and six children had transient episodes of oxygen desaturation that improved with repositioning of the airway. No child required placement of an endotracheal tube. No hypotension, cardiac arrhythmias or adverse neurologic effects secondary to propofol infusion were identified. None of the children experienced severe side effects or required hospitalization.

Conclusion: Nonanesthesiologists propofol sedation for endoscopy in children is safe and efficient.

Disclosure of Interest: None Declared
Objectives and Study: Whole exome sequencing (WES) was applied to identify the molecular defect causing severe auto immune enteropathy (AIE) with combined immunodeficiency in two siblings from consanguineous parents.

Methods: Mutation was identified by WES and confirmed by Sanger sequencing. mRNA expression was studied by RT-PCR and protein expression was analysed by western blot. Activation of NFκB was analysed in PHA (phytohemagglutinin)-T cell lines by flow cytometry after stimulation by Phorbol 12-myristate 13-acetate (PMA) and ionomycin.

Results: The girl (6 year-old) and her brother (4 year-old) displayed severe dermatitis and failure to thrive since birth. Progressively, they developed AIE with severe villous atrophy and an important lymphocytic infiltrate, without evidence of auto antibodies (AIE 75kD and anti-enterocytes). They displayed a wide spectrum of infections, including life-threatening pulmonary infections with adenovirus, Pneumocystis jirovecii and EBV. Immunological parameters were high IgE, low IgM, normal B cell counts but variable antibody titers to vaccination, elevated counts of activated/memory T lymphocytes, but reduced frequencies of Th1, Th2, Th17 and Treg.

WES identified a single autosomal recessive nucleotide variation (c.550G>T) in exon 4 of MALT1 predicting a deleterious p.Asp184Tyr amino acid change.

In agreement with the indispensable role of MALT-1 in the NFκB cascade downstream the T cell receptor (1), induction of interleukin-2 and degradation of IκBα in response to PMA and ionomycin were drastically impaired in PHA-T cell lines from the two siblings carrying the MALT1 D184Y mutation compared to cell lines derived from an unrelated healthy control and from both parents. MALT1 mRNA expression was comparable in PHA-T cell lines from the two patients, their parents and an unrelated healthy control, but the protein was undetectable in the two affected children. These results indicate that the mutant MALT1 D184Y is most probably unstable and rapidly degraded.

Conclusion: We describe the third (2, 3) loss-of-function mutation in the MALT1 gene as a cause of combined immunodeficiency and AIE.

MALT1 should be now considered as a candidate gene in AIE without auto-antibodies, especially in the context of immunodeficiency and multiple infections.


Disclosure of Interest: None Declared
A DEDICATED NETWORK FOR CONGENITAL DIARRHEAL DISORDERS: REPORT FROM LAST 8 YEARS OF ACTIVITY

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Objectives and Study: Congenital diarrheal disorders (CDD, [OMIM] 251850) are a group of rare heterogeneous chronic enteropathies with clinical onset in the first hours or days of life. Dedicated network and website (http://www.congenitaldiarrhealdisorders.net) were created at University of Naples “Federico II”, combining pediatric gastroenterology and clinical genetics expertise, in order to provide a rapid access to molecular analysis and other diagnostic and therapeutic procedures.

Methods: CDD patients database was investigated regarding the network activity from January 2007 to November 2014.

Results: During the study period DNA samples from patients suspected of CDD (n=95), and from their relatives (n=54) were analyzed. The molecular analysis showed mutations causative of disease in 66 patients: congenital chloride diarrhea (SLC26A3, n=44), congenital sucrase-isomaltase deficiency (SI, n=3), glucose-galactose malabsorption (SLC5A1, n=8), microvillous inclusion disease (MYO5B, n=2), congenital tufting enteropathy (EpCAM, n=2) and Shwachman-Diamond syndrome (SBDS, n=7).

Conclusion: Recent evidence in the understanding of genetics and pathophysiology of CDD are leading to significant advances in the diagnostic approach to these conditions. Molecular analysis is changing the scenario in CDD diagnosis and it is allowing to a reduction in the use of invasive and expensive diagnostic procedures. The activity of a dedicated network website made CDD molecular diagnosis readily available.

Disclosure of Interest: V. Pezzella Conflict with: Agenzia Italiana del Farmaco (AIFA), A. Elce Conflict with: Agenzia Italiana del Farmaco (AIFA), G. Terrin Conflict with: Agenzia Italiana del Farmaco (AIFA), G. Castaldo Conflict with: Agenzia Italiana del Farmaco (AIFA), R. Berni Canani Conflict with: Agenzia Italiana del Farmaco (AIFA)
FUNCTIONAL ANALYSIS OF ATYPICAL MICROVILLUS INCLUSION DISEASE PATIENTS

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Objectives and Study: Microvillus inclusion disease (MVID) is a rare congenital enteropathy that causes severe diarrhea resulting in dehydration, metabolic acidosis and the need for parenteral nutrition for survival. Recently, we identified that mutations in syntaxin 3 can cause atypical MVID. These patients also have enterocytic subapical accumulation of vesicles, partial microvillus atrophy and microvillus inclusion bodies, however they are different from classical patients because they can endure partial enteral feeding and show basolateral inclusions. It is still unknown to what extend cell polarity and nutrient uptake is affected in these atypical patients, we are currently addressing these questions by use of an in vitro organoid model.

Methods: We established intestinal organoids from two atypical MVID patients with mutations in syntaxin 3. By confocal microscopy we are assessing apical and basal polarity. Furthermore, we study the nutrient-uptake in a 2D-monolayer model with an accessible apical and basolateral side to measure sucrose uptake in these patients.

Results: Preliminary data show that organoids can be grown in 2D monolayers and some apical proteins are mislocalized, while others are not.

Conclusion: Mutations in syntaxin 3 in MVID patients cause partial mislocalization of apical proteins.


Disclosure of Interest: None Declared
CHEMOTHERAPY EFFECTS ON INTESTINAL GENE EXPRESSION PROFILES IN PIGLETS

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Objectives and Study: While limited knowledge is available from children, studies in animals indicate that cytotoxic therapy leads to marked changes in intestinal structure, function, immunity and of the microbiota. More detailed knowledge about chemotherapy-related expression patterns of intestinal genes may provide further insights into the mechanisms underlying chemotherapy-induced gut toxicity and help to identify biomarkers and targets for intervention.

Methods: Jejunal tissue samples were obtained from piglets, used as preclinical models of chemotherapy-induced gastrointestinal toxicity in children. Prior to tissue collection, the piglets were treated with either busulfan and cyclophosphamide (BuCy) (n=10), or a single dose of doxorubicin (Dox) (n=12) and compared to saline controls. Pigs were euthanized 9-11 days after chemotherapy in the Dox and BuCy experiment, respectively. Expression profiles were measured using the Agilent 4 x 44K porcine expression microarray (Design id: 026440) and global pathway analysis was done using Gene Set Enrichment Analysis.

Results: Gene expression analysis identified 1163 differentially expressed genes (570 down-regulated, 593 up-regulated) in the groups receiving chemotherapy. In the doxorubicin treated piglets, 594 genes were differentially expressed (396 down, 198 up). In piglets treated with busulfan and cyclophosphamide, 1328 genes were differentially expressed (657 down, 671 up). Bioinformatics analysis demonstrated repression of Gene Ontology (GO) terms and Kyoto Encyclopedia of Genes and Genomes pathways for treated vs. untreated animals related to cellular immunity and the adaptive immune system, including the intestinal network related to IgA production. Examination of the 137 genes sharing differential expression across the two chemotherapy regimens showed similarly repression of cellular immunity and the adaptive immune system. Several up-regulated genes were related to innate immune defense, suggesting a compensatory up-regulation of such genes after chemotherapy. These included surfactant protein D (SP-D), deleted in malignant brain tumors 1 (DMBT 1) and peptidoglycan recognition protein 2 (PGLYRP2), all related to primary defense against invading bacteria and virus on mucosal surfaces and important for epithelial growth and differentiation.

Conclusion: Innate immune factors, including SP-D, DMBT1 and PGLYR2, were differentially up-regulated in the intestinal tissue after chemotherapy. Further investigation into such genes will establish whether their corresponding proteins could be markers of gastrointestinal toxicity or have possible functional, prognostic or treatment-related implications.
Disclosure of Interest: None Declared
**Objectives and Study:** Protein Loosing Enteropathy (PLE) is a complication of Fontan operation. We will describe the effect of Budesonide treatment on serum albumin levels and infusion requirements in these patients.

**Methods:** A retrospective study of children <14 years who developed PLE post Fontan. PLE was defined as an albumin level < 30g/L with clinical manifestation of edema: facial swelling, lower limb swelling or ascites and positive albumin tagged scan. The outcome was measured by improvement in serum Albumin level > 30 g/L and reduction in transfusion requirements.

**Results:** 9 patients were identified with a median age of 108 months (48-192 months). The median age for developing PLE post Fontan is 53 months (20-143 months). All patients presented with edema with low serum albumin. The median serum Albumin value is 16 g/L (range 12-21 g/L) before and 39 g/L (range 31-44 g/L) after treatment. The increase in serum albumin above 30 g/L post treatment was statistically significant (P-value = 0.002). No side effects for Budesonide were reported. Only 2 patients relapsed on weaning Budesonide below 3mg/day.

**Conclusion:** Budesonide is effective in improving serum Albumin levels and reducing albumin infusion requirements in patients who develop PLE post Fontan. Relapse occurs once it is weaned below 3mg per day independent of age & weight.

**Disclosure of Interest:** None Declared
EXPANDING PHENOTYPIC AND ALLELIC HETEROGENEITY OF TRICHO-HEPATO-ENTERIC SYNDROME.

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Objectives and Study: Tricho-hepato-enteric syndrome (THES) also called syndromic diarrhea is a rare life limiting autosomal recessive bowel disorder. We describe the phenotypic/genotypic characteristics of patients with chronic diarrhea and abnormal skin hyperpigmentation with distinct distribution.

Methods: Six patients from four consanguineous Saudi families who were diagnosed with congenital chronic diarrhea were examined. Genomic DNA was extracted from whole blood using a standard salt precipitation method. DNA samples were quantitated spectrophotometrically and stored at -20°C. All participating individuals (affected and unaffected) were genotyped using an Affymetrix Axiom array.

Results: Families 1 and 4 had three and two affected siblings respectively, whereas family 2 and 3 had only one affected individual each. All children were products of first-degree consanguineous parents of Saudi origin. All patients presented with severe intractable diarrhea that occurred within the first two weeks of life. Facial dysmorphism (prominent forehead and cheeks, flat broad nose and hypertolerism) was observed in all patients. Hair showed an abnormal pattern with decreased shaft diameter in two patients. There was a picture of trichorrhexis nodosa in two other patients. Two patients had peg teeth. The skin lesions were consistent in all patients and were in the form of scattered tan-brown, hyperpigmented spots or maculae. They were different in size (0.5-5cm in diameter) and number (all >10). These lesions were not raised but had distinct borders and were all located in the lower half of the body (pelvic girdle and lower limbs).

Gastrointestinal biopsies were obtained from three patients. Small bowel biopsies showed normal villi with mild increases in the number of inflammatory cells in two individuals and partial villous atrophy with the same picture of inflammation in one girl. Immunological investigations did not show any specific abnormalities. Five patients received total parenteral nutrition for different lengths of time. One patient remained TPN dependent. The remaining patients managed well with elemental formula and/or a cow’s milk-free diet.

There was only 1 homozygous variant that was located in SKIV2L which has revealed a novel mutation: c.3559_3579del, p.1187_1193del in exon 28 of SKIV2L. The deletion includes several amino acids in the DOB1/SK12/helY-like DEAD box helicase C-terminal domain of SKIV2L (InterPro).

In the three other patients we identified a novel nonsense mutation: c.C4102T, p.Q1368X in exon 39 of TTC37 that was located in the tetratricopeptide–like helical domain of Thepsin (InterPro).

Conclusion: Our study expands allelic and phenotypic heterogeneity of SD/THES and highlights further the impact of allelism or perhaps modifier genes in specific ethnic populations.
Disclosure of Interest: None Declared
SYMPTOM QUESTIONNAIRE AS A TOOL TO AID THE DIAGNOSIS OF NON-IGE FOOD ALLERGIES AFFECTING THE GASTROINTESTINAL TRACT

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Objectives and Study: The prevalence of food allergy has increased in recent decades and there is paucity of data on time to improvement or symptom resolution using elimination diets in non-IgE mediated food allergies. We therefore aimed to assess the time required to improvement of symptoms using a symptom questionnaire for children with non-IgE mediated gastrointestinal food allergies (GIFA) on an elimination diet.

Methods: A prospective observational study was performed on patients with non-IgE mediated GIFA on an elimination diet who complete a questionnaire about nine most common food allergic symptoms before and after commencing an exclusion diet. The questionnaire measured symptoms individually from 0 (no symptom) to 5 (most severe) and collectively from 0 to 45. Children were only enrolled in the study if collectively symptoms improved with the dietary elimination within 4 or 8 weeks.

Results: Data from 161 children were suitable for the study, of which, 30 patients were excluded because they did not show any improvement in symptoms. Data from 131 patients were analysed. 90 boys and the median age of the cohort was 21 months [IQR: 7 to 66]. Based on the symptom questionnaire 129 patients (98.4%) improved after 4 week elimination diet and only 2 patients improved after 8 weeks. A statistical significant difference before and after commencing the elimination diet was seen in all nine recorded symptoms (all p <0.001), and in the overall median too.

Conclusion: This is the first study attempting to establish time to improve after commencing the diet elimination. Elimination diets rarely should be performed beyond 4 weeks, as almost all children will respond within this time frame.

Disclosure of Interest: None Declared
LONG-TERM OUTCOME OF CHILDREN RECEIVING HOME PARENTERAL NUTRITION: A 14-YEAR SINGLE-CENTRE EXPERIENCE IN 251 PATIENTS.

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Objectives and Study: Parenteral Nutrition (PN) is the main treatment for intestinal failure. The aim of this study was to review the indications for children treated with home PN (HPN) and describe outcomes for different underlying diagnostic groups over a 14-year period.

Methods: Retrospective study including all children referred to our institution and discharged on HPN between January 1st 2000 and December 31st 2013. The indications for HPN were divided into primary digestive diseases (PDD) and primary non digestive diseases (PNDD). Every child had a customized parenteral nutrition formula. Since October 2011, we started using Taurolidine locks (Taurolock®) in our unit for children who had 2 or more CRBSIs in a 12 months interval. The statistical analysis was performed using the R statistical software (http://www.r-project.org) and Microsoft Office Excel 2010 software. Risk threshold (mentioned as "p") was set in the whole study at 0.05.

Results: A total of 251 patients were recruited: 217 children (86%) had a PDD. The mean age at HPN onset was 3.2 ± 1.2 years with a mean duration of 1.9 ± 0.4 years. The major indication for HPN was short bowel syndrome (59%) secondary to midgut volvulus (16.7%), necrotizing enterocolitis (12.3%) and gastroschisis (12%). By December 31st 2013, 56% of children were weaned off HPN, 7.6% had intestinal transplantation and 9.6% of children were dead. The major complications of HPN were catheter-related blood stream infections (CRBSI, 1.7 per 1000 days of catheter) and intestinal failure associated liver disease (IFALD, 51 children, 20% of cohort). Children with congenital enteropathies had the highest rates of IFALD (44% of the sub-group). We had no significant deceleration of growth in SBS children 6 month after HPN weaning.

Conclusion: Children on HPN in our cohort have a shorter HPN duration to weaning, lower death rate and longer interval to catheter replacement than other studies. There is no statistical significance in the incidence of IFALD. We have an overall increased rate of CRBSIs compared to a study in our unit that was done between 1980 and 2000 but we see a decreasing trend since 2012. The incidence of CRBSIs secondary to staphylococcus aureus also increased. The results of Taurolidine line locks seem quite promising and despite the drop in CRBSI incidence in 2012 and 2013, it is too early to evaluate its efficacy on children in our unit. We see no deceleration of growth after 6 months of HPN weaning in SBS children. Nevertheless, data in literature show nutritional deficiencies on long term follow up of these children mandating close clinical and biological monitoring.
Disclosure of Interest: None Declared
PERIANAL FISTULAS AND ABSCESSES IN PAEDIATRIC CROHN’S DISEASE PATIENTS FOLLOWED IN THE GERMAN REGISTRY CEDATA-GPGE: INCIDENCE AND RISK FACTORS

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Objectives and Study: Perianal disease (PD), comprising fistula and abscess, is a severe complication in Crohn’s disease (CD). We aimed to examine the prevalence and incidence of PD and to identify risk factors for its development in a large cohort of newly diagnosed pediatric CD patients.

Methods: Data were obtained from the CEDATA-GPGE registry, a prospective, multi-center registry for pediatric inflammatory bowel disease (IBD) patients in Germany and Austria, established by the German Society for Pediatric Gastroenterology and Nutrition (GPGE) in 2004. Pediatric CD patients were included if they were registered within 3 months of diagnosis and had at least two follow up documentations in the first year. Eligible patients were censored if the time gap between the consecutive follow up case report forms (CRFs) after the first year was >200 days. The following items were considered as potential risk factors and examined with log rank tests and Kaplan Meier analysis: sex, family history of IBD, extraintestinal manifestation, disease localization according to Paris classification, and initial therapy with corticosteroids, exclusive enteral nutrition, or immunomodulators. The statistical significance was defined as p< 0.05.

Results: Of 2400 CD patients, 778 fulfilled the inclusion criteria with 59% patients being male. The mean age at CD diagnosis was 12.4 years (SD ±3.4). PD was prevalent in 47 patients (6.0%) at CD diagnosis (80.9% male). During a mean follow up time of 1.9 years (SD ±1.4) another 35 patients developed PD (80.0% male). The cumulative incidence of PD at 12 months after CD diagnosis was 4.0% and at 18 months 6.8%, excluding prevalent cases at diagnosis. Kaplan Meier analysis identified following items as potential risk factors for development of PD during follow up: male sex (log rank=7.3; p=0.007), initial induction therapy with corticosteroids (log rank=5.4; p=0.02) and extraintestinal manifestation at diagnosis (log rank=2.8; p=0.092).

Conclusion: Male sex and extraintestinal manifestation are associated with PD in pediatric CD patients. Initial therapy with corticosteroids may increase the risk for the development of PD during disease course.

Disclosure of Interest: None Declared
EOSINOPHILIC OESOPHAGITIS: SYMPTOMS, ENDOSCOPIC APPEARANCES AND HISTOLOGY FEATURES FAIL TO PROVIDE SUBGROUPS THAT PREDICT RESPONSE TO THERAPY.

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Objectives and Study: Consensus guidelines suggest treatment choices for eosinophilic oesophagitis should be tailored to avoid undue burden on the patient and family, with clinical trials suggesting both topical steroid and dietary therapy are both effective in a majority of patients. Predicting which would be effective based on disease subgroups would obviate serial therapeutic/dietary trials. We hypothesised that clinical, endoscopic and/or histological findings at diagnosis would be predictive for long-term treatment success.

Objective: to determine clinical, endoscopic and histological criteria in eosinophilic oesophagitis that are associated with treatment effect after a minimum of one year follow-up.

Methods: Endoscopy and pathology departmental databases identified 43 cases with confirmed eosinophilic oesophagitis, based on standard clinicopathologic criteria, diagnosed between 2008 and 2012; 32 were male, age range 22 months to 16 years (median 8 years). Details were extracted from case records to categorise symptoms at presentation, treatment with antacids, topical corticosteroid and dietary restriction. Endoscopic findings were categorised: normal, furrowing alone, multiple features (furrows, exudate, trachealisation, nodularity and/or stricture). Histology was categorised by the presence of pure eosinophilic or mixed eosinophilic/lymphocytic epithelial inflammation. Treatment effect was determined by response at one year follow-up by the treating clinician. Univariate analysis was performed using chi-square tests.

Results: Symptoms at presentation were: dysphagia (65%), vomiting (28%), abdominal pain (21%) and faltering growth (9%). Endoscopic findings were: normal (19%), furrowing alone (30%) and multiple features (51%). Two cases had stricture. Histology was pure eosinophilia in 15 (35%), and mixed in 28 (65%). Therapy administered was: topical corticosteroid (65%); targeted or compete dietary allergen avoidance (35%); antacid (32%). Dietary therapy alone was used in only 5 cases (11%). Overall, therapy was determined effective in 47% after one year, with treatment effect not recorded in a single case. There were no statistically significant associations between symptoms, endoscopic features or histology type.

Conclusion: No symptoms, endoscopic findings or histological type predicted response to drug or dietary therapy in clinical practice in a large cohort from a tertiary unit. Long-term dietary restriction was used as the single long-term therapy in only few cases.


Disclosure of Interest: None Declared
Objectives and Study: Intestinal microbiota composition may influence immunologic tolerance and defense from infections. The aim of our study was to evaluate the microbiota in infants at risk of atopy.

Methods: Within a randomized controlled trial on the role of supplementation of infant formula with prebiotic in prevention of atopy in infants at risk (314 enrolled), feces were collected from infants of less than 6 months of age. Fluorescence in situ hybridization (FISH) was performed to quantitatively detect Bifidobacteria, Bacteroidetes, Firmicutes, Faecalibacterium prausnitzii, Clostridium difficile and Clostridium cluster II and IX. Fecal calprotectin, fecal eosinophilic cationic protein and fecal IgA concentration were determined.

Results: Birth mode influenced the microbiota composition in the way that cesarean delivery was associated with a higher Firmicutes/Bacteroidetes ratio ($P=0.0073$) and a lower bifidobacteria colonization rate ($P=0.0164$). Clostridium difficile prevalence was 42%. Colonization with Clostridia Cluster II was associated with an increased risk of developing atopic dermatitis (AD) in the first year of life (adjusted odds ratio=2.3; 95%CI 1.1-3.2). Firmicutes/Bacteroidetes ratio influenced the occurrence of respiratory infections (odds ratioadjusted=2.4; 95%CI 1.28-3.5) and acute gastroenteritis (odds ratio=2.7; 95%CI 1.4-3.7).

Conclusion: These data support the role of microbiota in the development of AD, respiratory infections and acute gastroenteritis. Mode of delivery affect microbiota composition.

Disclosure of Interest: V. Buccigrossi Conflict with: The study was supported by Mead & Johnson Foundation., G. Ranucci Conflict with: The study was supported by Mead & Johnson Foundation., S. Zanconato Conflict with: The study was supported by Mead & Johnson Foundation., D. Piacentini Conflict with: The study was supported by Mead & Johnson Foundation., E. Borgia Conflict with: The study was supported by Mead & Johnson Foundation., G. Smania Conflict with: The study was supported by Mead & Johnson Foundation., M. Altieri Conflict with: The study was supported by Mead & Johnson Foundation., M. I. Spagnuolo Conflict with: The study was supported by Mead & Johnson Foundation., A. Guarino Conflict with: The study was supported by Mead & Johnson Foundation.
**Objectives and Study:** Proton pump inhibitor-responsive esophageal eosinophilia (PPI-REE) is a newly recognized entity that must be differentiated from eosinophilic esophagitis (EoE). The proportion of children with esophageal eosinophilic counts ≥ 15 eos/hpf that respond to PPI is unclear, as only retrospective data are available. The objective of this study was to determine the prevalence of PPI-REE in children and to identify clinical features associated with this entity.

**Methods:** This prospective study enrolled consecutive patients with esophageal dysfunction symptoms and esophageal eosinophilic counts ≥ 15 eos/hpf from two University Hospitals. Children received treatment with esomeprazol 2 mg/kg/day twice daily for 8 weeks and endoscopy was repeated. Complete response to PPI was defined as presence of < 5 eos/hpf and partial response if >5 and < 15 eos/hpf were found in post-treatment esophageal biopsies. Characteristics of responders and nonresponders were analyzed.

**Results:** Thirty-two patients (86.3% males) were enrolled (ages 1 through 15 years). Clinical improvement occurred in 28 (87.5%) patients. Histological response was observed in 22 (68.7%) children: 15 (46.9%) presented complete response and 7 partial response. Only 10 children (31.2%) were finally diagnosed of EoE.

There were no significant differences in familial and personal history of atopy, food allergy tests results and endoscopic score. Clinical symptoms were similar in both groups, except for food impaction that was present in 70% of children with EoE vs 13.6% of children with PPI-REE (p=0.005).

In 21 children pH-study was performed and only one patient finally diagnosed of EoE presented reflux index >7%. Pretreatment mean peak eosinophil count was significantly higher in EoE patients vs PPI-REE children (76.3±32.3 vs 44.3±30.7; p=0.012).

**Conclusion:** A significant proportion (68.7%) of children with esophageal eosinophilia responded to high dose PPI treatment. Clinical, endoscopic and results of pH study were similar in both groups, with the exception of food impaction that was more frequent among children with EoE. Mean peak eosinophil count was higher in nonresponders to PPI. These results support the published guidelines recommending a PPI trial prior to diagnosing EoE.

**Disclosure of Interest:** None Declared
EVALUATION OF THE VALUE OF THE FAECAL CALPROTECTIN IN DETERMINING THE ESOPHAGITIS ETIOLOGY

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Objectives and Study: To make differential diagnosis of esophagitis and to determine whether the diagnosis is eosinophilic esophagitis (EoE) or peptic esophagitis (PE) by evaluating faecal calprotectin (FC) levels.

Methods: In total, 40 newly diagnosed patients who were resistant to anti-reflux treatment and in between 6 months-18 years old were included (13 EoE, 27 PE) into the study. In all subjects, a complete blood count, C-reactive protein (CRP), total IgE, specific IgE, eosinophilic cationic protein (ECP), skin prick tests, serum IL-5, IL-13 and FC levels were assessed. The results compared with those of 24 healthy children and in between groups. The value of these tests in making distinction between EoE and PE was studied.

Results: Interleukin 13 levels were significantly higher in PE group than the healthy group (p=0.006), mean FC levels were not significantly different in between these two groups (p=0.571). Eosinophil count, CRP, total IgE, serum IL-5, IL-13 and FC levels in EoE were significantly higher than the healthy group (p values are <0.001, 0.013, <0.001, 0.010, 0.003, 0.033 respectively). Leukocyte count, eosinophil count, CRP, total IgE, ECP and serum IL-5 values were significantly higher in EoE group than PE group (p values are 0.003, 0.001, 0.016, 0.005, <0.001, 0.005, respectively). There was no significant difference between FC levels of EoE group and PE group (p=0.055). Total IgE (r=0.489) and ECP (r=0.810) were correlated with tissue eosinophil count (p=0.001; <0.001).

Conclusion: Faecal calprotectin and ECP could be used as a noninvasive marker for making the differential diagnosis of the EoE. However in order to use FC as a diagnostic marker more research containing larger number of patients is needed.

Disclosure of Interest: None Declared
Objectives and Study: This study is aimed at assessing frequency of interaction between non-alcoholic fatty liver disease (NAFLD) and ectopic fat deposition in the pancreas in obese and overweight children and at finding out common chains of pathogenesis.

Methods: This cross-sectional study was conducted among 150 children aged 11-15 years, included into 3 groups: 60 overweight children (1st group), 60 obese children (2nd group), and 30 healthy children (3rd group). Diagnosis of the NAFLD and non-alcoholic fatty pancreas disease (NAFPD) was based on sonographic data. Peculiarities of carbohydrates, lipid metabolism and pancreatic exocrine function and were investigated.

Results: Sonographic data compatible with NAFPD were found with equal frequency in overweight and obese children - 85% and 86.7% accordingly (p=0.88), whereas sonographic findings compatible with NAFLD were two times higher in children with obesity 56.7% vs. 30% (P =0.005). These results were associated with insulinresistancy, disturbances of the carbohydrates and lipid metabolism, decreasing level of the elastase-1 in 23.3% children with obesity.

In both groups were found changes in intestinal microbiota – in 66.7% overweight and 80% obese children (P =0.11). These changes characterized by increasing level of opportunistic flora (Proteus, Enterococcus, Clostridium) and decreasing level of Bifidum- and Lactobacterias.

Conclusion: Sonographic results compatible with NAFPD were found more than in 2/3 cases in overweight and obese children and they appeared earlier than sonographic results of NAFLD which were found only in 1/3 cases of overweight children and ½ cases of obese patients. These results were associated at first with insulinresistancy and carbohydrates metabolism disturbances, whereas in our study atherogenic dyslipidemia was not prominent. In 23% obese children with sonographic changes considered as pancreatic steatosis signs of mild exocrine insufficiency were found out. High frequency of microbiota changes detection needs in further exploration as a possible target of therapeutic intervention.

Disclosure of Interest: None Declared
DEVELOPMENT AND ACTIVITY OF THE INTESTINAL MICROBIOTA IN EXTREMELY- AND VERY PRETERM INFANTS

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Objectives and Study: Early life microbiota development is fundamental for health in later life by affecting development of the gastrointestinal tract and immune system through host-microbe interactions. In early life, the intestinal microbiota is dynamic with increased susceptibility to host- and environmental factors. Preterm birth is associated with organ immaturity, hospitalisation, antibiotic treatment and formula feeding, which may impact the development of the intestinal microbiota in preterm infants. Our aim is to study the establishment and functionality of the intestinal microbiota of preterm infants born at varying gestational ages (GA).

Methods: Faecal samples from 5 extremely preterm (EP, 25–27wks GA) and 5 very preterm (VP, 30wks GA) infants were collected during the first six weeks after birth. Faecal microbiota composition was investigated by 454 pyrosequencing of the 16S rRNA gene. To functionally characterise the intestinal microbiota, we studied the faecal metaproteome by LC-MS/MS.

Results: A temporal pattern in microbiota development is observed in all preterm infants, during which a highly diverse microbiota composition of meconium develops towards a Bifidobacteria dominated microbiota at postnatal weeks 3-6. At this time, Bifidobacterium spp. are significantly more abundant in VP than in EP infants (p<0.05), indicating delayed colonisation with Bifidobacterium spp. in EP infants. Faecal protein profiles of all preterm infants demonstrate a dominance of human proteins during the first six postnatal weeks. However, a rapid increase in microbial proteins is observed over time in all VP infants but not in all EP infants. In VP infants, proteins derived from Bifidobacterium spp. are most abundant, covering 68.5±10.8% of the total identified microbial proteins at postnatal weeks 3-6. Functionally, these proteins are mainly involved in milk fermentation. In EP infants, Bifidobacterium derived proteins are low at postnatal weeks 3-6 (4.8±5.3%) and fermentation processes are covered by facultative anaerobic Streptococcus, Enterococcus and Klebsiella species.

Conclusion: The transition towards a Bifidobacterium dominating state is delayed in EP infants compared to VP infants indicating that the degree of prematurity plays an important role in the development and activity of the intestinal microbiota. Which factors are most influential during this establishment, e.g. parenteral feeding, type of feeding, antibiotic treatment and intensive care stay, is under investigation.

Declared, I. Renes Conflict with: Employee of Nutricia Research, R. van Elburg Conflict with:
Employee of Nutricia Research, C. Belzer: None Declared, J. Knol Conflict with: Employee of Nutricia
Research
THE PAEDIATRIC NON-ALCOHOLIC FATTY LIVER INDEX-SCORE AND CARDIOVASCULAR RISK FACTORS IMPROVE AS RESULT OF A LONG-TERM AMBULATORY INTERDISCIPLINARY LIFESTYLE INTERVENTION IMPLEMENTED IN A CLINICAL SETTING IN OVERWEIGHT, OBESE AND SEVERE OBESE CHILDREN

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Objectives and Study: Liver pathology and increased risk of cardiovascular disease are most worrisome consequences of childhood overweight, an as yet increasing global problem. The most severe obese children are particularly at risk of these complications, while lifestyle interventions are often reported to be not effective in this group. Here, we studied whether a paediatric NAFLD index-score and cardiovascular risk factors improve in severe obese children as a result of an ambulant lifestyle intervention and compared it to the effect in overweight and obese children.

Methods: 172 children and adolescents (42% boys; 58% girls) with overweight, obesity, severe obesity or morbid obesity were included. They participated in the lifestyle intervention of the Centre for Overweight Adolescent and Children’s Healthcare (COACH) where they received ambulatory, personalized guidance on a monthly basis by an interdisciplinary team. The paediatric non-alcoholic fatty liver index-score (PNFI score) and the cardiovascular risk factors waist circumference, lipid spectrum, blood pressure, fasting glucose and HbA1c levels were evaluated.

Results: The COACH intervention resulted in a sustainable and on-going decrease of BMI z-score of -0.12±0.3 and -0.21±0.3 after 12 and 24 months respectively. Further, the PNFI score and important cardiovascular risk factors including waist circumference, diastolic blood pressure, levels of HbA1c, serum total cholesterol and LDL-cholesterol improved significant after 1 year of intervention. Most important, regarding long-term health benefits and weight loss, the intervention was equally effective for severe obese children compared to children with overweight and milder degrees of obesity.

Conclusion: The paediatric NAFLD index-score and cardiovascular risk factors improved significant in even the most severe obese children to the same extent as in overweight and obese children during a long-term, ambulatory, personalized lifestyle intervention carried out by an interdisciplinary team in a hospital setting and the children demonstrated significant weight loss.

Disclosure of Interest: None Declared
PECULIARITIES OF THE ADHESIVE INTESTINAL OBSTRUCTION IN ARMENIAN CHILDREN WITH FAMILIAL MEDITERRANEAN FEVER

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Objectives and Study: Familial Mediterranean Fever (FMF) is an ethnic disease for Armenian population with high frequency of carriers of MEFV mutations (1:3) and disease prevalence (14-100:10000). Apart amyloidosis, adhesive (mechanical) intestinal obstruction (AIO) is a second life-threatening complication of FMF. AIO is another type of abdominal involvements in FMF, which develops due to recurrent aseptic peritonitis and peritoneal adhesions. AIO is more typical for severe course of the FMF. It is especially important to diagnose it in time to diminish the risk of intestinal strangulation and necrosis. Objectives: to investigate the frequency and peculiarities of AIO in Armenian children with FMF.

Methods: We observed 715 children with FMF (438 boys and 277 girls (mean age 8.64±0.17). Diagnosis of FMF was based on Tel-Hashomer criteria and MEFV genetic analysis. The diagnosis of AIO was determined according to conventional surgical and radiological criteria.

Results: AIO was diagnosed in 23 (3.2%) FMF patients (14 boys, 9 girls). In 73.9% cases it occurred spontaneously, in 26.1% postsurgical. 30.4% of FMF patients developed AIO despite previous colchicine therapy. Most of children (16) had an early manifestation of FMF during the first three years of life (3.1y.). At the same time, FMF was diagnosed rather late (7.09±0.74 years) in comparison with the all observed FMF patients (5.25±0.15 years; t=2.207; p=0.03). Correspondingly, the colchicine therapy in this group was initiated later (on average after 7.3 years of the disease onset), which may also contribute to the complicated course of FMF. The association between AIO and the disease severity in primary admitted and untreated FMF patients was revealed ($c^2=6.65; p<0.04$). Most FMF patients with AIO (19 out of 23) had the predominance of $M694V$ mutation in different genotypes and 1/3 of them were homozygous. The frequency of AIO was 1.5-3.5 times higher in $M694V$ carriers ($c^2=1.94; p=0.75$).

Conclusion: 1. The revealed peculiarities of the AIO in Armenian children with FMF were the following: high disease severity, early manifestation of FMF, as well as late diagnosis and delayed start of colchicine treatment. $M694V$ mutation carriers with a severe course of disease, especially homozygotes were at higher risk of AIO development. 2. MEFV mutations screening is recommended for Armenian pediatric patients with AIO for diagnosis of FMF and starting colchicine therapy, which might improve the course of diseases and help to diminish the risk of surgical emergency.


Disclosure of Interest: None Declared
NERVE ENTRAPMENT AS A CAUSE OF CHRONIC ABDOMINAL PAIN IN ADOLESCENTS

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Objectives and Study: Unraveling the cause of chronic abdominal pain (CAP) in adolescents is challenging. When visceral and anatomic anomalies are excluded, focus may shift towards functional gastrointestinal disorders (FGID’s). Abdominal wall as an origin of pain is often neglected. ACNES (anterior cutaneous nerve entrapment syndrome) is an abdominal wall condition caused by entrapment of cutaneous end-twiggs of thoracic nerves. ACNES leads to a sharp abdominal pain aggravated by straining and severely interferes with daily function. Interestingly, a small portion of adult FGID patients were recently found to have ACNES. However, ACNES percentages in a pediatric FGID population are unknown. The objective of the present study is to estimate the prevalence of ACNES amongst pediatric patients with chronic abdominal pain.

Methods: Medical charts of chronic abdominal pain patients between 11-18 years of age analyzed in a pediatric department of a teaching hospital in 2011 and 2012 were retrospectively analyzed. FGID was assumed using ROME III criteria or based on the expertise of the consulting pediatrician. In contrast, ACNES was diagnosed if the following findings were present: A finger-tip small localized point of pain (trigger-point), a positive Carnett sign and altered pinch tests, and pain relief <15 minutes following a sub-fascial abdominal wall injection of 10cc of 1% lidocaine solution. Pain was determined before and after treatment using a VAS score (0-10).

Results: A total of 95 individuals with chronic abdominal pain were evaluated during the two year time period. All demonstrated a normal visceral diagnostic workup (female n=61, mean age 14 years, range 12-17). A FGID was diagnosed in the majority of children (n=83) whereas ACNES was thought probable in the remaining 12 adolescents. The ACNES population was one year older and contained more females compared to the FGID-population (15 years, 92% females vs 14 yr, 60% female) (both p<0.05). ACNES patients reported a verbal pain rating score of 7 (VRS 0-10, n=12) at presentation. Six weeks post treatment (42% infiltrations, 58% neurectomy), 92% (11/12) was pain free or was functioning with a non-obstructive pain level.

Conclusion: One of eight adolescents with chronic abdominal pain in the absence of structural visceral abnormalities may suffer from an abdominal wall condition termed ACNES (anterior cutaneous nerve entrapment syndrome). A simple treatment regimen including localized abdominal wall lidocaine injections or a neurectomy offers relief in the majority of adolescents.

Disclosure of Interest: None Declared
GENETIC POLYMORPHISMS ASSOCIATED WITH GASTROINTESTINAL SYMPTOMS IN FABRY DISEASE

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Objectives and Study: Gastrointestinal symptoms (GIS) are often among the earliest presenting events of Fabry disease (FD). It has been reported a wide range of intrafamilial phenotypic variability, both in terms of target-organs and severity of FD. Aim of this study was to evaluate if genetic polymorphisms could be responsible for phenotypic variability in GIS among patients with Fabry disease, even in family members harboring the same mutation.

Methods: We genotyped a cohort of 21 FD patients (6 families), 7/21 reporting GIS and 14/21 not complaining GIS. We also genotyped 3 healthy family members without GIS to use as controls. DNA extracted from peripheral blood cells was analyzed by the novel drug metabolizing enzyme and transporter (DMET) microarray platform (Affymetrix), enables highly multiplexed genotyping of 1936 known polymorphisms in Absorption, Distribution, Metabolism, and Elimination (ADME)-related genes (225). A total of 255 samples including patients previously genotyped because of breast cancer, lung cancer, multiple myeloma and healthy subjects randomly selected from the Affymetrix's genotype database were used as unrelated control group (no FD). The genotype association was calculated by Fisher’s exact test (two tailed).

Results: We first analyzed the genotype distribution in the FD group with GIS versus the FD group without GIS. A significant difference was found in the frequency of the rs55802895 SNP located in the nuclear receptor constitutive androstane receptor (NR1I3;CAR; CAR1; MB67) gene. We detected G/A diplotype in 5/7 FD patients with GIS while only in 1/14 FD patients without GIS (p=0.0055). The G/G diplotype occurred in 13/14 FD patients without GIS and in 2/7 FD patients with GIS. Interestingly, the G/G diplotype was found in all three healthy family members (no FD) without GIS (asymptomatic controls). Moreover, a significant difference of the G/A diplotype frequency was also found comparing the group of patients with FD and GIS (5/7) versus the wider control group (66/255) (p = 0.0177).

Conclusion: In conclusion, according to our preliminary findings, the heterozygous genotype G/A of the rs55802895 SNP in the NR1I3 gene seems to be associated with the altered gastrointestinal function in FD.

Disclosure of Interest: None Declared
HIGH PREVALENCE OF MALNUTRITION IN PATIENTS WITH SILVER-RUSSEL SYNDROME
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Objectives and Study: Silver-Russell Syndrome (SRS) is a congenital, genetic disorder characterized by intrauterine and postnatal growth retardation, triangular face with typical facial appearance, body asymmetry, and feeding difficulties. Due to the abovementioned characteristics of SRS patients, gastrointestinal conditions should be excluded in order not to overlook curable conditions. Hereby we present a unique, single center experience of gastrointestinal disorders associated with SRS.

Methods: This is a retrospective, single center analysis for the period of 1987-2013. The diagnosis of SRS was established on the basis of clinical manifestations and genetic studies. Collected data comprised nutritional status, method of feeding (oral, enteral, parenteral) and gastrointestinal disorders and performed surgeries.

Results: We collected data from 67 patients with SRS (F=30; M=37), all molecularly confirmed, with mean age of 4.6 years (2 months-17.5 years). In this group the mean BMI was 13.5 (range of 8.9-29.3). 57% (n=38) of patients were malnourished (BMI <3 percentile). Most of the patients were orally fed (n=63; 95%), three patients (4.5%) were fed through the gastrostomy due to insufficient nutritional status or severe feeding disorders. One patient had a history of parenteral feeding in infancy. Three patients (4.5%) presented with celiac disease and were given gluten-free diet. We found 4 patients with gastroesophageal reflux disease, another one with biliary reflux. Four patients (6%) had antireflux surgery performed, one of these procedures followed gastrostomy placement.

Conclusion: We presented a unique group of patients suffering from SRS. Malnutrition seems to be a common problem in SRS, still only a few patients received nutritional support with enteral feeding. Relatively high prevalence of celiac disease among SRS patients may result from more frequent screening due to the short stature in this group. Proper and regular nutritional screening and support should be advised for SRS patients in order to prevent malnutrition and its consequences.

Disclosure of Interest: None Declared
Objectives and Study: Barrett’s esophagus (BE) is a pre-neoplastic condition caused by chronic gastroesophageal reflux. Data on BE in children is limited. We aimed to establish the prevalence of BE in children and adolescents in Poland, while adhering to diagnostic guidelines, modes of treatment and follow-up in gastroenterology centers.

Methods: Retrospective analysis of clinical data of patients 1-18 years of age who underwent upper gastrointestinal endoscopy (UGE) from 1.01.2004 - 31.12. 2013 and were diagnosed with BE defined by endoscopic and histological findings.

Results: Data from 7 academic centers and 1 regional hospital were analyzed (39 936 UGE). BE was diagnosed in 88 patients (2.2 BE /1000 UGE), 51 boys (58%), mean age at diagnosis 13.3 years (1.2-17.9 y), 34 (49%) children had neurological disorders or congenital esophageal abnormalities. In children with neurodevelopmental and esophageal abnormalities, EB was diagnosed at a younger age (p=0.01) compared to children without chronic problems. The main clinical symptoms were vomiting (85.2%), abdominal pain (63.6%), heartburn (36%), dysphagia (19.3%), odynophagia (8%), retrosternal pain (9%), gastrointestinal bleeding (4%). The length of BE was 0.5cm-20 cm (mean 4.3 cm). Prague classification was applied in 2 cases. The mean number of biopsy samples was 2.1(1-7) and chromoendoscopy was done in 1 case. Intestinal metaplasia was found in 34 patients, (38.6%), gastric metaplasia in 44 (50%) and in 10 (11.4%) metaplasia was not specified. There was no dysplasia. Concomitant esophagitis was presented in 58 cases (65.9%), H.pylori infection in 12 children (13.6%). Mean duration of anti-secretory therapy was 7.3 months (2-6 months), 11 patients received prolonged treatment, 16 patients had fundoplication. Control endoscopy was done 1-19 months following diagnosis (mean 5mo), biopsies were taken in 47(53.4%) patients. 46 patients are still in pediatric centers, 15 in adult clinics, 27 patients were lost from observations.
**Conclusion:** The prevalence of BE in children in Poland is similar to other European countries. However, the diagnostic approach, treatment and follow-up program differs between centers. There is a need for guidelines for diagnosis and treatment of BE in children in order to establish uniform care. Additionally, a transition program from pediatric to adult centers should be developed.


**Disclosure of Interest:** None Declared
THE EFFECT OF BIFIDOBACTERIUM BREVE BBG-001 ON INTESTINAL PERMEABILITY IN PRETERM BABIES <31 WEEKS GESTATION

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Objectives and Study: Introduction

Several meta-analyses have suggested that probiotics significantly reduce the rates of necrotising enterocolitis (NEC) and NEC related death in preterm babies. As a result, some researchers have suggested that large randomised controlled trials are no longer needed. These recommendations come despite a lack of in vivo studies of probiotic mechanisms in this patient group.

Hypothesis

That randomisation to or proven colonisation with Bifidobacterium breve BBG-001 is associated with reduced intestinal permeability in preterm babies.

Methods: This study was conducted on a cohort of babies <31 weeks gestation, already enrolled to a randomised controlled trial of Bifidobacterium breve BBG-001 versus placebo for the prevention of NEC, sepsis and death (The PiPS Study). Intestinal permeability was assessed 14 days after birth by the sugar absorption test (SAT) using lactulose and mannitol and intestinal protein loss by stool alpha-1-antitrypsin (A1AT).

Results: The main PiPS Study recruited 1315 babies <31 weeks gestation. Administration of Bifidobacterium breve BBG-001 was not associated with a reduction in NEC, sepsis or death.

Thirty-six infants were enrolled to this study. Median (range) gestation was 27 weeks (24-30) and median birth weight was 900g (585-1460). Thirteen babies were randomised to BBG and 23 to placebo. As a result of cross colonisation, on stool culture at 2 weeks after birth, 19 babies were positive for BBG and 14 were not (culture not available in 3).

The mean (SD) lactulose:mannitol ratio (L:M) for all infants was 0.79 (1.2) and mean A1AT was 269 (326) mg/L. One sample was excluded from the final analysis. Results by randomisation and colonisation with BBG are presented in Table 1.

Table 1. Mean (SD) Lactulose:Mannitol Ratio and A1AT by Randomisation and Colonisation with BBG

<table>
<thead>
<tr>
<th>Results by Randomisation</th>
<th>Bifidobacterium breve BBG 001</th>
<th>Placebo</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactulose:Mannitol Ratio</td>
<td>0.43 (0.55)</td>
<td>0.97 (1.4)</td>
<td>0.16</td>
</tr>
<tr>
<td>A1AT (mg/L)</td>
<td>233 (267)</td>
<td>294 (366)</td>
<td>0.56</td>
</tr>
<tr>
<td>Results by Colonisation</td>
<td>Colonised with BBG</td>
<td>Not Colonised</td>
<td>P value</td>
</tr>
<tr>
<td>Lactulose:Mannitol Ratio</td>
<td>0.46 (0.53)</td>
<td>1.25 (1.7)</td>
<td>0.48</td>
</tr>
<tr>
<td>A1AT (mg/L)</td>
<td>314 (403)</td>
<td>233 (247)</td>
<td>0.79</td>
</tr>
</tbody>
</table>
Conclusion: In this cohort, administration of *Bifidobacterium breve* BBG-001 did not result in a statistically significant reduction in intestinal permeability or in intestinal protein loss. This is in line with the outcomes of the main PiPS study and highlights the importance of undertaking evaluations of mechanistic action. Studies such as these might in future be used to select the optimum probiotic species or probiotic combinations in order to achieve the maximum clinical benefit in this patient group.

Disclosure of Interest: None Declared
HEALTH-RELATED QUALITY OF LIFE, ANXIETY, DEPRESSION AND DISTRESS OF PARENTS OF CHILDREN WITH HOME PARENTERAL NUTRITION.

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Objectives and Study: Parents of children dependent on Home Parenteral Nutrition (HPN) may experience psychosocial problems due to the illness and intensive treatment of their child. We aimed to investigate the health-related quality of life (HRQOL) and levels of anxiety, depression and distress of these parents.

Methods: A cross-sectional, multicenter study was conducted in 21 mothers and 16 fathers of 21 children with HPN (response-rate 50%, mean age=5.7 years, SD=4.6). Parents completed online questionnaires: TNO-AZL Quality of Life Questionnaire (TAAQOL), Hospital Anxiety and Depression Scale (HADS) and the Distress Thermometer for Parents (DT-P) on the KLIK website (www.hetklikt.nu), designed for the use of Patient Reported Outcomes in daily clinical practice. The DT-P consists of a thermometer-score ranging from 0 (no distress) to 10 (extreme distress), with scores ≥4 indicating elevated distress, a list of possible problems and a question about a wish for referral. Mean scores of the TAAQOL and HADS were compared to reference groups of Dutch mothers and fathers, using Mann-Whitney U-tests and T-tests respectively.

Results: On the TAAQOL, no differences were found in HRQOL between HPN mothers and fathers compared to the reference groups. However, on the HADS, HPN mothers reported higher levels of depression compared to mothers in the reference group (Table 1). Also, 62% of mothers and 38% of fathers of children with HPN reported elevated distress on the DT-P. The most reported problems were fatigue (62%) by mothers and leisure activities/relaxing (63%) by fathers. Regarding the wish for referral, 43% of mothers and 38% of fathers indicated that they would like, or maybe would like to talk to a professional about their situation.

Table 1. Anxiety and depression (higher scores represent higher levels of anxiety and depression) in mothers and fathers of children with HPN in comparison to reference groups of Dutch mothers and fathers (mean scores)

<table>
<thead>
<tr>
<th></th>
<th>HPN parents</th>
<th>Reference group</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>N</td>
<td>M (S D)</td>
</tr>
<tr>
<td>Mothers</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Conclusion: HPN treatment of their child seems to be highly stressful for parents. Because of the small sample size, qualitative research can give more insight into the specific problems parents may experience. Then, targeted interventions can be developed and provided.

Disclosure of Interest: None Declared
HIGH MOBILITY GROUP BOX 1 (HMGB1) IS INCREASED IN PRETERM NEONATES WITH NECROTISING ENTEROCOLITIS

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Objectives and Study: High Mobility Group Box 1 (HMGB1) is a DNA-binding nuclear protein, released into the extracellular milieu actively, by innate immune cells in the presence of inflammatory stimuli, or passively, by any cells as consequence of tissue injury. In a previous study, we showed that HMGB1 is a very reliable and innovative fecal marker of intestinal inflammation (1. Am J Gastroenterol. 2011;106:2029-40). In the present study, we aimed to assess whether fecal HMGB1 could represent an early marker of necrotizing enterocolitis (NEC) in preterm neonates.

Methods: We studied 20 preterm neonates (gestational age <32 weeks): 3 with diagnosis of NEC and 17 without signs of NEC. We also evaluated 13 full-term neonates that served as controls. Stool samples were collected from each subject and stored at -20°C. HMGB1 levels were analyzed by western blot.

Results: Levels of fecal HMGB1 were markedly increased in preterm neonates with NEC as compared to full-term neonates (p<0.05); they were also increased as compared to healthy preterm neonates although not at a statistically significant level (likely because of a small sample size of NEC patients). Expression of HMGB1 in feces was also increased in healthy preterm compared with full-term neonates (p<0.05).

Conclusion: Our preliminary data, if confirmed by further studies in larger NEC populations, would suggest the use of fecal HMGB1 as a marker of this severe condition that affect premature babies

References:

Disclosure of Interest: None Declared
ROLE OF CHYMOTRYPSIN C(CTRC) MUTATIONS IN IDIOPATHIC PANCREATITIS IN CHILDREN.
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1 Hungarian Pancreatic Study Group., Szeged, Hungary

Objectives and Study: Chronic pancreatitis is a complex, multigenic disease, and affected individuals often carry more than one mutation in several disease-associated genes. It has been shown that loss-of-function alterations in chymotrypsin C (CTRC) predispose to pancreatitis by diminishing its protective trypsin-degrading activity. The aim of this study was to investigate the incidence of CTRC mutations, their association with PRSS1, SPINK1, and CFTR mutations and their effect on the age of onset in idiopathic pancreatitis in children.

Methods: The national registry of the Hungarian Pancreatic Study Group (HPSG) contains 24/35 children with idiopathic pancreatitis, 12/24 of them have had genetic testing up to now. Blood DNA was isolated from all patients. Mutations were detected in CTRC, the cationic trypsinogen gene (PRSS1), the serine protease inhibitor Kazal type 1 gene (SPINK1), and the cystic fibrosis transmembrane conductance regulator gene (CFTR) by direct DNA sequencing.

Results: 58% (7/12) of children had CTRC mutations. 4 patients were homozygous for and 3 patients heterozygous for p.G60G mutation. 43% (3/7) of the patients having CTRC mutations had additional mutations in different genes. These included mutations in the CFTR gene (p.F508delta heterozygous), the SPINK1 gene (p.N34S heterozygous) and the PRSS1 gene (p.R122H heterozygous). Patients having two mutations had earlier disease onset (5.7 vs. 8 years) than patients with only a single mutation.

Conclusion: CTRC mutations are often detected in children with idiopathic pancreatitis and seem to cause the disease in combination with other genetic risk factors. Age of onset appears to be earlier in patients carrying multiple mutations in different risk genes.

Disclosure of Interest: None Declared
INLET PATCH: A CASE SERIES WITH CLINICAL, ENDOSCOPIC AND HISTOLOGICAL FINDINGS

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Objectives and Study: An inlet patch (IP) is an area of heterotopic gastric mucosa of the proximal esophagus. It is an under recognized condition due to its location. There are only small numbers of studies in pediatric patients. Herein, we report clinical, endoscopic, and histological findings of our patients with inlet patch.

Methods: This retrospective study included all of the cases of IP recorded in last three years at our department. Data about demographics, clinical symptoms, endoscopic and histological findings, treatment, and outcome was collected.

Results: Retrospective review of last 3 years endoscopy records in our center revealed 6 cases with IP and 4 of them confirmed histologically (table). We found 0.3% incidence in local setting. The median age at diagnosis was 15.7 years (range 15–17 years). In our series one of the patients had a history of corrosive ingestion followed by stricture formation requiring multiple dilation procedures and dyspeptic symptoms, one had recurrent haematemesis and one of them had isolated dyspeptic complains and one had weight loss. All recovered after proton pump inhibitor treatment and did not recur. None of them had respiratory complains.

Table: Characteristics of the Patients

<table>
<thead>
<tr>
<th>Patient number</th>
<th>Age/sex</th>
<th>Symptom</th>
<th>Endoscopic/histopathological findings</th>
<th>Treatment/outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>17/F</td>
<td>Dyspepsia, heartburn</td>
<td>Solitary lesion, 7 mm in diameter/fundic type gastric mucosa, H. Pylori</td>
<td>PPI/asymptomatic</td>
</tr>
<tr>
<td>2</td>
<td>16/M</td>
<td>Poor appetite, weight loss</td>
<td>Solitary lesion, 4 mm in diameter/fundic type gastric mucosa</td>
<td>PPI/asymptomatic</td>
</tr>
<tr>
<td>3</td>
<td>15/F</td>
<td>Haematemesis</td>
<td>Three lesion, 1 cm in diameter/fundic type gastric mucosa</td>
<td>PPI/asymptomatic</td>
</tr>
<tr>
<td>4</td>
<td>15/M</td>
<td>Dyspepsia</td>
<td>Solitary lesion, 2 cm in diameter/antral type gastric mucosa</td>
<td>PPI/asymptomatic</td>
</tr>
</tbody>
</table>

Conclusion: Inlet patch is an under recognized condition due to its location. Although the majority of inlet patches are asymptomatic, it can be associated with severe complications and even malign transformation. Endoscopists should be aware of this condition and carefully assess the proximal esophagus especially if the patient has dyspeptic symptoms and no other findings on upper endoscopy.
Disclosure of Interest: None Declared
SELF BOUGIENAGE IN CHILDREN WITH OESOPHAGEAL STRCTURE; A CASE SERIES AND VIDEO DEMONSTRATION

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Objectives and Study: Oesophageal strictures (OS) in children are usually benign. Aetiology includes oesophageal atresia (57%); caustic ingestion (21%) and peptic oesphagitis (12%). Most need multiple dilatations with associated complications. We report 3 children who were successfully trained to swallow esophageal dilators as an alternative treatment modality for this complex problem.

Methods: All these children required multiple dilations on regular intervals. All children were taught to swallow the chosen Maloney Dilator by a consultant paediatric surgeon (SP). Cases 2 and 3 were also able to view a video demonstration by patient 1.

Results: Case 1: A 15 year old girl, with VATER anomaly, had an Oesophageal stricture following TOF repair. She had mid-OS which was aggravated by dysmotility. She had multiple dilatations since her 1st year of life. Self-bougienage was started at age of 8, no further dilatations required since. Upper endoscopy has shown no recurrence of stricture.

Case 2: An 11 year old boy diagnosed with Barrett’s oesophagus at 7 years of age. He had an Oesophageal stricture secondary to ulcerative oesophagitis. He required multiple balloon dilatations. He was trained to self dilatation and discharged with a size 28 Fr dilator. He remained asymptomatic since.

Case 3: A 15 yr old boy diagnosed with ulcerative oesphagitis 3 years ago developed a 6 cm lower Oesophageal stricture confirmed by barium and endoscopy; Biopsies were normal. He required multiple balloon dilatations. Self-bougineage started at 14 years of age. At present he does his self-dilatations twice weekly and remains asymptomatic.

We were unsuccessful in training a young 7 year old boy recently.

Conclusion: With appropriate patient selection and careful instruction oesophageal self-dilation is a safe and effective alternative treatment to current balloon or surgical dilatations. We have shown that such dilatations could be started as early as eight years of age.

References:

**Disclosure of Interest:** None Declared
CLINICAL EVALUATION OF THE CHILDREN DIAGNOSED ABDOMINAL TUBERCULOSIS: EXPERIENCE OF A SINGLE CENTRE
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¹Sisli Hamidiye Etfal Education and Research Hospital, Istanbul, Turkey

Objectives and Study: Abdominal tuberculosis (TB) includes infection of the gastrointestinal tract, peritoneum, mesentery, abdominal lymph nodes, liver, spleen, and pancreas and it is rare manifestation of childhood TB. It’s diagnosis is usually delayed as the symptoms were not specific in children, it can easily be confused with other conditions and sometimes it can result unnecessary surgery.

We aimed to report the experience of our clinic with children diagnosed abdominal TB for the last four years.

Methods: Eight children, diagnosed abdominal TB and followed in Şişli Hamidiye Etfal Training and Research Hospital, department of pediatric gastroenterology and pediatric infection between 2010-2014, were analysed from the patients’ records retrospectively.

Results: Eight patients (6 girls/2 boys) with mean age of 13.6±2.8 (7-16 years) were diagnosed abdominal TB during the last 4 years. The mean duration of symptoms before diagnosis was 2.5±1 months (1-4 month). All of the patients presented with abdominal pain and weight loss. Fever was seen in 4 patients and abdominal distension was seen in 6/8 patients. Six patients were followed as acute abdomen in Pediatric surgery and five of them underwent laparotomy. Household members with TB could be traced in three. All had BCG vaccination and 7 of them had positive tuberculin skin test. Seven patients had co-existing pulmonary findings. Abdominal TB involved peritoneum in 4, gastrointestinal tract in 2, both peritoneal and abdominal lymph nodes in 1 and both gastrointestinal tract and lymph nodes in 1 patient. Quantiferone test was positive in 4 patients. Mycobacterium tuberculosis was isolated from gastric aspirate or sputum in 1 patient and isolated in culture. The diagnosis of abdominal TB was confirmed histopathologically in 6 patients.

All of the patients had received quadruple antituberculosis treatment. Two patients had problem to use the drugs properly and one patient had neurological sequelae

Conclusion: It is difficult to diagnose abdominal TB in children. Although it was rare, it should be considered in the differential diagnosis of children with abdominal pain, weight loss in areas of high prevalence for TB and we should do confirmatory investigations to avoid unnecessary surgery.

Disclosure of Interest: None Declared
Objectives and Study: Anorectal lesions in children are still poorly-known issue and challenging problem for gastroenterologists. The aim of the study was to assess clinical characteristics, treatment and outcomes of anorectal disorders in children.

Methods: A retrospective review of medical records of 65 children hospitalized due to anorectal disorders in the Department of Paediatrics and Department of Paediatric Surgery and Traumatology from 2008 to 2013 was performed. Abstracted data included demographic details, symptoms and localization of lesions, duration of symptoms, underlying disorders, treatment and outcomes. Children were divided into two groups. Group 1 were infants younger than 12 months of age and Group 2 children aged 12 months to 18 years.

Results: Group 1 comprised 31 (97%) boys and 1 (3%) girl with mean age of 4±3 months. Twenty (62.5%) children presented with perianal abscess and 12 (37.5%) with perianal abscess and fistula-in-ano. The duration of symptoms was 1 day to 8 weeks (mean 1.5±2 weeks). All infants required systemic antibiotics. Surgical procedures were performed in 26 (81%) infants. Follow-up data were available in 20 children, of which 16 ended up with a satisfactory outcome and 4 had recurrence of perianal lesion.

Group 2 comprised 20 (61%) boys and 13 (39%) girls with mean age 10±5 years old. Sixteen (48.5%) children had IBD (15 with Crohn’s disease and 1 with ulcerative colitis), 8 (24%) functional constipation and 1 (3%) type 2 diabetes. Anal fissures were stated in 11 (33.3%), fistula-in-ano in 7 (21.2%), perianal abscess in 7 (21.2%), abscess and fistula-in-ano in 4 (12.1%) children. The duration of symptoms was 5 days to 72 weeks (mean 9 ± 18 weeks). In 10 (30.3%) cases surgical treatment was required. Antibiotic was used in 21 (63.6%) children. Follow-up data were available only in 10 children, of which 5 ended up with a satisfactory outcome and 5 had recurrence of perianal lesion.

There were significant differences in sex distribution (p<0.001), type of perianal lesion (p<0.001) and management (p<0.05) between both groups.

Conclusion: Perianal changes in children are more common in boys. In infants predominated perianal abscesses which were not associated with any underlying disease. The most common lesions in older children were anal fissures, fistula-in-ano and perianal abscesses. The majority of perianal lesions in older children are complication of underlying condition. Infants required surgical management and antibiotic therapy more frequently than older children.

Disclosure of Interest: None Declared
AUTOIMMUNE NATURE OF GASTRITIS IN CHILDREN WITH JUVENILE ARTHRITIS

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Objectives and Study: To estimate means of the early diagnostics of autoimmune gastritis in children with juvenile arthritis (JA).

Methods: We examined 35 children aged 9 to 16 years (mean age 13.9 ± 2.3 years) suffering from JA and CG (group 1).

The comparison group (group 2) consisted of 27 patients, suffering only from CG (group 2). All participants undergone standard gastroenterological examination with FGS including mucosa biopsies of the body and antrum of the stomach.

Histological examination of biopsies was performed using Sydney scale. Immunohistochemical study of gastric mucosa of Epstein-Barr virus (EBV) on paraffin-embedded biopsies was performed. Monoclonal antibodies were used as the first antibody to latent membrane proteins of the Epstein-Barr virus (manufactured by DAKO). As a positive control the tissue Hodgkin's lymphoma was used, the blocking serum was used as a negative control.

The detection of antibodies to gastric parietal cell (GPC) was performed by indirect immunofluorescence method using commercial kits (Euroimmun, Germany)

Results: The frequency of antibodies to gastric parietal cells in children with JA was higher than in the group 2 (25.71 % and 0 %, p<0.01). Antibodies to gastric parietal cell in children with JA was seen with a high frequency both with the persistence of EBV + HP (14.3 % and 0 %, p <0.01) and with the presence of HP only (8.6 % and 0 %, p <0.05). The increase only of antibodies to gastric parietal cell was seen in children with JA in 2.8 %. Among children with JA positive correlations were seen between the increase of antibodies to gastric parietal cell and HP (r=0.36, p<0.05), EBV persistence (r=0.28, p<0.05) and intestinal metaplasia (r=0.28, p<0.05) and the degree of mononuclear infiltration of gastric mucosa (r=0.28,
p<0.05). Studies suggest that correct etiologic diagnosis of CG in children with JA demands the identification of HP, EBV and antibodies to gastric parietal cell.

**Conclusion:** Autoimmune gastritis in children with juvenile arthritis was identified in 25.71% of cases. In children with juvenile arthritis the presence of HP and EBV + HP was one of the risk factors of autoimmune gastritis.

**Disclosure of Interest:** None Declared
EARLY-ONSET ECZEMA IS ASSOCIATED WITH BIFIDOBACTERIUM AND ROSEBURIA SUBPOPULATIONS BUT NOT MICROBIAL DIVERSITY IN STOOL SAMPLES OF CHINESE NEWBORNS

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Objectives and Study: Gut microbiota is increasingly recognised to play crucial roles in the pathogenesis of asthma, obesity and autoimmune diseases. Faecal microbiome is likely ethnic and diet-specific, but such data is lacking in Asians. This study characterised faecal microbial compositions of Hong Kong Chinese infants.

Methods: A total of 153 Chinese newborns with uneventful perinatal course and born in September 2012 in our university-affiliated teaching hospital were recruited. These babies were prospectively followed for the development of eczema. Random stool samples were obtained from 4-week-old infants with eczema (n=15) and without any allergy (n=15) at 9 months, which were subjected to next-generation sequencing to determine stool microbiome. Genomic DNA extracted by PowerSoil DNA Isolation Kit (MO BIO Laboratories) was sequenced using Ion PGM Sequencing 200 Kit v2, Ion 318 TM Chip v2 on Ion PGM System (Ion Torrent). Reads from each patient were filtered for low quality (Phred <20). Microbial diversity was evaluated using Shannon diversity index in Swedish (J Allergy Clin Immunol 2012;129:434-40).

Results: 5 controls had insufficient DNA for sequencing. Among top 5 genera, bifidobacterium was more commonly found in controls than cases (100% vs 60%; p=0.051). Relative abundance of roseburia was higher in controls (median 0, IQR 0-0.205) than cases (absent in all samples) (p=0.027). Shannon diversity index was similar between cases (median 1.252, IQR 0.863-1.746) and controls (median 1.401, IQR 1.236-1.660) (p=0.739). Comparing microbial compositions in our newborns and Swedish, Escherichia coli was found among top 5 genera only in both our cases and controls whereas enterobacter only in Swedish newborns. Clostridium, parabacteroides and lactobacillus were found only in Chinese eczema and healthy Swedish newborns. Bifidobacterium, bacteroides and streptococcus were found among top 5 genera among cases and controls in both populations.

Conclusion: Bifidobacterium and roseburia appear to be less frequently detected in stool of 4-week-old Chinese infants who subsequently develop eczema. Microbial diversity is not associated with eczema susceptibility. This study confirms ethnic-specific early-life faecal microbial compositions.

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Disclosure of Interest: None Declared
VITAMIN D STATUS OF ADOLESCENTS WITH GILBERT'S SYNDROME AND INFLAMMATORY DISEASES OF UPPER GASTROINTESTINAL TRACT

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Svetlana Vasilyeva 1
Tatyana Tvorogova 1
Nara Sugyan 1
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Objectives and Study: Our study was performed to assess the effect of hepatocellular disease (Gilbert's syndrome) and chronic gastroduodenitis on the status of serum vitamin D in adolescents.

Methods: The serum 25-hydroxyvitamin D (25-OHD) was measured in February with chemiluminescence enzyme immunoassay in 100 girls aged 11-17 years (mean age 14.3 ± 2 years). Vitamin D deficiency was defined as 25-OHD below 20 ng/mL; insufficiency as 25-OHD of 20 – 30 ng/mL; and sufficiency as 25-OHD of 30 – 50 ng/mL. Children were divided into 3 groups. The 1st one (n=14) with Gilbert's syndrome (of which at 12 - genetically confirmed, in 2 - clinically diagnosed by the presence of indirect hyperbilirubinemia), the 2nd one (n=20) with chronic gastroduodenitis and the 3rd comparison group (n=66) without inflammatory diseases of upper gastrointestinal tract and hepatocellular disease.

Results: A low vitamin D status was identified in all groups. The deficiency of 25-OHD in the 1st group with Gilbert's syndrome (10.48 ± 3.05 ng/mL) and 2nd group with chronic gastroduodenitis (11.77 ± 3.45 ng/mL) was greater than in the 3rd group (14.95 ± 4.0 ng/mL). The difference in the status of 25-OHD between the 1st group with Gilbert's syndrome and the 3rd group without inflammatory diseases of upper gastrointestinal tract and hepatocellular disease is significantly (p<0.05). Vitamin D intaked from food showed no significant differences in the examined groups (p>0.05). Clinically low vitamin D status in adolescent girls expressed by the presence of reduced growth rates at 16%, overweight and obesity - 7%, arterial hypertension - 6%, decreased bone mineral density - 6%, the frequent incidence of acute respiratory infections – 23%.

Conclusion: Inflammatory diseases of upper gastrointestinal tract (chronic gastroduodenitis), disrupted the process of absorption of vitamin D, are one of the leading risk factors for the formation of its low vitamin D status in adolescents. The most evident deficiency of 25-OHD with Gilbert's syndrome suggests the existence of multienzyme deficiency, including not only a violation glucuronidation processes, but also decrease the activity of the hydroxylation processes of vitamin D with slowing the formation of its active form.

Disclosure of Interest: None Declared
ARE PAEDIATRICIANS AWARE OF THE APPROPRIATE USE OF PROBIOTICS AND THEIR KNOWLEDGE OF THEM? RESULTS OF A MULTI-NATIONAL SURVEY

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Objectives and Study: Despite the scientific evidence accumulated during the last decade and the vast number of publications on the medical uses of probiotics, it is not clear whether this information reaches pediatricians properly and whether this evidence has an impact on their clinical practice.

To evaluate the knowledge level, attitudes and current practices of pediatricians (Peds) with regards to probiotics in 10 countries.

Methods: A closed-ended structured questionnaire was implemented in 10 different countries (Argentina, Peru, Spain, Italy, Hungary, Morocco, Turkey, Pakistan, India and China) online or face-to-face according to the country. Target and Sample Size: 30 to 70 Peds interviewed per country.

Total sample: 600. Representativeness: adapted criteria according to each country's reality (quota method).

Results: Most of Peds feel informed about probiotics (88%) with the highest prevalence in China (97%); however 30% Moroccan Peds expressed lack of information. 79% of Peds fulfilled the correct definition of a probiotic (95% Turkey vs 41% Pakistan) being well-known as a bacteria (68%) than a yeast (33%). There is a lack of consensus about strains with proven efficacy in acute diarrhea (AD) and antibiotic-associated diarrhea (AAD). There is a high level of confidence (89%) with differences across countries. Peds consider probiotics to be safe in children (83%) with the highest prevalence in Italy (96%) while in Morocco only 56% consider it safe. They prescribe probiotics for themselves (69%) or their relatives (80%) for AD (62.4%) and AAD (67.6%). Reasons for not prescribing are: no official guidelines (39%), not enough clinical trials (39%) and not having enough experience (35%).

Overall 93% Peds read at least 1 article/year. Information resources are professional (96%) and
public (52%). There was no correlation between knowledge/prescription score (0.036) and prescription/reading article (0.288) (Pearson Correlation Test).

**Conclusion:** Most Peds feel well informed about probiotics with a high level of confidence on their safety. More than 50% recommend probiotics for AD and AAD and use for their relatives or themselves. Lack of information is a key obstacle for not prescribing probiotics even though more than 90% read at least 1 article/year. Continuous medical education is key to promote the use of probiotics. This is the first multinational survey on probiotics.

**Disclosure of Interest:** None Declared
FATA JUNIOR GASTRO SIGENP: A FIRST ITALIAN SURVEY ON NONSTEROIDAL ANTI-INFLAMMATORY DRUGS (NSAID) AND UPPER GASTROINTESTINAL BLEEDING IN CHILDREN

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Objectives and Study: A retrospective population-based survey was conducted to assess the potential contribution of NSAIDs-related in upper gastrointestinal bleeding (UGIB) in pediatric population.

Methods: A national retrospective study from seven pediatric Gastroenterology Units (GU) and one adult GU was conducted. Patients aged between 2 months and 16 years were recruited. UGIB was defined as esophageal and/or gastric and/or duodenal bleeding. The odds ratios for UGIB and NSAID was assessed by comparing exposure during the 7 days preceding the date of hospitalization.

Results: A total of 51 children were included over 8 years. Hematemesis was present in most patients and melena was more frequent in group aged before 2 years. 88% of patients presented gastric lesions. The UGIB was associated with use of ibuprofen and paracetamol (adjusted OR 2.9, 95% CI 2.1 to 4.0). Paracetamol showed a lower risk compared to ibuprofen (OR 2.0 versus 3.7).

Conclusion: This is the first Italian pediatric study to assess an extensive analysis about adverse effects NSAIDs. The UGIB is rare but may be avoided with use of correct doses in most patients.

Disclosure of Interest: None Declared
**Objectives and Study:** There have been concerns that prolonged gastric acid suppression by proton pump inhibitors (PPIs) may lead to a number of gastrointestinal (GI) and systemic complications such as increased risk of gastroenteritis, pneumonia, osteoporosis and GI symptoms including diarrhea, abdominal pain and flatulence. Some of these complications may be associated with the development of small bowel bacterial overgrowth (SBBO).

Objectives: To evaluate whether a 3-month PPI treatment induces SBBO in children and if so, if it causes any symptoms. Additionally, the effect of omeprazole therapy on the presence of methanogenic flora in the gut was assessed.

**Methods:** Forty children (aged 3 to 17 years) diagnosed with reflux esophagitis by upper endoscopy and biopsies were treated with omeprazole (1 mg/kg/d, maximum 40 mg) for 3 months. Type and frequency of gastrointestinal (GI) symptoms were recorded, and a glucose breath test (GBT) to determine the presence of SBBO was performed prior to, and after PPI treatment.

**Results:** SBBO was detected in 2.5% prior to and in 22.5% of patients after 3 months of PPI treatment (p=0.011). Omeprazole treatment did not result in a significant change in the overall prevalence of methane producers (12.5% before vs. 10% after PPI use). After PPI treatment, SBBO-positive children, compared with SBBO-negative patients, showed a higher mean symptom frequency score for abdominal pain (p=0.004), bloating (p=0.001), eructation (p<0.001) and flatulence (p=0.024).

**Conclusion:** A three-month PPI treatment significantly increases the risk of SBBO. Patients who have been treated with a PPI and persist with GI symptoms should undergo a GBT in order to exclude SBBO rather than arbitrarily prolonging PPI treatment.


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

**GI Motility, GERD and Functional GI Disorders**

PO-G-0127

**IS ACID OR NON ACID REFLUX THE CULPRIT OF REFLUX ESOPHAGITIS?**

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**Objectives and Study:** To analyze the number of acid (AR), non acid (NAR) reflux episodes and the bolus clearance time (BCT) and to determine which of the three has the greater sensitivity and specificity for predicting esophagitis.

**Methods:** Review of multichannel intraesophageal impedance tracings (MII) performed between May 2006 and September 2014 in children suspected of gastroesophageal reflux. All patients underwent upper endoscopy with multiple esophageal biopsies followed by a 24 hr MII-pH study. Patients with esophageal atresia, achalasia, eosinophilic esophagitis and on PPI treatment were excluded. We analyzed AR, NAR episodes and BCT. Patients were divided into groups according to the presence or absence of esophagitis and to pHmetry results: E1 (esophagitis with normal pHmetry), E2 (esophagitis with pathologic pHmetry), N1 (normal mucosa with normal pHmetry) and N2 (normal mucosa with pathologic pHmetry). The t-test and chi square tests were used for statistical analysis.

We evaluated sensitivity and specificity of NAR in predicting esophagitis, using values from a recent publication (95th IQR = 34) (Curr Gastroenterol Rep, Mousa H et al. (2014)).

**Results:** One hundred and twenty children were evaluated; mean age: 9.78 yrs (r3-17yrs); of them 83 could be analyzed: E1: 28; E2: 16; N1: 27; N2: 12. Forty four patients had esophagitis on biopsies, 63.6% (28/44) of whom had normal pH score but a statistically significant higher number of NAR episodes (p=0.049(Table). When comparing E2 vs N2, there was a significant increase of NAR episodes (p= 0.016) (Table) but not in BCT and AR. The NAR values as predictor of esophagitis had a sensitivity of 25% and a specificity of 97%.

<table>
<thead>
<tr>
<th>MII Parameters</th>
<th>ESOPHAGITIS pH (28)</th>
<th>ESOPHAGITIS PH (16)</th>
<th>NAR (16)</th>
<th>p</th>
<th>MII Parameters</th>
<th>ESOPHAGITIS pH (16)</th>
<th>NORMAL MUCOSA</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACID</td>
<td>18.86 ± 14.68</td>
<td>49.31 ± 25.15</td>
<td>0.00</td>
<td></td>
<td>ACID</td>
<td>49.31 ± 25.15</td>
<td>54.67 ± 28.66</td>
<td>0.604</td>
</tr>
<tr>
<td>NON ACID</td>
<td>28.68 ± 19.75</td>
<td>17.63 ± 11.89</td>
<td>0.00</td>
<td>0.49</td>
<td>NON ACID</td>
<td>17.63 ± 11.89</td>
<td>8.42 ± 3.6</td>
<td>0.016</td>
</tr>
<tr>
<td>BCT</td>
<td>15.36 ± 4.84</td>
<td>17.56 ± 4.18</td>
<td>0.135</td>
<td></td>
<td>BCT</td>
<td>17.56 ± 4.18</td>
<td>17.17 ± 7.93</td>
<td>0.865</td>
</tr>
</tbody>
</table>

**Conclusion:** In children, the increase in A and NAR episodes is associated with esophageal injury. Higher values of NAR episodes seem to be more related to esophageal damage than other parameters and perhaps this could explain some of the failures of PPI treatment.

Disclosure of Interest: None Declared
THE NEONATAL INFLUENCE ON FUNCTIONAL GASTROINTESTINAL DISORDERS IN INFANTS

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Objectives and 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: This is a multicenter prospective longitudinal study. Preterm and at term babies born in different hospitals were recruited at birth. 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 a standardized phone interview were also used for missing data. Exclusion criteria were represented by: malformations, (any kind of) surgery, neurological, immune, metabolic, cardiac or renal diseases.

Results: 1021 infants (312 preterm, 31%, and 709, 69%, at term newborns) have currently completed the follow-up. Preliminary analysis showed an overall significantly higher incidence of FGIDs during the first year of life in preterm compared to at term newborns (86.5% vs. 74.9%, p<0.0001, OR 2.15). Antibiotics were used in neonatal period in 197 preterm and in 165 at term newborns. FGIDs were significantly more frequent in preterms treated with antibiotic compared to preterms not treated with antibiotics in the first weeks of life (90.9% vs. 78.3%, p=0.0018, OR 2.76). At term newborns treated with antibiotics had a slight, non significant, higher prevalence of FGIDs compared to the ones not treated with antibiotics (78.2% vs. 74%).

Conclusion: FGIDs are common disorders in infants. Preterm delivery and neonatal use of antibiotic are associated with an increased incidence of FGIDs in the first months of life. Caesarean section, formula feeding and longer hospital staying at birth may represent additional risk factors determining the higher prevalence of FGIDs in preterms compared to at term newborns and need to be further analysed.

Disclosure of Interest: None Declared
CURRENT SYMPTOMS AND QUALITY OF LIFE IN PATIENTS DIAGNOSED WITH ACHALASIA AT A PAEDIATRIC AGE (0-18YR)

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Objectives and Study: Achalasia is a rare chronic motility disorder with a big impact on Quality of Life (QoL), even in patients treated successfully. We aimed to prospectively assess current symptoms and QoL in patients diagnosed with achalasia in childhood (0-18yr).

Methods: Dutch children diagnosed with achalasia between 1990-2013 were contacted either by telephone or by mail and were asked to fill in 4 questionnaires. Severity of achalasia symptoms was assessed using the Eckardt score (suggestive for achalasia when >3) and the Reflux Disease Questionnaire (RDQ, suggestive for gastro-oesophageal reflux disease (GORD) when ≥mild heartburn/regurgitation occurred ≥2 days a week). Disease specific QoL was assessed with the Achalasia DS-QoL (when <18yr at time of study, 0= worst 100=best) or HRQoL (≥18yr, 0= worst 100=best). General QoL was measured with the KIDSCREEN-52 (<18yr, T-values over 10 domains relative to healthy norm, higher value suggests better QoL) or the SF-36 (≥18yr, 8 domains, 0= worst 100=best QoL per domain) and compared to healthy population norms.

Results: Sixty-three of 87 (72%) patients were prospectively reached. Median (InterQuartile Range) time since last clinical follow up was 1.5yr (0.5–6.5 yr). Twenty (32%) patients were <18yr. Median Eckardt score was 3 (IQR 2-5) with 30 patients (47.6%) having a positive score. Median RDQ score was 0.92 (0-1.73). GORD was reported relatively more frequent after initial treatment (IT) with Heller’s myotomy compared to pneumodilation (PD, P=0.04) and mean RDQ scores were higher for HM vs PD (1.71 (0.96 – 2.90) vs 0.58 (0 – 1.56), P=0.005). Eckardt and RDQ scores were similar for adult and paediatric patients (P=0.723 and P=0.454, respectively).

Overall HR-QoL score was 61.3 (45.1-80.0). General QoL (SF-36) in adults (n=43) was lower compared to healthy population norms for 7/8 domains, with scores on ‘bodily pain’ and ‘general health perceptions’ domains (18-25 yr) significantly lower compared to age adjusted norm (P=0.039 and P=0.002). SF-36 scores were similar for patients with IT PD and HM.

Paediatric achalasia DS-QoL score was 17.5 (8-29). Self-reported QoL (KIDSCREEN-52, n=20) was similar to population norms. On 2 domains (School Environment, Financial Resources) achalasia patients even scored better (P=0.038 and P=0.049).

Conclusion: Almost half of patients with achalasia diagnosed <18yr still have symptoms suggestive of active disease. This observation stresses the need for regular clinical follow-up and good transition to the adult gastroenterologist. Disease specific and general quality of life is lower for adult patients compared to paediatric patients. This suggests that the impact of achalasia increases with duration of disease.
Disclosure of Interest: None Declared
A MULTICENTRE, RANDOMISED, DOUBLE-BLIND, PLACEBO CONTROLLED, CROSSOVER TRIAL ON THE EFFICACY OF A MIXTURE OF THREE BIFIDOBACTERIA IN CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN.

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1 Federico II University, Department of Translational Medical Sciences, Naples, 2 University of Foggia, Department of Medical Sciences, Pediatrics, Foggia, Italy

Objectives and Study: Abdominal pain-associated functional gastrointestinal disorders, such as Irritable Bowel Syndrome (IBS) and Functional Dyspepsia (FD), are a common problem in pediatrics for which no safe and effective treatment is available. Probiotics have shown promising results in adult studies, but few studies have been published in children. Bifidobacterium infantis, Bifidobacterium breve and Bifidobacterium longum are among the most beneficial bacteria in pediatric subjects. We aimed to evaluate the efficacy of a mixture of these three Bifidobacterium species in children with IBS and FD.

Methods: Children 4 to 18 years old with IBS and FD, as defined by the Rome III criteria, were enrolled within 1 year in two Italian pediatric tertiary care centers. At diagnosis and at follow-up parents and/or their children completed a diary, to record weekly evacuative frequency, stool characteristics and gastrointestinal symptoms, and a quality of life questionnaire. They were then randomized to receive either a mixture of three Bifidobacteria or a placebo for 6 weeks. At the end, after a “wash-out” period of 2 weeks, each patient was switched to the other group and followed for further 6 weeks.

Results: A total of 34 children completed the study (61.8% males; 38.2% females, mean age 11.6 years). Preliminary data showed that although placebo was as effective as a mixture of three Bifidobacteria in several parameters, these probiotics were significantly superior to it in reducing abdominal pain/discomfort (P=0.03) and in improving family assessed-quality of life (P=0.03). No significant difference was found in the stool pattern.

Conclusion: A mixture of three Bifidobacteria is safe and associated with better control of abdominal pain and with improvement of the quality of life in children with IBS and FD than placebo.

Disclosure of Interest: E. Giannetti: None Declared, A. Alessandrella: None Declared, D. De Giovanni: None Declared, A. Campanozzi: None Declared, A. Staiano Conflict with: D.M.G. Italy, Conflict with: Valeas s.p.a., Milte Italia, Angelini, E. Miele: None Declared
THE RESPONSE RATE AFTER SINGLE AND REPEATED DOSES OF NEPADUTANT AS SYMPTOMATIC TREATMENT OF INFANT COLIC: THE NO-CRY PHASE II CLINICAL TRIAL


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Objectives and Study: Infant colic, affecting up to 30% of infants in the first 3 months of age, is widely recognised to impact on the mother-infant relationship and on the family wellbeing. The colicky crises usually start in the evening, when parents are less prone to cooperate and seek remedies which can shortly stop the fussing and inconsolable crying of their baby. In a double blind, placebo (P) controlled pilot study1 the oral administration of nepadutant -a potent and selective antagonist of the tachykinin NK2 receptors- significantly reduced the mean fussing and crying (F+C) time in colicky infants. The time to onset of the symptom relief after the 1st dose of nepadutant as well as after repeated doses was subject to an additional analysis, in view of its clinical relevance in the symptomatic management of colicky babies.

Methods: In a total of 112 colicky infants (mean age 11 weeks) belonging to the ITT population and exposed to oral nepadutant (0.1 or 0.5 mg/kg) or P at approximately 4 pm for 7 days, the mean F+C time recorded on the baby’s day diary by Barr at baseline (3 days prior to randomisation) was compared to that at steady state (last 3 days of treatment), and 3 days treatment withdrawal. Responders (achieved at least 50% decrease of F+C time vs baseline) were assessed at 4 hours (8 pm) and 8 hours (12 pm) post drug intake, after the 1st dose and steady state.

Results: Nepadutant given at 0.5 mg/kg showed a benefit after its 1st dose with response achieved in 55.3% of infants versus 26.3% and 22.2% of infants exposed to nepadutant 0.1 mg/kg dose and P, respectively (p=0.004) over the first 4 hours post-dose, i.e. approx. 8 pm representing the daily F+C peak of colicky babies. At steady state, the same magnitude of effect was shown over the first 4 hours post-dose with 55.3% responders at 0.5 mg/kg vs 36.8% and 25% at 0.1 mg/dose and P, respectively; p=0.009) and maintained also over 8 hours post dose (p=0.017).

Conclusion: Nepadutant, a first in class NK2 receptor antagonist, at 0.5 mg/kg dose showed a clinical benefit in 55.3% of colicky infant babies, with > 50% reduction of F+C time starting from the first 4 hours post-dose. The benefit over P was reached after the 1st dose and maintained over repeated doses. The magnitude of effect as well as the time of symptom relief make nepadutant a promising treatment deserving further investigations in infant colic.

References: 1 NCT01258153
IS LARYNGEAL INFLAMMATION ASSOCIATED WITH REFLUX?

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GianVincenzo Zuccotti 3 Patrizia Latorre 5 Yvan Vandenplas 6
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4 OspedalediParma, Parma, 5 ENT-OspedalediCircolo, Varese, Italy, 6 UZ Brussel, Brussels, Belgium

Objectives and Study: The association between gastroesophageal reflux (GER) and laryngeal inflammation is unclear. However, in many children acid inhibitors are started based on laryngoscopic findings. 

AIM: The aim of the study was to examine the correlation between laryngeal findings and esophageal impedance-pH monitoring (MII-pH) results.

Methods: This is a multicenter study with retrospective analysis of prospectively collected data. All children who underwent both flexible laryngoscopy and MII-pH were recruited. Exclusion criteria were represented by a time window between the two investigations above 1.5 months, reflux treatment started before the investigations, artifacts on MII-pH or incomplete laryngeal examination or report.

Laryngoscopy was considered as positive if it showed erythema and/or edema of arytenoids or postcricoid or vocal cord region or nodules. MII-pH analysis was focused on the reflux index (RI = 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. In this preliminary analysis we analyzed the laryngeal data according to RI >5% and >10% for acid, and to BEI >2% for total GER.

Results: 122 children (range 0.5-180 months, median age 42 months) were analyzed. Nearly 95% of the patients had respiratory symptoms and were referred by the ENT specialist because of suspected GER. The most common symptoms were chronic cough, recurrent respiratory infections and dysphonia in children and ALTE/apnea in infants. In the 107 patients (88%) with positive laryngoscopy, RI was >5% in 36 (34%) (with RI>10% in 12) and BEI was >2% in 50 (47%) (with normal RI in 31 patients, 29%). The presence of edema and erythema was not mutually exclusive and coexisted in 30 patients. In the 20 patients with negative laryngoscopy 4 had RI >5% (1 with RI>10%) and 5 (3 with normal RI) BEI >2%.

Conclusion: In our population the association between laryngeal inflammations and acid GER was limited to 1/3 of patients. In children, the empiric use of acid inhibitors only based on laryngoscopic investigation is not supported by our results. When both acid and weakly acid GER were considered we found a positive association between laryngeal findings and MII-pH results in nearly 60% of children. Pathological acid exposure may be present with completely normal laryngeal report.

Disclosure of Interest: None Declared
NORMAL VALUES FOR 3D HIGH RESOLUTION ANORECTAL MANOMETRY IN CHILDREN

Marcin Banasiuk1,* Aleksandra Banaszkiewicz 1 Piotr Albrecht 1
1 Department of Paediatric Gastroenterology and Nutrition Medical University of Warsaw, Warsaw, Poland

Objectives and Study: 3D high-definition anorectal manometry is the most precise tool to assess function and 3D topographic picture of pressures along the anal canal. Until now, it has been used only in adult population. The normal values have not been evaluated so far. The aim of the study was 3D manometric evaluation of anorectal function in children without symptoms from lower gastrointestinal tract.

Methods: Children without any symptoms from lower gastrointestinal tract were prospectively enrolled in the study. Manometry procedures were performed using a rigid probe (Covidien AG, Switzerland) without premedication. Pressures within the anal canal and 3D picture of sphincters were obtained. The volume of balloon to elicit rectoanal inhibitory reflex (RAIR) was established. If possible, defecation dynamics and thresholds of sensation were evaluated. Data were expressed as mean (5th and 95th percentile).

Results: 50 children (28 males; age: 2-17 years, mean: 7 years) were studied. Mean resting and squeeze sphincter pressures were 90.2 (65.3-123.7) mmHg and 201 (106-263.4) mmHg, respectively. The mean length of the anal canal was 2.72 (1.9-3.8) cm and it was correlated with age and height (p=0.000). Mean rectal balloon volume to elicit RAIR was 13 (10-30) cc. The first sensation, urge and discomfort were observed at 23.3 (10-101) ml, 45.3 (10-102) ml and 93.4 (30-180) ml of the balloon volume, respectively. There was no lesions of sphincters according to 3D topographic picture of the anal canal. There was no statistically significant difference in pressure profiles between males and females. Positive correlation between age and volume of balloon needed to elicit RAIR and discomfort was found.

Conclusion: Normative data of 3D high-definition anorectal manometry in children without symptoms from lower gastrointestinal tract were established. There were no significant gender differences concerning pressure results.

Disclosure of Interest: M. Banasiuk Conflict with: grant support from Covidien AG, A. Banaszkiewicz: None Declared, P. Albrecht: None Declared

Gastroenterology
GI Motility, GERD and Functional GI Disorders
PO-G-0133

NORMAL VALUES FOR 3D HIGH RESOLUTION ANORECTAL MANOMETRY IN CHILDREN

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1 Department of Paediatric Gastroenterology and Nutrition Medical University of Warsaw, Warsaw, Poland

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Disclosure of Interest: M. Banasiuk Conflict with: grant support from Covidien AG, A. Banaszkiewicz: None Declared, P. Albrecht: None Declared
SURGICAL TREATMENT FOR SEVERE REFRACTORY FUNCTIONAL CONSTIPATION IN CHILDREN

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Objectives and Study: In children with severe refractory functional constipation (RFC) surgical intervention is proposed as a treatment of last resort. Scarce data exist regarding the clinical characteristics and post-surgery outcome of these children. The aim of this study is to describe clinical features of children with RFC and their outcome after surgical intervention.

Methods: Children with RFC that received a surgical intervention in our tertiary hospital between 2011 and 2013 were identified retrospectively. Clinical characteristics were collected through chart reviews. Telephone questionnaires were used to collect data regarding their current symptomatology, their need for laxative treatment, and patient satisfaction after treatment on a scale of 1-10 (1 = I would not undergo this surgical procedure again, 10 = I am very satisfied with the result).

Results: All 23 children (17 girls) included were unsuccessfully treated with different oral and rectal laxative treatment regimens prior to surgery. The median age at presentation was 9.9 years and the median age at operation was 11.2 years (range 1-17 years). Surgical procedures performed were ileostomy (n=14, 61%), appendicocecostomy (n=5, 22%), colostomy (n=6, 26%), colectomy/sigmoidectomy (n=17, 74%), percutaneous endoscopic gastrostomy (n=5, 22%), sacral neuromodulation (n=8, 35%) and botulinum toxin injections (n=3, 13%). Eighteen patients (78%) experienced minor complications such as pain, infection, and stoma leakage. Nine patients (39%) underwent surgical revision, of which 6 were re-operated within one week after the primary operation. Eighty-six percent of patients rated the effect of the surgical intervention as 6 or higher on a scale of 1-10.

Conclusion: Surgical treatment for children with severe refractory functional constipation seems to be an effective treatment of last resort with high patient satisfaction rates; even though complications and reoperations occur frequently.

Disclosure of Interest: None Declared
NO EFFECT OF PROTON PUMP INHIBITORS ON CRYING AND IRRITABILITY IN INFANTS: SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS

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Objectives and Study: Proton pump inhibitors (PPIs) are increasingly being used to treat infants with crying and/or irritability based on the assumption that these symptoms are attributable to gastroesophageal reflux (GER). We aimed to examine whether PPIs are effective in the management of excessive crying and irritability in infants.

Methods: The MEDLINE, EMBASE, and Cochrane Library databases were searched up to July 2014 for published randomized controlled trials (RCTs) that compared the effects of a PPI with placebo or no intervention. Two registries for clinical trials (www.clinicaltrials.gov; www.clinicaltrialsregister.eu) were screened to identify published and ongoing studies. The references for identified studies were checked. There was no restriction on the language imposed. Participants had to be infants (i.e., birth to 12 months) with GER/GERD but otherwise healthy. The studies were recorded only if they reported outcomes related to crying/irritability such as the duration and/or number of episodes of crying and/or irritability, as assessed by the investigators. The secondary outcomes were adverse effects.

Results: Five, double-blind, placebo-controlled RCTs (involving 430 infants <12 month of age), with a parallel or crossover design, some with methodological limitations, were included. There was variability in how crying/irritability outcomes were reported, but all trials used reliable methods. Some trials showed a decrease in crying/irritability from baseline to the end of the intervention; a similar effect was observed in the control group. However, no significant differences between the treatment groups were observed.

Conclusion: This systematic review shows that PPIs are not effective in the management of crying/irritability.

Disclosure of Interest: None Declared
CORRELATION BETWEEN 24-HOUR OESOPHAGEAL PH MONITORING AND VIDEOFIBERSCOPE EXAMINATION OF LARYNX IN CHILDREN

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1 Medical University of Lublin, Lublin, Poland

Objectives and Study: Gastroesophageal reflux disease (GERD) is a common disorder affecting 20 to 40% of population. GERD typically manifests by oesophageal symptoms i.e. heartburn, regurgitation or chronic vomiting. However, it may be also presented with a wide spectrum of extraesophageal symptoms including chronic cough, laryngitis, hoarseness and asthma. The aim of the study was to investigate laryngeal disorders in patients with gastroesophageal symptoms and their correlation with 24-hour oesophageal pH monitoring.

Methods: Twenty children, including 9 (45%) girls (mean age 10.5±4.5 years) and 11 (55%) boys (mean age 9±4.5 years), with symptoms suggesting GERD underwent 24-hour oesophageal pH monitoring and videofiberscope examination of larynx.

Results: At initial presentation 15 (75%) children complained of oesophageal symptoms and 5 (25%) of extraesophageal symptoms. 24-hour oesophageal pH monitoring detected acid gastroesophageal reflux in 9 children, including 7/15 (47%) children with oesophageal symptoms and 2/5 (40%) with extraesophageal symptoms. In videofiberscopy 17 children, including 13/15 (87%) with oesophageal symptoms and 4/5 (80%) with extraesophageal symptoms, had laryngeal lesions i.e. posterior cricoid’s wall erythema, vocal cord erythema and oedema, or arytenoid erythema and oedema. All 9 patients with abnormal result of 24-hour oesophageal pH monitoring had laryngeal lesions suggesting chronic laryngitis. However, videofiberscopy revealed chronic laryngitis in 8 of 11 patients (73%) without signs of acid gastroesophageal reflux in 24-hour oesophageal pH monitoring.

Conclusion: Gastroesophageal reflux disease is associated with a wide variety of extraesophageal symptoms including chronic laryngitis. In our sample laryngeal lesions observed in videofiberscopy were recorded for both patients with acid gastroesophageal reflux and patients with normal pH-monitoring results. Children with extraesophageal symptoms suggesting gastroesophageal reflux may require additional tests for example esophageal impedance-pH monitoring to quantify reflux.

Disclosure of Interest: None Declared
PATTERNS OF COLONIC TRANSIT AND MUCOSAL ABNORMALITIES IN CHILDREN WITH REFRACTORY CONSTIPATION.

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1Great Ormond Street Hospital, London, United Kingdom

Objectives and Study: Refractory constipation, defined as failure to respond to optimum conventional therapy for a minimum of three months represents a diagnostic and therapeutic challenge, nonetheless, investigating underlying colonic disorders is required to guide therapy. Several methods were described to measure colonic transit time (CTT) of which radiopaque markers are simple to use and easy to interpret. The aim of this study was to measure CTT using radiopaque markers and to assess the incident of colonic mucosal abnormalities in children with refractory constipation.

Methods: Retrospective review of clinical, pathological and radiological data of children with refractory constipation who underwent colonoscopy and a radiopaque marker study in our institution between January 2010 and December 2013. Radiopaque marker studies were performed within two weeks after colonoscopy by ingesting one capsule per day for three successive days. An X-ray was taken on day 4. CTT was calculated using the following formula: number of markers*2.4

Results: 134 radiopaque studies were identified. 8 were excluded. Of the remaining 126, half were females and half were males. The mean age of patients (±SD) was 7.9 years (±3.6); range 1.8 to 17.1 years. 82 (65%) had slow transit constipation and 44 (35%) had colonic segmental delay of which 10 (8% of total) were side right, 18 (14%) left side and 16 (13%) were rectosigmoid hold up. The mean total CTT (±SD) for all children was 52.6 hours (±17), right colon transit 14.8 (±12.4), left colon transit 19.2 (±14.9) and rectosigmoid transit was 18.7 (±13.2). We then calculated CTT for each group. Children with slow transit constipation had CTT of 57.7 (±14.8), while children with segmental dysmotility had CTT as follow: right side CTT was 21.7 (±8.9), left side CTT was 40.1 (±20.95) and children with functional outlet obstruction had rectosigmoid CTT of 30.6 (±12.38).

109 children had colonoscopy within 2 weeks before taking the radiopaque makers. In 64 children (59%) the histology was normal and in 45 (41%) mucosal abnormalities were identified. 37 (82%) had increased inflammatory cells density in the lamina propria with eosinophils and lymphocytes are the dominant inflammatory cells. 3 (7%) had prominent lymphonodular hyperplasia, 3 (7%) had melanosis coli and 2 (4%) had focal cryptitis. Children with slow transit constipation had significant histological abnormalities (p value 0.03) however; the histological abnormalities were not significant in children with segmental delay.

Conclusion: More than half of children with refractory constipation had slow transit constipation and only 13% had functional outlet obstruction. Increased numbers of eosinophils and lymphocytes in mucosal biopsy was a significant finding in children with slow transit refractory constipation.

Disclosure of Interest: None Declared
YOGA THERAPY FOR CHILDREN WITH ABDOMINAL PAIN RELATED-FUNCTIONAL GASTROINTESTINAL DISORDERS. A RANDOMISED CONTROLLED TRIAL

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Objectives and Study: Psychological distress is strongly associated with abdominal pain in children and plays a role in the development of abdominal pain related-functional gastrointestinal disorders (AP-FGIDs). Yoga therapy has shown its efficacy in stress management and has been recommended as intervention in adults with irritable bowel syndrome (IBS). The aim of this study is to compare the effect of yoga therapy and standard care on the frequency and intensity of pain and quality of life (QoL) in children with AP-FGIDs.

Methods: Sixty-nine patients, aged 8-18 years, with an AP-FGID, were randomized to either standard medical care complemented with yoga therapy (YT) or standard medical care alone (SMC). Hatha yoga was given once a week for 10 weeks. Yoga sessions of 1.5h each were a mixture of classical yoga poses and relaxation exercises. SMC consists of education, reassurance, dietary advice and fibers/mebeverine if considered necessary. Pain intensity (0-5) and pain frequency (0-4) were scored daily in a pain diary and QoL was measured with the KIDSCREEN-27 (5 domains). Patients were followed up for twelve months. Treatment response was defined as a 50% reduction of weekly pain scores. Between-group differences were analyzed with generalized estimating equations.

Results: From baseline to 1 year follow-up, weekly pain intensity scores decreased from 17 to 8 (p<0.01) and from 16 to 12 (p=0.83) in the YT and SMC group, respectively. Weekly pain frequency scores decreased from 16 to 8 (p<0.01) in the YT group and from 16 to 14 in the SMC group (p=0.40). However, no difference in decrease in pain intensity and frequency was found between YT and SMC. A trend towards a lower pain intensity in the YT group compared to the SMC group was found in children aged 13-18 years (p=0.06). At 1 year follow up, treatment response was accomplished in 58% of the YT group and 29% of the control group (p=0.07). Although children in the YT group and their parents reported larger improvement in QoL compared to the SMC group, no significant difference was found (p>0.05 for all domains). A trend was reported for ‘psychological well-being’ in favor of YT (p=0.06). Percentage children who reported monthly school absence decreased in both groups at 1 year follow-up, from 55% to 7% after YT and from 65% to 33% after SMC.

Conclusion: Yoga therapy in addition to standard medical care resulted in a significant decrease of abdominal pain, improvement of quality of life and reduction of school absence, however, yoga therapy was not superior to SMC.

Disclosure of Interest: None Declared
**Objectives and Study:** Childhood constipation, one of the common gastrointestinal complaints in children, is most of cases absent of causal factors and therefore is defined as functional constipation (1-2). The treatment is long lasting and more than 30% still having problems beyond puberty probably because most of the therapeutic approaches are not clearly effective (3). Moreover there are few studies on a particular intervention, especially in the age range 2-5 years. Prebiotics are considered as a new option to treat constipation in children (4). Our aim was testing the beneficial effects of a daily dose of Orafti inulin-type fructans supplementation for 2-5 years old constipated children in a Pilot study.

**Methods:** Double-blind, randomized, placebo-controlled parallel group trial, where 2-5 y-old constipated children received 2 daily doses of 2g/d Orafti inulin-type fructans or the same amount of placebo (maltodextrin) during 6 weeks. Primary outcome was stool consistency assessed by a continuous daily bowel symptoms diary. Secondary outcomes were: stool frequency and gastrointestinal symptoms. Dietary intake as well as use of drugs or other products affecting gastrointestinal was controlled.

**Results:** Eleven children in each study group were recruited. From those, 17 completed the study protocol without any exclusion criteria (9 and 8 for control and intervention respectively). Baseline characteristics were similar in both study groups, except for the lower proportion of males and higher percentage of children who fulfilled the retention history inclusion criteria or higher score of abdominal pain among controls. Results showed that Orafti inulin-type fructans supplemented children showed softer stools compared to control group (p=0.003). The longitudinal analyses showed that whereas no significant changes were induced in controls, treated children softened their stool consistency after the intervention (p=0.040). Pain during defecation was reduced during intervention irrespectively of the study group.

**Conclusion:** Prebiotic inulin-type fructans improves the stool consistency in functionally constipated 2-5 y-old children.

**References:**

**Disclosure of Interest:** N. Ferre: None Declared, J. Escribano: None Declared, G. Castillejo: None Declared, V. Luque: None Declared, M. Gispert: None Declared, M. Zaragoza-Jordana: None Declared, C. Rubio-Torrents: None Declared, S. Theis Conflict with: Promoter employee, R. Closa: None Declared
MANAGEMENT OF GASTROESOPHAGEAL REFLUX IN INFANTS: CURRENT PRACTICE OF DIAGNOSIS AND TREATMENT IN A UK DISTRICT GENERAL HOSPITAL.

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Objectives and Study:
According to current ESPGHAN and NASPGHAN guidelines, gastroesophageal reflux (GER) is defined as the passage of gastric contents into the esophagus with or without regurgitation and vomiting. GER is considered to be physiological in the majority of young infants under the age of 12 months. Typically, episodes of GER in healthy individuals last <3 minutes, occur in the postprandial period, and cause few or no symptoms. In contrast, gastroesophageal reflux disease (GERD) is present when the reflux of gastric contents causes troublesome symptoms. Although clear guidelines on the diagnosis and management of GERD are widely available, in practice many children are being wrongly diagnosed and unnecessarily commenced on treatment.

Methods:
Medical records of 60 patients age 1 day to 1 year with a diagnosis of GOR or GORD where randomly collected. Patients were either treated as inpatients on the neonatal unit, paediatric ward, in the emergency department or seen in outpatient setting. Data recorded for each patient included: specific diagnosis, presence of clinical symptoms suggestive of GOR/GORD, choice of treatment and if the diagnostic criteria according to ESPGAHN guidelines were met.

Results:
In total 100% of patients included in this study were diagnosed with GOR, rather than GORD despite the presence of what could be considered as "troublesome symptoms". The two most frequently reported symptoms were poor weight gain n=6 (10%) and irritability n=40 (66%). Importantly, despite being "officially" diagnosed with GOR, 55 out of 60 children (91%) were commenced on anti-reflux medication (i.e. proton pump inhibitors or the H2 receptor blocker Ranitidine). Reassuringly, all parents were provided with education and guidance.

Conclusion:
Our small study provides insight into current clinical practice in a district general hospital and highlights major insufficiency in the understanding and management of GOR/GORD. Despite diagnosing GOR the majority of infants are commenced on medical treatment. Active advice and teaching to healthcare professionals in the primary and secondary sector is required to improve the situation in the long term.

Disclosure of Interest: None Declared
ENDEOSCOPIC AND HISTOLOGICAL FINDINGS CORRELATION IN PAEDIATRIC EOSINOPHILIC ESOPHAGITIS.

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Objectives and Study: Introduction
Eosinophilic esophagitis (EE) is a chronic disease with an accelerated incidence. Endoscopy plays an important role in EE evaluation in children. There are studies in adults who report sensitivity of endoscopic findings for the diagnosis in range of 50-90%. Currently in pediatrics is still unclear and need to be biopsied to establish the diagnosis by histopathological finding of a predominantly eosinophilic inflammation. This often delays the time to make treatment decisions.
Our aim was to determine diagnostic utility of endoscopic findings to correlate with histological finding in pediatric Eosinophilic Esophagitis using recent endoscopic score (ERFS) 1.

Methods: A retrospective review was performed about 86 endoscopic procedures in children under 18 diagnosed with Eosinophilic Esophagitis in period between January 2010 and September 2014. Endoscopies for diagnosis and follow-up were reviewed. EREFS was used to describe endoscopic findings. Eosinophil count per High Power Field (eos/hpf) was performed in proximal and distal esophageal mucosa biopsies. Correlation analysis was conducted of each endoscopic finding with eosinophils count and their prediction as a diagnostic tool in EE.

Results: A total of 86 endoscopic procedures were reviewed with a mean age of 10 years (R 3-16 years old), 74% male. Endoscopic and histological findings suggestive of EoE in 90% (77) and 86% (74) were found respectively. Three different patterns of endoscopic findings as furrow lines; furrow lines plus whitish exudate; and furrow lines, trachealization plus whitish exudates were present in 13%, 62% and 20% respectively. Eosinophils average count per endoscopic pattern in proximal and distal biopsies was: furrow lines 3 and 21 eos/hpf; Furrow lines plus whitish exudate; and furrow lines, trachealization plus whitish exudates were present in 13%, 62% and 20% respectively. Eosinophils average count per endoscopic pattern in proximal and distal biopsies was: furrow lines 3 and 21 eos/hpf; Furrow lines plus whitish exudate 40 and 52 eos/hpf; Furrow lines, whitish exudate and trachealization 45 and 54 eos/hpf. When performing statistical analysis found that endoscopic findings and histological findings in 91% correlated to determine the diagnosis of EoE with high statistical association (P <0.05). Furrow lines presence with whitish exudate of any grade had a statistically significant association (P <0.01) count ≥15 eos/hpf in 96% of endoscopy. Alone Furrow lines presence and combination of furrow lines, whitish exudates and trachealization correlates with count ≥15 eos/hpf in 55% and 95% of the endoscopy respectively, but achieve statistical association.

Conclusion: Endoscopic findings suggestive of Eosinophilic Esophagitis in children are highly correlated with the histological findings and could be useful as diagnostic criteria that allow therapeutic decisions while histological results were obtained.

Disclosure of Interest: None Declared
**Objectives and Study:** Patients (pts) with eosinophilic oesophagitis (EoO), a chronic immune-mediated disorder, may exhibit symptoms of disturbed food transit (i.e. dysphagia, impaction) or mimicking gastro-oesophageal reflux (GOR). We aimed at characterizing in EoO pts the intra-oesophageal pH pattern with 24-h multichannel intraluminal impedance (MII-pH) as well as the oesophageal motility with high-resolution manometry (EHRM).

**Methods:** During a 30 month period we studied 57 patients (pts), median age 11 years (range: 7-16): 25 with EoO, diagnosed according to widely agreed criteria (JPGN 2014;58:107-18; ESPGHAN guidelines) and 32 with GOR disease (GORD). All underwent oesophagogastro-duodenoscopy, MII-pH and EHRM. The pH-MII and data analysis were done according to ESPGHAN EURO-PIG protocol (JPGN 2012;55:230-4); variables analysed: reflux index, symptom index, number and type of liquid reflux, number of long lasting reflux episodes, correlation symptom-reflux. The test was diagnostic of GORD if at least ≥ 2 of the previous variables were positive. The EHRM was performed with water perfused catheters and swallow contractile patterns categorized using criteria recently reported by a paediatric group (Am J Gastroenterol 2010;105:460-7). Several motility variables were analysed (oesophago-gastric junction (EGJ) morphology, end-expiratory and end-inspiratory EGJ pressure, distal contractile integral (DCI), pressurization front velocity (cm/s), peristaltic propagation pattern.

**Results:** An abnormal MII-pH profile was markedly more common in GORD pts (27; 84.37%) than in EoO pts (4; 16%; p<0.001). On the contrary, EHRM irregularities were detected more commonly in EoO than the GORD pts: in particular, when motility tracing were analysed no significant difference for EGJ pressure and deglutitive EGJ relaxation was detected between the 2 groups; however, abnormalities such as peristaltic dysfunction (i.e. failed peristalsis, aperistalsis, and oesophageal spasm features) and lower distal contractile integral adjusted for oesophageal body length (DCIa) were more common in EoO (17; 68%) than in GORD pts (15; 46.8%) (p<0.05).

**Conclusion:** 1) The great majority of EoO pts have a normal MII-pH profile that doesn’t support the use of proton pump inhibitory therapy. 2) EoO pts exhibit higher prevalence of oesophageal motility abnormalities than GORD: this feature is likely sustained by the inflammatory infiltrate that characterizes the oesophageal wall in EoO and accounts for the oesophageal dysmotility complaints often detected in EoO pts.

**Disclosure of Interest:** None Declared
**Objectives and Study:** To describe the parameters of a paediatric sample of one Spanish Paediatric Unit of reference for the multichannel intraluminal impedance (MII-pH) technique, and correlate with patient age, sex and reasons for their request.

**Methods:** Single-center, retrospective, descriptive study. Analysis of the pH-Impedance data between 1/1/2012 and 1/11/2014. Register duration less than 8 hours or more than 25 hours are excluded, and also those in which there were an incident during the performance test. MII-pH (Greenfield™) catheter and (Ohmega) equipment were used in all patients. The recorded data were analysed with Medical Measurement Systems Software (MMS). (SAS 9.3) application for statistical analysis has been used. All statistical tests were considered bilateral and significant values those with p <0.05

**Results:** 324 records are analysed. Median time of test recording is 20.65 hours (standard deviation, SD, 1.572; Range 10-25). 59% are male. Average age is 53.70 months (SD 48.81; Range 0-196). 27.5% of the patients are younger than 12 months. Most frequent indications of the test are gastrointestinal (50%) and respiratory symptoms (28.4%). 132 tests (40.74%) are considered pathological according to the diagnostic criteria EURO-PIG ESPGHAN Working Group [61.4% by number and 38.6% for reflux symptoms index (SI)> 50%]. The percentage of patients <12 months with MII-pH pathological is higher than in the group of> 12 months (p = 0.002). In 13.27% of all records with an IR> 3, the MII-pH is normal. 46.6% of patients have one or more clinical symptoms during the test (35.18% associated with reflux). Of the 56 patients diagnosed with SI> 50%, 40 presented a symptom association probability (SAP)> 95%, but correlation between both parameters in different types of reflux, is not demonstrated. In children < 12 months, both non-pathological and pathological records, weakly acidic reflux predominates (p <0.05). In patients >12 months with respiratory symptoms, acid reflux predominates while weakly acid does in gastrointestinal symptoms (p <0.05).

**Conclusion:** Our study is one of the largest paediatric sample published from a european single center. In children less than 12 months weakly acid reflux predominates, with a percentage of pathological impedance-pH-monitoring significantly higher. There is still a diagnostic discrepancy with pH metry results. We observed no correlation between the symptom association probability and the symptom index. Therefore, with the current criteria that takes symptom index as a reference, we might tend to overdiagnose and overtreat the gastroesophageal reflux disease.
Disclosure of Interest: None Declared
IMPROVEMENT OF GASTROINTESTINAL DISTURBANCES AFTER SIX MONTHS WITH LOW-FODMAP DIET, IN PATIENTS WITH MIGLUSTAT THERAPY

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Objectives and Study: The intake of some foods in patients that receive Miglustat therapy has been related with gastrointestinal disturbances. The therapeutic effects of a low FODMAP (fermentable oligo, di, monosaccharides and polyols) diet on gastrointestinal symptoms in patients with receiving Miglustat therapy has not been explained so far. We aimed to identify if a low-FODMAP diet can reduce the prevalence of gastrointestinal symptoms in patients that receive Miglustat therapy.

Methods: Patients with Niemman Pick Type C or Gaucher Disease were recruited in seven different cities in Colombia. All the patients received the recommendations for a low-FODMAP diet during six months and were followed monthly by an expert dietitian. The main foods were provided during the diet period. Gastrointestinal symptoms like nausea, vomit, colic, diarrhea, constipation, bloating, pain and passage of wind were assessed, and Bristol’s scale was used to assess the stool consistency. Statistical analysis: X2 was applied for non-parametric parameters with SPSS 21.0.

Results: Twenty-six patients between 1 and 31 years were studied, 17 males. Lower prevalence of gastrointestinal disturbances was found after six months with low-FODMAP diet (p=0.028). Eighteen (18/26) patients had gastrointestinal disturbances before of the intervention with a low-FODMAP diet and just seven (7/25) six months later. Patients had greater satisfaction with stool consistency at 3 months to have started the low-FODMAP diet. Symptoms were minimal after six months of the diet. Bloating, pain, and passage of wind were reduced on the low-FODMAP diet. Colic was presented only in one child, and nausea and vomit was not present in any patient.

Conclusion: Gastrointestinal disturbances have a significant negative impact on quality of life of any patient. Dietary strategies like a low-FODMAP diet, is an efficacious therapeutic approach for control and also decreasing the prevalence of gastrointestinal symptoms in patients with Miglustat therapy, whenever an expert dietitian supervises it.

Disclosure of Interest: L. Ladino Conflict with: Private practice in Colombia for Biomarin, N. Sepulveda: None Declared, E. Ochoa: None Declared
BOWEL HABITS AND CONSTIPATION PREVALENCE IN JORDANIAN SCHOOL CHILDREN
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Objectives and Study: Little is known about bowel habits pattern in Jordanian children. Parents might not recognize constipation in school children, which could lead to delayed treatment and increase rate of complication. We aim to study the bowel habit pattern and prevalence of constipation in Jordanian school children.

Methods: Classes from academic years (grades) 6-8 were selected. A validated self-reporting questionnaire based on Pediatric Gastrointestinal Symptoms—Rome III Version (QPGS—RIII) - The official Arabic translation – was used. Data regarding bowel motions over the last two months was collected. Categorical data were analyzed using Fisher’s exact test, and continuous data were analyzed using t-test. P < 0.05 was considered significant.

Results: Out of 429 distributed questionnaires, 413(96.3%) were completed. Males made up 50.8% of the study population. Mean age was 12.7 yrs (11-16 yrs.). 252 (61%) reported opening their bowel at least once daily. Whereas 123 (29.8%) had two bowel motions or less weekly. 69 (16.7%) described their bowel motion as hard or very hard. 85 (20.6%) reported painful defecation. 115 (27.8%) withhold themselves once weekly or more. 69 (16.7%) reported fecal incontinence at least once weekly. Bulky stool was reported by 84 (20.3%). Boys reported infrequent bowel motions, hard, bulky motions and incontinence more frequently than girls (p<0.05). Constipation as per ROME III criteria was found in 59 (28.1%) and 51 (25.1%) in boys and girls respectively.

Conclusion: Most of Jordanian school children have a daily bowel motion without pain or withholding. Constipation affect about one fourth of Jordanian school children aged (11-16yrs).

Disclosure of Interest: None Declared
EPIDEMIOLOGY OF PAEDIATRIC FUNCTIONAL ABDOMINAL PAIN DISORDERS; A META-ANALYSIS

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Objectives and Study:
Childhood functional abdominal pain is a common problem in Western countries, with a serious disabling effect. We aimed to review the literature regarding the epidemiology of functional abdominal pain disorders in children and to assess its geographic, gender and age distribution including associated risk factors of developing functional abdominal pain.

Methods: The Cochrane Library, MEDLINE, EMBASE, CINAH L and PsychInfo databases were systematically searched up to February 2014. Study selection criteria included: (1) studies of birth cohort, school based or general population samples (2) containing data concerning epidemiology, prevalence or incidence (3) of children aged 4-18 years (4) suffering from functional abdominal pain disorders. Selection of eligible studies and quality assessment was done by two observers independently. Data were pooled using a random effects model.

Results: A total of 58 articles, including 196,472 children were included. Worldwide pooled prevalence for functional abdominal pain disorders was 13.5% (95% CI 11.8-15.3), of which irritable bowel syndrome was reported most frequently (8.8%, 95% CI 6.2-11.9). The prevalence across studies ranged widely from 1.6% to 41.2%, but pooled prevalence rates were more comparable across the continents (table). A higher pooled prevalence was reported when ROME III criteria were used. Functional abdominal pain disorders occur significantly more in girls (15.9% vs. 11.5%, pooled OR 1.5) and is associated with the presence of anxiety and depressive disorders, stress and traumatic life events.

Table. Pooled prevalence of functional abdominal pain disorders according to criteria used and geographical location

<table>
<thead>
<tr>
<th>Criteria used</th>
<th>Number of studies</th>
<th>Number of subjects</th>
<th>Pooled prevalence (%)</th>
<th>95% CI</th>
<th>Heterogeneity</th>
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<td></td>
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<tr>
<td>Self-reported criteria</td>
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<td>10.2-16.6</td>
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<tr>
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<td>12.9</td>
<td>9.9-16.2</td>
<td>97.8</td>
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<tr>
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<td>Rome III</td>
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<td>11</td>
<td>12</td>
<td>12.2</td>
<td>19.327</td>
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<tr>
<td>The Middle-East</td>
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<tr>
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</table>

**Conclusion:** Functional abdominal pain disorders are a common problem worldwide with irritable bowel syndrome as most encountered abdominal pain-related functional gastrointestinal disorder. Female gender, psychological disorders, stress and traumatic life events affect prevalence.

**Disclosure of Interest:** None Declared
Objectives and Study: Infant Colic-IC is a functional GI disorder affecting up to 30% of infants in first 3 months of age. Excessive inconsolable crying and fussing (C+F) are key diagnostic symptoms as per Rome III criteria. Current non pharmacological and pharmacological treatments are unsatisfactory, making IC an unmet medical need. The aim of this study was to assess the efficacy of nepadutant (NEPA), a selective tachykinin NK2 receptor antagonist, in IC based on its preclinical activity on visceral hypersensitivity and hypermotility.

Methods: A phase IIa, randomised, double-blind, pilot study in (otherwise healthy) infants from 10 centers in 5 Countries with no adequate response to available treatments aimed to assess the efficacy and safety of oral NEPA 0.1 or 0.5 mg/kg doses or placebo-P (n=40 pts/arm) given once daily at 4 pm for 7 days. The study encompassed a 4 to 7 day-screening with no study medication (last 3 days representing the baseline-bsl); a 7 day-treatment (last 3 days for efficacy assessment) followed by a 7 day-treatment withdrawal (first 3 days for withdrawal evaluation). Baby behaviour was recorded on the baby’s day diary, a validated patient reported outcome tool. Efficacy was evaluated as absolute and relative change of mean daily C+F time while on treatment vs bsl and as percentage of responders (infants achieving > 50% decrease of C+F time).

Results: A total of 115 out of the planned 120 infants were randomised (ITT n=113; PP n=97), mean age 11 weeks (range 4-20); 45% females; 98.2% whites. Bsl mean daily C+F was 280.6 min, with no difference between the 3 treatments. In the ITT analysis absolute change of mean daily C+F time while on treatment (primary end-point) favoured the 0.5 mg/kg arm (-119.2 vs -96.9 and -91.2 min for 0.1mg/kg and P, respectively, n.s.); statistical significance over P (p=0.039) was achieved when relative change is considered (-44% vs -35% and -31% for 0.1 mg/kg and P, respectively). NEPA 0.5 mg/kg was superior also in responders rate: 55.3% vs 36.8% and 19.4%, for 0.1 mg/kg and P, respectively (p=0.002). No differences in AEs between arms.

Conclusion: The first trial of NEPA demonstrated a favourable effect with the high, but not the low once daily dose, on C+F in colicky infants who showed a high placebo effect. The study revealed no evidence of a safety concern. Further clinical studies will confirm the potential benefit of NEPA in IC.

References: 1 NCT01258153
FUNCTIONAL GASTROINTESTINAL DISORDERS IN PALESTINE REFUGEE INFANTS IN JORDAN, THE WEST BANK AND GAZA

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Objectives and Study: Data about the prevalence of functional gastrointestinal disorders (FGDs), such as infant dyschezia (ID) and functional constipation (FC) in the Middle East and particularly among Palestine refugee infants are lacking. It is suggested that stress factors and early life events increase the prevalence of FGDs. We aimed to estimate the prevalence of ID and FC among Palestine refugee infants in a more secure community (Jordan) and less secure communities (West Bank and Gaza).

Methods: A cross-sectional survey was conducted from November 2013 to May 2014 at 12 health centers of United Nations Relief and Works Agency for Palestine refugees in the Near East (UNRWA) at Jordan, West Bank and Gaza. Infants (age 2 weeks–6 months) attending the well-baby clinic for growth monitoring/vaccination were randomly allocated. With a power of 80%, confidence level 95%, and a precision found to the nearest of 2%, the estimated sample size was 862. ID and FC were defined according to ROME 3 criteria.

Results: Mothers of 862 Palestine refugee infants were interviewed (mean age 3.1 months, 49% males, 432 in Jordan, 216 in Gaza, 214 in West Bank). The prevalence of ID was higher in Jordan (14%) than in the West Bank (8%, p=0.04) but comparable to Gaza (12%). The prevalence of FC was not significantly different between Jordan (10%) West Bank (7%) and Gaza (6%). Variables related to poor socio-economic condition and personal stress were more frequently reported in Gaza when compared to Jordan; such as higher number of siblings (p=0.02), higher father unemployment rate (p<0.001), more financial loans (p<0.001), frequent domestic violence to mothers (p<0.001) and higher trauma exposure (p<0.001).

Multiple logistic regression showed that risk factors for ID were being one of the first births in the family (p=0.04, OR 0.8 (95% CI 0.78-0.99) and a lower gestational age (p=0.002, OR=0.8 (0.74-0.93)). For FC, lower birth order (p=0.01, 0.8 (0.70-0.96)), lower birth weight (p=0.02, 0.99 (0.99-1.001)), abnormal growth (p=0.05, 0.57 (0.33-1.001)) and being male (p<0.001, OR 2.9 (1.70 - 5.05)) were predictive factors for FC.

Conclusion: Data show that the prevalence of ID among Palestine refugee infants is higher in Jordan compared to West Bank and similar to Gaza. The prevalence of FC is comparable between the three locations. Living in a stressful and violent environment was not a risk factor for functional gastrointestinal disorders among Palestine refugee infants.
Disclosure of Interest: None Declared
TRYPTASE STAINING OF MAST CELLS MAY SUPPORT THE DIAGNOSIS OF EOSINOPHILIC ESOPHAGITIS

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Objectives and Study: The broad clinical-inflammatory interface between eosinophilic esophagitis (EoE) and esophagitis due to gastroesophageal reflux disease (GERD) justifies the search for laboratory methods that may aid in the differential diagnosis of these conditions. This study objective was to evaluate the role of mast cell count in the esophageal epithelium as a tool for differentiating EoE esophagitis from GERD esophagitis.

Methods: Slides of esophageal biopsy from children and adult patients managed from 2009 to 2013 in a university hospital were retrospectively reviewed. Inclusion criteria for EoE were patients diagnosed according to international consensus guidelines, at least one symptom of esophageal dysmotility and ≥15 eosinophils/HPF collected from a treatment-naive patient for management of eosinophilic esophagitis or who failed to improve with prior use of acid-suppressive medication. Diagnosis of esophagitis due to GERD included at least one symptom and endoscopic signs consistent with erosive esophagitis, responsive to acid-suppressive medication or H2-receptor blockers. Archived pathology slides were re-reviewed to determine eosinophil count. Hematoxylin-eosin stained slides were masked to EoE or GERD status, and peak eosinophil density (eosinophils/HPF) was determined after examination of 10 microscopy fields. Immunohistochemistry for tryptase of mast cells included immunoperoxidase reaction with endogenous peroxidase block and the addition of Mast Cell Tryptase monoclonal primary antibody (Mouse monoclonal AA1 to Mast Cell Tryptase, 100µm, ab2378, Abcam) in a dilution of 1:1000, in bovine albumin. After an overnight period at 4° to 8°C, the incubation step was performed with Envision Dual Link during 1 hour at 37°C. Slides were stained with diaminobenzidine chromogen (DAB; Innovex Biosciences, Richmond, CA), and then counterstained with hematoxylin. Immunohistochemistry glass slides were scanned, converted to digital slides, and viewed with Image J software, version 1.48g, 2013. The maximum density of tryptase-positive cells in the esophageal epithelial layer measured in mast cells/HPF, was then determined after examination of 10 microscopy fields.

Results: Patients with eosinophilic esophagitis (N=22) have higher levels of tryptase-positive esophageal mast cells compared to GERD patients (N=19): the mean/HPF±SD were (15.8±4.2) and (7.5±4.6), p = 0.000, respectively. Tryptase-positive mast cells and eosinophil counts were only weakly correlated (0.06; R² = 0.059) in eosinophilic esophagitis.

Conclusion: A combination of mast cells count and eosinophil count may strengthen the reliability of eosinophilic esophagitis diagnosis.

Disclosure of Interest: None Declared
EVALUATION OF THE EFFECTIVENESS OF BIOFEEDBACK THERAPY IN THE TREATMENT OF FECAL INCONTINENCE (ENCOPRESIS) IN CHILDREN.

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Objectives and Study: Biofeedback therapy is helpful therapeutic method for the treatment of functional constipation with pelvic floor dyssynergia and fecal incontinence (encopresis) caused by abnormal function of the anal sphincters.

The aim of this study was to evaluate the effectiveness of biofeedback therapy in fecal incontinence (encopresis) in children.

Methods: Since 2002 to 2014, 19 patients (G 11 [57.9%], B 8 [42.1%], aged 6-18 years, medium 11 years), with symptoms of fecal incontinence caused by improper function of the anal sphincter muscle were enrolled into the study. During manometric recording, the patients were required to squeeze as to prevent defecation while being given visual feedback and verbal guidance on how to reach this goal. The patients average age of onset symptoms was 4.4 years. The first biofeedback exercises were performed at mean age 6.9 years. There was conducted average 2 sessions of anorectal exercises with the average number of exercises in one session 2.6.

Results: The improvement in the anorectal manometry was observed in 17 of 19 (89.5%) patients enrolled in the exercise due to abnormal function of the anal sphincters. Subjective clinical improvement was reported in 14 of 19 (73.7%) patients. After treatment 2 of 19 patients (10.5%) did not report on control visit.

Conclusion: Biofeedback therapy is effective treatment for fecal incontinence in children caused by abnormal function of the anal sphincters.

Disclosure of Interest: None Declared
A NEW METHOD TO ESTIMATE CATHETER LENGTH FOR OESOPHAGEAL MULTICHANNEL INTRALUMINAL IMPEDANCE MONITORING IN CHILDREN

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Objectives and Study: Multichannel intraluminal impedance combined with pH (MII-pH) is the gold standard test for diagnosing gastro oesophageal disease. Accurate catheter placement is essential to prevent erroneous recording of reflux events. In this study, we proposed a simplified method (GOSH Table) to estimate the length of insertion of MII-pH catheter from nose trill to the point where the pH sensor is approximately two vertebral bodies above the diaphragm. We compared our results to Strobel and Monreau formulae.

Methods: Retrospective data were collected from children who underwent MII-pH studies in the department of gastroenterology at Great Ormond Street Hospital between January to October 2014, including plain X-ray after initial catheter insertion and the position adjusted to align the pH sensor at two vertebral bodies above the diaphragm (desired catheter position). Children were divided into three age groups G1: 1 month to 3 years; G2: 3-10 years and G3: over 10 years.

Results: One hundred and forty four children were included with mean age was 5.1 (±4.5) years, 73 males and 71 females. The data were analysed as correlation (r) and mean difference (MD) between Strobel formula, Moreau formula, GOSH table and desired catheter position(DCP). The result were shown in table.

Conclusion: GOSH Table is an accurate method to estimate the insertion length of MII-pH catheters from nares to a point of approximately two vertebral bodies above the diaphragm in children. Although radiography is required to confirm final catheter position, using GOSH Table will reduce the need for
repeated catheter manipulation after initial insertion and will eliminate the use of a mathematically complicated formulae


Disclosure of Interest: P. Sintusek: None Declared, M. Mutalib Conflict with: Great Ormond Street Hospital for Children NHS Foundation Trust, N. Thapar Conflict with: Great Ormond Street Hospital for Children NHS Foundation Trust, K. Lindley Conflict with: Great Ormond Street Hospital for Children NHS Foundation Trust
LONG TERM RIFAXIMIN EFFICACY IN THE TREATMENT OF SIBO POSITIVE IBS CHILDREN

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Objectives and Study: Irritable bowel syndrome (IBS) is a common chronic functional gastrointestinal disorder in pediatrics. The natural history of the condition has been studied extensively, but few treatments have demonstrated to be effective. Furthermore few studies have examined the long term effects of those therapies. We had previously demonstrated a significant prevalence of small intestinal bacterial overgrowth (SIBO) in children with IBS, and that a short treatment course with Rifaximin was effective and safe in SIBO treatment and IBS symptoms improvement. We aimed to assess IBS symptoms recurrence in that group of children, at five year follow-up.

Methods: Patients who satisfied the Rome III criteria for IBS, who were also SIBO positive (retrospective diagnosis), were followed up by telephone interview and asked to attend an outpatient review at 5 years after their first attendance.

Results: Thirty-two participants from the original sample of 33 (97%) reported follow-up data at 4.4-5 years (mean 4.9 years), after completing treatment with Rifaximin. Intention-to-treat analysis showed that treatment gains were maintained on IBS symptoms in 75% children. Also quality of life and anxiety related to gastrointestinal symptoms were maintained with mainly large effect sizes. 6/32 (19%) patients performed more than one Rifaximin treatment course (mean 1.5 course), reporting benefit on IBS symptoms.

Conclusion: Rifaximin treatment appears to be related to long-term beneficial effects on IBS symptoms in children diagnosed with SIBO. Further studies on larger series, as well as placebo controlled once, are still needed to verify these findings.


Disclosure of Interest: None Declared
DELETERIOUS MUTATION IN THE NNOS GENE IS ASSOCIATED WITH INFANTILE ACHALASIA

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Objectives and Study: Nitric oxide (NO) is thought to play a role in the pathogenesis of achalasia. It was widely investigated in animal models but not well established in humans. We report genetic analysis of a family with two siblings with infantile onset achalasia.

Methods: Whole exome sequencing was performed in a single patient followed by segregation analysis of homozygous pathogenic variants in the family. Since NOS1 expressing tissue was not available for additional studies we measured the rates of NO synthesis and NADPH oxidation for purified wild-type and Y1197X. Furthermore, we calculated structural comparative models of the human wild type NOSred domain and the human NOSred mutant protein by using the software modeler.

Results: Exome analysis revealed homozygosity for a premature stop codon in the NOS1 gene (Tyr1202Ter mutation) encoding neural NOS (nNOS). The encoded nNOS protein catalyses NO biosynthesis via a reaction involving the conversion of l-arginine to l-citrulline. Tyr1202 resides in the C-terminal electron-supplying reductase module (NOSred). As predicted, NO formation was not detectable for rat nNOS Y1197X whereas wild-type rat nNOS exhibited a robust steady-state rate of NO formation (0.20 ± 0.07 s⁻¹). Similarly, the rate of NADPH oxidation for rat nNOS Y1197X was less than 5% of the rate observed for wild-type rat nNOS (0.013 ± 0.002 s⁻¹ versus 0.31 ± 0.04 s⁻¹) indicating a strong defect in NADPH oxidation for the truncated nNOS. Molecular modeling predicts that Tyr1202Ter mutation interfere with protein folding and cofactor binding. Heller myotomy had no effect but treatment with Sildenafil improved the ability to drink.

Conclusion: The finding recapitulates the previously reported phenotype in the NOS1 deficient mice which exhibits achalasia, implicating NO metabolism in the pathogenesis of achalasia in human.

Disclosure of Interest: None Declared
**GASTRIC EMPTYING IN CRITICALLY ILL CHILDREN MEASURED BY [14C] PARACETAMOL AND ACCELERATOR MASS SPECTROMETRY**

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**Objectives and Study:** In critically ill adults, gastric emptying is delayed as compared to healthy adults (paracetamol absorption test T_max 10-240 min vs 0-45 min) [1]. Most drugs are absorbed through the small intestines, therefore delayed gastric emptying will slow the time to peak concentration (T_max) and delay the onset of the action of a drug. Data from adults cannot be extrapolated to children, as age may also impact gastric emptying time, although reports are conflicting. A disadvantage of the paracetamol absorption test to study gastric emptying is the use of a therapeutic dose. Also the test is not possible when children already receive paracetamol for therapeutic reasons. A microdosing study, using a [14C]paracetamol ([14C]AAP) overcomes these limitations. In this pilot study, we aim to describe the gastric emptying using a microdosing study, using a [14C]AAP in critically ill children.

**Methods:** In a microdose pharmacokinetic pilot study, infants on a pediatric ICU (0-6 yrs of age) received a single oral/enteral [14C]AAP microdose as a liquid (3.3 ng/kg, 60 Bq/kg, 0.25 ml/kg). Gastrointestinal disorders, hepatic and circulatory failure were exclusion criteria. Blood samples were taken from an indwelling catheter. [14C]AAP levels were measured by accelerator mass spectrometry. PK parameters were estimated using standard methods. The T_max and the ratio of time to reach paracetamol peak to the maximum paracetamol concentration were used to describe gastric emptying (C_max/T_max).

**Results:** Ten infants (age 0.1 to 83.1 months) were included, one was excluded from data analysis as he vomited shortly after administration. 8 out of 9 patients were fed during the study. In 9 patients, T_max for [14C]AAP was 153 min (10-245). [14C]AAP was detectable at expected concentrations: C_max [14C]AAP 1.68 ng/L (0.75-4.76) and the ratio C_max/T_max was 0.011 (0.003-0.476).

<table>
<thead>
<tr>
<th>Patient</th>
<th>Feeding</th>
<th>T_max (min)</th>
<th>C_max/T_max (ng/L*min)</th>
</tr>
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<tbody>
<tr>
<td>1</td>
<td>No</td>
<td>161</td>
<td>0.005</td>
</tr>
<tr>
<td>2</td>
<td>Yes</td>
<td>245</td>
<td>0.003</td>
</tr>
<tr>
<td>3</td>
<td>Yes</td>
<td>37</td>
<td>0.068</td>
</tr>
<tr>
<td>4</td>
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<td>10</td>
<td>0.476</td>
</tr>
<tr>
<td>5</td>
<td>Yes</td>
<td>58</td>
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</tr>
<tr>
<td>6</td>
<td>Yes</td>
<td>193</td>
<td>0.006</td>
</tr>
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<td>7</td>
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<td>64</td>
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</tr>
<tr>
<td>8</td>
<td>Yes</td>
<td>153</td>
<td>0.011</td>
</tr>
<tr>
<td>9</td>
<td>Yes</td>
<td>178</td>
<td>0.011</td>
</tr>
</tbody>
</table>
**Conclusion:** This pilot study demonstrates the feasibility of a [14C]labeled microdose of paracetamol to study gastric emptying in critically ill children. Gastric emptying in critically ill children appears highly variable, and comparable to adult patients. When prescribing enteral drugs to critically ill children one should consider variable gastric emptying time and consequent delays to reach maximum plasma concentrations.


**Disclosure of Interest:** M. Mooij: None Declared, E. van Duijn Conflict with: TNO conducts microtracer studies and AMS analysis, W. Vaes Conflict with: TNO conducts microtracer studies and AMS analysis, B. Windhorst: None Declared, S. de Wildt Conflict with: This work was funded by a ZonMw grant (113202007)
Effectiveness of Three Follow-up Regimes in Childhood Functional Constipation. A Randomised Controlled Trail.

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Objectives and Study: Management of functional constipation in children hinges on information and follow-up. NICE guideline recommendations personalized follow-up including written and web-based information, face-to-face consultations, and telephone contact. However, recommendations on method of implementing follow-up are currently not available. Our aim was to examine the effect of three different follow-up regimes in children with functional constipation.

Methods: We conducted a prospective, single centre, randomized trial. Inclusion criteria were children who fulfilled the Rome III criteria of childhood constipation. Before randomization, the families received standardized education of childhood constipation followed by fecal disimpaction and maintenance treatment with polyethylene glycol. Hereafter, the children were randomly assigned to one of the following three follow-up groups for three months: (I) No planned contact (standard group), (II) Two pre-planned telephone contacts (telephone group) and (III) Self-administered access to web-based information on constipation (web group). The children were assessed at 3, 6 and 12 months after inclusion. The end-point was treatment success, defined as the presence of <2 Rome III criteria at the 12 month visit. Sub-categorization of responders was divided into persistent, delayed or late responders. Persistent responders met end-point criteria in all three visits; delayed responders met criteria at the first and last or second and last visit; late responders met criteria at the third visit.

Results: 235 children (52% boys) mean age 6.7 years ± 3.1 SD were included. At the 12 month follow-up, 152 children (65%) were successfully treated, 54 children (23%) were still constipated and 29 children (12%) were lost to follow-up. Of the 152 successfully treated children, 93 (61%) were persistent responders, 42 (28%) were delayed responders and 17 (11%) were late responders. In the web group there was a significantly higher number of persistent responders (p=0.036) compared to standard group (42% vs. 27%). No significant difference was found between web group and telephone group. Significantly less late responders (p=0.012) were present in the web group (12%) compared to standard group (59%). There was no difference between web group and telephone group or standard group and telephone group among late responders.

Conclusion: Self-motivated access of web-based information increased the possibility of persistent successful treatment and reduced the time to achieve response. Self-motivated access to information is a step towards more standardized and effective follow-up regimes in the treatment of childhood constipation.

Disclosure of Interest: None Declared
DEVELOPMENT AND VALIDATION OF A SPINA BIFIDA SPECIFIC PAEDIATRIC QUALITY OF LIFE QUESTIONNAIRE: THE SPINA BIFIDA PAEDIATRIC QUESTIONNAIRE, SBPQ

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Objectives and Study: A 'pubmed' search reports several studies on quality of life (QoL) in spina bifida (SB) patients. Most report disease-specific QoL instruments but score a certain aspect of the SB impairments. SB patients present a broad spectrum of problems, all having an impact on QoL. For children the pediatric QoL (PedsQL) is not applicable in children with mental and motor impairments. Hence, an instrument is needed to reliably measure the general QoL in SB children. The aim of the study was to develop and validate a Dutch SB Health-Related (HR)QoL questionnaire.

Methods: Based on existing questionnaires such as PedsQL 4.0, and patient interview a HR QoL questionnaire in SB children is created, the Spina Bifida Paediatric Questionnaire (SBPQ). Inclusion criteria: SB patients 6-18 years, Dutch-speaking. Exclusion criteria: presence of another disease (trauma, tumor) and mental age lower than 6 years. Written informed consent was obtained.

Ten SB patients of different ages and their parents, were asked to complete an ‘extended questionnaire’ of 35 items. A final questionnaire was retained when 3 consecutive patients did not give any suggestions for item modification. Parents and children with a mental development of at least 10 years answered on a 5-point Likert-scale. Younger children with developmental age of 6 to 10 years answered on a visual 3-point Likert-scale and were given additional visual clues. Lower scores designated better QoL. Validation was performed in patients, parents and controls: the same questionnaire was completed twice with a time-interval of 2 weeks.

Results: Thirty-nine patients and parents answered the questionnaire once, 20 patients and their parents the test-retest. Thirty-five controls answered the questionnaire once, 34 controls and their parents the test-retest. The test-retest showed a good to excellent agreement for child self-report in 5 domains (not for social functioning), for parent proxy report in all domains (6), for control self-report in 4 domains (not for domain home) and for control parent proxy report in all domains (5). Internal consistency reliability was good in child self-report and in parent proxy report. There was parent-child agreement for 4 out of 6 domains. Regarding social and emotional functioning, QoL was rated lower by parents than by children themselves.

Conclusion: The SBPQ has been developed. The questionnaire is tested, well accepted by children and parents and validated (after omitting one question from the social domain). This questionnaire is easy to complete and can be used by both young children and adolescents due to the visual clues.

Disclosure of Interest: None Declared
EFFECT OF BACLOFEN ON GASTROESOPHAGEAL ACID REFLUX IN NEUROLOGICALLY HANDICAPPED CHILDREN

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Objectives and Study: Baclofen is a derivative of gamma-aminobutyric acid and primarily used to treat spastality. It is proposed to be associated with lower frequency of gastroesophageal reflux (GER) through inhibition of transient lower esophageal sphincter relaxation. Majority of neurological handicapped children are reported to suffer from GER. So, we aimed to investigate whether baclofen is associated with lower frequency of GER

Methods: Neurologically handicapped children with gastrointestinal and feeding problems were included in the study. Patients were allocated to group 1 if they are taking baclofen and group 2 if they are not. All the patients are evaluated for GER by 24 hr Ph monitorization (Orion II Ph meter; Medical Measurement Systems BV; Holland). The groups were compared in respect to demographic features and GER.

Results: In total, 38 children (12 female, 31.6%) were included in the study. Median age, weight and height z scores were 3.00 (0.75-15.00), -4.18 (-14.75-1.40), and -2.30 (-8.08-2.91) respectively. Twenty-six patients (70.3%) had malnutrition. In total, 12 patients (31.6%) had pathologic gastroesophageal acid reflux. Both group 1 and 2 consisted of 19 patients. The age and gender distribution and the frequency of malnutrition were similar for both group 1 and 2. Although insignificant, pathologic GER was more frequent in group 1 compared to group 2 (9 patients (47.3%) versus 3 (8.3%) respectively, P=0.079).

Conclusion: In neurologically handicapped children, baclofen use does not seem to be associated with lower frequency of GER. In these population, the factors other than transient lower esophageal sphincter relaxation, such as dysmotility, delayed gastric emptying, hiatal hernia etc., may have been contributing to reflux. Additionally, non-acid or alkaline reflux that are not assessed in this study may be responsible from majority of GER episodes

Disclosure of Interest: None Declared
THE VALIDITY OF ROME CRITERIA III IN THE FOLLOW UP EVALUATION OF CHILDREN WITH FUNCTIONAL CONSTIPATION

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Objectives and Study: Study prospectively the response of constipated children, according to Rome III criteria, after therapeutic and behavioral interventions.

Methods: Child/adolescent with functional constipation (FC), according to the Rome III criteria, were included in the study (approved by the ethics committee) in a tertiary center between 2004 and 2014. At each query, behavioral and general clinical features, related to constipation characteristic were evaluated.

Results: A total of 278 patients were selected (54% males; mean age of 6.11 years) and this number decreased during the study down to 239, 188, 127 then 95, from the 1st to 5th appointment, respectively. The Rome criteria considered for analysis were: straining, retentive maneuvers, fecal consistency (Bristol-scale type 1, 2 or 3), and less than 3 bowel movements per week. The number of children who met 2 or more Rome criteria at each visit was 72.3%, 31%, 21.8%, 17.3% and 18.9%, respectively, from the 1st to 5th visit. Thus, there was significant reduction in the proportion of children with FC criteria between the 1st visit and the subsequent queries, and between the 2nd and the 4th visits. There was no difference in this ratio when comparing other consultations among themselves.

Conclusion: Treatment of FC resulted in a significant improvement of several variables, especially between the 1st and the 2nd consultations, and mainly the variables related to the Rome criteria III. There was also a progressive improvement, though less dramatic than the former, in subsequent visits.

It is noteworthy that the improvement of any particular variable was not associated, independently, with any intervention evaluated in the study, such as the use of polyethylene glycol without electrolytes, lactulose, mineral oil, milk of magnesia, dietary fibers, enemas or fecal desimpactation. The Rome III criteria correlated with severity, but were not effective for diagnosing and management of FC during the treatment. Rome did not guide the therapeutic interventions.


**Disclosure of Interest:** None Declared
Objectives and Study: Gastroesophageal reflux disease (GERD) is a frequent pathology in paediatric gastroenterology, but manifestations of the disease are often non-specific and change as the child grows. The main objective of our study was to evaluate the impact of patient’s age on the clinical features of GERD.

Methods: 98 patients (1-17 years old) with a diagnosis of GERD, admitted to our Department of Gastroenterology, were examined. Patients were assigned to upper endoscopy and pH monitoring. Particular attention was given to the study of their history, complaints, and comorbidities. The children were divided into groups according to their age: group 1 (1-6 years old; n=30), group 2 (7-12 years old; n=37), group 3 (13-17 years old; n=31). Males predominated in all groups.

Results: Evaluation of endoscopic changes of the esophagus revealed that GERD without esophagitis was observed more frequently in group 1 (56.7%, p<0.05), mucosal erythema – in group 2 (51.4%, p<0.05), erosions and ulcers – in third group (48.9%, p<0.05). Comparative analyses of the clinical features of GERD in different patients determined that younger children (1-6 years) often complained of vomiting, sometimes at night (p<0.001) and regurgitation (p<0.001). At the same time, older children (groups 2 and 3) often mentioned belching (39.7%). Heartburn is one of the most common symptoms in adult patients with GERD. However, this complaint was found in 30.9% of patients over 7 years old and almost never determined in younger children (p <0.05). Epigastric pain, chest pain, intensified at night or in the prone position, were observed in 30% of cases, with no significant differences in all groups.

Assessment of comorbidities in children of different ages revealed that adenoiditis (p <0.05), obstructive bronchitis (p <0.001) were more common in young patients (group 1). Also recurrent laryngitis and pneumonia were observed only in this group (11.1%). Patients of the second group often diagnosed sinusitis (18.9% of patients). Cardiac arrhythmias were detected significantly more often in patients older than 7 years (p <0.05).

Conclusion: There are significant differences in the clinical manifestations of GERD depending on the age of children. Careful study of these features will improve the diagnosis of the disease and reduce the frequency of visits to other specialists (otolaryngologist, cardiologist, etc.).

Disclosure of Interest: None Declared
ABDOMINAL PAIN-PREDOMINANT FUNCTIONAL GASTROINTESTINAL DISORDERS IN ADOLESCENT NIGERIANS

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Objectives and Study: Chronic functional abdominal pain is one of the main reasons school aged children in developing countries visit a paediatric gastroenterologist. Data are however lacking about the prevalence of abdominal pain-predominant functional gastrointestinal disorder (AP-FGD) in the African continent. Aim: To determine the prevalence of AP-FGD among Nigerian adolescents and its relationship with their socio-economic and psychological status.

Methods: A cross sectional study was conducted in two states of the South-South geo-political zone of Nigeria in June 2014. A total of 710 adolescents aged 10 – 18 years were recruited from 11 secondary schools using a stratified random sampling technique. A validated self-administered questionnaire on Rome III criteria for diagnosing AP-FGDs and its determinants were filled by the adolescents in a class room setting following parental consent and assent of participants.

Results: AP-FGD was present in 63 (8.9%) children. The prevalence was 9.1% in males and 8.0% in females. Sub-group analysis showed that 40 (6.5%) had irritable bowel syndrome (IBS), 17 (2.4%) had abdominal migraine, 14 (2.0%) had functional abdominal pain while 5 (0.7%) had functional dyspepsia. There was a statistically significant association between AP-FGD and change of school (p= 0.02), frequent punishment (p=0.03) and being bullied at school (p=0.02). The association between AP-FGD and socio-economic status or place of residence (urban vs. rural) was not statistically significant (p < 0.05).

Conclusion: AP-FGD is fairly common among Nigerian adolescents with irritable bowel syndrome as the most common sub-type. The condition is associated with some school-related stressful events.

Disclosure of Interest: None Declared
ASSOCIATION OF INFANTILE COLIC AND FUNCTIONAL GASTROINTESTINAL DISORDERS AND SYMPTOMS

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Objectives and Study: Infantile colic is a frequent, yet poorly understood condition. Although a gastrointestinal (GI) involvement has been broadly suspected, surprisingly little quantitative data is available to substantiate this link. As part of a randomized, controlled, double-blind, multicenter nutritional intervention study, we evaluated post hoc the association of infantile colic with other commonly observed functional GI disorders and symptoms at 4, 8, 13, and 17 weeks of age.

Methods: Healthy, term infants aged 0–28 days (n=432) were randomized to receive one of four different infant formulas until 17 weeks of age. Standardized 7-day diaries with daily entries on GI tolerance and crying were completed by the parents at 4, 8, 13, and 17 weeks of age. Parents were asked to score common digestive symptoms as absent, mild, moderate, or severe. Specific GI symptoms were considered relevant if the calculated mean score was above mild over the diary period. Infants were categorized independent of study intervention as “with colic”, or “without colic” based on adapted Rome III criteria. Data from the intention to treat population (n= 431) are presented, from whom a valid dairy was available for analysis.

Results: At the age of 4 weeks the overall incidence of colic was 16.1% (n=292), at 8 weeks 10.6% (n=284), at 13 weeks 2.2% (n=272), and at 17 weeks 0.7% (n=267). The most often reported GI symptoms with a score above mild at 4 and 8 weeks of age were flatulence (50% and 42.9% of infants), and regurgitation (25.7% and 24.3%). At 4 weeks and 8 weeks of age, the odds ratios of infants with colic versus infants without colic for flatulence were 4.9 (80% vs. 45.1%) and 4.0 (73.1% vs. 40.4%) respectively, for regurgitation (25.7% and 24.3%). At 4 weeks and 8 weeks of age, the odds ratios of infants with colic versus infants without colic for flatulence were 4.9 (80% vs. 45.1%) and 4.0 (73.1% vs. 40.4%) respectively, for regurgitation 3.3 (47.7% vs. 21.8%) and 3.1 (46.4% vs. 22.1%), for arching of the back 5.3 (38.1% vs. 10.5%) and 4.8 (20.0% vs. 5.0%), for abdominal distension 5.6 (37.2% vs. 9.6%) and 5.2 (30.8% vs. 7.9%), for diarrhea 3.8 (11.9% vs. 3.4%) and 2.9 (14.8% vs. 5.7%), and for constipation 4.9 (11.4% vs. 2.6%) and 4.4 (14.3% vs. 3.7%). At 13 and 17 weeks of age, the incidence of colic was too low for statistical assessment.

Conclusion: Functional GI disorders and symptoms were more frequently reported by parents in infants with infantile colic compared to infants without colic, in a preventive trial in healthy, term infants. These distinct functional disorders are common in infants and could be seen as a result of the interaction between the adaptation of the developing digestive system and microbiome to enteral nutrition.
Objectives and Study: A cross-sectional study (1) showed that normal colon transit time (CTT) associated with normal anal resting pressure in spina bifida (SB) patients is related to achieving spontaneous faecal continence. The aim of the study was prospectively evaluating CTT and anal resting pressure in 3 to 6 year old SB children as predictor of spontaneous faecal continence.

Methods: The study is performed at the SB Reference Center of the Ghent university hospital. All 3-6 year old SB patients are asked to participate. Data from the medical file is collected. The Rome III criteria for paediatric functional constipation are used. The SB patients are incontinent if involuntary faecal loss is > 1/month in children > 4 years old.

The control group for CTT are 16 healthy age-matched children. The control group for anorectal manometry (ARM) is based on the results by Kumar et al (1). CTT is measured using the 6-day method. ARM is performed in non-sedated children with a water-perfused latex-free catheter. Non parametric tests are used and multivariate analysis is performed.

Ethical approval (EC UZG 2010/348) is obtained.

Results: Seventeen out of 21 eligible patients consented to perform CTT, of which 12 also performed the ARM. The Rome III criteria confirm constipation despite treatment in 5/13 SB children. Three patients are spontaneously continent, 6 are pseudo-continent, overall 69% (9/13) is (pseudo)continent.

This prospective study confirms a former study (2), SB patients have a significant (P= 0.004) longer CTT compared to controls (median CTT 67.2h vs. 33.6h). Constipated SB patients have a significant longer CTT than the non-constipated (P=0.006) (median CTT 98.4h vs. 34.8h).

Spontaneously continent patients have a normal CTT (median 31.2h) and a normal resting pressure (median 46.5 mm Hg). There is a significant difference of CTT in continence status (P=0.028), with not spontaneously continent having an elongated CTT. For normal rectal pressure no significant difference is found (P= 0.14), but there is only one not spontaneously continent with a normal resting pressure and he has an abnormal CTT.

Conclusion: A former study and this prospective study confirms that a normal anal sphincter resting pressure is a prerequisite but not a guarantee for achieving spontaneous faecal continence. Combined with a normal CTT it predicts spontaneous faecal continence.

Disclosure of Interest: None Declared
CHARACTERISTICS OF ACHALASIA SUBTYPES IN GREEK PAEDIATRIC PATIENTS: A HIGH-RESOLUTION MANOMETRY STUDY

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Objectives and Study: Achalasia is a rare esophageal disorder and there have been very few reports about it, especially in children. High-resolution manometry (HRM) with pressure topography is used to subtype achalasia cardia, which has therapeutic implications. Our study aimed to evaluate and compare the clinical characteristics, manometric results and treatment outcomes of different subtypes of achalasia in Greek children using high-resolution esophageal manometry.

Methods: Ten consecutive children (median age 10.2; range 7–16 yrs) with achalasia were enrolled into the study. Presenting symptoms were vomiting (n = 8), dysphagia (n = 6), loss of weight (n = 5), recurrent respiratory infections (n = 3), cough (n = 2) and noisy respiration (n = 1). All patients underwent prolonged EHRM by using a solid-state catheter incorporating 36 unidirectional strain gauge pressure sensors, spaced at 1-cm intervals. Single wet swallows, multiple rapid swallows (MRS), and solid swallows were systematically studied. Based on the Chicago classification criteria achalasia is diagnosed as an impaired LES relaxation on deglutition (mean integrated relaxation pressure ≥ 15 mmHg) and aperistalsis of the esophageal body. The integrated relaxation pressure was defined as the LES relaxation pressure for 4 seconds (IRP-4s) within the relaxation window. Three achalasia subtypes were determined based on the Chicago classification. Clinical characteristics, manometric and treatment outcomes were compared. Eight age-matched children (5 males, median age 7.5 yrs, range 6–15 yrs) with non erosive reflux disease presenting with bolus impaction served as controls.

Results: In all, 2 patients were classified as type I, 6 as type II and 2 as type III. The mean overall length of lower esophageal sphincter (LES) in type II was significantly longer than those in the controls and type I patients (P<0.05), and abdominal LES length was significantly longer in type II than those in controls, type I and type III patients. All subtypes of achalasia had higher resting and residual LES pressures than those found in healthy controls (P<0.05). Resting upper esophageal sphincter (UES) pressure in all achalasia patients was significantly lower than those in healthy controls (P<0.05). There were no differences in UES function between patients and controls. Type II patients had a better response to the treatment than type I and III patients.

Conclusion: Achalasia subtypes classified by HRM may allow clinicians to direct therapy and predict outcomes of the disease. Type II is more common in Greek paediatric achalasia patients, and type II patients had better treatment outcomes than other types of patients.
Disclosure of Interest: None Declared
CHANGES IN THE PATTERNS OF COLONIC TRANSIT IN CHILDREN WITH FUNCTIONAL CONSTIPATION

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Objectives and Study: Functional constipation as described by Rome III criteria is common in children. Measuring colonic transit time (CTT) can help guide therapy. Several methods were described to measure CTT of which radiopaque markers are simple to use and easy to interpret. The aim of this study was to evaluate changes in patterns of constipation and CTT in children with functional constipation.

Methods: Retrospective review of clinical and radiological data of children with functional constipation who underwent more than one colonic transit measurement using radiopaque marker studies in our institution between January 2010 and December 2013. Radiopaque marker studies were performed by ingesting one capsule per day for three successive days. X-ray was taken on day 4. CTT was calculated using the following formula: number of markers*2.4.

Results: 19 patients were included in this study. The mean age (±SD) was 7.8 years (±3.0); range 2.8-13.4. M/F ratio was 15/4. Two radiopaque marker studies were performed for each patient. The average mean time between both studies (± SEM) was 1.8 years (±0.75); range 0.3-0.6. The baseline studies showed: 12 (64%) patients had slow transit constipation (STC) and 6 (37%) had colonic segmental delay of which 1 (5%) were right side (R-SD), 5 (26%) left side (L-SD) and 1 (5%) was rectosigmoid hold up (RS-SD). The mean total CTT hour (±SD) was 58.0 (±13.9), right colon transit (RCTT) 21.1 (±18.1), left colon transit (LCTT) 16.7 (±13.5) and rectosigmoid transit was (RSTT) 20.2 (±13.3). In the subsequent studies, 1 (5%) study was normal, 10 (53%) had STC and 8 (47%) had colonic segmental delay: 2 (11%) R-SD, 2 (11%) L-SD and 4 (20%) were functional outlet obstruction. The mean total CTT was 56.0 (±19.7), RCTT 20.3 (±20.7), LCTT 15.8 (±15.9) and RSTT 19.8 (±16.2). There were no changes in pattern of constipation in 11 cases (8 patients had STC, 2 had L-SD and 1 had RS-SD). The colonic transit patterns changed in 8 cases: in 1 patient from STC to normal; in 2 cases from STC to RS-SD; in 1 case from R-SD to functional outlet obstruction; in 1 from STC to R-SD; in 1 from L-SD to R-SD; in 2 cases from L-SD to STC. None of the changes in total and segmental colonic transit time were significant.

Conclusion: Measuring total and segmental colonic transit time with radiopaque markers allows the identification of types of colonic dysmotility and the appropriate choice of treatment. In this study, 47% of children had a different type of constipation in repeat radiopaque marker study. Total and segmental transit time was not statistically different between the first and second transit measurement likely due to small sample size. In children with chronic functional constipation who failed to respond to optimum therapy, repeating colonic radiopaque marker study may provide a useful guide to therapy.
Disclosure of Interest: None Declared
PREVALENCE OF FUNCTIONAL CONSTIPATION IN DANISH SCHOOLCHILDREN
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Objectives and Study: Prevalence rates of childhood constipation varies widely, from 0.7% to 29.6%.
Methodological issues makes comparisons difficult as diagnostic criteria vary between Rome III criteria and parents reports.

No data on the prevalence of functional constipation among schoolchildren are available in Denmark. A delay in initial treatment seems to be correlated with longer treatment duration. Thus, it is important to know the epidemiology of functional constipation. The present study aim to determine the prevalence of functional constipation among Danish schoolchildren.

Methods: A cross sectional study among children age 5-16 years were performed at randomly selected schools in Kolding Municipality. To ensure sufficient data to find the estimated prevalence at 5%, the study population included 2000 children.

A child was diagnosed with constipation when fulfilling at least two Rome III criteria. Questionnaires were emailed to parents addressing the Rome III criteria, urinary symptoms and demographic data. Parents were reminded of the study, through the school's email system.

Children only fulfilling one Rome III criteria, or who stating troubles finishing defaecating, were offered transabdominal ultrasound of the rectum to determine the presence of faecal impaction.

Results: Parents of 600/2138 children (28%) answered the questionnaire. Two or more Rome III criteria were found in 155/2138 children giving a prevalence of minimum 7.2%. Among children who fulfilled the questionnaire 26% fulfilled the criteria for constipation. Median age was 8.6 years, SD=2.8
Mean number of Rome III criteria among constipated were 2.6 (95% CI 2.5-2.8) and among the non-constipated 0.4 (95% CI 0.3-0.4). Distribution of Rome III criteria met by constipated vs. non-constipated children was: ‘Large diameter stools’ (68% vs. 18.2%), ‘Retentive posturing’ (68% vs. 8.5%), ‘Hard/painful bowel movements’ (45% vs. 2.9%), ‘Faecal incontinence’ (44% vs. 5.6%), ‘Feeling of faecal loading’ (26% vs. 0.45%) and ‘Defecation ≤2 times per week’ (12% vs. 0%).

17% of the constipated children had urinary incontinence, which overall was reported in 72 children with 39 children having enuresis, 18 children with day-urinary incontinence and 15 children with both day- and night urinary incontinence.

Conclusion: The prevalence of childhood constipation among Danish schoolchildren was minimum 7.2%. The sample is representative for Danish school children.

References:
Disclosure of Interest: None Declared
Gastrointestinal symptoms (GIS) are common in young people with eating disorders, and are associated with disordered motility. It is hypothesised that GIS reflect malnutrition. The aim of this study is to determine the prevalence of GIS and their relationship to nutritional status and comorbid psychopathology.

Methods: The data source was the HOPE (Helping Outline Paediatric Eating disorders) Registry a prospective register of tertiary eating disorder referrals and assessments. A multi-disciplinary paediatric eating disorders clinic assessed GIS, comorbid psychological characteristics (Child Depression Inventory (CDI), Multidimensional Anxiety Scale for Children (MASC), DSM V diagnosis, physical and nutritional status (BMI z score). GIS were assessed using a multi-item questionnaire modified for paediatric use, with GIS ranked none, mild, moderate severe for specific GIS and a cumulative GIS score recorded. Data were analysed with SPSS, using ANOVA, correlation and linear regression to explore models explaining GIS

Results: 332 new patients age 8.7-17.5 (mean = 14.4±1.4) years; 91% females, were assessed between 2012 and 2014. The table summarises population characteristics as mean value±sd.
Total GIS score ranged from 0-27 out of a possible 36, (mean 9.8). Early satiety, bloating and borborygmi were the most severe symptoms, followed by anorexia, nausea, cramps and constipation. GIS correlated positively with the CDI (0.43, p< 0.000), MASC (0.45, p< 0.000), age (0.22, p=0.003) and pubertal stage (0.22, p<0.000), but not BMI z score. In a regression model controlling for age and gender MASC (p= 0.003) and CDI (p=0.004) but not BMI z score predicted GIS.

Conclusion: GIS are associated with anxiety and depression and not malnutrition in children and adolescents presenting to a tertiary eating disorders service.


Disclosure of Interest: None Declared
EVALUATION OF THE EFFECTIVENESS OF BIOFEEDBACK THERAPY IN THE TREATMENT OF FUNCTIONAL CONSTIPATION IN CHILDREN.

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Objectives and Study: Defecation disorders are one of the most common problems in gastroenterology. It may be caused by the organic disease or more frequently it is a functional problem. The treatment includes fiber rich diet, proper education of patient, pharmacotherapy and in some cases the biofeedback therapy.

The aim of the study was to assess impact of parameters of anorectal manometry and their changes during biofeedback therapy on clinical outcome in children with constipation and pelvic floor dyssynergia.

Methods: Since 2000 to 2014, 44 children (aged 7-18 years, medium 12.5 years) with constipation and pelvic floor dyssynergia were retrospectively assessed in this study. All of them had pharmacotherapy for constipations with macrogoles as first choice drug and had one to four biofeedback series consisted of two to four sessions. Amplitudes between extremal and basic pressure during defecation maneuver during first and last session as well as difference between them both (amplitude in first session – amplitude in last session) were compared between group with clinical improvement after last session (n=38) vs. group with no clinical improvement (n=6). U Mann-Whitney test was used for analysis with p<0.05 regarded as significant.

Results: There were no significant difference found in amplitude in first session values [mmHg] 94, 65, 115 vs. 112, 55, 170 [median, Q1, Q3]; amplitude in last session values 36, 27, 52 vs. 41, -38, 66; as well as in difference between them both 71, 11, 124 vs. 81, 17, 109 in groups with clinical improvement after last session vs. group with no clinical improvement respectively.

Conclusion: Parameters of anorectal manometry and their changes during biofeedback therapies do not contribute to clinical outcome in children with constipation and pelvic floor dyssynergia.

Disclosure of Interest: None Declared
Objectives and Study: To detect infant low esophageal sphincter (LES) function with high resolution manometry (HRM), to help analysis the reason of infant vomiting.

Methods: Esophageal HRM was performed in neonates with vomiting, whose respiratory, metabolic and circulatory function was stable. Analyze the data of HRM with Mano View software.

Results: Esophageal HRM was performed successfully in 17 neonates. Neonate LES function is varied, LES pressure of some neonates is continuous low, some neonates had stable LES in resting period, but LES relaxed for even to 25 seconds after sucking and swallowing. Some neonates had multiple inefficient swallows without esophageal peristalsis, at the same time LES pressure was continuous low. But some preterm infants had high LES pressure without relaxation after swallow happened, even caused LES shift down. According the LES function, infant vomiting can be a symptom of gastroesophageal reflux because of low LES pressure, or consequence of milk retention in the esophageal because of high LES pressure without normal relaxation.

Image:
Conclusion: Infant LES function is immature, but not all the infants have low LES pressure, some infants have abnormal relaxation, some have high LES pressure. Infant vomiting has different reasons, esophageal HRM is helpful in distinguishing the reasons.


Disclosure of Interest: None Declared
**Objectives and Study:** Functional gastrointestinal disorders (FGIDs) are a group of conditions frequently misdiagnosed in children, associated with significant morbidity and high health-care cost. The first phase of this project aimed at assessing the diagnostic and therapeutic approach to children with suspected FGIDs by general paediatricians (GP) from different European countries.

**Methods:** A short form evaluating diagnostic approach, including the use of Rome diagnostic Criteria, and therapeutic management of irritable bowel syndrome (IBS), functional constipation (FC) and functional regurgitation (FR) was submitted to a large sample of GP.

**Results:** So far, 260 GP from 8 different countries (Italy, Spain, Greece, Israel, Serbia, Montenegro, Slovenia and Lebanon) returned the completed form. Regarding IBS, only 84/260 (32%) GP stated to use Rome III Criteria, whilst 110/260 (42%) of them considered IBS as an exclusion diagnosis, to be formulated after a complete diagnostic work-up. Of the surveyed GP, 212/260 (82%) based IBS therapy on the predominant complained symptom. The most prescribed treatments were: analgesics (29%) for pain control; dietary advices (35%) and osmotic laxatives (28%) for constipated patients; and dietary advices (32%) and probiotics (27%) for diarrhoeic IBS-subtype. About FC diagnosis, Rome III criteria were used by 96/260 (37%) of GP; diagnosis was mainly based on stool consistency (87%), bowel frequency (85%) and retentive posturing (80%). Moreover, 84% of GP considered the diagnosis of FC when a child presented with acute abdominal pain. Treatment of FC was based on dietary modifications (96%) and use of osmotic laxatives (93%); the most widely dietary treatment proposed was the increase in fiber and water assumption (78%), while the most used osmotic laxatives were PEG (59%) and lactulose (31%). Finally, Rome III criteria for FR diagnosis were used only by 76/260 (29%) GP, while 178/260 (68%) of them relied the diagnosis on personal experience. Reported treatment consisted mainly on reassurance (96%), supine positioning (66%) and thickened feedings (66%).

**Conclusion:** These preliminary data show that: (a) the use of Rome III diagnostic Criteria is not sufficiently widespread among GP; (b) there is still large variability in the treatment of FGIDs within the different countries.
ESOPHAGEAL HIGH RESOLUTION MANOMETRY IN NEUROLOGICALLY IMPAIRED CHILDREN AND GASTRO-OESOPHAGEAL REFLUX DISEASE

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Objectives and Study: Mechanism underlying the occurrence of Gastroesophageal reflux disease (GERD) in neurologically impaired children (NIC) is poorly understood. We sought to characterize, by Esophageal High Resolution Manometry (EHRM), alterations of esophageal motility associated with GERD in NIC and to compare with a group with a suspicion of GERD and normal psychomotor development (NPD).

Methods: EHRM and multichannel intraluminal impedance/pH-metry (MII/pH) were conducted in 7 NIC and 9 patients with suspicion of GERD and NPD. Esophagogastric junction relaxation (EGJr), the presence/pressure troughs of the oesophageal segments, the distal contractile integral adjusted for esophageal length (DCIa) and the pressurization frontal velocity (PFV) were analyzed by EHRM.

Results: Three out of 7 NIC (42.8%) and 4 out of 9 patients with NPD (44.4%) resulted positive to MII/pH (p=1). No statistical differences were observed for EGJr and PFV between NIC and NPD patients. DCIa was significantly lower in NIC subjects respect to NPD patients (p<0.01). Comparing NIC with GERD and patients with GERD and NPD we found that third segment was absent in 2/3 (66.6 %) of NIC respect to NPD patients (p<0.05) and that the third pressure trough was significantly lower in NIC respect to NPD patients (p<0.05). There were no statistical differences with respect to the first and second pressure trough between NIC and NPD patients.

Conclusion: NIC have esophageal motor dysfunction that can be detected by EHRM. Some esophageal manometric alterations could be predictive of GERD in NIC and could explain a different pathogenesis of GERD in NIC and in patients with NPD.

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**Objectives and Study:** The pathogenesis of irritable bowel syndrome (IBS) in children is not completely understood, but in adults IBS has been associated with low-grade inflammation. The aim of this study was therefore to evaluate the serum levels of cytokines to determine whether paediatric IBS is associated with increased immune activity.

**Methods:** In the population based birth cohort BAMSE (n=4089), adolescents were invited to participate in the 16-year follow up, of which 2547 agreed to undergo blood testing and clinical examination. Serum samples were obtained from 41 subjects with gastrointestinal (GI) symptoms and 97 individuals with no GI symptoms (controls). Children with GI symptoms fulfilled the Rome III criteria for IBS and were symptomatic at the time of blood sampling. MesoScale Discovery (MSD) multiplex immunoassay analysis was used for the measurement of serum cytokines.

**Results:** The overall profile of cytokines in serum did not differ between children with IBS and controls. However, children with IBS had increased serum levels of interleukin (IL)-6 as compared to controls with no GI symptoms. Also levels of tumour necrosis factor (TNF) and IL-8 tended to be increased in serum of children with IBS relative to controls. The levels of IL-6, TNF or IL-8 did not differ between children with IBS with or without constipation or allergy related diseases (asthma, eczema and/or rhinitis). Further, IL-2, IL-4, IL-5, IL-10, IL-12p70, IL-13, IL-17A were similarly expressed in children with IBS and controls.

**Conclusion:** Children with IBS have increased serum levels of pro-inflammatory cytokines, which mimics previously presented data from adults with IBS. Thus, paediatric IBS, similar to IBS in adults, is associated with increased immune activity.

**Disclosure of Interest:** None Declared
OUTCOME MEASURES FOR INFANT COLIC – WHAT DO HEALTH PROFESSIONALS THINK?
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Objectives and Study: Infant colic (IC) is a common problem with a prevalence of 5 – 25%. This self-limiting disorder can have negative long-term consequences such as increased susceptibility to abdominal pain, disturbed parent-infant interaction and even child abuse. To date, its etiology remains unknown, resulting in a wide variety in interventions. Previous research revealed that outcome measures used across therapeutic trials of IC are heterogeneous as well. In order to be able to compare results between trials and not to overlook important outcome measures, development of a core outcome set is necessary. Therefore, as a first step, we aimed to investigate which outcome measures are important to health professionals when treating IC.

Methods: In 2014 health professionals visiting two international paediatric conferences were personally invited to participate in our survey. One of our two investigators handed them a questionnaire on paper. They were asked to list up to 5 harmful and/or beneficial treatment outcomes, which they considered to be important and which guided their clinical decision making in both outpatient and inpatient setting. The questionnaire was completed at the conference. Answers were processed anonymously.

Results: 133 of 180 (74%) health professionals responded. They originated from 29 countries and included 63 paediatric gastroenterologists, 26 general paediatricians, 18 fellows, 4 residents, 4 nutritionists, 4 researchers, 2 neonatologists, 2 paediatric allergy specialists and 10 others. For the outpatient setting a total of 50 different outcome measures were reported – crying duration (63%), discomfort (26%) and sleeping time (19%) of the infant were considered to be the most relevant outcome measures. In the inpatient setting even 59 outcome measures were reported – crying duration (50%), duration of hospitalisation (23%) and discomfort of the infant (17%) were considered as most important outcome measures.

Conclusion: This study clearly shows that there is a large variation of outcome measures used by health professionals worldwide when treating IC. Therefore, there is a need to achieve consensus for which further development of a core outcome set is necessary.

Disclosure of Interest: None Declared
LONG-TERM OUTCOMES AND QUALITY OF LIFE AFTER SURGICAL MANAGEMENT OF HIRSCHSPRUNG’S DISEASE

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Objectives and Study: Investigate the long-term outcomes and the quality of life after Open or Minimal Invasive surgical managements (TERPT or LATEP) of Hirschprung’s disease (HD) in children operated in HUDERF.

Methods: We reviewed the patients who were operated for HD from 1987 - 2013. In all patients we investigated operative characteristics, postoperative complications and bowel function. For the patients older than 5 years of age without mental deficit we asked to full-fill a questionnaire of quality of life (QoL) and conducted a case control study comparing bowel function and QoL between operated children and controls.

Results: we included 45 operated patients and 48 controls. Sex ratio (male/female) was 2/1 and mean age was 13.8 +/- 7.1 years in the HD group compared with 2.4/1 and 14.6 +/- 9.1 years in the control group. Surgical procedures were: Soave (open) 73.4% (33 cases), TERPT 13.3% (6 cases), LATEP 13.3% (6 cases). Resected colons were: rectosigmoid: 71.1%, descending 15.6%, transversal 4.4%, total 8.9%. Postoperative complications were as follow: Torsion 2.2% (1 case), Intestinal obstruction 6.7% (3 cases), and dehiscence 4.4% (2 cases). 4 cases had multiple enterocolitis (3 of those had a total colon aganglionosis).

After questionnaire compelling, 10 patients were incontinent (22.2 %)) in the HD’s group compared with 4.2 % in the controls (P=0.03); 7 patients had constipation (15.5%) versus 6.2% in controls, 3 patients (6.7%) had more than 6 stools/day versus none in controls.

Overall, out of the 15 patients who had defecatory problems (fecal incontinence or constipation), 7 patients got better after adaptation of an intensive bowel management.

33 patients full-filled the questionnaire of QoL (patients suffering from Down Syndrome were excluded), 26 cases (78.8%) were good (9-12 score). The average score of QoL in the HD’s group was 9.9 +/- 2.5 versus the controls’ score 11.9 +/- 0.3 (P<0.001, T-test; 95% CI:1.16 -2.79). Rate of school absence, unhappiness, food restriction and peer rejection was 6 (18.2%), 9 (27.3%), 12 (36.4%) and 4 (12.1%) respectively. After 10 years of age, most of the patients had a normal life, except those with severe defecatory troubles.

Conclusion: Incontinence and constipation have an important impact on long-term outcome and quality of life in patients with HD. Continuous follow-up with enough attention for treating constipation and incontinence with laxatives and intensive management is imperative to obtain a better result.
Surgeons, gastroenterologists, the patient and his family have to be aware that also after surgery caring for these patients is challenging, but necessary to obtain a better quality of life.

**Disclosure of Interest:** None Declared
OBJECTIVES AND STUDY: Infant formulas containing prebiotics are useful for relieving constipation in infants, but trials including children are scarce. This study objective was to determine the effect of 4’ galactooligosaccharide on functional constipation as defined by the Rome III criteria.

METHODS: From 2010 to 2012, 23 constipated patients (4-16 years) sought a primary healthcare unit, 20 patients were enrolled in a double-blind, placebo-controlled, crossover clinical trial. Eleven children received galactooligosaccharide (1.7g) 30 days along, followed by a 15-day washout period and, after, a 30-day period of placebo (Maltodextrin), remaining 9 patients received placebo (Maltodextrin) for 30 days, followed by a 15-day washout period and, after, a 30-day period galactooligosaccharide (1.7g). Primary outcome were bowel movements per week, straining during defecation and stool consistency, such symptoms were ranked in a numeric scale, according intensity and data recorded at baseline, at the 15th and 30th day in each 30-day crossover period. Oral anal transit time was determined at baseline and 30th day of each period. Repeated-measures analysis of variance (ANOVA) was used to analyze the findings over time.

RESULTS: At baseline there were no statistically significant differences between groups in symptoms intensity (p=0.45). Galactooligosaccharide increased bowel movement frequency, p<0.0001, relieved defecation discomfort, p<0.0001, and decreased stool consistency, p=0.0014 when compared to placebo. Oral anal transit time was lower during galactooligosaccharide ingestion, p<0.0001. A significant time/effect and time/ galactooligosaccharide interaction for symptoms intensity was found. Patients have not referred side effects during galactooligosaccharide use.

Clinical data and time effect (clinical scores values over time) using analysis of variance (ANOVA) for comparison between two groups of constipated patients. Cross-over study during two four-week periods, when galactooligosaccharide (GOS) or Placebo were ingested, alternately. Clinical data were evaluated with a score based on bowel frequency, fecal consistency and defecation symptoms were recorded at baseline and each 2 weeks in two crossover periods.

CONCLUSION: Galactooligosaccharide was effective at improving clinical symptoms in constipated children.

Key words: child, constipation, functional food, therapy

Disclosure of Interest: None Declared
OUTCOME OF FUNDOPLICATION IN CHILDREN WITH AND WITHOUT NEUROLOGICAL IMPAIRMENT

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Objectives and Study: The utility of fundoplication in patients with neurological impairment (NI) is debated, and it is assumed that NI patients have inferior results compared to those without NI (NI-). However, only two prospective studies have compared outcome in children with and without NI (1). The aim of the study was to assess postoperative complications, recurrence of GERD, gastrointestinal symptoms, feeding problems, and the child`s overall well-being in a cohort of children with and without NI.

Methods: 87 out of 107 patients undergoing Nissen fundoplication (NF) at the two centers Rikshospitalet and Ullevål between 2003 and 2009 were included in this prospective cohort study. At admission patient demographics, gastroesophageal reflux disease (GERD) symptoms and feeding problems were recorded. Complications occurring the first 30 days after NF were graded using the Clavien-Dindo system and scored from 0-100 by the comprehensive complication index (CCI). An upper gastrointestinal (UGI) contrast study, 24-hour pH monitoring and clinical examination were scheduled 6 months postoperatively. Phone-interviews recording GERD symptoms and parental evaluation was performed 1, 2 and 4 years after NF.

Results: 46 NI and 41 NI- children were included. Median age was 3.1 [0.2-15.2] and 5.0 [0.4-15] years in NI and NI-, respectively (p=.14). Preoperatively, 39 NI and 6 NI- had a feeding tube (p<.001). Of the 87 patients, 46% had vomiting ≥4 days/week, 60% had regurgitation ≥4 days/week, 28% had retching ≥4 days/week, 21% were fed >3 hours/day, and 25% had ≥4 pulmonary infections treated by antibiotics/year. Postoperatively, there was no statistical difference in the number of patients with early complications (NI: 59% vs NI-: 53%) or total CCI score (NI: 20.9 [0-44.9] vs NI-: 8.7 [0-40.6]). Duration of hospital stay was 9 days [4-57] in NI and 4 days [2-16] in NI- children (p<0.001). Median follow-up time was 4.2 [0.2-8.9] years. One year after NF vomiting, retching and regurgitation was significantly reduced in both groups (p<.05). Parental evaluation was positive, and >90% in both groups said that the child`s overall condition was improved, that their expectations were fulfilled, and that they would have chosen NF again 1, 2 and 4 years postoperatively. During the total follow-up period, recurrence of GERD was diagnosed in 12 NI and 7 NI- patients (p=.31).

Conclusion: NI children have longer duration of hospital stay after NF than NI- children. Over 90% of parents reported that their child`s well-being was improved and that they would have chosen NF again.

Disclosure of Interest: None Declared
Objectives and Study: To explore the association between lifestyle and abdominal pain-related functional gastrointestinal disorders (p-FGID) at 5 years. We also aimed to classify 5-year-old children with Irritable Bowel Syndrome into subtypes according to the adult version of the Rome III criteria.

Methods: The prospective birth cohort ALADDIN (N=470) was followed to 5 years of age. Before the child’s birth, parents answered questionnaires and families were characterized regarding lifestyle; anthroposophic, partly anthroposophic and nonanthroposophic. Prevalence of p-FGID according to Rome III criteria was measured with questionnaires and structured interviews at age 5 years. We had complete follow up data for 75% (n=354) of eligible children. Children with functional constipation (n=31), with cow’s milk protein allergy (n=1) and children with abdominal pain but who did not fulfill the p-FGID-criteria (pain frequency <1/week and/or duration <2 months, n=131) were excluded from the main analyzes. We used logistic regression to calculate the Odds Ratios (ORs) and 95% Confidence Intervals (CIs) for p-FGID at 5 years as a function of family lifestyle and adjusted for the potential confounder presence of older siblings.

Results: The prevalence of p-FGID among eligible children with complete follow up was 15% (Irritable Bowel Syndrome 8%, Functional Abdominal Pain 7%). The study population (n=191) consisted of families with anthroposophic (26%), partly anthroposophic (39%) and nonanthroposophic (35%) lifestyles and 54 of these children had p-FGID (28%). Children in families with an anthroposophic lifestyle as well as children in families with a partly anthroposophic lifestyle more often had p-FGID at 5 years (adjusted OR; 95%CI: 2.61; 1.15-5.94, p=0.022 and 2.46; 1.01-5.98, p=0.048 respectively). Mixed IBS was the most prevalent subtype of IBS.

Conclusion: A family lifestyle with anthroposophic characteristics is associated with an increased risk of p-FGID in 5-year-old children. The mechanisms are unclear but we speculate in psychological and dietary explanations.

Disclosure of Interest: None Declared
EFFICACY AND SAFETY OF TREATMENT OF ACUTE DIARRHOEA WITH LACTOBACILLUS RHAMNOSUS GG (LGG) – THE DIALAGG TRIAL
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Objectives and Study: A recent metaanalysis concluded the need for more studies to confirm efficacy and safety of the treatment of acute diarrhoea with LGG.

Aim: A randomised multicentre double blind placebo controlled study was conducted in infants and toddlers with acute gastroenteritis with the trial hypothesis that the mean duration of diarrhoea under LGG plus ORS is shorter than that for placebo plus ORS.

Methods: Patients and methods: N= 150 infants and toddlers (age 28d – 24 mo) with acute diarrhoea (>3 watery/loose stools) during the last 24h were recruited. Duration of treatment with LGG+ORS or Placebo+ORS was for a maximum of 10 days.

Results: Safety and full analysis set (FAS) included N=73 LGG and N=77 plac, per protocol analysis (PP) N= 70 LGG and N=76 plac. Time until success (<3 watery stools) in FAS: 2,7±2,5d (LGG) and 3,9±2,9 (plac) = -1,27d (95%CI -2,1 to -0,35d) (p=0,0066) and PP: 2,6±2,5d (LGG) and 3,9±3,0d (plac) = -1,27d (95%CI -2,16 to -0,37d) (p=0,0061, two-sided t-test). Patients treated with LGG had approximately one diarrhoeal stool less per day than patients in the placebo group. (p <0,05, two-sided, except day 2). Furthermore, significantly less vomiting events occurred in the LGG group at all time points from day 3 to day 9 (p < 0,05, Fisher exact test two-sided). There was no difference in adverse events.

Conclusion: LGG in addition to ORS significantly shortens the duration and severity of diarrhoea and furthermore significantly decreases vomiting events and diarrhoeal stools over time. No severe adverse events occurred in both groups.

*Study sponsored by InfectoPharm Heppenheim, Germany

INHIBITION OF GROWTH OF CLOSTRIDIUM DIFFICILE AND TIME TO RESOLUTION IN INFECTED PAEDIATRIC PATIENTS FOLLOWING USE OF A BIOACTIVE POLYPHENOL SUPPLEMENT: RESULTS OF IN VITRO AND IN VIVO STUDIES

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Objectives and Study: Use of antibiotics can cause Clostridium difficile-associated diarrhoea, which may require repeated doses of additional antimicrobial agents that can perpetuate the infection cycle. The objectives of this study were to determine (1) whether a bioactive polyphenol supplement inhibits growth of the bacterium in vitro, and (2) its capability to halt diarrhoea and eliminate C. difficile toxin in patients' stool.

Methods: Minimum inhibition concentration (MIC) was determined by standard protocol; the supplement (LiveLeaf Bioscience) was serially diluted 10 times and combined with a 150 microlitre volume of C. difficile (ATCC BAA-1803) added to agar test wells, incubated for 24 hours, and evaluated for growth. With parental consent, a prospective open-label study was conducted in a paediatric gastroenterology outpatient clinic on patients with C. difficile enterotoxin A positive chronic diarrhoea (> 3 weeks) who had not responded to standard treatment. A polyphenol-based supplement was given daily in serving sizes based upon weight. Symptoms were monitored for up to 21 days and stools retested for toxin A one week after the treatment period.

Results: The MIC for the bacterium was equivalent to one serving of the supplement. A total of 13 patients, ranging in age from 1 month to 16 years, with chronic diarrhoea and additional symptoms of abdominal pain, rectal bleeding, and growth failure, were monitored and treated. Following consumption of the supplement, diarrhoea resolved completely in 9 (69%) of the patients, with the median time to resolution within 14 days. Ten (77%) of the patients were toxin A negative in post-treatment stool sampling. Of the 3 patients who remained toxin A positive, one had complete symptom resolution, one had reduction in diarrhoea, and one with comorbidity of Crohn's disease had no improvement in symptoms. No adverse events were reported.

Conclusion: In patients with C. difficile infection, resolution of diarrhoea without antibiotics is the goal. This bioactive polyphenol supplement could inhibit growth of C. difficile at a level equivalent to one serving size. Use of this bioactive polyphenol supplement resulted in resolution of diarrhoea and elimination of C. difficile toxin A from stool cultures in the majority of paediatric patients, with no side effects. Resolution of diarrhoea and normalization of bacterial flora with this supplement make it an attractive alternative to repeated antibiotic treatments.

Disclosure of Interest: A. Dahlstrom: None Declared, H. Pavis: None Declared, N. Patel Conflict with: LiveLeaf Inc
THE EFFECTS OF BIFIDOBACTERIUM LACTIS, BIFIDOBACTERIUM LACTIS PLUS INULIN, INULIN AND PLACEBO ON THE DURATION OF DIARRHOEA IN CHILDREN: A RANDOMISED, MULTI-CENTRE, DOUBLE-BLIND PLACEBO CONTROLLED CLINICAL TRIAL

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Objectives and Study: We aim to evaluate the effect of Bifidobacterium lactis with or without inulin, or inulin alone on the duration of acute diarrhoea in children.

Methods: A prospective, multicenter, randomized, double blind clinical trial was performed in 280 children (3-60 months) with acute watery diarrhoea in Turkey. Children received oral rehydration with Bifidobacterium lactis (5x10^9 CFU) plus inulin (900 mg), B. lactis (5x10^9 CFU), inulin (900 mg) and placebo for 5 days. The primary endpoint was the duration of diarrhoea (hours). Secondary outcomes were duration of hospitalization (hours) and percentage of children without diarrhoea 72 hours after the onset of treatment. Adverse events were also recorded.

Results: In total, data from 245 children could be evaluated. The duration of diarrhoea was significantly reduced in the B. lactis plus inulin group and B. lactis comparing the inulin alone and placebo group (p<0.001). There are no statistical difference between B. lactis plus inulin and B. lactis, and also between inulin and placebo. After 72 hours, the % of children that was diarrhea-free was significantly larger in the B. lactis plus inulin and B. lactis group comparing the inulin alone and placebo group (p<0.01). Mean length of hospital stay was approximately 24-30 hours lower in B. lactis plus inulin group and B. lactis group comparing the placebo group (p<0.001). No adverse effects were noted.

<table>
<thead>
<tr>
<th></th>
<th>B. lactis and inulin n=60</th>
<th>B. lactis n=64</th>
<th>Inulin n=58</th>
<th>Placebo n=63</th>
</tr>
</thead>
<tbody>
<tr>
<td>Duration of diarrhea (hours)</td>
<td>65.7±26.7</td>
<td>67.5±24.7</td>
<td>97.6±30.1</td>
<td>94.2±42.3</td>
</tr>
<tr>
<td>Percentage of diarrhea free children at 72 hours</td>
<td>24/60 (40%)</td>
<td>25/64 (39%)</td>
<td>7/58 (12%)</td>
<td>10/63 (15.8%)</td>
</tr>
<tr>
<td>Duration of hospitalization (hours)</td>
<td>84.4±30.9</td>
<td>90.1±20.7</td>
<td>107.5±29.1</td>
<td>114.6±28.9</td>
</tr>
</tbody>
</table>
Conclusion: *B. lactis* plus inulin and *B. lactis* alone reduce the duration of diarrhoea in the same way with ~ 30 hours. There is no effect of inulin alone on the duration of diarrhoea.

PRIMARY ANTIMICROBIAL SUSCEPTIBILITY CHANGES IN CHILDREN WITH HELICOBACTER PYLORI INFECTION OVER 13 YEARS IN NORTHERN ITALY

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Objectives and Study: During the last years, the widespread use/abuse of antibiotics, particularly for respiratory tract infections, led to the increasing resistances of Helicobacter pylori (HP) infection to common antibiotics, mainly to clarithromycin that is almost doubled over the past 10 years. ESPGHAN/NASPGHAN guidelines recommend antibiotic susceptibility testing for clarithromycin before starting clarithromycin-based triple therapy in areas/populations with a known high resistance rate. The aim of the study is to evaluate the variations in primary antibiotic susceptibility over last 13 years in children with HP infection in Parma, northern Italy comparing with our previous results obtained in 1998/99.

Methods: From January 2011 to December 2012 we diagnosed by endoscopy and histological examination 74 naïve children with HP infection aged between 39 to 192 months (16 years old). Endoscopic biopsy specimens were taken in all subjects for histology following Sydney Criteria (two from the gastric antrum, and two from the gastric corpus-fundus), and microbiological culture (one from the antrum). Antimicrobial susceptibility testing were performed for ampicillin, tetracycline, metronidazole, and clarithromycin.

Results: Culture developed in 54/74 patients (74.3%) with a reduction of 10% than those performed 13 years before with no statistically significant value. Throughout the last 13 years, we obtained a significant reduction in metronidazole resistant (57% vs 33%) (p=0.014), while the clarithromycin resistance evidently increased although with no statistically significant value (16% vs 26%) (p=0.142). During these years resistance to amoxicillin has been confirmed very low or absent (3% in 1998/99 and none in 2011/2012) as well as that to tetracyclines (2% in 1998/99 and none in 2011/12); in the same way the combined resistance to metronidazole and clarithromycin together has not been changed, staying very low (8% in 1998/99 and 7% in 2011/12).

Conclusion: Comparing this study with the previous one, some changes in antibiotic resistance rate occurred over the last 13 years. Metronidazole resistance significantly decreased and that to clarithromycin increased although with no statistically significant value. Furthermore we confirmed that the resistance rate of HP to amoxicillin is very rare. Therefore before recommending HP eradication therapy, we should know either the antibiotic susceptibility of patient or the local distribution of antibiotic resistance rates to have higher successful probabilities.
Disclosure of Interest: None Declared
**Probiotic Prescriptions in Children with Acute Gastroenteritis: A Survey in Italian Inpatient and Outpatient Settings**

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**Objectives and Study:** Probiotic strains with proven efficacy (Lactobacillus GG and S. boulardii) are currently recommended by ESPGHAN/ESPID guidelines as a first line treatment for children with acute gastroenteritis (AGE) in adjunct to oral rehydration solution. Although there is a global interest in the field, little is known about practice pattern in childhood. Aim of this study was to investigate pediatricians’ prescriptions of probiotics for the management of AGE in Italian inpatient and outpatient settings.

**Methods:** Data on prescriptions were collected through an online clinical reporting form in 31 Italian hospitals and a web-survey questionnaire delivered by 185 pediatricians working in outpatient setting in different Italian regions and compared with the European standard recommendations for adherence.

**Results:** A total of 588 (228 inpatients and 360 outpatients) prescriptions of probiotics in children < 5 years with AGE were collected. Significant differences in prescribing patterns emerged. The strains recommended (Lactobacillus GG and S. boulardii) were used in 68/228 hospitalized patients and in 299/360 children seen in outpatient setting (25% vs 83%; P<0.001). Strains with a weakly recommendation (Lactobacillus reuteri, L.acidophilus LB) were prescribed in 116/228 inpatients and in 48/360 outpatients (51% vs 13%; P<0.001). No recommended probiotics were prescribed in 44/228 admitted children and in only 13/360 outpatients (20% vs 4%; P<0.001).

**Conclusion:** Primary-care pediatricians are fairly adherent to guidelines’ recommendations. In contrast, inappropriate probiotic prescriptions were more common in hospital, where usually only one probiotic strain is included in the hospital drug code. Health care policies should drive physicians’ prescriptions of probiotics.


**Disclosure of Interest:** None Declared
**Objectives and Study:** Our multicenter, randomized, prospective, controlled clinical trial in children with acute watery diarrhea showed that the duration of diarrhea was approximately 24 hours shorter in the *Saccharomyces boulardii* CNCM I-745 group, that the mean length of hospital stay was shortened with more than 36 hours and that the mean length of admission at the emergency care unit was shortened with more than 19 hours. Because of these findings, it was emphasized there could be a social and economic benefit of *Saccharomyces boulardii* CNCM I-745 in adjunction to ORS in acute infectious gastroenteritis in children.

**Methods:** We calculated direct cost related with acute infectious diarrhea treated in ambulatory care, emergency care unit and in hospitalized children. These data were extrapolated to the number of all cases of rotavirus diarrhea during one year period.

**Results:** In hospitalized children, *S. boulardii* CNCM I-745 significantly reduced the cost: 186±70 US$ vs. 242±69 US$ in the control group (p<0.001). A 19 hours reduction of emergency unit stay reduced the direct cost significantly: 48.4±16.4 US$ vs. 80.7±21.2 US$ (p<0.001). In outpatients, cost was higher in the *S. boulardii* group than in the control group: 26.8±3.9 US$ vs. 22.2±6.3 US$ (p<0.01). When we extrapolated these findings to the yearly number of rotavirus gastroenteritis in Turkey, total cost related to hospitalization and emergency care unit stay was reduced with 25% or 51 US$ per patient. In one year perspective, if *S. boulardii* would be administered to all rotavirus cases under 5 years, total cost was reduced with 23% or 11.3 US$ per patient.

**Conclusion:** The administration of *S. boulardii* CNCM I-745 to children that are treated at the emergency care of are hospitalized reduces significantly direct treatment cost. Further analysis with a potential addition of reduced indirect cost is now needed.

**References:** 1- Dinleyici EC et al. *Saccharomyces boulardii* CNCM I-745 reduces the duration of diarrhea, length of emergency care and hospital stay in children with acute diarrhea. Benef Microbes 2014 (in press)
Objectives and Study: Background: In the second year of life, milk continues to be essential part of a child's diet. Providing a milk formula designed to improve its intestinal tolerability and to maintain an adequate nutritional intake, have an effect on enteral symptom duration. **Objective:** To evaluate LFP effectiveness in children 1-2 years of age with not complicated acute gastroenteritis.

Methods: All patients at admission underwent a complete medical history and examination, stool test and Rotatest. Patients were randomized into two groups: The control group received a diet and 45 mEq/Lt rehydration solution (RS). Group 2 received the same treatment plus LFP. Evaluations at start, third and fifth day were performed. Weight, number and consistency of bowel movements, duration of diarrheic symptoms, duration of oral rehydration therapy, and anti-diarrhea diet were assessed at beginning and end of the study. SPSS Statistics (v 17.0) was used for statistical analysis. X² or Fisher's exact test and Student's test were used. Significance value was 0.05.

Results: 32 patients without dehydration were included, with a mean age of 17.2 months, of which 2 were excluded. In the 30 patients who completed the study, there were no differences in demographic characteristics. The duration of diarrheic symptoms was 3.41 days in group 1, and 2.43 in group 2 (p =0.038, CI .316-1.952). Bowel movements on third day in group 1 were 2.64, and 1.81 in group 2 (p =0.02, CI 0-0.027-1.081), on fifth day there was no difference (p =0.89). Children in group 2 at the beginning of the study had more watery bowel movements than group 1 (p =0.001). On third day, there was no difference, and at the end of the study showed more formed stools (p =0.001). RS was administrated for 3.41 days in group 1, and 2.43 in group 2 (p =0.025, CI 0.177-1.733). The days of using diet had no difference between the two groups. Number of peristaltic movements improved faster in children receiving LFP (p=0.005) and were similar at the end of the study. Body weight of group 1 had an average of -230 g at the end of the study with regard to that at admission, and group 2 had an average of +230g with respect to that at admission (p=0.43).

Conclusion: LFP shortened disease duration in one day. Bowel movement pattern significantly improved on third day when using LFP. Need of oral rehydration was shorter with LFP. LFP use prevented not only loss of weight, but contributed to its increase. Evidence obtained in the study is limited by test group size. Therefore, it is concluded that the use of LFP demonstrated to be more effective than traditional management. Of note, shortening of symptom duration is similar to that observed with other drugs. Studies with a larger number of children comparing different therapeutic options are recommended.

Disclosure of Interest: None Declared
**Gastroenterology**  
**Inflammatory Bowel Disease**  
PO-G-0185

**IMMUNOGENICITY OF 13-VALENT PNEUMOCOCCAL CONJUGATED VACCINE IN PAEDIATRIC PATIENTS WITH INFLAMMATORY BOWEL DISEASE**

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**Objectives and Study:** There are only a few studies on immune response to pneumococcal vaccines in patients with inflammatory bowel disease (IBD); all of them assessed polysaccharide vaccines only. The aim of the study was to evaluate the immunogenicity and safety of 13-valent pneumococcal conjugated vaccine (PCV13) in IBD pediatric patients compared with healthy controls.

**Methods:** This was a multi-center, prospective and controlled study on children and adolescents aged 5-18 years with IBD with no history of pneumococcal immunization or documented pneumococcal infection. The subjects for the study belonged to one of the following groups: patients with IBD on no immunosuppressive therapy (Group A), those on TNF agents or immunomodulators (Group B) and healthy controls (Group C). The study population received one intramuscular injection of PCV13. The primary outcome measure was adequate vaccine response defined as post-vaccination titer ≥0.35 µg/mL to all 13 serotypes. Geometric mean titers and geometric mean titer rises (GMTRs) were measured for all serotypes. The evidence of local and systemic adverse effects for five days after the vaccine was registered.

**Results:** A total of 178 subjects (122 patients and 56 controls) completed the study course. There was no significant difference in the rate of adequate vaccine response between IBD patients and controls measured 4-8 weeks after vaccination (90.4% vs. 96.5%, p=0.5281). Children in group A had higher GMTRs than children in group B (p = 0.0369). There were no serious adverse events related to PCV13 during the study.

**Conclusion:** PCV13 is both immunogenic and safe in pediatric patients with IBD.

**Disclosure of Interest:** None Declared
KRILL OIL IMPROVES INTESTINAL EPITHELIAL RESTITUTION AND PROTECT AGAINST AIEC ADHESION/INVASION DURING INFLAMMATION

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Objectives and Study: Inflammatory bowel disease (IBD) is a model of inflammatory disorder with a chronic disabling course. The therapeutic approach is often a real challenge for clinicians. A specific causal treatment of IBD is still not available and drugs currently used for the management of human IBD are not devoid of potentially serious side effects. Thus, the development of new treatment strategies that combine efficacy and safety is an important goal in IBD therapy. Our hypothesis is that krill oil (KO), which is rich of phospholipids, omega-3 and astaxantin and has a demonstrated anti-inflammatory activity without side effects, could be useful in flanking conventional therapies.

The aim of the work is to assess the KO efficacy in decreasing inflammatory markers and maintaining epithelial morphology and function in human intestinal epithelial cells primed with pro-inflammatory cytokines or adherent and invasive Escherichia coli (AIEC) strains.

Methods: Human colonic adenocarcinoma cell lines, CACO2 and HT29, were pre-treated with KO [100mg/ml] for 18h. Inflammation was induced by exposing cells to a cytomix (TNFα [10ng/ml] +IFNγ[250ng/ml]) for 18h or to AIEC strain LF82 (MOI 10:1 for CACO2 and 100:1 for HT29) for 3h. Quantitative PCR, immunofluorescence, western blotting, scratch test, cell death by flow cytometry and adhesion/invasion assays were used.

Results: In both cell lines, pretreatment with KO: 1) significantly reduced (p<0.05) the expression levels of IL-8 and TNFα mRNA after exposure to AIEC bacteria; 2) significantly increased (p<0.001) the epithelial restitution and decreased cell death after exposure to cytomix; 3) strongly reduced the formation of inflammatory stress fibers (F-actin polymers) and improves tight junction regulation (e-cadherin) that was disorganized after the exposure to cytomix ; 4) significantly reduced the ability of AIEC strains to adhere (p<0.05) and invade (p<0.01) intestinal epithelial cells.

Conclusion: We show for the first time that KO is able to significantly reduce inflammation, increase wound healing and recovery epithelial cell morphology. Moreover, KO protects intestinal epithelium against the immunostimulatory and pro-inflammatory activity of AIEC bacteria.

We believe that KO could be a very useful and innovative tool for the treatment of human IBD.

Disclosure of Interest: M. Costanzo: None Declared, V. Cesi: None Declared, L. Stronati: None Declared, E. Prete: None Declared, A. Negroni: None Declared, F. Viola: None Declared, F. Civitelli:
None Declared, M. Aloi: None Declared, S. Cucchiara Conflict with: Develop Registry, Johnson & Johnson
INFLAMMATORY BOWEL DISEASES CHARACTERISTICS IN CHILDREN WITH ASSOCIATED IMMUNOMEDIATED HEPATOBILIARY DISEASES: A COMPARATIVE STUDY FROM THE ITALIAN PAEDIATRIC IBD REGISTRY

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Objectives and Study: Immunemediated hepatobiliary diseases (IHBD) are reported in up to 7.8% of paediatric inflammatory bowel disease (IBD) and a distinct IBD phenotype has been suggested. This study aimed at evaluating: 1) the prevalence of IHBD in the Italian paediatric IBD population; 2) the features of patients with IHBD compared to IBD patients without IHBD.

Methods: Information were obtained from the Italian Paediatric IBD Registry from January 2009 to June 2014. Patients with at least 6 months of follow-up were considered eligible for comparison.

Results: IHBD was detected in 5.2% of the 752 patients recorded in the Registry. Thirty-six patients with IHBD (19 sclerosing cholangitis, 2 autoimmune hepatitis type 1, 14 overlap syndrome, 1 unclassified cholangitis) and 471 controls were compared. Age at IBD diagnosis, duration of IBD symptoms, sex, familiarity and other extraintestinal manifestations did not differ between patients with IHBD and controls. Compared to controls, patients with IHBD were more likely to have UC or indeterminate colitis (IC) than Crohn’s disease (CD) (UC 72.2% vs 49.5%; IC 13.9% vs 4.0%; CD 13.9% vs 46.5% p <0.00). Pancolitis was significantly more common in UC patients with IHBD than controls (80.8% vs 54.9% p 0.01) while no differences in anatomic localization and disease behaviour were found in patients with CD. Use of third line therapies, intestinal resection or colectomy were similar between patients with IHBD and controls.

Conclusion: In Italy the prevalence of IHBD in children with IBD is 5.2%. In this study, IHBD was found to be associated with the diagnosis of UC, especially with pancolitis, and IC. No other distinguishing features were found.

References: On behalf of the SIGENP IBD Group
Disclosure of Interest: None Declared
Objectives and Study: An increased incidence of Crohn’s disease has been associated with more hygienic elements of modern urban life, greater exposure to air pollution, artificial preservatives in processed foods, and antibiotics (1). Global mapping also indicates a higher rates of Crohn’s Disease in northern latitudes located in alluvial flood plains with municipalities delivering soft water. We explored the relationship of soft water in potentiating post treatment emerging contaminants in municipal water.

Methods: Using published figures of Crohn’s disease incidence in 67 community health districts from the province of Quebec, Canada, we identified units with high or very high incidence of Crohn’s to those with low or very low Crohn’s disease incidence (2). We mapped disease specific data on 57 health units to government published description of water quality in these administrative areas segregating units with high or very high water hardness (greater than 10 ppm of calcium) to those with low or very low soft water (less than 3 ppm calcium). Data were compared by Fisher’s Exact T-Test with significance defined as < 0.05.

Results: Fourteen of 21 administrative units were characterized as having soft water and high incidence of Crohn’s Disease vs. 6 of 34 units with soft water and low levels of Crohn’s, significant at a level of P < 0.0004.

Conclusion: This analysis suggests an association between municipalities with soft or very soft water and health units with a high incidence of Crohn’s disease among adults. Because of their intrinsic diversity, larger urban municipalities with >100,000 populations do not figure in the calculation. The majority of the municipalities with soft water and high Crohn’s disease incidence lie in the St. Lawrence alluvial flood plain. We are exploring the role of soft water in potentiating the influence of synthetic detergents on intestinal microbiota and/or intestinal permeability as a predisposing factor to the development of Crohn’s disease. Alternative agents could include antibiotics, heavy metals among other emerging water contaminants.

2. Pascal Michel P, St-Onge L, Lowe A, Bigras-Poulin M Brassard P. Geographical variation of Crohn's disease residual incidence in the Province of Quebec, Canada Int J. of Health Geographics.com/content/9/1/22 2010

Disclosure of Interest: None Declared
**Objectives and Study:** The pathomechanism of Crohn’s disease (CD) is not fully understood, however several data suggest that inflammation, oxidative-nitrative stress and consequential poly(ADP-ribose)polymerase (PARP) activation are involved. As PARP activation in CD has not been examined in a human setting yet, therefore our aim was to examine the colonic PARP activation in paediatric patients suffering from CD. Previously, it has been suggested that TNF-α, which is a key molecule of CD, can influence the expression of PARP in other inflammatory disorders. However, the connection of TNF-α and PARP activation is not examined in CD. Therefore, we investigated the connection between TNF-α and PARP activation in HT-29 colon epithelial cell line.

**Methods:** Colon biopsies of children with CD, with macroscopically intact (CDintact: n=7) and inflamed (CDinflamed: n=10) mucosa, and controls (C: n=12) were analyzed. Paraffin embedded sections of biopsies were immunostained with anti-PAR (end product of PARP) antibody to estimate the localization of active PARP. The amount of PAR was determined by a blinded experimenter (scoring: 1-10). PARP-1 mRNA expression was measured by real-time PCR in fresh-frozen colon tissue samples and also in TNF-α treated HT-29 colon epithelial cells.

**Results:** The amount of PAR was significantly higher in the colon tissues of CD than in the controls (CDintact vs. C, p≤0.05; CDinflamed vs. C, p≤0.001). However, there was no significant difference according to the macroscopic image (CDintact vs. CDinflamed, p=ns.). This increment correlated with the elevated Paediatric Crohn’s Disease Activity Index, the neutrophil, lymphocyte counts and the C-reactive protein. PARP-1 expression was significantly elevated in CD biopsies (CD vs. C, p≤0.05) and in TNF-α treated HT-29 cells (TNF-α vs. C, p≤0.05) compared to the controls.

**Conclusion:** PARP activation can be observed in the colon mucosa of children with CD. PARP activity correlated with the severity of intestinal inflammation and the clinical activity of CD. The elevated expression of PARP in the TNF-α treated HT-29 suggests that TNF-α is significantly involved in the regulation of PARP activation in colon epithelial cells. Further studies are required to explore the possible role of PARP in the pathomechanism of CD or its usage as therapeutic target.

**References:** Acknowledgment: This work was supported by grants OTKA-PD113022,-K105530, -PD83431, -PD105361, “Lendület” Research Grant LP008/2014 and KMR_12-1-2012-0074. Horváth E. M. is holder of the János Bolyai Research Scholarship.
Disclosure of Interest: None Declared
Objectives and Study: The identification of Crohn’s disease in children can at times be delayed when there is predominance of small bowel involvement. MR enterography (MRE) has become the new standard of care for the its identification. We have performed videocapsule endoscopy since 2006 to identify small bowel Crohn’s disease in children. MRE became routinely available in our centre in 2012. We compared the results of videocapsule studies to MRE in children to establish a diagnosis or relapse of Crohn’s disease.

Methods: A retrospective observational study was carried out at Sainte-Justine Hospital, from January 2012 to September 2014. Of 41 patients who underwent a videocapsule study to rule out active Crohn’s disease (based on clinical grounds, despite normal or non-specific upper endoscopy or colonoscopy findings), we excluded 15 patients who lacked an MRE study. Therefore, a total of 26 patients with an average age of 14.9 years (6 - 18 years) at the time of the study, 14 girls and 12 boys, were evaluated.

The capsule studies were all readblinded to the MRE results. There were no adverse events related to the capsule.

Results: 50 % (13 exams) of the MRE were abnormal. In 4.1% (3 exams) the MRE exams revealed specific ileal changes, 22.7% (5 exams) of MRE exams revealed non-specific ileal changes, 22.7% (5 exams) showed only left colonic involvement.

57.69% (15 cases) of the video capsule had significant findings typical of Crohn’s disease.

The mean interval between the two examinations was 5.3 months (1 -24 months)

For small bowel involvement only:

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<th>Study</th>
<th>normal MR enterography</th>
<th>abnormal MR enterography</th>
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<td>Normal Video capsule</td>
<td>11</td>
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<td>Abnormal Video capsule</td>
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In 11 cases the results were discordant between the 2 tests. In 9 cases with normal small bowel MRE, a videocapsule study showed typical lesions of Crohn’s disease with more than 5 deep mucosal ulcers with peripheral erythema and fibrin (5), mucosal thickening, cobblestoning, pseudopolyp formation (4) and circumferential ulceration with luminal narrowing (3) leading to the diagnosis of 4 new cases of Crohn’s disease and 4 cases of relapsed Crohn.

In 4 additional cases, videocapsule studies clearly demonstrated no Crohn’s disease while the - MRE had suspected findings.
**Conclusion:** Videocapsule endoscopy appears to be more sensitive than MR enterography in the detection of small bowel Crohn's disease in an experienced centre.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Over the past few years mucosal healing (MH) in patients with Crohn’s disease has become a discussed issue. MH has emerged as a perspective goal in clinical trials in patients with Crohn’s disease. The main aim of the study is to assess if the combination therapy infliximab (IFX) + azathioprine (AZA) is more effective than AZA therapy alone in achieving of the mucosal healing in paediatric patients with Crohn’s disease.

**Methods:** Retrospective (2004-2012) a prospective (2013) observation of newly-diagnosed paediatric patients (N=50) with Crohn’s disease in the Department of Paediatrics, University Hospital in Hradec Kralove. Based on the therapy the patients were divided into two groups: 1. Infliximab (IFX) + Azathioprine (AZA) ± corticosteroids ± 5-ASA (N=15) and 2. AZA + corticosteroids ± 5-ASA (N=35). Based on the MH were patients also divided into two groups …MH YES* and …MH NO*. MH was defined as a complete endoscopic disappearance of all mucosal ulcerations and lesions without any signs of mucosal inflammation (erythema, edema) in the terminal ileum and the large bowel. In the case of normal endoscopic findings but the histological signs of high inflammatory activity were presented the patients were classified as the …MH NO*.

**Results:** MH was observed in 47 % (8/15) patients in the combination therapy group in comparison with 17% (6/35) patients in AZA group, p = 0,04. Median dose of IFX was 5.1 mg/kg/dose. Median dose of AZA in both groups was 1.9 mg/kg/day. The interval between first and second colonoscopy was in the first group 692,70 ± 83,44 days and 774,30 ± 79,51 in the second group, p=0,35.

**Conclusion:** The combination therapy (IFX+AZA) is significantly more effective in achieving of the MH in paediatric patients with Crohn’s disease.

**Disclosure of Interest:** None Declared
ANCA AND ASCA IN > 400 CHILDREN WITH IBD-UNCLASSIFIED (IBD-U), CROHN'S COLITIS (CC) AND ULCERATIVE COLITIS (UC) - A LONGITUDINAL REPORT FROM THE PORTO PEDIATRIC IBD GROUP OF ESPGHAN

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Objectives and Study: Serology can help differentiate Crohn's disease (CD) from UC, but the bigger clinical challenge is differentiating IBD-U from isolated Crohn's colitis (CC) and UC. No study to date has longitudinally evaluated ANCA and ASCA in pediatric IBD-U as compared with CC. In this largest study to date, we aimed to explore the diagnostic utility of the serological profile in these IBD subgroups and to assess whether serology can predict disease severity and long term outcomes.

Methods: This was a multicenter retrospective longitudinal study including 406 IBD children from 19 centers affiliated with the Porto IBD-working group of ESPGHAN (mean age 10.5 ± 3.9, 221 (54%) males); 118 (29%) with CC, 142 (35%) with UC and 146 (36%) with IBD-U, classified by the Porto criteria. Median follow-up period was 2.8 [IQR 1.6-4.2] years when outcomes and the last diagnosis was recorded.

Results: The most prevalent serologic profile in IBD-U was pANCA-/ ASCA- 37 (41%), followed by pANCA+/ ASCA- 31 (34%) and pANCA-/ ASCA+ 15 (17%). They had a high PPV but very low NPV to differentiate IBD-U from either CC or UC (table). UC patients with pANCA+/ASCA- had less often mild disease at diagnosis than those negative for this profile (36 (62%) vs 22 (38%), p=0.033) and had more often severe disease course, defined as the need for calcineurin inhibitors, biologics or colectomy (25 (80%) vs 6 (20%), p=0.026). In contrast, pANCA-/ ASCA+ profile was not associated with disease progression or severity in the CC group.

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<th>Sensitivity %</th>
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<td>IBD-U vs. CC (pANCA-/ ASCA+)</td>
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<td>83%</td>
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<td>IBD-U vs UC (pANCA+/ ASCA-)</td>
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<td>CC vs UC</td>
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Conclusion: In this first comparison of serology in IBD-U and isolated CC, serology seems less accurate than previously reported when comparing UC vs. CD, with high PPV and very low NPV for disease phenotype. Moreover, whereas serology profile was predictive of severe disease course in UC, this was not demonstrated in CC, questioning the utility of serology testing in clinical practice of children with CC.

Disclosure of Interest: None Declared
INTERLEUKIN-24 IS A MODULATOR OF TISSUE REMODELING IN INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Therapies targeting cytokines of the interleukin (IL)-10 family came into focus as potential treatment strategy for IBD. IL-24, a new member of IL-10 family was suggested to be involved in immune regulation, however its role in IBD is not clarified. Thus we aimed to investigate the potential role of IL-24 in IBD.

Methods: Colonic biopsy samples from children with newly diagnosed IBD and controls (n=16/each group) were collected. Expression and localization of IL-24 and its receptor were investigated by real-time RT-PCR and immunofluorescence staining, respectively. Effect of IL-24 treatment on the proliferation and apoptosis of CCD18Co colonic fibroblast and HT-29 colonic epithelial cells was assessed by MTT-test and Annexin V and PI staining. Following IL-24-treatment the amount of tumor growth factor (TGF)-β1 was determined in CCD18Co and HT-29 cells by flow cytometry. Effect of IL-24 or TGF-β1 treatment on the collagen-I and -III expression of CCD18Co cells were measured by real-time RT-PCR. Expression of collagen-I and -III after IL-24 treatment was determined in the colonic mucosa of C57Bl/6J mice by real-time RT-PCR as well.

Results: We found elevated expression of IL-24 compared to controls in the colonic mucosa of children with IBD. Strong IL-24 receptor immunopositivity was detected in mucosal epithelial and fibroblast cells. IL-24 had no effect on cell proliferation and apoptosis, but it enhanced the production of TGF-β1 in HT-29 colonic epithelial and CCD18Co fibroblast cells. Moreover, IL-24 induced the collagen-I and -III expression of CCD18Co cells and also that of in the colonic mucosa of mice.

Conclusion: Increased expression of IL-24 in the colonic mucosa of children with IBD suggests its role in disease pathophysiology. We observed that IL-24 has a more pronounced effect on collagen production of colonic fibroblasts than TGF-β1, which was previously mentioned as a key inducer of tissue remodeling. We suggest that IL-24 promotes tissue remodeling shifted toward an excessive deposition of extracellular matrix components. However further studies are required, our data suggest that therapeutic inhibition of IL-24 may have an antifibrotic effect in patients with IBD.

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Disclosure of Interest: None Declared
ENVIROMENTAL RISK FACTORS IN PAEDIATRIC IBD ACCORDING TO THE HYGIENE HYPOTHESIS: A CASE-CONTROL STUDY

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Objectives and Study: Inflammatory Bowel diseases (IBD) are chronic, relapsing, intestinal disorders whose pathogenesis is still unknown, being the result of multifactorial agents contribution. Even if the importance of genetic predisposition has been strongly demonstrated, the primary role of environmental influence on IBD onset has been recently stressed. We investigated the impact of the emerging “Hygiene Hypothesis” (HH) in a cohort of pediatric IBD patients, in order to find a correlation between the exposure to specific environmental factors and the risk to develop both Crohn’s disease (CD) and Ulcerative Colitis (UC).

Methods: A total of 698 subjects aged 1-18 years, were enrolled between January and June 2014. Among these 262 were IBD patients, 230 were IBD healthy siblings and 171 were age- and sex-matched healthy controls (HC). All patients underwent a multi-item questionnaire including 5 different groups of potential environmental IBD risk factors: family history of IBD, perinatal period, home amenities and domestic hygiene, childhood diseases and vaccinations, infant and child diet.

Results: A positive family history of IBD was one of the strongest risk factor for developing both CD and UC (p<0.001). A lower gestational age was found to be more frequent in controls than in IBD (p=0.006), whereas a less frequent recurrence of hospitalization during the first month of life was more frequent in IBD (p=0.017), confirming that exposure to infections early in life could be protective towards IBD onset. According to the hygiene hypothesis, protective associations were found for an higher number of siblings (p<0.001), bed sharing (p=0.005), consumption of tap water (p=0.014), pet owning (p<0.001), a positive family history for intestinal parasitosis (p<0.001) and H. Pylori infection (p=0.003) and father stable employment (p<0.001). Instead family stressing events (p<0.001) were more frequently found in IBD group. Breastfeeding, with a duration > of 3 months was a risk factor for IBD (p=0.001) as well as gluten introduction in child’s diet before the 6th month of age (p<0.001) both recurring more frequently in IBD than in healthy controls. In contrast, the adherence to Mediterranean diet (p<0.001) was considered protective being less followed by IBD patients compared to controls.

Conclusion: Our work confirms that environmental factors are closely linked to IBD onset and that HH can partly explain the rise of IBD in developed countries. However, prospective studies are necessary to validate these results, in order to offer both a better disease care for patients, already suffering from IBD, and possible interventions for IBD prevention in genetically predisposed individuals.
Disclosure of Interest: C. Strisciuglio: None Declared, F. P. Giugliano: None Declared, M. Martinelli: None Declared, L. Greco: None Declared, S. Cenni: None Declared, A. Staiano Conflict with: D.M.G. ITALY, Conflict with: VALEAS s.p.a, ANGELINI, MILTE ITALIA, E. Miele: None Declared
Gastroenterology

Inflammatory Bowel Disease

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CHARACTERISATION OF THE TEMPORAL INTESTINAL MICROBIOTA COMPOSITION AND DIVERSITY IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE

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Objectives and Study: In the aetiology of IBD, including its phenotypes Crohn’s disease (CD) and ulcerative colitis (UC), intestinal microbiota has been considered to play a crucial role. However, data on paediatric cases is limited and conflicting. Here we aimed to describe the intestinal microbiota composition in a large cohort of children with newly diagnosed IBD, from active disease upon achieving clinical remission, linked to temporal composition of healthy controls.

Methods: Faecal samples were collected from newly diagnosed IBD patients, prior to bowel cleansing (t0) and at week 1, 3, 6 and 18 after initiation of therapy. Disease activity was assessed by Global-Physician-Assessment (GPA) score, substantiated by faecal calprotectin and CRP. Microbiota profiles were compared to profiles of healthy controls, collected at similar time-points. All samples were analysed by IS-pro, a validated PCR-based profiling technique.

Results: In this prospective study, performed at two tertiary centres in the Netherlands from March 2011 until now, faecal samples of 104 newly diagnosed IBD patients (70 CD, 34 CU, median 14.0 years) and 63 healthy controls (median 8.8 years) were collected through time (totally 819 samples). 95% of IBD patients were in clinical remission at t6. At t0 microbiota profiles of CD, UC and controls were distinguishable. At t0 diversity and total abundance of the phylum Firmicutes in CU were significantly higher compared to controls, (p0.003 and p0.001 respectively). At t6, total abundance of Firmicutes increased even further (p0.039). In both UC and CD, total abundance of phylum Bacteroidetes at t0 was lower compared to controls (p0.003 and p0.07 respectively). Diversity and total abundance of the phylum Proteobacteria at t0 was higher in CD compared to controls (p0.041 and p0.001 respectively). From active disease upon achieving clinical remission, overall microbiota composition changed towards normal profiles in CD, while this effect was not observed in UC.

Conclusion: Microbiota-analysis demonstrated clear differences in composition between paediatric-IBD and controls, affecting all major phyla. Changes were disease specific and reversion towards normal control microbiota was only seen for CD patients.

Disclosure of Interest: None Declared
**Objectives and Study:**
TPMT testing is recommended routinely prior to initiating treatment with thiopurines (6-mercaptopurine and azathioprine) to identify individuals who may be at risk of toxicity. TPMT can be measured either by biochemical enzyme activity (phenotype) or through genetic analysis for polymorphisms (genotype). Based on TPMT activity, patients can be classified as having normal activity (2 functional alleles of the active gene), intermediate activity (heterozygous, with one allele) and no/low activity (presumed homozygous with 2 variant deficient alleles) [1]. More than 20 different haplotypes have been described [2, 3]. In this study, we assess the phenotype-genotype correlation through analysis of exome data in an existing cohort of paediatric IBD patients. We also present a novel variant, predicted to be highly deleterious through in silico analysis.

**Methods:** Exome data from 90 paediatric IBD patients was interrogated for TPMT genetic variations and correlated with TPMT enzyme activity. Genetic variants were assessed using various bioinformatic and in silico data mining tools to annotate potential functional impact.

**Results:** Nine out of 90 patients (10%) had low enzyme activity, 81 patients (90%) normal enzyme activity and none were deficient. Interrogation of exome data found 7(8%) individuals with a low activity haplotype (TPMT *3A, *3C or *3B); 4 of these had low enzyme activity and 3 normal activity. Two of the three patients with a low activity haplotype, but normal enzyme activity developed severe drug toxicity. Of particular interest was a novel variant identified in an individual, predicted to be a highly deleterious through in silico analysis. This patient had normal TPMT enzyme activity, but developed severe drug toxicity necessitating discontinuation of the drug.

**Conclusion:** This study demonstrates the strength of next generation sequencing as a powerful tool in identifying patients who are likely to develop toxicity despite having normal TPMT enzyme levels. However, a more comprehensive genotype-phenotype profile for all coding variants is necessary for accurate interpretation and precedes routine sole use of NGS technology to guide treatment.


**Disclosure of Interest:** None Declared
Objectives and Study: Transition of adolescent IBD patients to adult health care is often troublesome. Transitional programs are designed to provide a successful transfer. Self-efficacy is important in the process of transition and reflects the level of independence that an adolescent thinks and says he has in dealing with his disease. In 2008, we developed an IBD-specific questionnaire measuring IBD-knowledge and self-efficacy, called “IBD-yourself”. The presented follow-up study aims to evaluate the success of transition in IBD patients and to assess the predictive value of “IBD-yourself” for successful transition and transfer to adult care.

Methods: This follow-up study was performed in the study population from 2008. In 2008, 50 adolescent IBD patients attending our IBD transition clinic were recruited to complete the “IBD-yourself”. In 2013, when all patients had been transferred to an adult gastroenterologist, these patients were asked to participate in this study. First, an index scoring system was developed reflecting the outcome of transition based on a) adherence to visits to the outpatient clinic b) adherence to therapy and c) qualitative evaluation of transition by the patient. Total scores reflected successful-, moderately successful- or failed transition. Secondly, the relationship between “IBD-yourself” and success of transition was studied by comparing the domains of the “IBD-yourself” to the outcome of transition. Additionally, confounding factors (demographic and disease factors) were studied in relation to success of transition.

Results: Informed consent was obtained in 36 out of 50 patients. Transition was successful in 24 (66.7%), moderately successful in 11 (30.6%) and failed in 1 patient. Comparing success of transition to the “IBD-yourself” showed that adolescents with successful transition had significantly higher scores only on the domains “actual behavior medication use” and “actual behavior outpatient clinic”. Ethnicity, age at diagnosis and transfer, IBD type, transfer to a regional hospital or the Erasmus MC or presence of a transfer letter were of no importance for success of transition. Clinical remission at time of transfer was associated with successful transition. Boys had higher rates of successful transition, while higher educational level and divorced parents appeared to have a negative impact on success of transition.

Conclusion: In this study we have developed a scoring system reflecting the outcome of transition. The “IBD-yourself” questionnaire did not seem predictive of successful transition. We showed that 67% of the adolescents had a successful transition after attending our IBD transition clinic.

Disclosure of Interest: None Declared
Objectives and Study: The biological therapy audit aims to measure efficacy, safety and use of anti-TNFα therapy in patients with inflammatory bowel disease (IBD) in the UK.

Methods: A prospective audit; all UK paediatric IBD (PIBD) teams providing biological therapy were asked to identify patients starting biological therapy during 12/9/11-28/4/14. Disease severity was assessed using Physician Global Assessment (PGA) +/or Paediatric Crohn’s Disease Activity Index (PCDAI).

Results: 22 of 25 (92%) UK specialist PIBD centres plus 8 additional UK paediatric centres submitted data for analysis. 524 patients were included; 429 Crohn’s disease (CD), 76 ulcerative colitis (UC) and 19 IBD unclassified (IBDU). Commonest starting indication was active luminal CD 78% (355/458) or chronic refractory UC/IBDU 57% (58/102). Most patients had concomitant co-immunosuppression (thiopurine or methotrexate) at biologic start; 79% (386/488) infliximab (IFX) and 78% (58/74) adalimumab (ADA). 429 CD datasets were analysed further (267 male); median age at diagnosis 12 years (IQR 9, 14). 396 had initial treatment with IFX and 63 with ADA; 30 CD patients received both. Median time from diagnosis to treatment 1.42 years (IQR 0.63-2.97). At initial treatment, PGA was mild 8%, moderate-severe 92% (N=179); median PCDAI score (N=255) was 28 (IQR 20, 38). This suggests disparity between PGA vs PCDAI severity scoring; PCDAI implies many with mild disease but 92% moderate-severe on PGA. Where induction response was recorded, 77% CD patients had response and 65% gained remission. Children with CD receive biological therapy significantly earlier in disease course than adult CD; 1.42 vs 5.23 years (p<0.001).

1389/1414 IFX treatments seen for follow up at some point; 10% (32/316) CD patients had ≥1 adverse event. No deaths or malignancies were recorded.

Surgery rates 6 months pre/post initiation were comparable; 7%/5% (N=524). Perianal abscess drainage was significantly less common in CD after biologic start 26% (27/102) vs 7% (3/42) after (p=0.01).

Conclusion: Our audit suggests biologics are generally safe and effective treatments for IBD but the current length of follow up of this national cohort is relatively short. Disparity between disease severity scoring tools needs to be addressed, perhaps with weighted PCDAI. Adverse events are uncommon but loss of response is an important clinical issue; longer term follow up data than this is required.
Disclosure of Interest: None Declared
**Objectives and Study:** Exclusive Enteral nutrition (EEN) is recommended as first-line therapy for pediatric Crohn’s disease (CD) (1). It has been shown to be superior to steroids in inducing mucosal healing, with comparable clinical remission rates (2).

Our aims were:
1. To compare short- and long-term outcomes of CD patients initially managed with EN versus corticosteroids, notably clinical remission, linear growth and steroid avoidance.
2. To evaluate differences in response to EN therapy depending on disease location using the Paris classification (3).

**Methods:** A single centre, retrospective analysis (1985 to present) of 229 pediatric patients with CD receiving either EEN (n=153) or steroid induction therapy (n=76). EEN was used for a 12 week induction, followed by EN (50% total daily calories) + regular diet as maintenance. Disease activity was assessed at week 0, 8, 26, 52 and at 24 and 36 months. Clinical remission was defined by PCDAI<10. Height z-scores were calculated based on WHO charts. A propensity analysis by logistic regression with nearest-neighbour matching, a 1:2 replacement, Caliper = .15 (SD of estimated propensity score) was used to create comparable groups to examine effectiveness of EEN versus steroid therapy over time.

**Results:** There were no significant differences across disease locations based on response to EN therapy at 8 weeks, length of time on EN or remission status at 1 year. EEN (n=69) and corticosteroid groups (n=70) were then matched on baseline characteristics (gender, age, weight, and height, PCDAI, and Paris disease location), using a propensity analysis to maximize group comparability. Patients treated with EEN were more likely to be in clinical remission at 8 weeks (68% vs 85%, p=0.03) Compared with steroids, EEN showed a significant positive impact on linear growth (height z-score over three years follow-up, p=0.004). Initial EEN therapy significantly decreased the risk of exposure to corticosteroids: EEN propensity matched patients remained steroid-free over 1 and 3 years follow-up in 76% and 66%, respectively.

**Conclusion:** Long-term success of EN (length of time, or remission rates at 1 year) was not related to Paris disease location. EEN therapy was associated with more favourable outcome during induction of remission as well as over time, due to significant changes in linear growth and avoidance of corticosteroids over a 3-year follow-up period.

**References:**
3. Levine et al. IBD 2011

**Disclosure of Interest:** J. Van Limbergen Conflict with: Aptalis, Janssen, Abbvie, Nestle, A. Grant: None Declared, N. Griffin: None Declared, G. Mahdi: None Declared, M. Rashid: None Declared, T. Otley: None Declared
**Objectives and Study:** Iron deficiency anaemia is one of the most common systemic manifestations in patients with Inflammatory Bowel Disease (IBD) and studies showed a negative impact in the quality of life. Current intravenous (IV) infusions seem to be safe and well tolerated according to adult studies, but data concerning childhood are scarce and the best iron formulation is not completely established. The primary objective of the study is to document the safety of treatment with iron carboxymaltose infusions when compared with iron dextran in the correction of anaemia.

**Methods:** We conducted a retrospective, non-randomized, case-control study in IBD paediatric patients of the Department of Gastroenterology at Addenbrookes hospital, with iron deficiency anaemia submitted to treatment with iron carboxymaltose (cases) and iron dextran (controls). The statistical analysis was performed using STATA13® and data were presented as mean±SD. Chi-square and Fisher’s exact test were used to compared adverse reactions between 2 treatments and two sample t-test to compare the mean values of Hb after treatment between the 2 iron infusions. A CI of 95% and a statistical significance of <0.05 were assumed.

**Results:** Clinical files of 38 treatments with IV iron (iron carboxymaltose:18; iron dextran:20) were analyzed. Patients having an iron infusion with iron carboxymaltose had mean age of 13,0 years old (SD±3,2), 9 were male (50%) and the majority had a diagnosis of Crohn’s disease (CD) (CD:77,8%; Ulcerative colitis (UC): 16,7%, IBD unclassified (IBD-U): 5,5%). The mean Hb before treatment was 92,3±23,3 g/l, with a mean ferritin of 8,1± 8,2. After treatment an increase in Hb was identified (Mean Hb 124,8±11,3g/l). Only one patient had an adverse reaction (6,3%) after the treatment, characterized by pruritus in arms and legs. The control group treated with iron dextran patients had a mean age of 12,7±3,6, 13 were male (65%) and the majority had similar to the previous group a diagnosis of CD (CD: 80%; UC: 10%; IBD-U: 5,5%). The mean Hb before treatment was 103,3±18,8 g/l, (mean ferritin of 16,24± 20,7 ug/dl) and after treatment was 122,3±10,9 g/l. Four patients (22,2%) experienced adverse reactions: 2 anaphylaxis, 1 with urticarial rash and 1 with mild temperature. When comparing the 2 treatments for the number of adverse reactions, no statistical significance was identified (p:0.189). No differences in mean Hb after treatment were found (p:0,53).

**Conclusion:** This study shows that treatment with iron carboxymaltose has no disadvantages when compared with iron dextran, for adverse reactions and improvement in Hb. As iron carboxymaltose infusion requires fewer infusions and a shorter length, it may become the treatment of choice for patients and providers.
Disclosure of Interest: None Declared
DE NOVO INFLAMMATORY BOWEL DISEASE FOLLOWING PAEDIATRIC LIVER TRANSPLANTATION: A CASE SERIES OF THREE PATIENTS AND WORLD LITERATURE REVIEW.

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1 Paediatric Gastroenterology Department, Bristol Royal Hospital for Children, Bristol, 2 Department of Paediatric Gastroenterology and Nutrition, Royal Hospital for Sick Children, Edinburgh, 3 Paediatric Liver Unit, Birmingham Children's Hospital NHS Foundation Trust, Birmingham, 4 Paediatric Gastroenterology Department, Bristol Royal Hospital for Children, Bristol, United Kingdom

Objectives and Study: Following solid organ transplantation (SOT), recurrent and de novo IBD have been described despite immunosuppressive therapy. The majority of de novo IBD cases in adults occurred post liver transplantation (LT) (136/175) with 96/136 patients originally transplanted for sclerosing cholangitis (SC) or autoimmune hepatitis (AIH). In paediatrics, 14 cases of de novo IBD have been described post liver, heart and renal transplant. 9 cases have been described post LT (3/9 cases transplanted for SC/AIH). Various risk factors have been implicated in the development of post-transplant IBD. Herein, we describe 3 cases of de novo IBD post LT for causes other than SC/AIH.

Methods: Case 1 was the index case and the other 2 patients were identified through an electronic search of the Birmingham Liver Unit Paediatric Transplant database (782 LT patients between 1983 and 2014). Medline and Embase were searched for “de novo inflammatory bowel disease” and “transplantation”. The search was extended by scanning reference lists of related articles and free text web search. A total of 46 articles were included in the systematic review.

Results: 2 patients were originally transplanted for α1 antitrypsin deficiency and 1 for extra-hepatic biliary atresia. Risk factors for the development of post LT IBD are shown in table 1. Mean age at the time of de novo IBD diagnosis was 7.3 years (range 3-11 years) with a mean of 4.6 years post LT. Diarrhoea was the presenting symptom in 2 patients and intermittent rectal bleeding in 1. IBD diagnosis was based on Porto criteria. The patients underwent on average 2.6 upper and/or lower GI endoscopies prior to diagnosis, while the time of presentation to diagnosis varied from 3 months to 1 year. Crohn’s Disease was diagnosed in 2 patients and IBD-unclassified (IBDU) in 1. Infliximab was used in 1 patient while the other 2 were treated with 5-aminosalicylic acids. All patients were in clinical remission at last follow-up.

<table>
<thead>
<tr>
<th></th>
<th>Case 1: CD</th>
<th>Case 2: IBDU</th>
<th>Case 3: CD</th>
</tr>
</thead>
<tbody>
<tr>
<td>CMV mismatch (donor / recipient)</td>
<td>-ve/-ve</td>
<td>+ve / -ve</td>
<td>-ve / -ve</td>
</tr>
<tr>
<td>CMV infection post LT</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Acute / Chronic Rejection</td>
<td>No / Yes</td>
<td>No / No</td>
<td>No / No</td>
</tr>
<tr>
<td>Biliary stasis</td>
<td>No</td>
<td>No</td>
<td>No</td>
</tr>
</tbody>
</table>
### PMHx of Autoimmunity
No

### FHx of Autoimmunity
No

### Immunosuppression at presentation with de novo IBD
<table>
<thead>
<tr>
<th></th>
<th>Tacrolimus, Prednisolone, MMF</th>
<th>Cyclosporine</th>
<th>Cyclosporine</th>
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</thead>
</table>

### Immunosuppression after diagnosis with de novo IBD
<table>
<thead>
<tr>
<th></th>
<th>Tacrolimus, Prednisolone, AZA</th>
<th>MMF, Prednisolone</th>
<th>MMF, Prednisolone</th>
</tr>
</thead>
</table>

### Other IBD Tx following diagnosis
Infliximab  Mesalazine  Mesalazine

**Conclusion:** *De novo* IBD does occur following liver transplantation in children but is rare. *De novo* IBD should be considered in the differential diagnosis of chronic diarrhoea post-transplant.

**Disclosure of Interest:** None Declared
Objectives and Study: The relationship between celiac disease and inflammatory bowel disease (IBD) is controversial. Our aim was to determine the celiac disease in newly diagnosed children with IBD and to analyze frequency of elevated tissue transglutaminase antibodies (tTG) and histological signs of celiac disease at the time of diagnosis of IBD.

Methods: We have investigated frequency of celiac disease, villus atrophy and tTG in the cohort of the Hungarian Pediatric IBD Registry. A total of 296 patients with IBD were registered between January 1st of 2012 and December 31st of 2013 (CD: 188, UC: 89; IBD-U: 19). Previously diagnosed celiac disease, level of tTG antibodies; macroscopical and microscopical appearance of duodenum were recorded at registration of newly diagnosed IBD patients.

Results: At the time of diagnosis 7 patients had celiac disease (2.4%) (Crohn disease: 5, ulcerative colitis: 1, IBD-Unclassified 1). Two-hundred and five patients had tTG screening at the time of diagnosis, 9 (3%) of them had positive result. Five children were known patients with celiac disease without any sign of celiac disease at duodenoscopy at the time of diagnosis of IBD. The rest of the children with positive tTG had no villous atrophy, intraepithelial lymphocytosis (IEL) or crypt hyperplasia. Furthermore, 9 children had histological symptoms of celiac disease. Villous atrophy was found in 6 (2 partial villous atrophy) children (2[M1] %) with Crohn's disease, IEL with cryptitis was described in one IBD-unclassified case and one patient with ulcerative colitis had villous atrophy with IEL.

Conclusion: Celiac disease seems to be more frequent in children with IBD (2.4%), than in healthy children (1.4%) in Hungary. Elevated tTG may be a non-specific phenomenon in IBD, and villous atrophy may be a sign of inflammation in Crohn's disease. As a result the diagnosis of celiac disease during the course of IBD can be a challenge.

Disclosure of Interest: None Declared
HISTOLOGICAL IMPROVEMENT AFTER INDUCTION THERAPY WITH INFlixIMAB PROVIDE PROLONGED CLINICAL REMISSION DURING MAINTENANCE THERAPY IN CHILDREN WITH CROHN’S DISEASE.

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1Children's Memorial Health Institute, Warsaw, Poland

Objectives and Study: Recently, so-called "deep remission" has become a conceptual, more "extended" goal that contribute to achievement of long-term clinical remission and may even alter the long-term natural history of the disease in selected patients. Since data on that issue are limited, especially in pediatric population, the aim of this study was to assess impact of histological healing during biological therapy for maintenance of Crohn disease (CD) remission.

Methods: 33 patients aged 16.7±4 years with moderate to severely active CD who had clinical response following induction therapy with infliximab (IFX) and continued with maintenance therapy during 1 year were included into the study. Colonoscopy and gastroscopy with samples collection were performed in all patients at baseline (week 0), after three injections of IFX (week 10), and after 1 year of maintenance therapy with IFX. Histological changes were evaluated with numerical scoring system (0-no inflammation; 1-nonactive inflammation; 2-crypt distortion, abscesses; 3-active inflammation, ulcerations). Histological scorings at week 0 and week 10 were compared between 2 subgroups: patients with remission at week 52 present (n=26) vs. patients with no remission (n=7). Discriminant ability was assessed with ROC curve analysis.

Results: Neither histological scoring at week 0 nor at week 10 did not differ significantly between subgroup with remission at week 52 present vs. subgroup with no remission, whereas difference between scoring at week 0 and at week 10 was significantly higher in subgroup with remission. Area under ROC curve for this parameter (scoring week 0 – scoring week 10) was 0.76 and optimum cut-off point greater or equal 2 discriminate subgroups with sensivity 0.62 and specificity 1.

Conclusion: Histological improvement after induction therapy with at least 2 points provides prolonged clinical remission, whereas 40% patients with less histological improvement have CD flare during maintenance therapy with IFX.

Disclosure of Interest: None Declared
AZATHIOPRINE BIOTRANSFORMATION IN YOUNG PATIENTS WITH INFLAMMATORY BOWEL DISEASE: CONTRIBUTION OF GLUTATHIONE-S TRANSFERASE M1 AND A1 VARIANTS

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1 University of Trieste, 2 Institute for Maternal and Child Health IRCCS Burlo Garofolo, 3 Sanitary Services Agency 1, Trieste, 4 Centro di Riferimento Oncologico, IRCCS, Aviano (Pordenone), Italy

Objectives and Study: Azathioprine (AZA) continues to be first-choice approach to maintain remission for young patients with IBD; however AZA efficacy displays significant interindividual variability. Genetic variants of enzymes involved in AZA biotransformation TPMT and GSTM1 are associated with its pharmacokinetics and efficacy in young patients with IBD; however, the role of GSTA1, known to activate AZA in vitro, has not been explored in patients yet. Therefore, the objective of this study is to evaluate the contribution of candidate genetic variants TPMT rs1142345, GSTM1 deletion and GSTA1 rs3957357, involved in AZA biotransformation, on AZA efficacy and pharmacokinetics in young patients with IBD.

Methods: AZA doses, metabolites and clinical effects were assessed after at least 3 months of therapy. AZA dose was titrated on therapeutic efficacy (remission and adverse effects). Clinical efficacy was defined as disease activity score below 10. AZA metabolites thioguanine nucleotides (TGN) and methylmercaptopurinenucleotides (MMPN) were measured by HPLC-UV. Candidate genetic variants were determined on patients' DNA by PCR based assays.

Results: 114 young IBD patients (female 47.4%, Crohn’s disease, CD, 55%, median age 15.1, interquartile range, IQR, 12.4-17.2) were enrolled and 257 measurements of AZA metabolites were performed (median 2 per patient, IQR 1-3). Clinical efficacy was better in ulcerative colitis (UC) than in CD patients (76% vs 63% responders, p=0.015, linear mixed effect model, LME). For the pharmacological variables, TGN/dose ratio at the first evaluation was higher in responders to AZA (p=0.003, ANOVA). For the genetic variants, TPMT (4.6% of patients) was associated with increased TGN, TGN/dose ratio and decreased MMPN, as well established. GSTM1 deletion (57.9% of patients) was associated with 18.6% decrease in TGN/dose ratio (p=0.011, LME) and 15.4% decrease in clinical efficacy (p=0.020, LME). GSTA1 variant (12.3% of patients) showed a trend for an association with decreased clinical efficacy (p=0.049, LME), however no significant effect on AZA pharmacokinetics was found.

Conclusion: GSTM1 deletion was more frequent among patients not responding to AZA treatment, possibly related to the reduced concentration of AZA active metabolites already described (1). GSTA1 variant was more frequent in AZA non-responders, however no significant effect for GSTA1 could be detected on AZA pharmacokinetics requiring further investigation in a larger patients’ cohort.

References: (1) Stocco et al., Inflamm Bowel Dis 2007
Disclosure of Interest: None Declared
**Objectives and Study:** The aim of the study was to compare the effectiveness of metronidazole and rifaximin in the treatment of *Clostridium difficile* infection (CDI) in pediatric patients with inflammatory bowel disease (IBD).

**Methods:** It was a prospective, double-blinded, randomized trial of children aged 12-18 years with IBD. Crohn’s disease (CD) and ulcerative colitis (UC) were diagnosed according to Porto criteria. CDI diagnosis was based on a positive stool VIDAS® *Clostridium difficile* toxin A/B ELFA (bioMerieux, France) test. Patients were randomly assigned to receive metronidazole or rifaximin for 14 days in doses based on weight. Stool samples were collected before and 4 weeks after the end of treatment.

**Results:** 26 patients were enrolled (mean age 14.3 years), including 9 with CD and 17 with UC. 14 received metronidazole and 12 received rifaximin. No statistically significant differences were found in age, gender and disease type between the study groups. 4 weeks after the end of treatment *Clostridium difficile* toxins were found in 5/14 (36%) patients in metronidazole group and in 4/12 (33.3%) patients in rifaximin group (p=NS).

**Conclusion:** Metronidazole and rifaximin are equally effective in the treatment of CDI in pediatric patients with IBD.

**Disclosure of Interest:** None Declared
**Objective and Study:** Primarily, our aim was to assess health-related quality of life in pediatric patients diagnosed with Inflammatory bowel disease (IBD) living in Minho (Portugal), using IMPACT-III© questionnaire. Secondly, to compare the obtained results from the "body image" domain of IMPACT-III© with a healthy control group.

**Methods:** A cross-sectional study was performed applying the IMPACT-III© questionnaire to pediatric IBD patients who met the necessary criteria: having IBD diagnosis for more than 6 months and age above 9 years. The control group (without IBD) was created by pairing each individual with 4 others of the same age and gender, in a convenience sampling process.

**Results:** From an initial sample of 137 pediatric IBD patients (Crohn’s Disease (CD) = 94, Ulcerative Colitis (UC) = 40 and IBD-undetermined (IBD-U) = 2), 59 patients met the IMPACT-III© criteria and 32 agreed to fill out the questionnaire, corresponding to 54.2% of the eligible group. No significant differences were found between the total score and domains between IBD types (CD (Mean (M) ± Standard Deviation (SD) = 136.9±17.2); UC (M±SD=135.0±28.2; t(5.892)=0.154, p=0.88). When comparing between domains, systemic symptoms (M±SD=82.9±16.6%) and social functioning (M±SD=83.2±11.6%) had the higher scores, unlike the emotional functioning (M±SD=70.5±17.3%) and treatment/interventions (M±SD=69.0±19.1%) that scored lower. It was also found that age at completion of the questionnaire negatively related to body image (ρ=-0.404, n=32, p=0.022), but no relation was found between body image and delayed diagnosis (ρ=-0.178, n=32, p=0.330) or time after diagnosis (ρ=-0.127, n=32, p=0.489). Comparing body image between groups, no significant differences were found between the diagnosed group (M±SD=11.8±2.4, n=32) and control group (M±SD=11.4±2.1, n=128, t (158) =-0.798, p=0.43). In diagnosed group, gender does not influence the score and age affects it negatively (B=-0.427; β=-0.432; p=0.014). In the control group, male gender obtained better results (B=1.281; β=0.304; p=0.001) and no age influence was found.

**Conclusion:** IMPACT-III© questionnaire was easily understood and has good internal consistency. The health-related quality of life found in this study was similar to that found in literature. Regarding body image domain, despite the absence of significant differences between groups in final scores, a tendency analysis showed that different variables influence the results in each group. Regardless of illness duration and diagnosis delay, older teenagers with IBD, possibly due to a different
understanding of the disease, tend to have worse body image and the difference between genders tends to fade.

Disclosure of Interest: None Declared
**Inflammatory Bowel Disease**

PO-G-0207

Efficacy and Safety of Adalimumab for Paediatric Crohn’s Disease – Systematic Review.

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1 Department of Gastroenterology, Hepatology and Feeding Disorders, The Children’s Memorial Health Institute, 2 Department of Pediatrics, The Medical University of Warsaw, Warsaw, Poland

**Objectives and Study:** The aim of this study was to systematically evaluate the published evidence on the efficacy and safety of adalimumab for CD treatment in children.

**Methods:** MEDLINE, EMBASE, the Cochrane Library and abstracts from the main gastroenterologic meetings in the last 5 years were systematically searched up to September 2014 for interventional and observational studies.

**Results:** 13 studies performed in 12 study populations (1 randomized controlled trial, 11 case series) altogether including 731 pediatric patients were found. (tab.1) The studies differed from each other with respect of patients characteristics (eg. percentage of Infliximab naïve patients, CD duration, site of the disease), induction and maintenance ADA doses, treatment duration and follow-up period. The remission rates evaluated at the end of the study ranged from 23% to 97%. Severe adverse events (included 2 deaths in one study) were estimated from 0% (6 studies, n=131, follow-up maximum 1 year) to 45% at the 5 year follow-up study.

<table>
<thead>
<tr>
<th>Study ID</th>
<th>Study design</th>
<th>Patient s No</th>
<th>Age (±)</th>
<th>mean PCDAI at entry</th>
<th>Adalimumab Dose</th>
<th>Duration of therapy (mo)</th>
<th>Clinical remission (pts %)</th>
<th>Serious adverse events (pts %)</th>
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<td>Retro CS</td>
<td>37 ± 14.7</td>
<td>&gt;30</td>
<td>NA</td>
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<td>10</td>
<td>62</td>
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<tr>
<td>Jacob 2013</td>
<td>Retro CS</td>
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<td>NA</td>
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<td>Retro CS</td>
<td>40 ±12.6</td>
<td>±25</td>
<td>Induction 160/80 N=55% Maintenance 40 N=100%</td>
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<td>97</td>
<td>50</td>
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<td>NA</td>
<td>Induction</td>
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<td>Age</td>
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<td>N (%)</td>
<td>Maintenance</td>
<td>N (%)</td>
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<td>2010</td>
<td>CS</td>
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<tr>
<td>Rosh</td>
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<td>115</td>
<td>±15.8</td>
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<td>80/40</td>
<td>N=44%</td>
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<td>4%</td>
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<td>50%</td>
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<tr>
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<td>Week 3</td>
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<tr>
<td>Noe 2008</td>
<td>Prosp CS</td>
<td>7 ±15.7</td>
<td>12</td>
<td>-</td>
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<tr>
<td>Viola 2009</td>
<td>Prosp CS</td>
<td>23 ±16</td>
<td>?</td>
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<td>Hyams 2012</td>
<td>RCT</td>
<td>188 ±13.5</td>
<td>&gt;30</td>
<td>52</td>
<td>33,3</td>
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<td>Rosh 2014</td>
<td>as above</td>
<td>as above</td>
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</tbody>
</table>

CS-case series, RCT- randomized controlled trial, PCDAI- Pediatric Crohn Disease Activity Index, NA-non available

**Conclusion:** There is still a paucity of high-quality evidence available on effectiveness and safety of adalimumab for paediatric CD.

**Disclosure of Interest:** None Declared
A COMPREHENSIVE ASSESSMENT OF NOD PATHWAY VARIATION IN PAEDIATRIC IBD
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Objectives and Study: Next generation sequencing technology has facilitated the analysis of rare and private variations. It is known that rare and private mutations have a stronger impact in the susceptibility of complex diseases compared to common variants (1). For rare mutations, single variant association testing has limited power because such large sample sizes are required. In order to overcome this problem, several statistical tests in which rare and common variants are jointly analysed within a gene or a region have been developed. We present the application of the joint test SKAT-O for detecting association with IBD affection status using 132 PIBD patients and 56 controls for 40 genes across the NOD receptor pathway on data derived from next generation sequencing.

Methods: Cases and controls were recruited through tertiary referral clinics at University Hospital Southampton. For all exomed patients, genomic DNA was extracted using the salting out method and the samples were exome sequenced at the Wellcome Trust Centre in Oxford. Data were aligned and tested for quality control by using the in-house pipeline and customised scripts. Variants different from the reference human genome (hg19) were annotated for each individual and retained in the analysis if depth >4 and Phred > 20 to increase the quality of the call.

Results: Ten genes within the NOD receptor pathway have been previously implicated by GWAS in IBD. Mutations were found in all but two genes involved in the pathway (CCL5 and CCL2). Despite the small sample size, association analysis revealed five genes associated with disease status at p<0.05 with SKAT-O test prior to Bonferroni correction. All five genes play key roles in innate immunity.

Conclusion: The field of statistical tests dealing with rare variant analysis is currently an active field of research. SKAT-O test suggested an association with IBD for previously unreported genes. Currently we are conducting functional assays on the specific patient samples where the SKAT-O test suggested a possible abrogative gene involved in IBD.


Disclosure of Interest: None Declared
EFFECT OF ADALIMUMAB ON CLINICAL LABORATORY PARAMETERS IN PAEDIATRIC CROHN’S DISEASE PATIENTS FROM IMAGINE 1

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Objectives and Study: Adalimumab (ADA) was shown to be effective for inducing and maintaining clinical remission in children with moderately to severely active Crohn’s disease (CD) in IMAGINE 1. Changes in laboratory values indicative of systemic inflammation were evaluated.

Methods: Patients (pts), 6-17 years-old, with baseline (BL) Paediatric CD Activity Index >30 received open-label induction ADA at weeks (wks) 0/2 by body weight (<40kg, 80/40mg; ≥40kg, 160/80mg). At wk 4, pts were randomized to double-blind (DB) higher-dose (HD) ADA (<40 kg, 20mg every other wk [eow]; ≥40kg, 40 mg eow) or lower-dose (LD) ADA (<40 kg, 10 mg eow; ≥40 kg, 20 mg eow) for 48 wks. The proportion of pts with abnormal values at BL, who later achieved normal values at wk 52 were evaluated. Albumin levels of >3.4 g/dL, platelet counts of <500x10^9 platelets/L, and CRP levels of <1 mg/dL were considered normal. Mean change in hemoglobin from BL to wk 52 was also assessed. Last observation carried forward (LOCF) was used for missing data.

Results: Overall, HD ADA-treated pts with abnormal laboratory values at BL achieved normal albumin levels (75%), platelet counts (53%), and CRP levels (64%) at wk 52 (Table). HD ADA also improved mean hemoglobin levels at wk52 (mean change from BL LD -0.96 v. HD 3.43 g/L, p<0.001).

<table>
<thead>
<tr>
<th>Normalization of laboratory values in pts with abnormal values at BL (LOCF)</th>
<th>Wk 52</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LD</td>
</tr>
<tr>
<td>Albumin (N=36)</td>
<td>6/24 (25.0)</td>
</tr>
<tr>
<td>Platelet count (N=75)</td>
<td>11/30 (36.7)</td>
</tr>
<tr>
<td>CRP (N=103)</td>
<td>28/53 (52.8)</td>
</tr>
</tbody>
</table>

**p<0.01 for HD v. LD by Pearson’s chi-square test and Fisher’s exact test
Conclusion: ADA led to normalization of laboratory values in clinically meaningful proportions of pts who had abnormal albumin levels, platelet counts, and CRP levels at BL in IMAGINE 1. Improvements in hemoglobin levels were also observed at wk 52.

References: 1.Hyams et al Gastroenterol 2012;143:365

INFLIXIMAB TROUGH LEVELS ARE ASSOCIATED WITH DISEASE ACTIVITY IN PAEDIATRIC INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Low serum trough levels (TLs) of infliximab (IFX) and antibodies to IFX (ATIs) are associated with loss of therapeutic response in adults with inflammatory bowel disease (IBD) receiving IFX. Until now, pediatric data are scarce. Therefore, we aimed to cross-sectionally investigate the association between ATIs and IFX TLs, and clinical and biochemical disease activity in children receiving IFX for IBD.

Methods: Children aged <18 years receiving IFX maintenance treatment for Crohn’s disease (CD) or ulcerative colitis (UC) at three Dutch hospitals were included. Prior to two consecutive IFX infusions, IFX TLs and ATI levels were measured. Clinical disease activity was determined by PCDAI and PUCAI, for CD and UC, respectively. Biochemical disease activity was assessed by serum CRP and fecal calprotectin (FC). Clinical remission was defined as a PUCAI or PCDAI score of <10. Therapeutic range of IFX was considered 3-7µg/mL.

Results: 39 patients were included (31 CD; 16 females). Median age was 15.0 years. Median IFX TL was 3.5µg/ml [IQR 2-7]. Subtherapeutic and supratherapeutic TLs were found in 38.5% and 23.1% of children, respectively. ATIs were detected in 4 patients. A correlation was found between IFX TL and CRP [r_s=-0.51; p<0.01] and FC [r_s=-0.49; p<0.01]. However, when only clinical disease activity was considered, no difference in median TL was found between remission and active disease (resp. 3.5µg/ml [IQR 2-5] and 2.3µg/ml [IQR 0.3-4.6]; p=0.2).

Conclusion: IFX TLs are related biochemical markers of disease activity. This could provide a rationale for monitoring TLs in children receiving IFX for IBD.

Disclosure of Interest: D. Hoekman: None Declared, J. Brandse Conflict with: served as a speaker for Abbvie, MSD and Takeda, T. de Meij: None Declared, T. Hummel: None Declared, M. Löwenberg Conflict with: served as speaker for Abbvie, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme and Tramedico., M. Benninga Conflict with: Janssen Biologics, G. D’Haens Conflict with: Abbott Inc, Jansen Biologics, Given Imaging, MSD, Dr. Falk, Photopill., Conflict with: Abbott Laboratories, Actogenix, Centocor, Cosmo, Engene, Ferring Pharmaceuticals, GlaxoSmithKline, Jansen Biologics, Millenium Pharmaceuticals, MSD, Novonordisk, PDL Biopharma, Pfizer, SetPoint, Shire, Takeda, Teva, UCB, Conflict with: served as a speaker for Abbott Inc, Tillotts, Tramedico, Ferring, MSD, UCB, Norgine, Shire, A. Kindermann Conflict with: Janssen Biologics
INTERMITTENT VANC
OMYCIN AND GENTAMICIN AS EXCLUSIVE THERAPY FOR SEVERE
VERY EARLY ONSET INFLAMMATORY BOWEL DISEASE
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Objectives and Study: Very Early Onset Inflammatory Bowel Disease (VEO-IBD) is a unique subtype of IBD and many patients are resistant to standard therapy. VEO-IBD is more often associated with monogenic etiologies, particularly those with infantile onset. While children with both PSC and IBD treated with vancomycin have been reported to incidentally show improvement in IBD as well, vancomycin has never been studied as exclusive therapy for VEO-IBD.

Methods: We report here our experience using oral vancomycin and gentamicin (V&G) to successfully treat two patients with VEO-IBD refractory to standard treatments.

Results: Patient 1, with severe Crohn's colitis, presented at 5 months with hematochezia and subsequent diarrhea, failure to thrive and elevated inflammatory markers. Colonoscopy revealed aphthous ulcerations in the rectosigmoid and cecum with granulomas. Investigation for immune deficiency and interleukin-10 defects was negative. Treatment with corticosteroids, exclusive enteral nutrition, sulfasalazine and infliximab was unsuccessful; he had an allergic rash on azathioprine. At the age of 14 months he fully responded (PUCAI=0) within 5 days to oral V&G following 6 months of chronically active disease (PUCAI 20-85). Over the next 14 months he received no maintenance treatment; he had 2 exacerbations which were successfully treated with 2 week courses of V&G. Seven months after completing the third course, he continues to be in complete clinical remission with no medications.

Patient 2 had intermittent hematochezia starting at 8 months of age. At 2.5 years she presented with bloody diarrhea along with elevated transaminases and GGT. Colonoscopy demonstrated pancolitis and liver biopsy was consistent with PSC. Investigation for immune deficiency and interleukin-10 defects was negative. She was refractory to 5-ASA. Over the next 7 months she received three courses of oral V&G with prompt and complete remission each time of both her colitis symptoms and her liver markers, including normalization of CRP. At last follow-up she is in complete clinical remission with normal transaminases and GGT without any maintenance treatment.

Conclusion: We have reported the first two cases of VEO-IBD successfully treated with only oral antibiotics, using intermittent courses of vancomycin and gentamicin. The treatment also resulted in normalization of liver enzymes in a patient who had concurrent PSC. Both antimicrobial and immunomodulatory effects, including stimulation of regulatory T cells, may play a role in the mechanism of action. As VEO-IBD is often difficult to treat, our findings represent a potential treatment and should be further investigated in controlled trials.
Disclosure of Interest: None Declared
SCHOOL ATTENDANCE IN CHILDREN WITH FUNCTIONAL ABDOMINAL PAIN AND INFLAMMATORY BOWEL DISEASES

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Objectives and Study: Inflammatory bowel disease (IBD) is associated with debilitating symptoms, frequent medical visits and procedures as well as treatment related severe adverse effects. Thus, IBD have the potential to significantly disrupt school functioning. To date, it is not known whether School absenteeism in IBD is distinct from more benign gastrointestinal disorders as compared to healthy controls. Thus, this study aim was to assess school related quality of life and School absenteeism in children and adolescents with IBD, functional abdominal pain (FAP) or functional abdominal pain syndrome (FAPS) and healthy controls.

Methods: School absenteeism data as well as data regarding participation in school and extracurricular activities for the 2013-14 school year were obtained for 42 children with crohn's disease, 30 children with ulcerative colitis, 40 children with FAP/FAPS (diagnosed according to Rome criteria) and 30 age-matched healthy controls. Parents and children were interviewed using a semi-structured questionnaire which included questions specifically addressing the impact of gastrointestinal symptoms on the child’s school and extracurricular functioning. In order to diminish recall bias, absenteeism data were cross matched with patient’s official school annual report cards. Medical records were assessed to evaluate disease related associated factors.

Results: Children with IBD and FAP/FAPS missed significantly more school days than age-matched healthy controls (21±12 and 18±10 vs. 5±1, respectively, p<0.0001). Absenteeism due to abdominal pain was similar in IBD and FAP/FAPS (10±9 vs. 9±8 days), significantly greater than healthy controls 0.7±0.5, p<0.0001). Compared to children with FAP/FAPS, Absenteeism due to medical appointments and hospitalization was significantly greater in children with IBD (9±7 vs. 5±4, p=0.003).

Participation of children with IBD and FAP/FAPS in various school activities (such as gym classes) and extracurricular activities (such as afternoon group classes) was significantly affected compared with healthy controls. Interestingly, there was no difference in school attendance and functioning between children with IBD and FAP/FAPS.

Conclusion: Functional abdominal pain has a significant impact on school attendance and functioning similar to the effect of IBD related symptoms. These findings may explain potential psychosocial and academic difficulties faced by children with FAP/FAPS.

Disclosure of Interest: None Declared
SERIOUS CUTANEOUS ADVERSE EVENTS UNDER INFLIXIMAB IN A PAEDIATRIC IBD COHORT

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Objectives and Study: Cutaneous adverse events are well known and described in patients treated with anti-TNF agents. In the paediatric population, skin lesions seem to be different than in adult patients with a major infectious part. The main objective of our study was to describe skin lesions under infliximab therapy in a paediatric monocenter inflammatory bowel disease (IBD) cohort.

Methods: The studied cohort was composed of n=65 paediatric IBD patients treated with infliximab during January to July 2014. For each patient clinical and biological data were collected in a database, including the occurrence of skin alterations during anti-TNF treatment. In the present study we defined as a cutaneous event only skin manifestations that needed a specific therapeutic management.

Results: Twelve of 65 PIBD patients (18%) with skin lesions were identified during the six month period.

The median age at diagnosis was 11 years in these patients. Nine patients had Crohn’s disease, one ulcerative colitis and 2 indeterminate colitis. The average time between diagnosis and first infusion of infliximab was 16 months. Four patients had a personal history of atopy.

Various skin lesions were found during the follow up: eczema, folliculitis, impetigo, herpes, molluscum contagiosum, abscess, adenitis, perleche, and psoriasis. Folliculitis (92%) and eczema (83%) were predominant.

Eight patients had positive microbiological sampling and 10 needed antibiotic therapies (5 local and 7 systemic antibiotics). Bacteriologic samples were positives in 54% of folliculitis, each time with staphylococcus aureus, 82% of folliculitis received a local antibiotic, and 45% a systemic antibiotic. In 48% of the cases, local therapy was ineffective.

The average time between the first infusion of infliximab and onset of skin lesions was 10.6 months. Nine patients were on combination therapy with azathioprine at the time of skin lesions, the others received infliximab monotherapy.

Eight children (66%) were in clinical remission at onset of skin lesions, and 9 (75%) had negative CRP (<5mg/l).

In 2 patients infliximab was stopped because of infectious cutaneous adverse events.

Skin lesions appeared during puberty in 83% of patients. Only one patient reported skin lesions before puberty. 38% of lesions were self-resolving after the end of puberty.

Conclusion: Cutaneous adverse events occurred more frequently in paediatric patients treated with infliximab compared to adult IBD patients and the type of lesions differs from adult skin lesions, with...
less psoriasis but more infectious folliculitis. The development of skin lesions seems not to be related to active disease. Since these inflammatory/infectious skin lesions occur during puberty one might speculate about the role of sexual hormones in the development during anti-TNF medication.

**Disclosure of Interest:** None Declared
Inflammatory Bowel Disease

Objective and Study: Cytomegalovirus (CMV) infection is detected frequently during inflammatory bowel disease (IBD) immunosuppressive treatment in adult patients. The infection causes increased morbidity and mortality, related with colectomy. We have limited data CMV infection in pediatric IBD population. We aim to evaluate CMV infection in pediatric IBD patients receiving immunosuppressive agents.

Methods: All study patients were diagnosed with Crohn Disease (CD) or ulcerative colitis (UC) between January 2006 and January 2013. The disease activity, laboratory/histological findings, immunosuppressive treatment features were evaluated. CMV colitis was diagnosed by histology, DNA PCR, antigenemia and/or serum specific antibodies.

Results: During the study period, over a total of 31 pediatric IBD patients hospitalized for a flare-up of active colitis. Among the patients, 13 CMV infection in the colonic mucosa were identified in seven patients (5 UC, 2 CD; 22.5%). Three of them were steroid resistant and four were steroid dependent. Total steroid dose was found higher in patients with CMV colitis than in CMV negative patients (p=0.03). Intravenous ganciclovir was administered for CMV colitis with immunosuppressive dose reduction. After the treatment clinical remission and histological improvement was provided in six patients. In one patient CMV clearance was provided from colonic mucosa, but remission in active colitis did not observed, and total colectomy was performed.

Conclusion: CMV co infection was seen in 22.5% of pediatric moderate-severe IBD patients treated with immunosuppressive agents. Treatment with high dose steroid was associated with CMV colitis. The children with steroid refractory or dependent IBD, should be screened for CMV infection before changing immunosuppressive therapy.


Disclosure of Interest: Y. Ozturk Conflict with: Professor of Pediatric Gastroenterology in DEU University Hospital. Data collection, reviewing and interpretation, P. Kuyum Conflict with: Resident in
ACCURACY OF FECAL CALPROTECTIN, BOWEL ULTRASONOGRAPHY AND INFLAMMATORY INDEXES IN THE DIAGNOSIS OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE

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Objectives and Study: To assess the accuracy of non invasive parameters including fecal calprotectin (FC), bowel ultrasound wall thickening (BWT) and blood inflammatory indexes (BII) alone or in combination as a diagnostic tool for paediatric inflammatory bowel disease (IBD).

Methods: Subjects aged 2-18 years referred to our paediatric gastroenterology clinic from 2007 to 2013 for recurrent abdominal pain and/or altered bowel habits were retrospectively considered. Subjects who underwent laboratory tests (FC, BII: white blood cell count [WBC], C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]) and bowel ultrasound as initial assessment were eligible. Exclusion criteria were: signs or symptoms highly suggestive for IBD (perianal disease or haematochezia), known organic disease, previously performed endoscopy. Eligible patients were followed-up for one year.

Results: Seventy-seven patients (mean age 11.3, 44 males) were retrospectively included. One-year diagnoses were: 23 (29.9%) IBD (8 ulcerative colitis, 12 Crohn’s disease, 3 indeterminate colitis), 54 (70.1%) non-IBD diseases. Mean values of WBC, CRP, ESR (p<0.001) and at least one BII pathological value were higher in IBD vs non-IBD patients (65.2% vs 11.1%, p<0.001). Pathological BWT (> 3 mm) and FC (> 200 µg/g) were more frequent in IBD than in non-IBD patients (69.6% vs 3.7%, p<0.001 and 95.7% vs 27.8%, p<0.001 respectively). Considering 3 (BII + FC + BWT) or 2 parameters together (FC + BWT, FC + BII) IBD patients had more simultaneous pathological results than non IBD-patients (52.2% vs 0%, p<0.001; 69.6% vs 0%, p<0.001; 65.2% vs 3.7%, p<0.001 respectively). Diagnostic accuracy of considered parameters are described in table 1.

<table>
<thead>
<tr>
<th>Variables</th>
<th>Se, % (95% CI)</th>
<th>Sp, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>BII (at least one altered)</td>
<td>65.2 (45.8-84.7)</td>
<td>88.9 (80.5-97.3)</td>
<td>71.4 (52.1-90.7)</td>
<td>85.7 (76.5-94.9)</td>
</tr>
<tr>
<td>BWT (&gt;3mm)</td>
<td>69.6 (50.7-88.4)</td>
<td>96.3 (91.3-100)</td>
<td>88.9 (74.4-100)</td>
<td>88.1 (80.0-96.4)</td>
</tr>
<tr>
<td>FC (&gt;200 µg/g)</td>
<td>95.6 (87.3-1)</td>
<td>72.2 (60.3-84.2)</td>
<td>59.5 (436.75.3)</td>
<td>67.5 (92.7-1)</td>
</tr>
<tr>
<td>FC + BWT + BII</td>
<td>52.2 (31.8-100)</td>
<td>100</td>
<td>100</td>
<td>83.1 (74.0-</td>
</tr>
</tbody>
</table>
Table 1. Se = sensitivity. Sp= specificity, PPV= positive predictive values, NPV= negative predictive values.

**Conclusion:** In initial work-up for IBD, FC alone presents highest sensitivity but poor specificity. The combination of FC + BWT presents the highest accuracy in identification of patients needing further invasive procedures in the short term.

**Disclosure of Interest:** None Declared
IMPACT OF INDUCTION THERAPY WITH 3 DOSES OF INFLIXIMAB ON DEEP REMISSION IN PAEDIATRIC PATIENTS WITH ACTIVE CROHN'S DISEASE.

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Objectives and Study: The aim of this study was to assess the impact of induction therapy with IFX on deep microscopic remission in pediatric patients with CD.

Methods: Fifty-six children (32 boys and 24 girls) aged 13.0±9.3 years with moderate to severely active CD diagnosed at the mean age of 5.5±0.83 years were included into the study. Colonoscopy and gastroscopy with sample collection were performed in all patients before and after three injections of IFX. Clinical activity of the disease was assessed using the Pediatric Crohn's Disease Activity Index (PCDAI), and the endoscopic activity was scored using the Simple Endoscopic Score (SES-CD). Histological changes were evaluated by a previously described numerical scoring system

Results: Thirty-nine patients (69.6%) reached clinical remission (PCDAI ≤10). When comparing data at baseline and at week 10, significant decrease was observed in median PCDAI, and in SES-CD score, a non-significant decrease (p=0.63) was reported in histological scale. Three (5.4%) patients had a score of 0 in the control histological examination. The correlation was found only between histological score and SES-CD score. Clinical remission correlated better with mucosal healing expressed by a decrease in SES-CD score than with microscopic changes

Conclusion: Biological therapy with infliximab enables mucosal healing in pediatric patients with CD, which is not necessarily associated with histological evidence of suppression of inflammation. Mucosal healing correlates better than microscopic healing with clinical remission


Disclosure of Interest: None Declared
**Objectives and Study:** The number of children diagnosed with early-onset of Inflammatory Bowel Disease (IBD) is rising worldwide and, over the last 5 years, this category of paediatric patients has been thoroughly investigated and described. Nevertheless, it hasn't been fully clarified yet whether children with an earlier onset of IBD (5-11y) present with disease characteristics and progression, which differ from patients diagnosed during adolescence. The aim of this study was to investigate whether the presentation and course of IBD amongst children diagnosed in the earlier years (<11y) differ from those diagnosed during adolescence (11-16y).

**Methods:** Retrospective cohort study conducted at two Paediatric Gastroenterology Units, in the United Kingdom and in Italy. Each cohort consisted of two age-groups of patients, with earlier onset (EO, <11y of age) and later onset (LO, 11-16y) of IBD. A total of 160 children were recruited. For the statistical analyses, a descriptive elaboration including Student's-t, Mann–Whitney, Chi-square and Fisher's exact tests was first performed. Subsequently, a multiple logistic regression analysis was conducted (SAS package 9.1).

**Results:** 1. Disease presentation: the disease activity at diagnosis (assessed through PCDAI and PUCAI scores) was more severe amongst the children with EO (OR 1.04; CI 1-1.08), irrespective of their country of origin. An L2 localisation of CD (Paris classification) was found to be more frequent amongst the British children with EO (P 0.04). In regard to the signs and symptoms at disease presentation, the British
children with EO presented more frequently with diarrhoea (P 0.04), PR bleeding (P 0.06), urgency (P 0.01), nocturnal symptoms (OR 1.6; CI 0.7-3.1) and joint pain (OR 1.45; CI 0.6-3.4). 2. Disease outcomes: The children with EO received more often early treatment with Thiopurines (i.e. within 3 months since diagnosis; OR 1.3; CI 0.7-2.7) and underwent endoscopic assessment more frequently during the follow-up (OR 1.49; CI 0.7-3.1).

**Conclusion:** Our data outlines that children diagnosed with IBD in their earlier years tend to have a more severe disease presentation than those diagnosed as adolescents. Moreover, children with EO of IBD appear to be more prone to a severe disease course. Further prospective studies on a larger scale should be prompted in order to confirm our findings as well as investigate the potential requirement for adjusting treatment at diagnosis in children with EO-IBD (i.e. top-down instead of step-up approach).

**Disclosure of Interest:** None Declared
CHARACTERISTICS OF A LARGE PAEDIATRIC CROHN'S DISEASE COHORT IN ISRAEL

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Objectives and Study: Our aim is to describe the presenting parameters of children diagnosed with crohn's disease (CD) among Schneider Pediatric Inflammatory Bowel Disease (SPID) cohort which was recently established. This cohort is based on a large retrospective single center registry of more than 700 children diagnosed with inflammatory bowel disease (IBD) since 1981.

Methods: A retrospective chart review of children diagnosed with CD was performed. Diagnosis of CD was based on clinical, radiologic, endoscopic and histological examinations.

Results: Seven hundred and five children diagnosed with IBD between 1981 and 2013 were included, 479 (68%) of whom were diagnosed with CD. Mean age at diagnosis was 13.4 y (range 2-18y) with a male to female ratio of 1.41; median duration of symptom prior to diagnosis was 4 m (range: 0.5-48m). Distribution of origin showed that 96% of children were Jewish (36% Ashkenazi, 29% Sephardi, 30% mixed, 1% Ethiopian) and 4% were non-Jewish. Familial history of IBD was reported in 22.5% of children (73% of whom had CD, 17% UC, 7% IBD-unclassified and 3% had familial history of both CD and UC). The initial symptoms were dominated by abdominal pain (84%), diarrhea (83%) and weight loss (66%). Thirty four % of patients presented with BMI z-score < -1 standard deviations. At diagnosis, linear growth delay was demonstrated in 23%, peri-anal involvement in 34% (62% of whom with perianal fistulae, abscesses or both) and extra-intestinal manifestations in 25%. Anemia was observed in 76% of patients, elevated C-reactive protein in 87%, and hypoalbuminemia in 32%. Disease location according to Paris classification demonstrated ileal distribution in 44%, ileo-colonic in 36%, colonic in 17% and 3% with isolated upper gastrointestinal involvement. Complicated behavior was observed in 24% of children (stricturing 18%, penetrating 2% and both 4%). Histologically, granulomas were present in 33% of patients.

Conclusion: A large Israeli cohort of children with CD demonstrates frequent prevalence of peri-anal disease and extra-intestinal involvement at diagnosis with a striking frequency of positive family history.

Disclosure of Interest: None Declared
CLINICAL AND PHENOTYPES PATTERNS OF EARLY ONSET PAEDIATRIC INFLAMMATORY BOWEL DISEASES: REVIEW OF SINGLE CENTRE EXPERIENCE

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Objectives and Study: Early-onset inflammatory bowel diseases (e-IBD) are chronic diseases of the gastrointestinal tract diagnosed in children less than 5 years of age. They include Crohn's disease (CD), Ulcerative colitis (UC) and Indeterminate Colitis or IBD-unclassified. The incidence of childhood IBD ranges from 0.3-10.9/100,000/years, and epidemiological and natural history studies demonstrate a rising incidence in this population, especially with regard to early-onset CD. Recent data demonstrated showed that the incidence of IBD had statistically increased from 1994 to 2005 (from 23.9 to 31.6/100,000 for CD and 16.2 to 19.7/100,000 for UC). An important difference between early-onset and late-onset IBD is a prevalence in males in early-IBD CD-like, while there is females prevalence when diagnosed in adolescence age. We examined the phenotype and clinical disease course of patients with IBD diagnosis under 5 years of age (e-IBD).

Methods: We have evaluated retrospectively data collected from a cohort of pediatric patients (1-18 years of age) with IBD who were enrolled from January 2006 to January 2014. We included all patients in whom the diagnosis of UC or CD was confirmed by clinical, laboratory, radiological, endoscopic and histological criteria, according to Paris classification, and we studied their clinical characteristics, the familiar history, age of diagnosis, disease phenotype and occurrence of therapies.

Results: 14 patients were diagnosed with early onset IBD (21% with CD, 79% with UC); 4 of them had a positive familiar history. Prevalence symptoms were bloody (71%) and watery diarrhea (7%), rectal bleeding (71%) and abdominal pain (43%); furthermore associated symptoms were oral aphtous lesions (14%), perianal disease (21%), tenesmus (14%), weight loss (7%), severe anemia (7%), fever (7%) and weight loss (21%). The phenotype included 50% of pancolitis (14% CD, 36% UC) and 50% (7% CD, 43% UC) of left colitis. 36% of patients are resulted steroid-resistant at the onset; at 1 year of follow-up, 50% started azathioprine and 21% cyclosporine. Moreover, 21% started biologics and 14% needed colectomy in the same period.

Conclusion: Our data confirm that early-onset IBD is a severe and extensive diseases, with a predominant colonic involvement and a greater impact of positive familiarity. The symptoms were severe at onset with high prevalence of resistance to steroids. At 1 year, more than half of the patients needed treatment with immunosuppressive or biological therapies, and no of the our patients was diagnosed perianal disease. These data confirm that the early-onset phenotype of IBD is a severe disease which differs from late-onset IBD.

Disclosure of Interest: None Declared
Gastroenterology
Inflammatory Bowel Disease
PO-G-0220

A NATIONWIDE SURVEY OF POST-OPERATIVE MANAGEMENT OF CROHN'S DISEASE IN CHILDREN IN UK

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Objectives and Study: Despite advances in immune-modulators and biologic therapy, the risk of surgical resection for paediatric onset Crohn’s disease was 48±5% by the age of 30 years and disease recurrence is 80-100% within 3 years without post-operative treatment. There is currently no proposed consensus guidelines for the management of post-operative Crohn’s disease in paediatrics. Our aim was to review the current practice throughout UK for the post-operative management of paediatric Crohn’s disease.

Methods: An online survey of all tertiary paediatric gastroenterology centres across UK was undertaken by advertising on the BSPGHAN website and also by contacting units individually.

Results: In this survey our response rate from gastroenterology centres was 18/23 (78.2%). Pre-operative steroid weaning policy: 53% used low dose steroids, 33% had withdrawn completely and 13% used either low dose steroids or off steroids. Risk Factors for post-operative recurrence: 33% used ECCO guidelines to define risk factors, 16% followed departmental protocol, 11% used both and 38% had no specific policy. Post-operative prophylaxis: 14% did not use prophylaxis until relapse or endoscopy, 57% used immediate prophylaxis with immune-modulators if there are risk factors, 21% used anti-TNF for high risk patients and 7% used antibiotics. Duration of post-operative prophylaxis: 23% used regular ileocolonoscopy to decide about the duration of prophylaxis, 23% used both ileocolonoscopy and CDAI score, 30% used clinical symptoms and biological markers and 7% used combination of all. Reassessment of the disease: 66% used endoscopy post-operatively only at time of relapse and 13% reassessed the disease with endoscopy at 6 months. Treatment: 61% started immune-modulators from no prophylaxis if there was endoscopic recurrence and 76% continued the same in the maintenance phase. Follow up: 43% followed their post-operative patients in IBD clinic, 25% in combined gastro-surgical clinic and 31% in both clinics.

Conclusion: This survey demonstrates that there is significant variability in the treatment modalities of paediatric post-operative Crohn’s disease in UK. It highlights the need for developing consensus guidelines/algorithm based on risk stratification to reduce variability in practice and to deliver the optimal post-operative treatment in children.

Disclosure of Interest: None Declared
LONG-TERM OUTCOMES AFTER RESTORATIVE PROCTOCOEKTOMY AND ILEAL POUCH ANAL ANASTOMOSIS IN PAEDIATRIC PATIENTS; MORE THAN 20 YEARS OF EXPERIENCE IN A TERTIARY CARE FACILITY

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Objectives and Study: Restorative proctocolectomy with ileal pouch anal anastomosis (IPAA) has become the surgical treatment of choice in paediatric patients who have failed medical therapy or in familial adenomatous polyposis (FAP). A higher incidence of postoperative complications is expected in IBD, since these patients are in a more disease-affected state. However, data regarding the long-term outcomes in these patients compared to FAP patients are limited.

Methods: The aim of our study is to compare the long term outcomes between paediatric patients with IBD and FAP who underwent restorative proctocolectomy with IPAA.

In a retrospective study, 53 (27 ulcerative colitis, 3 indeterminate colitis, 4 Crohn’s disease, 19 FAP) consecutive children (<19 years) that underwent IPAA between February 1991 and September 2014 were identified. Perioperative characteristics were collected by chart review. Pouch outcomes of IBD patients with a median age of 16 years (IQR, 14–17) were compared to FAP patients with a median age of 16.5 years (IQR, 15–17) at the time of surgery. The mean follow-up was 4.1 years (range, 1.2–22.3 years) and was comparable between both groups.

Results: IBD patients were in a more disease-affected state than FAP patients with an ASA score of more than 2 (73.2% vs 14.7%, p=0.001). In line with this, 48.3% of IBD patients were treated with steroids and 3.3% with biologicals (< 3 months before surgery) compared to no treatment in FAP patients. Most IBD patients had a pouch in multiple stages, that is an initial subtotal colectomy followed by completion proctectomy with IPAA at a later stage (76.5% vs 36.8%, p=0.007). The short-term anastomotic leak rate was comparable between IBD and FAP (15.8% vs 17.6%, p=0.863). Although not significant, fewer IBD patients had strictures compared to FAP (3.8% vs 16.7%, p=0.146). IBD patients had higher fistula (19.2% vs 0%, p=0.048) and pouchitis rates (57.7% vs 11.1%, p=0.002) compared to FAP patients. However, long-term results showed comparable pouch failure rates between both groups (15.8% vs 11.8%, p=0.691).

Conclusion: Surgeons perform multi-staged procedures in paediatric IBD patients in order to wean of medication and restore their nutritional state before restoring the continuity. However, postoperative complications rates are high which is possibly due to the inflammatory state of the resected colon in IBD compared to FAP patients. On the long term, pouch failure rates remain comparable between both patient groups. Although these complications do not alter the clinical course, attention should be paid on lowering the high fistula and pouchitis rates since it may negatively affect a child’s life.
Disclosure of Interest: None Declared
RELATIONSHIP AMONG THE VALUES OF FECAL CALPROTECTIN AND THE AGE IN A HEALTHY PAEDIATRIC POPULATION

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Objectives and Study: To establish the normal levels of FC in a population of healthy children younger than 4 years and to evaluate the possible relationship with gestational age, chronological age, weight, gender and type of feeding

Methods: A descriptive, cross-sectional and prospective study was conducted during the period of May 2013 to June 2014. The sample was selected among healthy pediatric population. Stool samples from healthy children of different ages of our departmental area were studied, from newborn to 4 years. The FC was determined as a quantitative test by fluoroenzymoimunoanalysis. Collection of data was performed by a structured telephone interview with the parents or guardians of the participating children; socio-demographic and clinical data was included. The results were analyzed using SPSS statistical software 17.0

Results: A total of 158 participants were included in the study (79 boys and 79 girls). The participants were divided into 4 subgroups according to its age. The average values of FC in each of the groups were: 160 mg/Kg in children 0 to 2 months, 52 mg/Kg in children 12 to 24 months, 33 mg/Kg in children 24 to 36 months, and 17mg/Kg in children 36 to 48 months. Significant differences were observed between the groups 24-36 months and 36-48 months compared to the 0-12 month group (p < 0.001); FC values were significantly higher in children under 12 months compared to the other groups. No correlation was observed between FC values and gestational age, birth weight or weight at the time of the sample collection. There were no differences regarding the type of food (breastfeeding or formula feeding).

Conclusion: Fecal calprotectin values decrease with age, having the highest levels in the first year of life, which could be explained by the immaturity of the intestinal flora in this age of childhood. It does not seem that factors such the type of feeding during the first months of life, gestational age, weight or gender are related to the values of FC.

Disclosure of Interest: None Declared
INCIDENCE OF BOTH CROHN’S DISEASE AND ULCERATIVE COLITIS HAS CONTINUED TO RISE OVER THE LAST 10 YEARS WITHIN THE SOUTHWEST REGION OF ENGLAND.

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Objectives and Study: The first prospective national survey of paediatric Inflammatory Bowel Disease (pIBD) documented an incidence of 5.2/100,000 children per year1. A higher incidence was noted in the north (Scotland: 6.5) as compared to the south (England:5.2) and Ireland (4.4). This prospective study aimed to document change in pIBD incidence in Southwest England (SWE).

Methods: Bristol is the single specialist paediatric gastroenterology centre for SWE to which all children suspected of having IBD from the 12 paediatric centres are referred for endoscopy. Prospective data was collected on all new pIBD cases between 2004–2013 including types of IBD, gender and postcode address.

Results: 461 new cases of pIBD were diagnosed with 40 cases in 2004 compared to 63 in 2013. The incidence of pIBD in SWE increased from 4.5 (2004) to 6.7 (2013). Male (n=269) to female (n=192) ratio was 1.4:1. Crohn’s disease increased from 2.61 to 3.54, Ulcerative Colitis 1.48 to 2.25 and IBD-unclassified 0.45 to 0.96. The 5-year cumulative incidence rates for the city of Bristol were much higher than the whole SWE and increased from 9.2 (2004-2008) to 11.0 (2009-2013).

Image:
Conclusion: Annual incidence of Crohn’s disease and ulcerative colitis in SWE has continued to increase during 2004–2013 (4.5-6.7) with male preponderance. This study documents significantly higher incidence in the city population (9.2-11.0) supporting role of environmental factors.


Disclosure of Interest: None Declared
TRANSITIONAL CARE IN INFLAMMATORY BOWEL DISEASE – A SINGLE CENTRE EXPERIENCE

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Objectives and Study: Introduction: Inflammatory bowel disease (IBD) is a chronic disease with a natural history of relapses and remissions. Approximately 25% of the IBD patients are diagnosed before the age of 16 years. There are many differences between children and adults in terms of the ideology of care, service provision and approach to investigations and treatment. This difference between the pediatric and adult population emphasizes the need for an organized and planned transition process. The aim of our study is to describe our experience in IBD transitional care clinic.

Methods: We conducted a retrospective case-controlled study to characterize patients treated in a novel transitional IBD clinic. Our clinic consists of a combination of a pediatric and an adult gastroenterologist, an IBD nurse, dietitian and a psychologist. We used a self-efficacy questionnaire (the “IBD-yourself”) to assess patients’ skills for self-management of chronic conditions, their self-advocacy, and their healthcare utilization before and after visiting our transitional clinic program. We have also compared their readiness according to disease extent, disease duration and therapeutic strategy.

Results: During the years 2013-2014, 21 patients visited our transitional clinic, 15 of them completed the transition process (11 males, 4 females). Crohn's disease was significantly more common (14/15). Average age was 19.4 years (range 17-27) with average disease duration of 4.9 years (range 0.67-10 years). The transitional process included an average of 3-4 meeting over an average time of 7 months. The following domains were found to have statistically significant higher self efficacy score after completing the transition: knowledge of IBD (P=0.01), knowledge of diagnostic tests (P=0.0004), medication use (P=0.003), actual behavior outpatient clinic (P=0.016), knowledge of transition process (P=0.0001) and self readiness for transition (P=0.013). We noted a positive correlation between number of meeting and coping with IBD (r=0.56, p=0.029). No correlation was found between disease extent, disease duration, therapeutic strategy and change of readiness during the transition.

Conclusion: We have described our experience with an organized IBD transition process from the pediatric to the adult healthcare system. Most domains in the self efficacy questionnaire showed statistically significant higher ability score after completing the transition process. The transition process is a major part o a successful transfer to the adult gastroenterologist.
Disclosure of Interest: None Declared
NEW BIOMARKERS IN INFLAMMATORY BOWEL DISEASE: THE ROLE OF HMGB1

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Objectives and Study: High Mobility Group Box 1 (HMGB1) has recently received a great deal of attention as a clinical biomarker in inflammatory diseases. This biomarker is, in fact, a DNA-binding protein with various functions, which depend on its localization. Nuclear HMGB1 regulates transcription, whereas cytosolic HMGB1 works as a pro-inflammatory cytokine. Furthermore, HMGB1 is involved in several autoimmune and inflammatory disorders, such as rheumatoid arthritis, type 1 diabetes, systemic lupus erythematosus and sepsis. In recent studies, the role of faecal HMGB1 as a marker of IBD was demonstrated. Moreover, HMGB1 proved to be a reliable non-invasive marker of both clinical and subclinical inflammation. Aims of our study were to assess role and significance of serum HMGB1 in a group of paediatric patients with IBD.

Methods: We have included a total of 46 paediatric patients: 18 with Crohn’s Disease (CD) (average age: 14; range: 8-18), 16 with Ulcerative Colitis (UC) (average age: 14; range: 7-18), and 12 controls (average age: 8; range 7-11). Evaluation of serum HMGB1 was carried out by using a colorimetric commercial kit (IBL INTERNATIONAL HGMBH, Hamburg, Germany on licensed by Shino-Test Corporation), the test was performed via immunoenzymatic assay (ELISA).

Results: Serum levels of HMGB1 were significantly higher in patients with IBD compared with the controls (p<0.05) (CD: 65,42±65,42 ng/ml; UC: 68,82±60,95 ng/ml; control: 3,41±1,06 ng/ml; CD vs control: p<0.0021; UC vs control: p<0.008), whereas no significant difference was shown between patients with UC and CD. Distinct types of therapies did not interfere with serum levels of the HMGB1. Furthermore, no relevant differences were reported among patients with different age or localisation of the disease: high levels of HMGB1 were always documented in the serum of patients with IBD. Lastly, serum levels of HMGB1 did not correlate to CRP (C-Reactive Protein) in patients with IBD: patients in remission showed normal CRP but constantly high levels of HMGB1.

Conclusion: High correlation between IBD and serum HMGB1 was confirmed in our study. HMGB1 was a reliable indicator of IBD regardless of age, treatment or state of the activity of the disease. Hence, we believe that serum HMGB1 should be considered as a new biomarker of pediatric IBD. In addition, serum HMGB1 could be adopted as a screening test prior to more invasive investigations when IBD is suspected. The next step could be studying the relationship between serum and faecal HMGB1, assuming that faecal HMGB1 may be better related with the state and the extension of the disease.

Disclosure of Interest: None Declared
APPLICABILITY OF COLON CAPSULE ENDOSCOPY (CCE) IN PAEDIATRIC CROHN'S DISEASE
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Objectives and Study: Endoscopy has a crucial role in patients (pts) with Crohn's disease (CD) since it allows assessment of disease extension, helping in therapeutic decisions. While endoscopic capsule exploration of small bowel (SB) has been repeatedly described, data on endoscopic capsule of the large bowel are rare. We showed that colon capsule endoscopy (CCE) (Endoscopy 2014;46:485-92) is an alternative to colonoscopy in pediatric ulcerative colitis; CCE can also allow to explore SB and colon concurrently. We investigated prospectively the accuracy of CCE in evaluating disease activity of the SB and colon in CD, by comparison with magnetic resonance enterography (MRE), SB contrast ultrasonography (SICUS) and colonoscopy

Methods: We enrolled 40 consecutive pts (22 males, 18 females, mean age 13.1±3.1 years) with CD of SB and colon (mean disease duration: 37.3±26.1 months) and candidates for endoscopy. All underwent SICUS, MRE, CCE and colonoscopy sequentially over 5 days. All investigators were blinded to the patient history and to all test results, and independently analysed the different tools. Patients were classified as “active” or “inactive” either for the SB and the colon according to specific criteria for each tool (SES-CD, Lewis score, US and MR parameters of activity). Statistical analysis was applied with calculation of specificity (SP), sensitivity (SE), positive predictive value (PPV) and negative predictive value (NPV) of CCE. For colonic mucosa evaluation, colonoscopy was the gold standard, while for the SB, due to the lack of a gold standard, CCE was compared with a consensus reference standard (panel with an investigator for each technique to achieve a consensus to the presence of active disease). Two patients were excluded from the analysis due to inability to swallow CCE.

Results: Sensitivity of CCE to detect colonic inflammation was 89% and specificity was 100%. The PPV and NPV of CCE for colonic inflammation were 100% and 91% respectively. Regarding the SB, CCE showed 90% SE, 94% SP, with PPV and NPV of 95% and 89% respectively. Accuracy parameters for SICUS (SE: 89%, SP: 85%) and MRE (SE: 85%, SP: 89%) were lower than those for CCE. No serious adverse event related to the CCE procedure or preparation was reported

Conclusion: We showed for the first time in CD pediatric age that CCE is of great usefulness in evaluating SB and colon mucosa. By this single and non-invasive tool it is possible to evaluate simultaneously both the SB and the colon with high diagnostic accuracy. Future multicenter studies will promote CCE in the routine management of pediatric CD patients.

Disclosure of Interest: None Declared
FIRST OBSERVATIONS OF THE USE OF BIOSIMILAR INFLIXIMAB FOR TREATMENT OF ULCERATIVE COLITIS IN PAEDIATRIC POPULATION.

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Objectives and Study: Biological treatment in ulcerative colitis (UC) is employed after the failure of standard treatment. Introduction of biosimilar infliximab (INF) (Remsima/Inflectra) in European Union allows gaining first experience with this medicine in children with ulcerative colitis. Biosimilar infliximab was authorised in all indications on the basis of in-depth review of preclinical and clinical data. However, the use in children with ulcerative colitis was not reported previously.

Methods: Six patients starting treatment with biosimilar infliximab Remisma (5 mg/kg) was assessed at week 10 after receiving 3 doses at weeks 0, 2 and 6. Disease activity (PUCAI) and laboratory values (CRP, ESR, platelet count) was assessed at the start of the biological therapy and at week 10. Mean and range of clinical values is reported.

Results: Median age of 6 patients was 12.3 years (range 8.5-17.5). Mean PUCAI before infliximab initiation was 47.5 (range 5-80). Mean (range) CRP, ESR and platelet count before initiation were 1.8 mg/dL (0.03-8.1), 24 mm (5-33) and 370x10⁹/L (260-530x10⁹). For one patient it was the second course of biological treatment (3 doses of the reference INF received 9 months ago. For 2 patients (33%) treatment was discontinued, in 1 due to lack of response after first dose (disease flare), in second due to anaphylactic reaction during dose 3 infusion. For the latter patient that was the second course of infliximab treatment. As of November 2014 3 patients (50%) received 3 doses and were evaluated at week 10. For these patients initial values of PUCAI, CRP, ESR and platelet count were not different than for all 6 patients. After 3 doses of biosimilar infliximab PUCAI values decreased to 28.3 (range 5-50). CRP, ESR and platelet count were 0.3 (0.02-0.68), 20 (10-28) and 418x10⁹ (236-706), respectively.

Conclusion: Initial observations point to efficacy and safety of biosimilar infliximab in the treatment of pediatric patients with ulcerative colitis. Further studies with larger patient groups are required. Data for more patients and longer observation time will be collected and presented.

Disclosure of Interest: None Declared
GOLIMUMAB IN PAEDIATRIC PATIENTS WITH CROHN'S DISEASE REFRACTORY TO PREVIOUS TUMOR NECROSIS FACTOR ANTIBODY

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Objectives and Study: Treatment with antibody to tumor necrosis factor (TNF)-α such as infliximab (IFX) or adalimumab (ADA) is associated with inducing and maintaining clinical remission in children with Crohn’s disease (CD). There are no data about the use of a third introduced subcutaneous TNF antibody, golimumab, in the treatment of paediatric CD.

We evaluated the efficacy of golimumab for children with moderate/severe CD who failed previous treatments with TNF antibody.

Methods: Retrospective data analyses were done in all 7 (5 girls) children who received golimumab at a median age of 17 years for a median of 7.2 months. Before golimumab, they have received IFX for median of one year (range:0.5-1.9) and ADA for median of 1.4 year (range:0.3-3.3). Paediatric Crohn’s disease activity index (PCDAI), full blood count, inflammatory markers, use of corticosteroids and adverse events were recorded.

Results: With golimumab treatment 5 of the 7 children were PCDAI responders and 2 entered remission (PCDAI<10). There was a significant increase in haematocrit after 2 weeks, (p=0.04), faecal calprotectin was significantly reduced after 4 weeks of golimumab compared to baseline (p=0.05). Out of five children, steroid withdrawal was possible in one and steroid reduction in two cases. There were no serious side effects in the study subjects.

Conclusion: Golimumab induced and maintained clinical response in the majority of children with moderate/severe CD who failed previous treatment with IFX and ADA. The majority of children were PCDAI responders, in most of them steroid sparing was possible. Golimubab might be a well-tolerated and effective rescue therapy in refractory CD even if previously treated with TNF antibodies.

References:

Disclosure of Interest: None Declared
EXTRA-INTESTINAL MANIFESTATIONS ASSOCIATED WITH MUTATIONS IN THE IL-10 PATHWAY

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Objectives and Study: Loss of function in the IL-10 axis in infancy results in severe enterocolitis and extra-intestinal manifestations, the latter currently remain ill-defined.

Methods: Clinical history and results for 3 patients with IL-10 axis dysfunction, identified between 2010 to 2012, were reviewed.

Results:

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Mutation</th>
<th>Origin</th>
<th>Colectomy</th>
<th>HSCT</th>
<th>Respiratory</th>
<th>Sensorineural Hearing Loss</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>8y</td>
<td>IL-10</td>
<td>Northern Pakistan</td>
<td>16m</td>
<td>4y</td>
<td>Bronchiolitis wheeze, emphysematous bullae</td>
<td>moderate-3y</td>
<td>Microcephaly Eczema</td>
</tr>
<tr>
<td>2</td>
<td>4y</td>
<td>IL-10</td>
<td>Northern Pakistan</td>
<td>-</td>
<td>14m</td>
<td>Wheeze</td>
<td></td>
<td>Klebsiella sepsis Eczema</td>
</tr>
<tr>
<td>3</td>
<td>1y</td>
<td>IL-10Rβ</td>
<td>Indian</td>
<td>-</td>
<td>10m</td>
<td>Respiratory failure</td>
<td></td>
<td>Inotrope-sensitive</td>
</tr>
</tbody>
</table>

Table 1: Clinical history and systemic analyses.

Impaired mucosal/skin defence: A predominance of upper respiratory symptoms (4 with intermittent symptoms and 1 had HFOV+NO with a febrile episode) in early childhood were recorded. Sensorineural hearing loss in early childhood was detected following developmental concerns. Recurrent and severe infections, including Klebsiella sepsis requiring ICU admission, indicated increased susceptibility to infections. Eczematous lesions seen were resistant to conventional topical treatment, suggesting compromised skin immunity.

Impaired adaptive immunity: Low T (CD3, CD4 and CD25) and B (CD19) cells counts, and PHA stimulation test were recorded. Raised IgA seen in all patients confirm mucosal immune dysfunction. IgM, IgE, IgG1 and IgG3 were also variably increased. EBV-driven lymphoma occurring later in immunosuppressed, non-transplanted patient has been reported. Severe infections in infancy is likely to have contributed to microcephaly seen in a patient.

Conclusion: In addition to its well-established effects on gut homeostasis, defects in the IL-10 pathway leads to immune deficiency and impaired mucosal defence. Understanding this rare disease may enable prompt referral to other specialists and early treatment. It also offers to opportunity to better understand childhood IBD.
Disclosure of Interest: None Declared
Objectives and Study: Combining infliximab with immunomodulating therapy, including azathioprine and methotrexate, may reduce the risk of antibody formation directed against infliximab. [1] [2] [3] [4] Antibodies to infliximab (ATI) have been associated with loss of response in adults [5], but studies in children are limited. The objective of this study was to evaluate the impact of concomitant immunomodulator use (combination therapy vs infliximab monotherapy) on ATI formation and the impact of ATIs on developing loss of response in children with Crohn’s disease.

Methods: From two academic centres in the Netherlands, we collected clinical, biochemical and histological data of children diagnosed with Crohn’s disease treated with infliximab between 2009 and 2014.

Results: A total of 101 children were identified (67 men, median age at start of infliximab 13 years) of whom 39 patients received exclusively combination therapy. Median duration of infliximab treatment was 29 months, including 12 months combination therapy. Ten patients developed ATIs (2 had combination therapy at that time, 8 received infliximab monotherapy after initially combination therapy in 7 of 8 patients). Seven out of 10 patients (70%) developing ATIs had loss of response, versus 18 of 91 patients (20%) without ATIs (p=0.0005).

Conclusion: Also in children, ATIs are associated with loss of response. Since most patients with ATIs were on infliximab monotherapy, our data suggest that combination therapy may prevent ATI formation and hereby loss of response.

Disclosure of Interest: None Declared
**Objectives and Study:** Faecal calprotectin has been increasingly used as a non invasive marker to diagnose IBD in children with chronic diarrhea. It is known to have high sensitivity and specificity both for new IBD diagnosis and monitoring disease activity. We report cases of children with normal faecal calprotectin and active new disease confirmed on endoscopy and histopathology.

**Methods:** Review of children (less than 16 years old) with confirmed IBD and normal faecal Calprotectin at the time of referral to our tertiary gastroenterology unit between 2009-2014. Our centre / laboratory looks after more than 1000 patients (adult and children) with IBD. The clinical presentations on referrals, blood results, faecal calprotectin, endoscopic findings and histopathology results were analysed. Children who were already on immunosuppressant medications (for another co) were excluded.

**Results:** All children were referred for assessment of chronic diarrhea. We identified 6 symptomatic children (18 months to 15 years) with low/normal faecal calprotectin (normal value used <60mcg/g) and normal or low inflammatory indices too. They were all scoped and noted to have erythema, ulcers, stricture and pseudopolyps, changes were noted in ileum, colon or both, histopathology was in keeping with inflammatory bowel disease with crypt abscess or granuloma. The calprotectin levels were normal in both ulcerative colitis and Crohn’s disease neither was a correlation with area of disease or age/sex of the children.

<table>
<thead>
<tr>
<th>Age (Years)</th>
<th>Sex</th>
<th>Facal calprotectin (mcg/g)</th>
<th>Findings</th>
<th>Site</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.8</td>
<td>boy</td>
<td>95</td>
<td>Erythema and ulcers</td>
<td>ileum and colon</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>9</td>
<td>girl</td>
<td>10</td>
<td>Erythema</td>
<td>ileum</td>
<td>Crohn’s disease</td>
</tr>
<tr>
<td>13</td>
<td>girl</td>
<td>36</td>
<td>Fraible mucosa</td>
<td>Rectum and left colon</td>
<td>Ulcertaive colitis</td>
</tr>
<tr>
<td>13</td>
<td>girl</td>
<td>77</td>
<td>Ulcer</td>
<td>Caecum and right colon</td>
<td>Ulcerative colitis</td>
</tr>
<tr>
<td>14</td>
<td>girl</td>
<td>67</td>
<td>Stricture and pseudopolyps</td>
<td>Ileum</td>
<td>Crohn’ disease</td>
</tr>
<tr>
<td>15</td>
<td>boy</td>
<td>27</td>
<td>Ulcers</td>
<td>Colon and ileum</td>
<td>Crohn’s disease</td>
</tr>
</tbody>
</table>
Conclusion: Faecal calprotectin may be used as a guide in children with chronic diarrhoea but not as a absolute marker for diagnosis of IBD. Children with suspected IBD with normal Calprotectin must have endoscopy to confirm the diagnosis.

Disclosure of Interest: None Declared
OUTCOME OF VERY EARLY ONSET IBD: OVERVIEW OF A SINGLE CENTRE EXPERIENCE
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Objectives and Study: IBD develops during childhood or adolescence in up to 25% patients. Very early onset IBD (VEOIBD), before 6 years old, has been reported in 15% of paediatric patients with IBD. We analysed the outcome of a population of VEOIBD followed in a single centre IBD group.

Methods: We retrospectively evaluated VEOIBD patients followed at Bambino Gesù Children’s Hospital between 1999 and 2014. Collected variables were: median age at diagnosis, sex, onset age, diagnosis of Crohn’s Disease (CD) or Ulcerative Colitis (UC), disease extension, behaviour, severity, therapy and outcome.

Results: Thirty consecutive patients (15 males, age at diagnosis: 9-72 months, median age: 38.2 months) with diagnosis of VEOIBD were enrolled. At the onset, 7 patients had CD diagnosis (3 males) and 23 patients (76.6%) had UC diagnosis (12 males). Of 250 Paediatric IBD patients followed in our centre, 30 had a VEOIBD (12%). According to Paris Classifications, CD localization at diagnosis was in 3 patients ileo-colonic (L3), in 1 ileal (L1), in 1 ileocolonic and upper disease (L3-L4), in 1 colonic and upper disease (L2-L4), in 1 isolated upper disease (L4). Disease behaviour in 1 child was classified as B2, while in 6 children was classified as B1. UC extension was pancolitis (E4) in 19 children and left colitis (E2) in 4 children. During the follow up two UC developed a small bowel involvement and a penetrating IBD after 19 and 16 months respectively from diagnosis, with a clinical shifting from UC to CD diagnosis, confirmed by histology. One patient with UC showed ileitis after colectomy. About therapy, 15 patients (65.2%) with UC and 5 (71.4%) patients with CD received azathioprine. Rescue therapy was administered to 11/23 UC patients (47.8% UC). One child avoided surgery; ten (43,5% UC) underwent colectomy because of no-response to medical treatment. Furthermore, one patient (4.3% UC) had complications during diagnostic endoscopy and underwent emergency colectomy. One patient with CD received anti-TNFalpha therapy, another patient with CD had a short -intestinal resection (14.2%).

Conclusion: VEOIBD was associated with frequent colonic disease extension. As the first IBD diagnosis may be changed during the follow up, a rigid classification at onset should be avoided. It is mandatory to study small bowel involvement. The large use of immunosuppressant drugs, the high percentage of rescue therapies and surgery may be representative of a more aggressive disease in the VEOIBD population.

Disclosure of Interest: None Declared
CHARACTERISTICS OF A PAEDIATRIC ULCERATIVE COLITIS COHORT IN ISRAEL

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Objectives and Study: Our aim is to describe presenting parameters of children diagnosed with ulcerative colitis (UC) among the Schneider Pediatric Inflammatory Bowel Disease (SPID) cohort which was recently established. This cohort is based on a large retrospective single center registry of more than 700 children diagnosed with inflammatory bowel disease (IBD) since 1981.

Methods: A retrospective chart review of children diagnosed with UC was performed. Diagnosis of UC was based on clinical, radiologic, endoscopic and histological examinations.

Results: Seven hundred and five children diagnosed with IBD between 1981 and 2013 were included, 188 (27%) of whom were diagnosed with UC. Mean age at diagnosis of UC was 12.3 y (range 2-18 y) with a male to female ratio was 1.18; median duration of symptom prior to diagnosis was 4 m (range: 0.5-34 m). Distribution of origin showed that ninety six % of children were Jewish (28% Ashkenazi, 38% Sephardi, 30% mixed) and 4% were non-Jewish. Familial history of IBD was reported in 23% of pediatric cases of UC. The initial symptoms were dominated by bloody stools (95%), diarrhea (77%) and abdominal pain (51%). Extra-intestinal manifestations were observed in 28% of patients within the first year of follow-up. Twenty % of patients presented with BMI z-score < -1 standard deviations. At diagnosis, anemia was observed in 49%, elevated C-reactive protein in 30% and hypoalbuminemia in 11% of patients. Defined by Pediatric UC activity index (PUCAI), 6 % of patients had severe disease at diagnosis, 49% and 45% had moderate and mild disease, respectively. Severe disease was documented in 30% within the first year of follow up.

Proctocolectomy with ileal pouch–anal anastomosis (IPAA) was performed in 8 patients (4%) within the first year post diagnosis. Over up to 32.7 years of follow up, 18% of the cohort required IPAA. According to Paris classification 32% of patients had pan-colitis, 14% extensive colitis, 32% left-sided colitis and 22% had proctitis.

Conclusion: A large Israeli cohort of children with UC demonstrates a striking frequency of positive family history. Although minority of pediatric UC presented with severe disease, a significant proportion of patients demonstrated aggressive disease course within the first year of follow-up.

Disclosure of Interest: None Declared
Objectives and Study: Diagnostic delay (DD) in Inflammatory Bowel Disease (IBD) has important clinical impact. There is increasing evidence showing a higher success rate when treatment is administered early in the disease.

Objective: To evaluate DD in pediatric IBD in Spain.

Methods: Multicentric prospective observational study including IBD patients diagnosed in 2013 and 2014 in 20 pediatric centers. Data from 18 months were analyzed. Information was obtained from a questionnaire filled in by the treating pediatric gastroenterologist (PG). Data were analyzed with the program SPSS 18.

Results: Data from 80 patients (51 males) were obtained. Mean age at diagnosis was 11.24 years. Disease distribution: Crohn’s disease (CD) 50 patients (62.5%), ulcerative colitis (UC) 27 (33.8%), IBD unclassified (IBDU) 3 (3.8%). Median DD was 19.64 weeks (interquartile range [IQR] 37.46), being significantly longer (p=0.005) in CD (27.85 w; IQR 39.71) than in UC (16.57 w; IQR 18.54). Family IBD history was not associated with shorter DD. Median time from appearance of symptoms to consultation with the first physician involved in the process was 2 weeks (IQR 4.07), from this first visit to being sent to the pediatric gastroenterologist (PG) 7.3 weeks (IQR 20.71); from referral to the PG visit 0.93 weeks (IQR 4.14), and from this visit to the diagnosis 2 weeks (IQR 5.18). The time span from the first physician consultation (FPC) to the PG referral was significantly longer in CD (10.43 w, IQR 35.29) than in UC (6.57 w; IQR 18.54). There were no differences in the rest of the time intervals. The median of physicians visited before the PG was 2 (IQR 2), but 25.6% of patients went to 3 or more physicians. A negative correlation between the DD and the z-score for height in CD patients was observed (r=-0.36, p=0.015)
**Conclusion:** DD in CD was significantly longer as compared to UC. The major component responsible for DD in IBD was the time spent between the FPC and the PG referral. DD in CD could be partially responsible for growth impairment in pediatric patients.

**Disclosure of Interest:** None Declared
Gastroenterology
Inflammatory Bowel Disease
PO-G-0235

SERUM HEPcidIN AND IRON ABSORPTION IN PAEDIATRIC IBD: A PROSPECTIVE, COMPARATIVE, CROSS-SECTIONAL STUDY.

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Objectives and Study: Anemia in patients with Inflammatory Bowel Disease (IBD) has a multifactorial origin, including blood loss, iron malabsorption (IM), and anemia of chronic inflammation (ACD). Hepcidin regulates iron homeostasis. We sought to correlate hepcidin serum levels in patients affected by IBD with disease activity, inflammatory markers and iron load test (ILT) and to compare with a group of coeliac and healthy patients.

Methods: One-hundred-forty-five subjects (50 IBD, 45 coeliac patients and 50 healthy controls; mean age: 10.8 years) were included in the study between December 2012 and June 2013. At the enrollment all patients underwent the following: full blood count, serum hepcidin, serum iron, ferritin, transferrin, soluble transferrin receptor, transferrin saturation, total iron binding capacity, C-reactive protein (CRP), and erythrocyte sedimentation rate (ESR). In order to evaluate the efficacy of iron absorption in IBD patients ILT was performed and change in iron levels between baseline and 2 hours (Δ[Fe]2hr) was also calculated. In addition in IBD patients PUCAI, PCDAI, disease localization, disease duration and IBD therapy were also evaluated and a fecal sample for calprotectin collected.

Results: The prevalence of anemia in IBD patients was significantly higher compared with both coeliac group and healthy controls (p=0.03 and p=0.001, respectively). In details, 9 out of 17 IBD patients (53%) were affected by IDA, 2/17 (11.7%) by ACD and in 6 out of 17 (35.3%) IBD children a combination of IDA and ACD was identifiable. Forty-three out of 50 IBD patients (86%) correctly performed ILT. Twelve out of 43 (27.9%) patients showed a pathological ILT. Patients with iron malabsorption showed significant higher values of ESR and CRP compared with patients with normal iron absorption (p=0.02 and p=0.001). Eight out of 12 (66.7%) children with a pathological ILT showed an active disease compared with 6/31 (19.3%) children with normal iron absorption (p=0.01). Serum hepcidin was significantly higher in IBD patients with a PCDAI/PUCAI ≥30 compared with both coeliac patients and healthy controls (p=0.02, p=0.005; p=0.003 respectively). Hepcidin levels directly correlated with serum ferritin and CRP (p=0.001, r=0.457; p=0.001, r=0.351 respectively). An inverse relationship was found with Δ[Fe]2hr and transferrin (p=0.001, r=-0.474; p=0.0001, r=-0.311, respectively).

Conclusion: This prospective, comparative, cross-sectional study clearly demonstrates that serum hepcidin is increased in IBD children with active disease and it is responsible for iron malabsorption.
Disclosure of Interest: M. Martinelli: None Declared, C. Strisciuglio: None Declared, A. Alessandrella: None Declared, R. Auricchio: None Declared, S. Perrotta: None Declared, B. Nobili: None Declared, A. Staiano Conflict with: D.M.G. Italy, Conflict with: Valeas s.p.a., Angelini, Miltè italia, E. Miele: None Declared
**NATURAL HISTORY OF PAEDIATRIC IBD AROUND TRANSITION TO ADULT SERVICES: A REGIONAL COHORT STUDY**

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**Objectives and Study:** Effective transition of young people with paediatric-onset IBD (PIBD) is essential, but paucity of data exists in this area. We aimed to describe the transition of PIBD patients in South East Scotland (SES) with regard to natural history (disease activity, therapy escalation and service utilisation) both at the point of transfer and post-transition.

**Methods:** A prospective PIBD database identified a cohort of all patients discharged from our regional service since 01/01/10. A retrospective study of patients leaving as a result of graduation from paediatric to adult IBD services through a transition process, a transition event (single joint clinic) or transfer until 30/09/13 was conducted, with data at a minimum of 1 year follow-up (FU) post-transition collected.

**Results:** 74 patients had transition; 52 Crohn’s disease (CD), 13 ulcerative colitis (UC) and 9 IBD-unclassified (IBDU). Median age at transition was 17.9yrs (IQR 17.6-18.4). 81% of patients were in steroid-free remission (SFR) at time of transfer, and 5% had moderate-severe disease. 75% of CD patients had ileocolonic involvement and 60% pan-enteric disease; 73% of UC/IBDU patients had extensive disease. 80% of patients had been exposed to thiopurines, 46% to methotrexate (MTX) and 24% to anti-TNFα therapy in paediatric services. Only 18% of patients had never required immunosuppression. 11% had major IBD-related surgery prior to transfer and 3 patients (4%) had pan-treatment refractory IBD (primary non-response, complete loss of response or non-recoverable intolerance to all of thiopurines, MTX, infliximab and adalimumab). Median follow-up post-transition was 2.2yrs (IQR 1.4-3.8). At last adult FU 6 patients had transferred out of SES and 3 had defaulted from clinic. 85% of the remaining 65 were in SFR; 8% had moderate-severe disease. The rates of ileocolonic CD and pan-enteric CD had already increased to 80% and 67% respectively; 65% of UC/IBDU patients had extensive disease. 15% of patients had their first thiopurine exposure, 3% their first MTX exposure and 19% their first anti-TNFα exposure in adult services. 14% had major IBD-related surgery in adult services and pan-treatment refractory IBD increased to 11%.

**Conclusion:** PIBD patients have significant disease at transfer to adult services with 24% having required anti-TNFα therapy and 82% at least one immunosuppressant. Disease severity progression continues; 19% of patients required their first anti-TNF agent in adult services and the rate of pan-treatment refractory IBD almost trebled to 11%.

**Disclosure of Interest:** None Declared
CLINICAL VALUE OF ANTIMICROBIAL PEPTIDES ASSESSMENT IN STOOL AND PLASMA IN CHILDREN WITH INFLAMMATORY BOWEL DISEASES

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Objectives and Study: Recent findings suggest a central role of the bacterial microflora and the innate mucosal barrier interactions in the pathogenesis of inflammatory bowel diseases (IBD). Important factors providing mucosal barrier are antimicrobial peptides like elafin, alpha 1-3 defensins and cathelicidin, which modify bacteria-host interactions. There is little known about their concentrations in children with IBD up to now. The objective of our study was to assess stool and plasma elafin, alpha 1-3 defensins and cathelicidin concentrations in children with Crohn's disease (CD) and ulcerative colitis (UC).

Methods: Thirty six children were enrolled to the study, including 15 children with newly diagnosed CD (8 boys, 7 girls, mean age: 13.8 yrs, range: 6.3 – 17.8 yrs), 21 with newly diagnosed UC (11 boys, 10 girls, mean age: 12.7 yrs, range: 6 -17.5 yrs) and 18 healthy controls. Elafin, alpha 1-3 defensin and cathelicidin concentrations were assessed in stool supernatants and plasma at the baseline, before the treatment and after 2 weeks of treatment using ELISA immunoassays (Hycult Biotech, the Netherlands). 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.

Results: We found increased stool and plasma elafin concentrations at the baseline in CD group as compared to UC group (p<0.05) and controls (p<0.05). Assessing stool and plasma alpha 1-3 defensin concentrations at baseline, they were comparable to CD and UC group, but elevated when compared to controls (p<0.05). During the treatment alpha 1-3 defensin concentrations in stool and plasma increased after 2 weeks in UC group (p<0.05) and decreased in CD group (p<0.05). Stool and plasma cathelicidin concentrations were comparable to CD and UC group at baseline and decreased during the treatment.

Conclusion: Increased stool and plasma elafin concentrations in CD and alpha 1-3 defensin concentrations in UC suggest different influence of bacterial microflora on mucosal barrier in pathogenesis of these diseases. Stool and plasma elafin and alpha 1-3 defensin assessment may be a useful clinical marker in differential diagnosis between CD and UC in children.

Disclosure of Interest: None Declared
THE ROLE OF MAGNETIC RESONANCE ENTEROGRAPHY IN ASSESSING PAEDIATRIC CROHN'S DISEASE ACTIVITY

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Objectives and Study: Children affected by Crohn's disease undergo magnetic resonance enterography (MRE) in order to identify to which extent the small and large bowels are involved, and to assess the disease activity. The aim of this study was to investigate the role of MRE in the disease staging at diagnosis and during the follow-up, to compare this technique with endoscopy and to study possible correlations through the use of SES-CD (Simple Endoscopic Score for Crohn Disease) and of the clinical score PCDAI (Pediatric Crohn Disease Activity Index).

Methods: 35 MRE investigations from 35 children (24 males; mean age 11.6 years; range 2.01-15.09) were retrospectively evaluated. MRE was performed using a 1.5T machine, and a protocol based on bowel preparation and distension with PEG as oral contrast was used. Patients underwent colonoscopy during the same admission. An imaging-based score of disease activity was obtained by applying the MaRIA Index (Magnetic Resonance Index of Activity, Rimola et al.) and the MEGS Index (Magnetic Resonance Enterography Global Score, Makanyanga et al.) For the statistical analysis, the Spearman coefficient was used in order to correlate the imaging-based Indexes (MGES and MaRIA), with the endoscopic score and the PCDAI. Non-parametric Mann Whitney test was used for independent sampling with non-normal distribution.

Results: Adverting to the Paris classification, 24 patients (68.6%) were L3, 5 (14.3%) L1, 5 L2, 1 (2.8%) L4, 8 (22.8%) B2, 27 (77.1%) B1. Six patients had perianal lesions: 1 (17.1%) B2p and 5 (83.3%) B1p. Three patients (8.6%) presented with growth delay (G1). Compared to the endoscopic investigation, MRE yielded a sensitivity of 71% for the assessment of the terminal ileum, and of 94% for the colonic location (51% looking at the single colonic segments). Moreover, the study of the small bowel segments other than terminal ileum was enabled by MRE in 13 patients. A significant high grade correlation between MaRIA Index and SES-CD score (r=0.70; p<0.05), and a significant moderate grade correlation between MaRIA Index and PCDAI score (r=0.50; p<0.01) were identified.

Conclusion: The MRE protocol used in this study allows a correct evaluation of small and large bowel involvement in paediatric Crohn's. Such technique yields accurate imaging-based quantification of the disease activity, which should be considered along with the endoscopic, clinical and biochemical assessments.
Disclosure of Interest: None Declared
**Objectives and Study:** Nutrition is involved in many aspects of Inflammatory Bowel Disease (IBD) including aetiology. Adult IBD studies have identified animal protein and Omega 6 lipids as risk factors for Crohn’s Disease (CD) and Omega 3 lipids as protective factors for Ulcerative Colitis (UC). Data on the role of diet in development of paediatric IBD is scanty. The aim of our study was to evaluate pre-illness dietary intakes in paediatric patients with newly diagnosed IBD and compare the findings with dietary consumption of healthy subjects. The objective of this comparison was to identify nutrients which could potentially be involved as dietary risk or protective factors for the development of disease.

**Methods:** Dietary consumption 12 months prior to symptom onset was assessed in 25 children and adolescents with newly diagnosed IBD aged 6-17 years (CD n=13, UC n=10, Undetermined Colitis (IBDU) n=2). Data on dietary consumption was collected by a dietitian, through a 7-day dietary recall and analysed with Software *MètaDieta*, which calculated the mean intakes of macro- and micronutrients from the diet. The same dietary recall was performed in healthy controls (HC; n=25), matched for age and gender. The nutrient intakes were expressed as percentage of the recommended dietary intakes for the Italian population (*RDI-Livelli di Assunzione di Energia e Nutrienti Raccomandati per la Popolazione Italiana LARN 2012*) and compared between IBD and HC groups. In IBD group, comparison of nutrient intakes between CD and UC subjects was also done.

**Results:** Energy intake (% of estimated energy requirements, EER) and protein intake (% of population reference intake, PRI) were higher in IBD vs HC group (p=0.017 and p=0.0001 respectively). Lipid intake (% of reference intake range for macronutrients, RI) was higher in HC vs IBD group (p=0.0417). Animal/Vegetable protein ratio and Omega 6/Omega 3 lipid ratio were higher in IBD vs HC group (p=0.0225 and p=0.0523 respectively). No between group differences were observed for carbohydrates and for micronutrients except for iron and vitamin E. Iron intake (% PRI) was higher in IBD vs HC group (p=0.0286). Intake of vitamin E (% of adequate intake, AI) was lower in IBD vs HC group, with values close to statistical significance (p=0.0752). Main results are represented in figure 1. In IBD group, no significant difference of nutrient intakes was observed between CD and UC subjects.

**Image:**
Conclusion: Our results suggest that specific nutrients may be implicated in pathogenesis of paediatric IBD. High intake of animal protein, Omega 6 lipids and iron may have a role as risk factors, whilst high consumption of Omega 3 lipids and vitamin E may be protective for the development of paediatric IBD.

Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0240

**INCREASED EXPRESSION OF MIR-146A AND MIR-155 IN THE DUODENAL MUCOSA OF PAEDIATRIC PATIENTS WITH CROHN’S DISEASE**

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**Objectives and Study:** The exact pathomechanism of Crohn’s disease (CD) is unknown, despite the fact that in the last decades very intense researches were in progress. In recent studies there is an increased interest in epigenetic factors, such as non-coding RNAs, the microRNAs (miR). Certain miRs have been observed to be dysregulated in CD. There are only a limited number of studies which examine the expression of miRs in paediatric patients suffering from CD. None of the studies examine the miR expression in the upper GI tract. Our aim was to analyze the expression of miR-146a, miR-155 and miR-122 in the duodenal mucosa of paediatric patients CD, based on our previous study performed in colonic mucosa.

**Methods:** Formaldehyde-fixated paraffin embedded biopsies were analyzed: duodenal biopsy with CD (CD: n=20), with macroscopically intact (uninflamed) (CD intact: n=10) and inflamed (CD inflamed: n=10) duodenal mucosa, and healthy controls (C: n=10). The expressions of different miRs were measured by real-time PCR.

**Results:** The expression of miR-146a and miR-155 were significantly higher in the intestinal mucosa of children with CD compared to the control group (CD vs. C, p<0.05, p<0.005, respectively). The increment of the expression levels of these miRs was significantly higher in the macroscopically inflamed intestinal biopsies compared to either biopsies derived from intact duodenal mucosa or from healthy controls (CD inflamed vs. C, p< 0.05; CD inflamed vs. CD intact, p<0.005). In contrast with our previous study, there was no significant difference in the expression of miR-122 between the CD and control group.

**Conclusion:** Our results suggest that miRs play an important role in the patomechanism of CD. Expressions of miRs differ regarding the disease severity, location, and the site of the biopsy. Elevated miR-146a and -155 levels were specific for inflammation, but independent of the location. Further studies are required to explore the function of these miRs regarding their role in the pathomechanism and possible usage as therapeutic targets.

**References:** Acknowledgment: This work was supported by grants OTKA-PD113022, OTKA-K105530, PD83431, PD105361, “Lendület” Research Grant LP008/2014 and KMR_12-1-2012-0074.

**Disclosure of Interest:** None Declared
Objectives and Study: Guidelines for the treatment of Ulcerative Colitis (UC), both in adult and pediatric patients, recommend the use of salicylates as first-line maintenance treatment even in moderate-to-severe disease after steroid-induced remission. Our aim is to compare the efficacy of two maintenance strategies (mesalamine and azathioprine) for pediatric UC after steroid-induced remission at diagnosis.

Methods: Patients with UC diagnosed in our center (January 2008-December 2013), who needed treatment with systemic steroids to induce remission were retrospectively studied. Patients receiving mesalamine and those receiving azathioprine (AZA) were compared.

Results: 16 patients were included. Seven patients received mesalamine (group 1) and 9 AZA (group 2). PUCAI at diagnosis, extension, and duration of steroid treatment were comparable.

Group 1: Mean time until first relapse was 22 weeks. During the follow-up all the seven patients (100%) needed a change in maintenance treatment due to relapse of the disease.

Group 2: Mean time until first relapse was 30 weeks. During the follow-up 5 patients (55%) needed a change of treatment; 1 patient was switched to 5ASA after toxicity attributable to AZA and 4 patients after relapse.

We found statistically significant differences in the number of patients with failure of initial treatment (100% in group 1, 55% in group 2, p<0.04).

Conclusion: Treatment with azathioprine is more effective than salicylates for maintaining the steroid-induced remission in pediatric UC at diagnosis. The course of the disease in these patients is severe enough to determine the need for treatment escalation in 55% of the patients even on AZA since diagnosis.

Disclosure of Interest: None Declared
**Objectives and Study:** The aim of this study was to assess the impact of biologic therapy with ADA on MH and microscopic remission in pediatric patients with CD.

**Methods:** Twenty three children aged 13.0±9.3 years with moderate to severely active CD were included into the study. Seven patients (30.4%) had been previously treated with infliximab and switched to ADA due to intolerance or loss of response. Colonoscopy and gastroscopy with sample collection were performed in all patients before and after induction treatment with ADA. Clinical activity of the disease was assessed using the Pediatric Crohn's Disease Activity Index (PCDAI), and the endoscopic activity was scored using the Simple Endoscopic Score (SES-CD). Histological changes were evaluated by a previously described numerical scoring system.

**Results:** Four patients (17.4%) reached clinical remission (PCDAI ≤10). When comparing data at baseline and at week after ADA treatment, a significant decrease was observed in median PCDAI, and in SES-CD score between the initial and control colonoscopies. We reported a decrease in histological scale which was not statistically significant. The correlation was found between PCDAI and SES-CD score.

**Conclusion:** Biological therapy with adalimumab has a positive impact on mucosal healing in pediatric patients with CD, which is not associated with histological evidence of suppression of inflammation. Mucosal healing correlates better than microscopic healing with clinical remission.

**References:**

**Disclosure of Interest:** None Declared
**Objectives and Study:** Faecal calprotectin (FC) is a good marker in monitoring mucosal healing in adults with ulcerative colitis. Its concentrations in faeces is closely related to state of mucosa observed in endoscopy. There are a few studies concerning FC in mucosa status assessment in paediatrics population with UC. The aim of the study was to assess the usefulness of FC as a biomarker of endoscopy proven mucosal healing in monitoring of children with UC.

**Methods:** 66 patients with UC (F 36, M 30, ±14,16 years) were involved to the study and had elective colonoscopy performed, FC level and erythrocyte sedimentation rate (ESR) within a week before endoscopy measured. Each patient had also body mass index (BMI) and paediatric ulcerative colitis activity index (PUCAI) calculated. Mucosa status during endoscopy was assessed with Baron score. Full mucosal healing was defined as Baron score=0. We have identified two subgroups: those with full mucosal healing, and patients with inflamed gut mucosa. The receiver operating characteristic curve (ROC) was used as a statistical method to establish cut-off points. The cut-off points are calprotectin threshold for simple model and posterior probability threshold for the linear discriminant analysis (LDA). The area under the curve (AUC) assesses the differentiation quality of the study group based on the model score. To increase sensitivity at high specificity the LDA with FC, ESR, BMI and PUCAI was taken.

**Results:** AUC for the simple model was 0.90. The selected cut-off level of discrimination between subgroup with full mucosal healing vs. subgroup with mucosal inflammation present was 189 μg/g with sensitivity 0.96 and specificity 0.75. When specificity was outweighed over sensitivity the cut-off point was 62 μg/g with sensitivity 0.50 and specificity 0.95. Due to the low sensitivity accompanying high specificity we used LDA with other parameters to increase sensitivity rate. With LDA used on FC, ESR, BMI and PUCAI the AUC was 0.90, and we could discriminate our patient with sensitivity 0.61 and specificity 0.97.

**Conclusion:** FC is a good marker of mucosal healing in monitoring of children with UC. FC above 189 μg/g enable to select 75% of patients with active inflammation in gut mucosa. LDA with FC, ESR, BMI and PUCAI let us select 61% of patients with full mucosal healing. Using these two methods, step by step, we could discriminate patients with unknown mucosa status, that requires endoscopy.

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

**Inflammatory Bowel Disease**

PO-G-0244

**EARLY-ONSET INFLAMMATORY BOWEL DISEASE CONDITIONED BY A NOVEL IL10RA MUTATION THAT LEADS TO AN ABERRANT IL-10 SIGNALING**

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**Objectives and Study:** The very early onset inflammatory bowel disease (EO-IBD) has been explained by defects in the interleukin 10 (IL-10) signaling pathway. We reported a case of EO-IBD by a novel IL-10 receptor alpha (IL-10RA) mutation with its clinical and genetic features.

**Methods:** PBMC of the clinically suspected child was collected for DNA sequencing of genes IL-10 and IL-10 receptors and functional assays. Complete immunological investigations were done to rule out others known abnormalities.

**Results:** A term boy with consanguineous parents started recurrent infections and diarrhea in the first months. At the sixth month he showed anal fissures with significant growth failure. He was treated with amino acid formula that lead to diarrhea improvement but with continuing recurrent infections. At the end of the first year a bloody diarrhea started, and the endoscopy and colonoscopy showed nodular duodenitis, perianal fissures and fistulae, florid colitis of the sigmoid colon and ileocecal valve. No granulomata were seen on histology. There was no improvement with corticosteroid and azathioprine treatment. He had multiple courses of antibiotics for perianal, intestinal, respiratory infections and sepsis. The total enteral nutritional with amino acid formula showed partial improvement of diarrhea and a gastrostomy tube was placed. Currently at 3 years of age, he has height Z score -3.33, weight Z score -2.02, BMI Z score + 0.38 and maintaining recurrent infections. A novel homozygous mutation in the IL-10RA was detected, which was described as c.598G>A (p.T247Tsfs242_247del). The mutation has caused important conformational changes in the extracellular portion of the IL-10RA as shown by bioinformatics. To demonstrate if the mutation was functional, the PBMCs of the child was submitted to LPS and LPS/IL-10 stimuli, and TNFα levels in the supernatant were measured by ELISA. Partial binding of the IL-10 to IL-10RA was also shown by flow cytometry. Interestingly, an impaired IL-10 signaling was demonstrated by exacerbated TNFα production under the LPS+IL-10 treatment, when similar levels were expected in both stimuli. There was not other defined primary immunodeficiency.

**Conclusion:** An aberrant IL-10 signaling was demonstrated in this novel IL-10RA mutation. Any treatment used could not keep the symptoms under control, although the total amino acid enteral nutritional has improved partially the diarrhea and kept a satisfactory nutritional state. Further investigations are under way to demonstrate the origin of the mutation and how anti- and pro-inflammatory pathways are cross-talking using agonists and antagonists in PBMCs of both parents.
and child.

Disclosure of Interest: None Declared
SURGICAL INTERVENTIONS IN CHILDREN WITH ULCERATIVE COLITIS
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Objectives and Study: Previous studies have reported 10-year colectomy rates of over 35% in adult patients with ulcerative colitis (UC). Data regarding colectomy rates in pediatric UC is limited. We sought to analyze the occurrence of surgical interventions in pediatric UC patients during a long-term follow-up and to assess its association with disease severity at diagnosis.

Methods: We performed a chart review of pediatric UC patients using the Schneider Pediatric Inflammatory Bowel Diseases (SPID), cohort database, including pediatric UC patients (aged: 2-18 yr) with up to 32 years of post diagnosis follow-up.

Results: Median follow-up was 8.55 years (range 1-32.7 yr). Among 188 patients with UC, 37 (20%) underwent surgery, 33 of whom (89%) underwent proctocolectomy with ileal pouch–anal anastomosis (IPAA) including 8 (24%) who were operated within the first year post diagnosis. The other four patients underwent proctocolectomy with ileoanal anastomosis, right hemicolectomy, sigmoidectomy or anterior rectal resection. Median duration from diagnosis to first surgical intervention was 9.6 yr (range 0.27-21.2 yr). Of patients who underwent IPAA, 21 (64%) developed pouchitis; acute in 30%, chronic in 25% and extended (crohn’s like disease) in 9%. Four patients underwent second surgical procedure during follow-up with a median duration from diagnosis to second intervention of 18.4 yr (range 11.8-28.7 yr). Defined by Pediatric UC activity index (PUCAI), 6 % of patients (12/188) had severe disease at diagnosis, 49% (92/188) and 45% (84/188) had moderate and mild disease, respectively. Patients with severe disease at diagnosis had a 50% colectomy rate during follow-up (6/12) compared with 21% (19/92) and 9.5% (8/84) of patients with moderate and mild disease, respectively (p=0.001).

Conclusion: The colectomy rate in a large Israeli pediatric UC cohort is lower than reported in previous several adult series. The risk for colectomy was associated with disease severity at diagnosis with a high rate of pouchitis demonstrated in operated patients with IPAA.

Disclosure of Interest: None Declared
**Gastroenterology**  
**Inflammatory Bowel Disease**  
PO-G-0246

**BONE MINERAL DENSITY AND VITAMIN D STATUS IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE**

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**Objectives and Study:**  Patients with inflammatory bowel disease (IBD) are at increased risk of metabolic bone disorders and decreased bone mineral density (BMD). Multiple factors have been implicated in significantly impaired BMD including chronic inflammatory state, steroid therapy, malabsorption, malnutrition and growth failure. The aim of the study was to evaluate BMD and identify clinical factors associated with low bone density in children with IBD.

**Methods:** Forty two children with IBD including 17 at the time of IBD diagnosis, 16 in IBD remission, 9 with IBD exacerbation, and 46 healthy controls were studied. Patients with IBD underwent bone density assessment by dual-energy X-ray absorptiometry of the lumbar spine. Low bone mineral density was defined as BMD z-score ≤-2SD. Laboratory tests included serum calcium, phosphate, magnesium, alkaline phosphatase, 25-hydroxy vitamin D (25(OH)D), C-reactive protein, total protein and albumin. Serum 25(OH)D concentration was measured using 25-OH-Vitamin D direct ELISA kit. Vitamin D serious deficiency was defined as 25(OH)D level <30nmol/L, deficiency as 30-75nmol/L and sufficiency as >75nmol/L. Statistical significance was defined as p<0.05.

**Results:** Study group comprised 26(62%) children with ulcerative colitis (UC) and 16(38%) with Crohn’s disease (CD). The mean age was 14±3 years old. The median disease duration was 6 months. BMD z-score ranged from -3.3 to 1 with median -0.7. Low BMD was stated in 11(26%) children with IBD, including 7/26(27%) with UC and 4/16(25%) with CD. There was no significant difference between BMD z-score in children with CD and UC (p=0.7). No significant correlation was found between BMD z-score and either disease duration (p=0.2) or severity (p=0.5). The virtually significant negative correlation was found between BMD z-score and C-reactive protein (p=0.058). In IBD children 30(71.4%) had vitamin D deficiency, 11(26.2%) serious deficiency and only 1(2.4%) child had sufficient vitamin D level. In healthy controls 37(80.4%) had vitamin D deficiency, 3(6.5%) serious deficiency and 6(13.1%) had sufficient concentration of vitamin D. The difference in 25(OH)D concentration between IBD children and healthy controls almost approached significance (p=0.054). There was no correlation between 25(OH)D level and BMD z-score (p=0.6).

**Conclusion:** In this sample the frequency of low bone mineral density was considerably high and occurred in one quarter of children with IBD. BMD may not be affected by vitamin D status, IBD severity or duration. Further studies are needed to clarify mechanism of impaired bone metabolism in children with IBD. We recommend screening and monitoring BMD in children with IBD.

**Disclosure of Interest:** None Declared

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Vol. 60, Supplement 1, May 2015
LONG TERM OUTCOMES OF ANTI-TNF TREATED PAEDIATRIC INFLAMMATORY BOWEL DISEASE PATIENTS AFTER TRANSITION TO ADULT SERVICES

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Objectives and Study: Anti-TNF therapy use in paediatric IBD (PIBD) is increasing worldwide with evidence of short-term effectiveness and safety. Longer term outcomes are less clear due to lack of follow-up (FU) of young people after transition to adult services. We aimed to assess effectiveness and safety of anti-TNF therapy in PIBD post-transition to adult care.

Methods: A retrospective case review of PIBD patients treated with anti-TNF (Infliximab (IFX) or Adalimumab (ADA)) in the SE Scotland regional PIBD unit at RHSC, Edinburgh and then transitioned to the regional adult specialist IBD centre at WGH, Edinburgh, during 01/01/00-30/09/13. Data (including outcome and duration of anti-TNF therapy, dose escalation, adverse events and discontinuation/re-start of therapy) were collected prior to, at the time of transition from PIBD services, and to study end point (transfer out of region, loss to FU, death or ongoing adult care at 31/07/2014), a minimum 10 months FU.

Results: 34 children (30 Crohn’s disease (CD), 4 ulcerative colitis (UC)) had anti-TNF exposure in PIBD services then a median (range) duration of FU post-transition of 2.9 (0.7-9.3) years. At transition, 19/34 were still on anti-TNF (12 IFX and 7 ADA). 10/12 IFX were in steroid-free remission (SFR) and 8/10 remained in SFR at last FU; 2 discontinued IFX due to loss of response (LoR), both then had ADA with 1 ADA LoR and 1 SFR on ADA at last FU. 1/12 IFX patient with moderate disease at transition then achieved remission, had planned drug withdrawal (PDW) then relapsed, restarted IFX and had mild disease at last FU. 1/12 IFX patients had response with mild disease post-induction IFX but transitioned and had primary non-response (PNR) by 6 doses IFX, and switched to ADA with moderate disease activity at last FU. 3/7 ADA patients at transition were in SFR; 1 stopped as PDW in prolonged remission but 2 stopped due to adverse events. 2/7 ADA patients with mild disease at transition then achieved sustained remission up to last FU. 2/7 ADA patients had moderate disease at transition; one had ADA LoR and moderate disease at last FU, the other gained remission so had PDW, relapsed but was in remission at last FU. There were no deaths or malignancies associated with anti-TNF use.

Conclusion: Anti-TNF therapy post-transition is effective at maintaining remission in those with remission prior to transition, although some may require a 2nd anti-TNF agent to maintain remission. Those previously not in remission can achieve sustained remission, usually if just starting anti-TNF maintenance at transition; others do not and have a more complicated disease course. Loss of response remains a key reason for stopping anti-TNF therapy.

References:
Disclosure of Interest: None Declared
THE DEVELOPMENT OF ANTI-INFLIXIMAB ANTIBODIES IN CHILDREN WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Infliximab is proven effective in the treatment of inflammatory bowel disease in children and leads to dramatic improvement in the life of patients. Development of infliximab antibodies indicates the cessation of treatment and poses challenges to clinicians. We present our experience in children with inflammatory bowel disease who developed antibodies against infliximab.

Methods: 27 pediatric patients (13 boys, median age 11.5 years) were treated with infliximab for ulcerative colitis (7 patients) and Crohn’s disease (20 patients) at King’s College Hospital in 2013-2014. The clinical response, activity of disease and infliximab levels/antibodies were reviewed.

Results: Infliximab treatment was discontinued in 4/27 patients (14.8%) due to poor response despite the absence of infliximab antibodies and therapeutic infliximab serum levels. 5 patients (18.5%) (1 boy) developed infliximab antibodies. Patient's age, diagnosis and duration of disease, concomitant treatment, duration/number of infliximab infusions, dose of infliximab, activity index, and titer of serum infliximab and infliximab antibodies at the time of antibody identification are shown in table 1. 3/5 patients developed antibodies within a year and 5/5 in less than 2 years. 2/5 patients had measurable serum infliximab levels in the presence of high titer antibodies. Patient 1 and 3 were subsequently treated with adalimumab. Patient 2 is due endoscopic reassessment. Patient’s 4 endoscopy revealed mildly active chronic pancolitis-proctitis. Following endoscopy the patient was treated with steroids and is currently off biologics. Patient 5 is in clinical remission and still on infliximab.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (years)</th>
<th>Diagnosis</th>
<th>Duration of the disease (years)</th>
<th>Treatment</th>
<th>Duration (months)/ number of infusions</th>
<th>Infliximab</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient 1</td>
<td>9</td>
<td>Perianal Crohn’s</td>
<td>5</td>
<td>Azathioprine</td>
<td>18/ 11</td>
<td>10</td>
</tr>
<tr>
<td>Patient 2</td>
<td>16</td>
<td>UC/AILD</td>
<td>5</td>
<td>Mesalazine, Prednisolone, Azathioprine</td>
<td>4/ 5</td>
<td>5</td>
</tr>
<tr>
<td>Patient 3</td>
<td>13</td>
<td>Crohn’s</td>
<td>1</td>
<td>Azathioprine</td>
<td>8/ 6</td>
<td>5</td>
</tr>
<tr>
<td>Patient 4</td>
<td>6</td>
<td>UC</td>
<td>1.7</td>
<td>Mesalazine, Azathioprine, Sulphasalazine (enema)</td>
<td>8/ 6</td>
<td>5</td>
</tr>
<tr>
<td>Patient 5</td>
<td>12</td>
<td>Perianal Crohn’s</td>
<td>1</td>
<td>Mesalazine</td>
<td>13/10</td>
<td>5</td>
</tr>
</tbody>
</table>
Table 1.
UC: ulcerative colitis, AILD: autoimmune liver disease, PUCAI: pediatric ulcerative colitis activity index, PCDAI: pediatric Crohn’s disease activity index, FC: faecal calprotectin

**Conclusion:** The development of infliximab antibodies in children with inflammatory bowel disease results in loss of response and necessitates different treatment strategy. In selected cases infliximab serum levels remain measurable despite the presence of antibodies and the drug is effective to sustain clinical remission.

**Disclosure of Interest:** None Declared
**Objectives and Study:** The frequency of surgical interventions in crohn's disease (CD) patients has diminished significantly in the era of biologic targeted therapies. Data describing the incidence and the risk factors for surgical interventions in pediatric CD is scarce. We sought to assess the rate of surgical interventions in a large pediatric CD cohort during a long-term follow-up period.

**Methods:** We performed a chart review using the Schneider Pediatric Inflammatory Bowel Diseases (SPID), cohort database, including pediatric CD patients (aged: 2-18 yr) with up to 30 years of post-diagnosis follow-up. Diagnosis of CD was based on clinical, radiologic, endoscopic and histological examinations.

**Results:** Median follow-up was 8.5 years (range 1-30.4 yr). Among 479 patients with CD, 147 (31%) underwent a surgical procedure, 36 of them (25%), during the first year of follow-up. Median interval from diagnosis to first intervention was 5.5 yr (range 0.42-26.2 yr). Ileocecal resection was performed in 52% of operated patients, right hemicolectomy in 22%, fistulectomy in 10% and small bowel resection in 9%. Twenty two patients (5%) underwent at least 2 surgical operations during follow-up. At diagnosis, 44% (211/479) patients presented with ileal disease (L1), 17% (81/479) with isolated colonic disease (L2), 36% (173/479) with ileo-colonic disease (L3) and 3% (14/479) with isolated upper gastrointestinal involvement according to Paris classification. Among patients who presented with ileal disease, 43% (90/211) underwent surgical intervention, compared to 25% (44/173) and 16% (13/81) of ileo-colonic and colonic disease respectively (p<0.001). Complicated disease behavior (defined as stricturing, penetrating or both) was observed in 24% (115/479) at diagnosis. Among these patients 45% (52/115) underwent surgical intervention compared to 26% (95/364) for those with uncomplicated disease (p<0.001). Ten-year surgical intervention rate was 31% (58/187) prior to the year 2000 and 19% (55/292) afterwards (p=0.002).

**Conclusion:** In our cohort, a significant proportion of pediatric CD patients underwent surgical interventions during prolonged follow-up. Ileal disease phenotype and complicated behavior at presentation predicted a higher rate of surgical interventions during follow-up. We observed a significant decrease in surgical intervention rate in recent years which could be attributed to the emergence of biologic therapies.

**Disclosure of Interest:** None Declared
HAS THE RISING INCIDENCE OF PAEDIATRIC INFLAMMATORY BOWEL DISEASE IN SOUTH WALES STABILISED?

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Objectives and Study: The incidence of paediatric inflammatory bowel disease (IBD) has risen significantly across Europe in the last 20 years, although our own Welsh data had suggested that this had plateaued by 2004. We have now studied the data from the same area over the last decade and compared them with our previous published studies from South East Wales (1983-2003).

Methods: All cases of IBD < 16 yrs old residing in a defined location within South Wales (Cardiff and Vale) were prospectively recorded from January 2004 to March 2014. The incidence, age, gender and disease type were analysed and compared to our data from 1983-2003 from the same region.

Results: Between 2004 and 2014, there were 57 new patients compared to 39 (1996-2003) and 28 (1983-1993). The overall incidence of IBD was 5.9 per 100,000 per year, Crohn’s disease (CD) 3.7 per 100,000 per year and Ulcerative colitis (UC) 2.07 per 100,000 per year compared with 5.4/100,000 for 1996 to 2003. There is no statistically significant difference between the two groups. The median age at diagnosis remains at 12 years with a male- to- female ratio of 1.7:1

Image:

Conclusion: The incidence of paediatric IBD in a defined geographical area within South Wales has remained similar for over 15 years suggesting that the previous exponential rise in incidence has reached a stable state.

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Arch Dis Chid 1996;74:460-1
Disclosure of Interest: None Declared
**Gastroenterology**

**Inflammatory Bowel Disease**

PO-G-0251

**DICKKOPF-1 IS CORRELATED WITH INFLAMMATION IN CROHN’S DISEASE**

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**Objectives and Study:** Dickkopf-1 (DKK-1) is a secreted glycoprotein that has been demonstrated to act as a potent inhibitor of the canonical Wnt/β-catenin signaling pathway. To explore the potential role of DKK-1 and β-catenin in Crohn’s disease (CD) and to evaluate the effect of a tumor necrosis factor (TNF)-α inhibitor (infliximab) on Wnt signaling in patients with CD.

**Methods:** We enrolled 21 patients who received infliximab treatment for one year and who achieved clinical remission during the treatment period. Peripheral blood and colonic mucosal specimens were collected from all 21 CD patients and from 14 healthy control individuals. DKK-1 levels in serum were detected by enzyme-linked immunosorbent assay (ELISA). Total RNA for DKK-1 and β-catenin from the frozen colonic tissue was obtained real-time quantitative reverse transcription-polymerase chain reaction (RT-PCR). Serum C-reactive protein (CRP) levels, erythrocyte sedimentation rates (ESR), albumin and the Pediatric Crohn Disease Activity Index (PCDAI) were also measured in patients with CD before and after infliximab therapy.

**Results:** The serum level of DKK-1 was significantly higher in patients with CD than in healthy controls (P = 0.003) and decreased in CD patients treated with infliximab (P = 0.026). The serum DKK-1 level was correlated with levels of ESR (r = 0.527, P = 0.025), CRP (r = 0.502, P = 0.034), albumin (r = 0.363, P = 0.021) and PCDAI (r = 0.462, P = 0.054) in CD. DKK-1 mRNA expression in the colonic mucosa was higher in patients than in controls and decreased after infliximab treatment. β-catenin expression in the colonic mucosa was lower in patients than in controls and increased after infliximab treatment. However, there were no statistical differences (P>0.05).

**Conclusion:** DKK-1, as an important mediator, might be associated with the process of the pathogenesis of CD. The change of DKK-1 level may serve as a biomarker of inflammation in patients with CD.

**Disclosure of Interest:** None Declared
ADALIMUMAB IN THE TREATMENT OF PAEDIATRIC PATIENTS WITH CROHN’S DISEASE NAIVE TO BIOLOGICAL THERAPY – A SINGLE CENTRE EXPERIENCE

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**Objectives and Study:** Adalimumab (ADA) was recently approved for use in paediatric patients with Crohn’s disease (CD). Previously, ADA was used in clinical practice mainly as second-line therapy in patients who failed to infliximab. Until now, there are very limited data in the literature concerning use of ADA as first line biological therapy in paediatric patients with CD (ref. 1,2).

**Methods:** In the years 2013 and 2014, ADA therapy was commenced in 12 patients (8 boys, 4 girls) naive to biological therapy in our tertiary referral center. Average age at start of the treatment was 14.5 years (10.5-18), median time of duration of the treatment was 0.5 years (0.2-1.5). Patients had various phenotypes of CD (L1 (n=5), L3 (n=7), +L4 (n=5), B1 (n=6), B2 (n=1), B3p (n=4)). All patients had concomitant treatment with azathioprine (n=11) or methotrexate (n=1).

**Results:** Six patients (50 %) achieved clinical remission (one of them started ADA after ileocaecal (IC) resection due to residual disease), 3 patients (25 %) had clinical response, 2 patients (17 %) developed stricture in the IC area leading to operation. Two patients (17 %) had to be intensified to every-week dosage. One patient remains active in spite of intensification and will undergo re-evaluation. In 2 patients (17 %) faecal calprotectin remains significantly high (over 1800 ug/g) in spite of clinical remission. No major safety concerns during the treatment were detected.

**Conclusion:** Our data suggest that ADA is effective and safe as first-line biological therapy in treatment of paediatric patients with CD. Longer follow-up is necessary to evaluate rate of long-term response and remission and failure rate.

Study was supported by research grant VZ FNM 64203/6001 and Centrum detske gastroenterologie a vyzivy.

**References:**

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

**Inflammatory Bowel Disease**

PO-G-0253

**SIGNIFICANCE OF “INTESTINAL ALKALINE PHOSPHATASE" AS A HISTOLOGICAL MARKER IN MONITORING INFLAMMATORY BOWEL DISEASES ACTIVITY**

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**Objectives and Study:** Intestinal alkaline phosphatase (iAP) is an intestinal brush border enzyme that has significant roles in maintaining intestinal mucosal defense mainly through the detoxification of bacterial endotoxins. iAP has been thought to be one of the factors involved in the pathogenesis of inflammatory bowel disease (IBD).

**Methods:** The aim of this study is to investigate the relation between iAP and IBD activity and role of iAP in the monitoring of IBD activity. Pre-/post-treatment colonoscopic biopsy specimens of IBD patients consisting of Crohn’s disease (CD) and Ulcerative colitis (UC) and control group (CG) were stained immunohistochemically with anti-human iAP antibody and degree of iAP staining in different localizations was graded. Hematoxylin-eosin (HE) sections were used to determine inflammatory activity. The histopathological findings were compared in pre and post-treatment biopsies of each group and with CG. The relation between histological findings and Paediatric Crohn’s Disease Activity Index (PCDAI), Paediatric Ulcerative Colitis Activity Index (PUCAI) were evaluated.

**Results:** A total of 24 IBD patients (mean age of 12 CD patients was 11.5 and of 12 UC patients was 12.9 years) and 20 controls were included in the study. Mean time between pre and post-treatment colonoscopies was 22 months. Intestinal alkaline phosphatase staining was reduced in IBD patients compared to CG. For CD and UC patients no significant difference was detected for iAP staining in pre-treatment and post-treatment biopsies of any segment. In terminal ileum (t. ileum), iAP staining was remarkably concentrated in region 1 (apical surface, brush border and epithelial cells) and a significant negative correlation was found between grade of iAP staining and inflammatory activity both in pre and post treatment biopsies (p=0.008 and p=0.02, respectively) in CD patients. In UC patients no significant correlation between iAP staining and inflammatory activity was detected for t. ileum or any colonic segment in pre and post treatment biopsies. Pre-treatment biopsies of t. ileum and colon taken from IBD patients and CG were compared according to the grade of staining with iAP. There were a statistically significant difference in region 2 (lamina propria and goblet cells) of t. ileum and both in region 1 and 2 of colon (p=0.015, p=0.006, p=0.000 respectively) in three groups. We did not find a significant correlation between inflammatory activity and disease activity indices in all regions of t. ileum and colon.

**Conclusion:** Immunohistochemical staining with iAP antibody may be used as an additional marker predicting the activity of IBD especially for CD. Further studies with large number of patients are needed.

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Disclosure of Interest: None Declared
**Objectives and Study:** In order to correctly evaluate the severity of Crohn’s disease at the time of diagnosis and the response to treatment, the most commonly used tool in everyday clinical practice is PCDAI, the clinical index of severity. It has been known that there is no strong correlation between clinical symptoms and changes in intestinal mucosa. Our aim was to evaluate the correlation of Pediatric Crohn’s Disease Activity Index (PCDAI) and Simple Endoscopic Score for Crohn’s Disease (SES-CD) at the time of diagnosis.

**Methods:** We prospectively analyzed 32 patients with newly diagnosed Crohn’s diseases admitted to the Department of Pediatrics in Clinical Hospital Centre Rijeka from 2008 to 2014. All the patients had undergone upper and lower endoscopy in deep sedation. SES-CD score was evaluated by the investigator. PCDAI was made at the time of admission. Pearson test was used to test the correlation.

**Results:** In our study there were 23 boys (72%) and 9 girls (28%), with mean age 13.25 years, range 3-17. According to PCDAI, 11 patients (34%) had inactive disease, 14 (44%) had mild disease, while 3 (10%) had moderate and 4 (12%) severe disease. At the contrary, after calculating SES-CD 50% of patients (16) had inactive disease, while the same number of patients (8, 25%) had mild and moderate disease. None of them had severe disease. When comparing the scores there is moderate, but statistically significant correlation between SES-CD and PCDAI, R=0.5093 (p= 0.00291, p<0.05).

**Conclusion:** PCDAI is clinically well established parameter in evaluating disease severity, but with no adequate reliability in detecting mucosal inflammation. We found SES-CD score clinically usable tool in clinical practice with statistically significant correlation with PCDAI which can both be used for detecting disease severity at the time of diagnosis and follow up in monitoring response to treatment.

**Disclosure of Interest:** None Declared
EOSINOPHILIC X PROTEIN CAN BE USED AS NON INVASIVE MARKER TO DIAGNOSE INFLAMMATORY BOWEL DISEASE IN CHILDREN WITH CHRONIC DIARRHEA

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Objectives and Study: Eosinophilic Protein X (EPX) is a cationic protein, which is released from eosinophils during inflammation, and can be measured within the stool. Although non-specific, evaluation of EPX offers an indication of eosinophilic activity associated with food allergy or parasitic infection. There are a number of invasive procedures that assess eosinophilic activity in the intestinal mucosa, including histologic observation, immunochemistry markers, and gut lavage. However, all of these tests have limited utility because they require colonoscopy or biopsy. In addition, EPX is not prone to many of the clinical drawbacks of other noninvasive inflammatory markers.

Methods: After obtaining appropriate consent, we measured EPX randomly in children presented to the tertiary gastroenterology clinic and asked for stool sample. We reviewed the clinical notes regarding age, sex, clinical presentation and diagnosis.

Results: Total of 41 (17 male and 24 female), aged from 1 year to 19 years, children's fecal sample was used to analyze the EXP. Total of 41 (17 male and 24 female), Normal level was reported as less than 60 ug/l, levels varied from 43.2ng/ml to >3,220ng/ml. 12 children were known to have IBD, level was high in all these children ranged from 1717 to above 3,200 (normal less than 60), 3 children was confirmed to have EGID (Eosinophilic Gastrointestinal disease), level ranged from 188 to 878. 4 children was seen with history of chronic diarrhoea with suspected food allergy, levels varied from 67 to 2,800. 1 child had confirmed coeliac diagnosis and the level was 190.17, 17 children was seen with history abdominal pain, reflux or food allergy but not confirmed.

Conclusion: Faecal assay of Eosinophil protein X (EPX) offers a sensitive, noninvasive alternative to these invasive procedures. EPX offers increased sensitivity for evaluating inflammatory disease including Eosinophilic gut disease as an alternative to faecal Calprotectin.

Disclosure of Interest: None Declared
DECREASED SERUM IGA RESPONSES TO MILK AND MITE ALLERGENS DURING EARLY CHILDHOOD ASSOCIATED WITH ALLERGY AT AGE 5.
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Objectives and Study: Allergy afflicts up to one third of children, impacting quality of life and socio-economic aspects. These disorders may remain difficult to diagnose in very young patients, while there is no validated predictive tests. The objective of this study was to determine whether we could identify immune features that may predict the development of allergy during infancy.

Methods: We recruited a birth cohort of 200 subjects, followed to 60 months of age. Subjects were examined at birth and at 2, 6, 12, 18, 24, 36, 48 and 60 months, and skin prick and specific IgE responses to common (including milk and mite) allergens were performed at 6, 18, 36 and 60 months. In addition, serum from age 2, 6, 18, 36 and 60 months were assayed for anti-β lactoglobulin (LG) and anti-Dermatophagoides pteronyssinus (Der p) IgA1 antibodies.

Results: At 36 months, among 161 subjects for whom data were available, 41 were classified as allergic children. Mean levels of serum anti-βLG IgA1 at 2 months of age were significantly lower in these allergic subjects, as compared to non-allergic children (p<0.0117). A similar finding was observed at 36 months (p<0.001, Table). In addition, a strong inverse correlation was observed between levels of serum anti-Der p IgA1 at 2 months and of anti-Der p IgE at 5 years of age (R² 0.83, p<0.0122). Moreover, anti-Der p IgA1 levels at 2 months were significantly lower in the future atopic children as compared to non-allergic children (1.19 (95%CI 0.25-5.56, n=11) vs 8.87 (95%CI 5.83-13.48, n=14), p<0.0022).

<table>
<thead>
<tr>
<th>Allergy at 36 months</th>
<th>n</th>
<th>Age (months)</th>
<th>Serum βLG-IgA1 (mean, AU)</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>9</td>
<td>2</td>
<td>18.5</td>
<td>13.07-26.18</td>
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<tr>
<td></td>
<td>5</td>
<td>2</td>
<td>6.96</td>
<td>3.22-15.04</td>
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<td>2</td>
<td>6</td>
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<td>93.41-166.87</td>
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<td></td>
<td>2</td>
<td>36</td>
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<td>No</td>
<td>1</td>
<td>2</td>
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<td></td>
<td>0</td>
<td>36</td>
<td>71.85</td>
<td>58.72-87.92</td>
</tr>
</tbody>
</table>
Conclusion: Lower levels of serum specific IgA1 to milk and mite allergens in 2 months-old infants are associated with the development of allergy and atopy later on. Future studies should confirm this relationship and whether it relates to deficient mucosal immunity to allergens.

Disclosure of Interest: None Declared
RESEARCH DURING PAEDIATRIC GASTROENTEROLOGY TRAINING: RESULTS OF A SURVEY

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Objectives and Study: Promoting child health not only relies on good clinical practice, but also on well conducted research. Paediatric Gastroenterology (GI) training should be a perfect time to start and continue research.

Methods: A survey among paediatric GI trainees in the European Crohn’s and Colitis Organization (ECCO) and the European Society for Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) was conducted from 2012 until 2013 inquiring about research opportunities during paediatric GI training.

Results: There were 104 responses from various European countries and a few other countries with a mean age of the trainees of 32.9 years, 62% were female. 43.3% have already undertaken a dedicated period of research during their paediatric GI training, 31.1% of them are applying for, are doing or have completed a PhD, 2.2% are doing an MSc. 5.8% wish not to do any research and 8.7% feel pressured to do research. 48.1% think that doing research will improve their job prospects in the long term and 14.4% are doing research in order to find out if they would enjoy research. 43.3% are doing research for an academic career. 36.5% have not perceived any opportunity to do research, and of those 89.5% would like to do research.

54.8% would be able to undertake a dedicated period or research where they are currently working, and 8.7% of those who have an opportunity to do research would rather go elsewhere. 73.1% consider going to another country if the opportunity became available.

17.3% know how to get funding and 26.7% of those who want to pursue an academic career know how to get funding.

Conclusion: Since less than half of the Paediatric GI trainees have already conducted research, and only a little more than 50% would be able to conduct research where they are currently working it becomes obvious that Paediatric GI trainees need more time and means to conduct research during their training. Actually, roughly 40% have not perceived any opportunity to do research. A solution to this may be that during Paediatric GI training there should be allotted time dedicated to research, e.g. one or two years of research during a three year programme. A little less than half of the Paediatric GI trainees are planning to pursue an academic career and less than 10% wish not to do any research or feel pressured, which may be skewed by the fact that only subspecialty trainees took part in the survey. Almost three quarters of the Paediatric GI trainees are considering going abroad if they had the opportunity, highlighting the need for international cooperation and financial grants. However, less
than 20 % know how to get funding which again underscores the need for research training, which should be offered to all Paediatric GI trainees.

**Disclosure of Interest:** None Declared
**NEW APPROACH TO PREDICT THE EFFECT OF FOOD-DRUG INTERACTIONS ON ORAL BIOAVAILABILITY OF DRUGS IN CHILDREN**

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1 TNO, 2 TNO Triskelion, Zeist, 3 Erasmus MC - Sophia Children’s Hospital, Rotterdam, Netherlands

**Objectives and Study:** An accurate prediction of oral bioavailability of drugs in children is very difficult, especially when food-drug interactions and off-label dosing needs to be taken into account. We aimed to design a new approach for optimal prediction of the effect of food-drug interactions on the oral bioavailability of drugs in young children. To demonstrate our approach, we selected paracetamol syrup as a model drug, since paracetamol syrup is often given in combination with food.

**Methods:** First, the fraction of paracetamol accessible for absorption across intestinal tissue was determined using a dynamic paediatric gastro-intestinal model (TIMpaediatric) using age-related food matrices. Thereafter, the *in vitro* apparent permeability (Papp) of paracetamol, using porcine intestinal tissue (mounted in InTESTine™) was determined. Furthermore, the expression levels of metabolic enzymes and transporters in porcine intestinal tissue were determined and compared to known expression levels in the intestine of young children. Intestinal and hepatic metabolism of paracetamol was estimated by extrapolation of *in vitro* metabolism data.

**Results:** We have previously shown that intestinal permeability of a wide range of compounds is comparable between (adult) human and porcine intestinal tissue (Westerhout et al., 2014). There is, however, no Papp data available of paracetamol across intestinal tissue of children. Therefore, we applied a physiologically-based scaling approach to predict the intestinal absorption of paracetamol in children based on intestinal absorption using porcine tissue. The results indicated that by scaling the expression levels and Papp values to the specific situation in children, the oral bioavailability can be predicted. Moreover, we showed a unique combination of porcine InTESTine™ system with luminal samples collected from the gastrointestinal model (TIM) studying the permeability of compounds in the presence of undiluted biorelevant samples without the loss of intestinal barrier integrity.

**Conclusion:** The results show that permeability measurements across porcine intestinal tissue with biorelevant matrices, together with abundance data, metabolism data, and physiologically-based scaling offers a unique combination for predicting oral bioavailability in children.


**Disclosure of Interest:** None Declared
EVOLUTION OF HELICOBACTER PYLORI ASSOCIATED GASTRO-DUODENAL ULCERS OR EROSIONS OVER THE LAST 23 YEARS: DECLINE OR STEADY STATE?

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Objectives and Study: Recent data suggest that, in children, the proportion of gastro-duodenal ulcers/erosions associated with Helicobacter pylori infection is currently lower than expected. In this study, we trace this proportion over two decades.

Methods: Retrospective review of the reports of all upper GI endoscopies with biopsies for culture over the last 23 years. Helicobacter pylori status was evaluated using a combination of several invasive methods and its rate compared in different time periods between children with lesions and controls.

Results: A total of 7849 endoscopies were performed in 5983 children (2874F/3109M, median age 7.6 y, range 0.1-17.9 y). At their first endoscopy 12.2% of the children presented gastric and/or duodenal ulcers or erosions (35.4% of them infected by Helicobacter pylori) while no such lesions were identified in 87.8% (controls, 21.3% being infected). The exposure factors associated with such lesions were older age (p < 0.001), male gender (p 0.002) and Helicobacter pylori infection (p < 0.0001). Gastric ulcers were not significantly associated with Helicobacter pylori (23% infected) while only 55% of duodenal ulcers are associated with an infection, 33% of gastric erosions and 48% of duodenal erosions. The proportion of gastro-duodenal lesions associated with Helicobacter pylori remained stable over time. Children with Helicobacter pylori infection and ulcers were older than those with Helicobacter pylori without ulcers (p < 0.001).

Conclusion: Our study confirms that, in our paediatric population, the proportion of ulcers without Helicobacter pylori infection is higher than previously suggested and that this prevalence has not changed over the two last decades.

Disclosure of Interest: None Declared
**Objectives and Study:** Although the frequency of Helicobacter pylori (Hp) infection in Polish children shows some regional differences, it is still 30%. The symptoms of the infection might be scanty or absent or not be felt by a child because it comes from the very early childhood and the patient gets used to it. Ongoing infection associated by gastric inflammation finally can lead to indigestion; worsen intestinal absorption, and impaired growth of a child. Ghrelin is a hormone that stimulates release of growth hormone and IGF-I, it also regulates meal intake. The aim of this study was evaluation Hp influence on growth and on weight, ghrelin and IGF-I and leptin secretion in children with idiopathic short stature.

**Methods:** Among the first group analyzed 121 children with short stature, 85 patients met the inclusion criteria for the study (no endocrine and other than Hp infection gastrointestinal diseases influence the growth and body weight). The study involved 100 children, 85 (43 girls and 42 boys) at the age of 5 - 15 years (mean 10.17±3.10 y) with short stature that exceeded -2.0 SD, in which, according to hormonal diagnostics growth hormone deficiency and hypothyroidism were excluded. 15 healthy children without growth disorders was the control group. The concentrations of IgA and IgG antibodies to Hp were measured; upper GI endoscopy with urease test and biopsy pathology exam was performed.

**Results:** Hp infection was confirmed in 28 children comprised Hp(+) group, and excluded in 57 children - Hp(-) group. 15 healthy children were the controls. There were no significant differences between Hp(+) and Hp(-) groups with reference to children’s age (11.28 ± 2.87 years vs. 10.1±3.39 years), height insufficiency (-2.52±0.66 SD vs. -2.43±0.97 SD), and BMI value (15.77±1.82 kg/m2 vs. 15.52±2.23 kg/m2). Significantly lower ghrelin and significantly higher leptin concentration was observed in Hp(+) children in comparison with Hp(-) children: 1014.02±406.2 ng/ml vs. 1585.41±911.17 ng/ml, and 4.18±5.13 vs. 9.76±8.70 pg/ml respectively. IGF-I SDS concentration was lower in Hp(+) as compared to Hp(-) group, but no significant differences were noted (-1.44±1.41 vs. -0.93±1.07). In Hp(-) group, statistically significant negative correlation between ghrelin and BMI values (r=-0.52, p<0.05) and between concentration of ghrelin and IGF-I SDS (r=-0.45, p<0.05) was observed, while in Hp(+) group no such relationship was noted.
Conclusion: Hp infection results in lower ghrelin and IGF-I and higher leptin synthesis in children. In contrast to healthy individuals, in children with Hp infection, ghrelin secretion stops to be dependent on a child's nutritional condition.

Project supported by NSC grant number N N407 570038

References:

Disclosure of Interest: None Declared
The role of Bifidobacterium lactis containing synbiotic for Helicobacter pylori eradication in children: A randomised controlled trial

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Objectives and Study: Standard triple therapy remains the first choice treatment for Helicobacter pylori (H. pylori) infection in children. The eradication rate of the standard triple regimen is decreasing in children because of poor patient’s compliance, antibiotic resistance and side effects. We aimed to investigate the role of Bifidobacterium lactis containing synbiotic as an adjuvant therapy in children with symptomatic H. pylori infection.

Methods: One hundred children who underwent upper gastrointestinal endoscopy for different indications at Sisli Hamidiye Etfal Hospital, department of pediatric gastroenterology between August 2013 and August 2014 who were found to be positive for H. pylori infection by histopathologic evaluation of the antrum and/or corpus biopsies were enrolled the study. The patients were randomized into two groups. In the first group, 50 patients have been conducted to the standard therapy with amoxicillin (50 mg/kg/day, -2 dose -14 days) + clarithromycin (15 mg/kg/day, -2dose-14 days) + lansoprozole (1 mg/kg/day, once daily 30 days) and Bifidobacterium lactis containing synbiotic once a day for 14 days. In the second group, 50 patients have been treated by the standard triple therapy in two weeks period concurrently. Successful eradication was defined as a negative stool antigen test result 1 month after therapy discontinuation.

Results: H. pylori eradication was achieved by group 1 who received standard therapy with additional synbiotic in 88% (44/50) and 72% (36/50) in children receiving the standard therapy in group 2. The ratio of eradication was high in the first group, the difference between two groups was statistically significant (p=0.046). The ratio of the patients in the second group who suffered from abdominal pain more in the 3.-4.-5.-6.-7.-8.-9.-10.-11.-12.-13.- 14. day of the treatment than first group (p<0,05). There was no significant change of the vomiting rate between the day 1 to 7( p=0,046) but any day between 8 to 14 vomiting rate was higher in the second group (p<0,027). The addition of probiotics to the triple therapy significantly lessened the frequency of diarrhoea but no significant difference the frequency of metallic taste (p=0.04, p=0,418 respectively ).

Conclusion: We found that the addition of bifidobacterium lactis -containing synbiotic to the triple therapy is effective for eradicating H.pylori infection in children and the side effects such as diarrhea, vomiting and abdominal pain were observed less in synbiotic group in our study.

Disclosure of Interest: None Declared
Immune Status in Children with Chronic GastroDuodenitis

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Objectives and Study: The aim of the work was to study the features of cellular and humoral immunity and cytokine concentration in children with chronic gastroduodenitis (CG).

Methods: Patients and methods. The study included children aged 9 to 15 years. Of the 54 patients in the acute stage of CG in 26 was detected erosive (group 1) and in 28 superficial (group 2) pathological process. The control group consisted of 16 healthy children. Statistical processing of data was performed with the expectation of the median and interquartile range [25 to 75 percentile].

Results: A reduction in the percentage of CD3+ of patients in the first group to 48 [47; 49] and in the second group up to 51 [50; 52] in comparison with the control (p < 0.05) were observed. Registered CD4+ level reduction up to 27 [25; 29] and 31 [29; 33] in the respective groups as compared to healthy children (p < 0.05). Reducing the proportion of CD4+, while increasing that of CD8+ resulted in a significant reduction ratio CD4+/CD8+ and 1.0 [0.9; 1.1] in patients with erosive gastroduodenitis and 1.3 [1.1; 1.6] with the surface form, whereas normally it was 2.1 [1.9; 1.6]. In all patients, regardless of CG is registered as increased concentration of immunoglobulin of class M and G and a sharp increase in the levels of inflammatory cytokines in normal concentration of contra inflammatory interleukin-4. The concentration of IL-1β in the first group increased to 142.07 [130.52; 159.23], in the second - to 130.97 [118.32; 145.06] compared with control 20.25 [19.23; 21.63] (p < 0.05). All of these cytokines were increased in patients from 4.0 to 7.1 times compared with healthy (p < 0.05). In the analysis of cytokine content depending on the presence or absence of H. pylori were found that in patients with Helicobacter pylori - associated Cg elevated levels of interferon -α to 147.83 [123.12; 169.45] vs 80.81 [63.14; 95.37] pg/ml in uninfected patients (p < 0.05). A direct significant correlation between the level of antibodies to H. pylori and the concentration of tumor necrosis factor-α (r = 0.41; p < 0.05) were found.

Conclusion: During an exacerbation CG imbalance is developing in the immune system. Indicators such as immunogram and cytokine levels can serve as informative diagnostic criteria for pathological process activity of CG in children

Disclosure of Interest: None Declared
Objectives and Study: Currently available empiric first-line treatment options for children with Helicobacter pylori (H. pylori) infection comprise various combinations of proton pump inhibitors (PPIs) and antimicrobial agents including amoxicillin, clarithromycin and metronidazole for a duration of 7-14 days. Antimicrobial resistance of H. pylori is the leading cause of eradication failure. Consequently, antibiogram guided first-line treatment has recently been proposed by the ESPGHAN H. pylori working group to increase eradication success. The aims of our study were (1) evaluate antibiogram guided therapy and (2) to determine antimicrobial resistance of H. pylori in Slovenian children not previously treated for H. pylori infection.

Methods: Consecutive patients aged 1-18 years with proven and not previously treated H. pylori infection, between October 2011 and February 2014, were included in this multicentre retrospective cohort study. Basic demographic, treatment characteristics and H. pylori antimicrobial susceptibility data were analysed. Eradication was confirmed with the urea breath test or monoclonal stool antigen test at least 4 weeks after the treatment.

Results: A total of 109 patients were evaluated. 92.7% (n=101) of those (63.4% girls), with a median age 12.7 years (IQR 9.2–15.8 years) met the inclusion criteria. Primary antimicrobial resistance rates for amoxicillin (AMO), clarithromycin (CLA), metronidazole (MET), levofloxacin and tetracycline were 0%, 19%, 17%, 1% and 0%, respectively. 65.3% (n=66) of patients received CLA-based triple therapy either with AMO 62.4% (n=63) or MET 3.0% (n=3). 31.7% (n=32) of patients received AMO-based triple therapy, 25.7% (n=26) with MET, 3.0%, (n=3) with ciprofloxacin and in 3.0% (n=3) with tetracycline. One patient (1.0%) received quadruple therapy with AMO, CLA and MET and 2 patients (2.0%) were not treated. Mean duration of therapy was 12.5 days with the majority of patients (74.7%, n=71) being treated for 14 days (data available for 95 patients). Test-of-cure results were available for 70.3% (n=71) of patients. Eradication was achieved in 85.9% (n=61) of them. Adverse effects were reported by 21.1% (n=15) of patients, the most common being nausea, followed by abdominal pain and vomiting.

Conclusion: High resistance rates to CLA and MET detected in our clinical H. pylori isolates support the need for susceptibility testing and guided therapy for initial H. pylori eradication therapy. However,
far from ideal eradication rates in our study call for further optimisation of first-line eradication treatment for children.

**Disclosure of Interest:** None Declared
HELICOBACTER PYLORI, CAGA, AND VACA STATUS AND CLINICAL PRESENTATION IN CHILDREN

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Objectives and Study: Seroprevalence of H. pylori infection in Iran exceeds 65% of pediatric population. In this study, we intended to find association between the virulence genes (cagA and vacA) and clinical presentations.

Methods: H. pylori isolates were achieved from the gastric mucosa of children. In each case, the gastric biopsy specimens were cultured and the organisms identified. Detection of different genotypes was carried out by PCR method.

Results: A total of 106 biopsy specimens were cultured and 33 H. pylori isolates obtained. Among these 33 H. pylori strains 24 (73%) were cagA-positive. Genotypes of vacA s1m2, s1m1, s2m2, and s2m1 were 45.5%, 30.3%, 21.2%, and 3%, respectively. Most female patients were infected with genotype s1m2. The vacA-m1 strains were significantly more common in patients with nodular gastritis. There were no statistical differences between the vacA and cagA genotypes and clinical outcomes.

Conclusion: The frequency of cagA genotype was high. In this study, nodular gastritis was a common finding and was rather significantly associated with m1 allele of vacA.


Disclosure of Interest: None Declared
Fecal Calprotectin in Helicobacter Pylori Gastritis

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Objectives and Study: There are few studies showing the relationship between fecal calprotectin levels and upper gastrointestinal diseases. The aim of this study is to demonstrate if there is a difference between the levels of fecal calprotectin in H. pylori positive and negative patients; and to show its relation with degrees of neutrophil activity in antral biopsies.

Methods: Children older than 5 years who applied to Pediatric Gastroenterology Departments of Başkent University, Faculty of Medicine and Dr. Sami Ulus Children’s Hospital between November 2013 and May 2014 with complaints related to upper gastrointestinal system diseases were evaluated. Fecal calprotectin testing and parasitologic assessment were performed to 89 patients who underwent upper gastrointestinal endoscopy. Patients with gastric, duodenal ulceration, and erosive esophagitis were excluded.

Results: Endoscopy results and reports of gastric antral biopsies of the patients were evaluated, fecal calprotectin levels of H. pylori positive 51 (57%) and negative 38 (43%) patients were compared. Mean fecal calprotectin levels were 74.8 µg/g and 52.7 µg/g in H. pylori positive and negative groups, respectively. The difference was statistically significant (p=0.039). Cut-off level for detecting H. pylori positivity is calculated as 30.49 µg/g. With this cut-off level sensitivity and specificity of fecal calprotectin testing for detection of H. pylori are 60.8% and 63.2% respectively. Gastric activity and inflammation degrees according to Updated Sydney Classification were not related with fecal calprotectin levels (p>0.05).

Conclusion: Fecal calprotectin levels are higher in H. pylori positive group, but the sensitivity and the specificity of the test are low. Also, fecal calprotectin levels are not found to be related with gastric neutrophil activity degrees. Therefore routine measurement of fecal calprotectin levels in diagnosis of H. pylori gastritis is not advisable.

Disclosure of Interest: None Declared
Objective and Study: Alagille syndrome (AGS, OMIM #118450) is an autosomal dominant multisystem disorder affecting the liver, heart, face, eyes and skeleton. In early infancy AGS may mimic biliary atresia (BA) and extrahepatic bile ducts might not be visualised by endoscopic retrograde cholangiopancreatography (ERCP) or postoperative cholangiography. Our aim was to confirm the diagnosis in patients with suspected AGS (n=4) and to identify carriers of JAG1 mutations among patients with BA (n=72), all aged 2 months on average.

Methods: 310 children with neonatal cholestasis were hospitalized at the Department of Pediatrics, Faculty Hospital Motol, Prague, between January 1998 and January 2012. ERCP was indicated in 127 patients with suspected BA based on clinical and laboratory examinations. Subsequent surgical revision was performed in 96 patients with pathological findings on the bile ducts. Mutational analysis of the JAG1 gene was done in a subset of 72 living patients with isolated BA and in 4 patients with suspected AGS and normal extrahepatic biliary tree.

Results: Sequence analysis of JAG1 revealed seven novel mutations including one missense [c.401G>T (p.Leu135Phe)], one nonsense [c.1998T>A (p.Cys633*)] and five frameshift mutations [c.327_330delCAAG (p.Lys110Profs*50), c.1313_1314delGT (p.Cys438Serfs*10), c.879_880delTG (p.Cys293*), c.2913-2914delAC (p.Pro971Argfs*10), c.2050delG (p.Asp684Thrfs*59)], and one known nonsense mutation [c.960T>A (p.Tyr320*)]. All 5 patients with proven JAG1 mutations presenting initially as BA developed clinical signs typical for AGS before 3 years of age. By contrast, no JAG1 mutation was present in the remaining 67 patients with BA.

Conclusion: Biliary atresia is not associated with JAG1 mutations in Central Europeans. In addition to liver histology, early molecular diagnosis of AGS could be useful in diagnosis of the “grey zone” AGS patients presenting as extrahepatic biliary atresia in early infancy.

Disclosure of Interest: T. Dedic Conflict with: GA UK No. 630512, M. Jirsa: None Declared, M. Rygl: None Declared, S. Jiri: None Declared, R. Keil: None Declared, R. Kotalova: None Declared
Objectives and Study: Malignant cells express specific proteins on their cell surface. It is widely believed that it is these proteins that the immune system uses to recognise tumours and eventually eradicate them. When this process goes wrong, a tumour forms.

Aim: (1) To identify tumour specific MHC class I phosphopeptide antigens on lymphoblastoid cell lines LCL’s (an in vitro model for PTLD) as well as hepatic tumour tissues. (2) T-cells are immune cells which are notoriously difficult to maintain in long-term culture and as a result it is difficult to establish an ‘off the shelf’ T-cell product, however the aim of this project was to explore potential modalities for capturing the T-cell receptor (TCR), important in recognising tumour specific antigens and the resultant product could be used to establish a non patient-specific, but tumour specific product.

Methods: Paediatric and adult patients were identified with hepatic malignancy and consented as per current policy. Cells were isolated and tumour specific phosphopeptide antigens were identified. These provide the targets for T-cells, and more specifically TCR’s. Having identified these antigens, modalities have been explored for expanding these cells. Hybridoma technology is long established in immortalising B-cells, and this study aims to explore its potential with immortalisation of T-cells.

Results: A number of novel phosphopeptide antigens have been identified both in vitro as well as on patient tissues. This information has been used to identify potential T-cell targets and by formation of hybridomas we have established a method for expanding specific T-cell’s in vitro. Although these hybridomas are currently unstable due to their tetraploid status, we aim to modify this protocol further to allow for stable expansion of hybridoma cells which possess the relevant TCR motif.

Conclusion: Identifying a modality for expanding cells with a specific TCR repertoire clearly allows us to target tumour specific phosphopeptide antigens and has the potential to be developed as an immunomodulatory therapy in patients with hepatic tumours or PTLD.

References: Cobbold M, De La Pena H, Norris A et al 2013 MHC Class I-associated phosphopeptides are the targets of memory-like immunity in Leukaemia. Sci Trans Med, 5, 203ra125
Depontieu F, Qian J, Zarling A et al 2009 Identification of tumor-associated MHC class II-restricted phosphopeptides as targets for immunotherapy. Proc Natl Acad Sci USA, 106, 12073-8

Disclosure of Interest: None Declared
ANIMAL MODELS FOR PAEDIATRIC (TYPE 2) NON-ALCOHOLIC STEATOHEPATITIS: AN EXTENSIVE SYSTEMATIC REVIEW

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Objectives and Study: Animal models are widely used in the study of non-alcoholic fatty liver disease (NAFLD). A range of models have been produced to reflect the spectrum of disease, including non-alcoholic steatohepatitis (NASH) and fibrosis. Most children with NASH have evidence of zone 1 (portal) inflammation, known as type 2 NASH, rather than the centrolobular inflammation of adult, type 1 NASH. We performed a comprehensive systematic review to identify whether any animal models reflect type 2 NASH.

Methods: MEDLINE search for all articles (in English) including “animal model” and “non-alcoholic steatohepatitis” or “non-alcoholic fatty liver disease”. Only primary research papers with animal models were included. Models were described by animal, genetic modifications, diet, and if toxic insults were used. Models were assessed for concordance with features of NAFLD: obesity, insulin resistance, steatosis, portal steatohepatitis, centrolobular steatohepatitis, and development of hepatocellular carcinoma (HCC).

Results: MEDLINE search identified 951 articles, 472 were excluded (230 not relevant, 132 reviews or comments, 70 papers could not be obtained, and 39 had no animal model).

Data was extracted from 479 studies, which used 208 different animal models of NAFLD: 72 dietary, 35 genetic, 11 toxic, 4 offspring, and 86 combination models. The most frequently used models were: high fat diet (HFD) in mice (83/479), HFD in rats (64/479), and methionine-, choline-deficient (MCD) diet in mice (64/479).

No studies specifically described an animal model for paediatric NASH; only 1/208 models demonstrated a predominance of portal inflammation. Mice fed an ad libitum high-fat, high-fructose diet (=4800 kcal/kg diet) for 16-weeks (used by 4/479 studies) most closely reflects paediatric type 2 NASH, with portal fat infiltration, zone 1 steatohepatitis, and portal fibrosis.

129/208 models had evidence of Type 1 (“adult”) NASH, with predominance of zone 3 inflammation or panacinar steatohepatitis. 19/208 models demonstrated development of hepatocellular carcinoma.

Conclusion: A 16-week high-fat, high-fructose diet in mice most closely reflects paediatric type 2 NASH. There are a large number of published models, with variable phenotypes and histology.

Disclosure of Interest: None Declared
CONFOCAL STUDY OF APOPTOSIS AND AUTOPHAGY IN PROGRESSION OF LIVER DISEASE IN PATIENTS WITH ALPHA-1- ANTITRYPsin DEFICIENCY

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Objectives and Study: Homozygous (PIZZ) α-1-antitrypsin deficiency (ATD) is associated with the development of liver damage in children, chronic liver injury and hepatocellular carcinoma in adults. The progression of liver disease varies ranging from normal liver tests to early cirrhosis. PiZ mouse model studies revealed that hepatocytes containing the mutant protein ATZ, are more susceptible to death than globule-devoided cells while hepatocyte death has never been examined in human liver biopsy specimens in relation to disease prognosis. The aim of the study was to determine hepatocyte death associated with variable course of ATD compared to controls with biliary atresia.

Methods: We reviewed 17 liver tissue samples from 17 patients (PiZZ), divided into 2 groups: with unfavourable prognosis (I group, n=8, age of biopsy sampling 0.3(0.15-0.55)y[median(Q1-Q3)] presenting liver cirrhosis in course of the disease and with good prognosis- without cirrhosis (II group, n=9, 0.17(0.13-0.17)y). Liver biopsies obtained from patients with biliary atresia served as a control group (III group, n=10, age of biopsy sampling 0.17(0.13-0.17)y). The follow up in the I group until LTx or death was 10.3 (1.9-17)y [median(min-max), while in the II group was 10.5(0.5-18)y. Liver sections were investigated on confocal microscopy (FV-1000, Olympus) using antibodies anti-active caspase-3 (apoptosis) and beclin-1 (autophagy marker) and ultrastructurally with iTEM morphometric program. Cells with positive reactions (in case of beclin-1 when reaction was intensive in whole cell) were counted with CellSense program (Olympus).

Results: Significant higher (p<0.01) percentage of hepatocytes demonstrated apoptosis (26.85 ± 21.32) and autophagic death (56.64±24.54) in I group in comparison to II group ((9.41±SD 11.29) and (32.34±SD 23.43), respectively). Intensity of apoptosis and autophagy in III group was 21.00 ±19.15 and 38.41± 22.49, respectively: there was no significant difference related to apoptosis compared to I group (p=0.054) and significant difference in range of autophagic death (p 0.0001). Analyses of mitochondria revealed their lower volume density in I group vs. II group (11% vs 15%) and presence of long mitochondria in about 30% of cells in I group.

Conclusion: Apoptosis and autophagy- the mechanisms of increased death of hepatocytes, may be an important element of the unfavorable course of liver disease in ATD. In the context of previous results of mitochondria analysis in patients with varying course of ATD mitochondrial changes in the group with bad prognosis may predispose to an increased cell death.

Disclosure of Interest: None Declared
RESULTS OF TREATMENT AND ANALYSIS OF PROGNOSTIC FACTORS IN CHILDREN WITH BILIARY ATRESIA

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Objectives and Study: Kasai hepatopancreatostomy (HPE) and liver transplantation (LTx) dramatically improved prognosis in children with biliary atresia (BA). The restoration of intestinal bile flow can slow down or even stop the progress of BA, however most of the children eventually are liver transplantation candidates. The aim of the study was to analyze the risk factors and outcome in children with BA.

Methods: We performed the retrospective chart review of 383 children (226 females, 157 males) with BA treated in The Children’s Memorial Health Institute between 1984 and 2014. The following parameters were analyzed: age at Kasai operation, age at LTx, anatomical type, bilirubin level before operation, outcome of HPE, co-existence of congenital abnormalities, survival with native liver (SNL), survival after LTx (TS). Statistical analyses were based on Kaplan-Meier method and log-rank test.

Results: HPE was performed at the mean age of 72 days (SD+/-23) and was successful in 187 (49%) patients. The overall 5 and 10 year actuarial survival with native liver was 38% and 29% respectively. Restoration of bile flow was the main indicator of good prognosis. If total bilirubin dropped below 2mg% within 6 months after HPE the actuarial 5 and 10-year SNL was 70% and 56%. There was no significant correlation between age at HPE and the outcome. Anatomical type of BA, and direct bilirubin level before operation (<8mg%) proved to be important predictive parameters. In 116 (33,8%) patients we determined at least one congenital anomaly: polysplenia (n=27), intestinal malrotation (n=20), abdominal situs (n=7), preduodenal portal vein (n=9) and heart defect (n=53). BASM abnormalities did not correlate with worse prognosis. LTx was performed in 181 patients with 5-year survival of 92%.

Conclusion: Treatment of BA is surgical with favorable long-term outcomes. Early HPE, but without strict age threshold, and optimal timing of LTx warrant the best results.

Disclosure of Interest: None Declared
Objectives and Study: Transition of adolescents with chronic disease requires a shared and planned program to avoid psychophysical complications. This gradual process implying the switch of care from pediatricians to adult specialists is well documented for some major conditions, but not yet for childhood onset chronic liver disease. We therefore surveyed opinions and knowledge of pediatric and adult liver experts preliminarily to aiming for specific joint guidelines.

Methods: We proposed to European adult hepatologists (AH) and pediatric hepatologists (PH) two pilot online questionnaires focusing on both 1) Transition’s general issues, and 2) Specific matters usually presenting in emerging adults with pediatric liver diseases.

Results: From February to June 2014, 34 PH and 13 AH from 18 European countries responded.

- In most cases a Transition Program either does not exist (39%) or is still under development (33%).
- Main criteria for starting Transition remains to be focused on age (PH 61% and AH 77%) although recent evidence indicates the need also for other emerging discriminators.
- AH report that major barriers are represented by the adult medicine approach itself which is felt unfriendly by young patients (50%), parents interference (34%) and some lack of trust in the new specialist (42%). PH instead mainly report poor communication and collaboration with AH (26%).
- Finally, AH and PH different views on proper management of emerging adults’ hepatobiliary diseases mainly refer to autoimmune liver diseases (52-78%), some common metabolic disorders [e.g. Wilson Disease (62-84%)], biliary atresia (70-89%) and newer forms of genetic cholestasis (60-75%).
**Conclusion:** General and disease-specific modalities of transitioning from pediatric to adult healthcare adolescents with chronic pediatric-onset hepatobiliary diseases are still uncertain even among experts. Our pilot results confirm the absolute urgent need for pediatric and adult hepatologists agreeing on specific clinical practice recommendations based on existing evidence.

**Disclosure of Interest:** None Declared
UTILITY AND ACCURACY OF TRANSIENT ELASTOGRAPHY IN DETERMINING LIVER FIBROSIS IN CHILDREN WITH CHRONIC LIVER DISEASE.

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Objectives and Study: Transient elastography (TE) is a non-invasive and reproducible tool for assessment of liver fibrosis with limited information in children and none so far from Asia. We conducted a prospective study to find out the utility and accuracy of liver stiffness measurement (LSM) by TE in children with chronic liver disease (CLD).

Methods: From January to October 2014, 62 children (aged, 5-18 years), 40 with CLD (diagnosed on the basis of clinical, biochemical, imaging and liver biopsy) and 22 healthy controls were enrolled prospectively. Liver biopsy fibrosis was scored according to the metavi staging and the pathologist was blinded to TE results. TE (Echosense touch 502 France) was done in dorsal decubitus position without sedation in fasting state with probe selected on basis of chest circumference (mainly S2). The study was approved by research ethics committee of the institute.

Results: Median age of cases and controls were 12.1 (range, 5-17.3) years and 9.6 (range, 5.6-17) years respectively (p= ns) with male to female ratio of 2:1 vs. 1:1 respectively (p=0.27). TE was successful in all children. In controls, median LSM was 4.8 (range, 2.8-7.3) kPa with 95th centile value of 7.3KPa. LSM did not vary significantly with age (p=0.7) or sex (p=0.8). In cases aetiologies were chronic hepatitis B 15, autoimmune liver disease 11, Wilson 4, nonalcoholic fatty liver disease 3, chronic hepatitis C 2, cryptogenic 5. TE values correlated positively to fibrosis stage (Spearman \( r = 0.78, p=0.0 \)), gammaglutamyl transpeptidase (Spearman \( r = 0.53, p=0.0 \)), spleen size (Spearman \( r = 0.71, p= 0.0 \)) and negatively to platelet counts (Spearman \( r = -0.58, p=0.0 \)). TE was not a good discriminator of any fibrosis (≥F1) from no fibrosis (F0) (p=0.11) but good for significant fibrosis(≥F2) from minimal/no fibrosis (<F2) (p=0.03); severe fibrosis (≥F3) from less severe fibrosis (<F3) (p=0.0); cirrhosis (F4) from no cirrhosis (<F4) (p=0.02) with AUROC for ≥F2, ≥F3, F4 using TE was 0.71, 0.93, 0.91 respectively. Optimal cut-off for significant fibrosis was 10.7kPa (sensitivity 73% specificity 60%), severe fibrosis 15.4kPa (sensitivity 92% specificity 85%), cirrhosis 21.8kPa (sensitivity 100% specificity 78%). AUROC for significant fibrosis (10.7 KPa) in children with platelet count of <150,000 was 0.82 (sensitivity 76% specificity 65%).

Conclusion: This study showed that TE is good in detecting significant fibrosis (F2 to F4) and best in severe fibrosis/cirrhosis (F3,F4) but not good in diagnosing early fibrosis. Significant fibrosis is uncommon in children with normal platelet counts.

References: Fitzpatrick E, Quaglia A, Vimalasvaran S, et al. Transient elastography is a useful noninvasive tool for the evaluation of fibrosis in paediatric chronic liver disease. JPGN 2013; 56: 72-76
Disclosure of Interest: None Declared
FIBROSIS AND INFLAMMATION HISTOLOGY SCORES PREDICT DISEASE REMISSION IN PAEDIATRIC AUTOIMMUNE HEPATITIS UNDER IMMUNOSUPPRESSIVE THERAPY

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Objectives and Study: To investigate the fibrosis evolution and indicators of disease remission in paediatric autoimmune hepatitis (AIH) under immunosuppressive treatment.

Methods: Retrospective analysis of a cohort of 40 children (24 females, median age 10.5 years, range 9m-15y) with established AIH (9 type I, 7 type II, 2 seronegatives, 4 coombs+, 18 overlap) and immunosuppressive therapy (median follow-up 4 years, range 0-19y). Biopsy histology scores (ISHAK and LUDWIG) were compared at baseline (n=38) and follow-up (n=19) (median 4 years, range 3m-16y). Remission was defined as normalisation of AST, ALT and gammaglobulin levels, and absence of clinical symptoms. Long term prognostic indicators for remission and fibrosis progression were analysed by logistic regression, including baseline and follow-up demographic, clinical, biochemical, immune, histological and treatment parameters. The subgroup of overlap syndrome was also analysed separately for fibrosis progression.

Results: In the entire series, fibrosis score decreased from 3.2 ± 1.6 to 2.2 ± 1.9 (p=0.03) and inflammation decreased from 3.1 ± 1 to 2.4 ± 1.1 (p=0.02). Logistic regression showed that inflammation evolution was predictive of fibrosis progression (OR 16.2 ; p=0.03). Disease remission was predicted by (1) fibrosis score at diagnosis (OR 1.9 ; p=0.03), (2) fibrosis score at follow-up biopsy (OR 2.6 ; p=0.03), and (3) inflammation score at follow-up biopsy (OR 3.8 ; p=0.04). The best predictive factor for disease remission was the follow-up fibrosis score (ROC 85% ; p<0.05). When overlap syndrome group was analysed separately, the fibrosis score remained unchanged over time (3.71 ± 1.25 to 3.57 ± 2.23 ; p=0.99), while the improvement was confirmed in the other categories (3.25 ± 1.22 to 1.42 ± 1.08 ; p=0.001).

Conclusion: Under immunosuppressive treatment both fibrosis and inflammation scores decreased significantly. Improvement of inflammation significantly predicted fibrosis regression. Pre-treatment and follow-up fibrosis scores as well as follow-up inflammation score were predictive factors for the long term disease remission. The subcategory of overlap syndrome had no favourable progression of fibrosis.

We conclude that fibrosis regresses under treatment in paediatric AIH except for overlap syndrome, and that the fibrosis and inflammation scores at follow-up biopsy are predictive of long term outcome.
Disclosure of Interest: None Declared
FEASIBILITY AND ACCEPTABILITY OF ANTENATAL SCREENING FOR HEPATITIS C INFECTION
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Objectives and Study: Hepatitis C is not currently included in the UK antenatal screening programme, although regular knowledge updates keep this under review. The latest update highlighted a need to determine the sero-prevalence of hepatitis C in the pregnant population. This study investigated the prevalence of hepatitis C infection in pregnant women in Sandwell and West Birmingham and collected data on the feasibility and acceptability of antenatal screening in this population.

Methods: Women were approached in hospital antenatal clinics and counselled about HCV. Those who consented to participation in the study had blood taken which was tested for hepatitis C antibodies. Positive results were confirmed by polymerase chain reaction. Women completed a questionnaire which explored their understanding of viral screening and opinion on the acceptability of antenatal hepatitis C screening. Their views on the counselling they had received were also evaluated.

Results: 489 patients participated in the study. The overall seroprevalence of HCV was 0.2%. Knowledge about blood borne viruses was limited. Only 55% of our population sample had heard of hepatitis C. Women were interested in the idea of screening for hepatitis C, with 99% of women suggesting that hepatitis C testing should be available to pregnant women. Women felt the counselling they received was useful and delivered in an acceptable manner.

Conclusion: Whilst routine antenatal screening for hepatitis C virus is not currently recommended, our study has demonstrated that any future antenatal hepatitis C screening programme would be feasible to carry out and acceptable to the majority of the target population.

Disclosure of Interest: None Declared
PO-H-0276

EARLY PREDICTORS OF MODERATE/SEVERE ACETAMINOPHEN-INDUCED HEPATOTOXICITY IN 10-17 YEAR OLD CHILDREN - A NATIONAL DANISH PROSPECTIVE STUDY

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Objectives and Study: To explore the following in a pediatric population with acetaminophen (APAP) overdose due to suicide attempt:
1) The dose–response relationship between ingested APAP and the degree of hepatotoxicity.
2) Validation of multiple episodes of vomiting as an early predictor of hepatotoxicity.
3) The impact of early initiation of NAC treatment on liver outcome.
4) The incidence of nephrotoxicity.
5) The impact of repetitive suicide attempts with APAP on the development of hepatotoxicity.

Methods: Data was collected as a national prospective study of 381 children aged 10 to 17 years old, admitted to 19 different Danish pediatric departments due to suicide attempt with APAP.

Results: Highly significant relationships were found between the number of pre-hospital vomiting episodes and e.g. maximal INR (p<0.001), γ-glutamyltransferase (p=0.008), and maximal alanine aminotransferase (ALT) (p<0.0001). The results remained highly significant when adjusting for the ingested dose. There was also a highly significant relationship between the number of in-hospital vomiting episodes and relevant biochemical parameters e.g. maximum aspartate aminotransferase (AST) (p<0.0001), maximum bilirubin (p<0.001), and maximum INR (p<0.0001). In all there was no significant relationship between the ingested amount of acetaminophen and the degree of hepatotoxicity.

The latency time before NAC initiation was a determining factor, and highly significant relationships were found between the latency time before NAC initiation and e.g. maximum creatinine (p = 0.002), maximum INR (p<0.001), and maximum ALT (p < 0.0001).

The frequency of nephrotoxicity in children with acetaminophen poisoning may be higher than previously recognized. In our study population, 7.6% (n=29/381) had a maximal creatinine level of ≥75 µmol.

Children who had repetitive suicide attempts, by means of APAP, were more likely to develop hepatotoxicity than children who only overdosed once e.g. maximum AST (p<0.001), maximum bilirubin (p=0.002), and maximum ALT (p<0.001).

Conclusion: Children and adolescents at increased risk of developing hepatotoxicity can be identified at time of admission. Our results show that the number of pre- and in-hospital vomiting episodes, increased latency time before the initiation of NAC treatment, and repetitive suicide attempts are independent highly significant risk factors of hepatotoxicity in pediatric patients with APAP poisoning. Furthermore, the amount of ingested acetaminophen appears to have no influence on the degree of
hepatotoxicity, in contrast to the findings in adult studies. Finally, the presence of nephrotoxicity was higher in our pediatric population compared with adult studies.

Disclosure of Interest: None Declared
DIAGNOSIS OF MONOGENETIC METABOLIC HEPATOPATHIES: POTENTIAL ROLE FOR NEXT GENERATION SEQUENCING?

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Objectives and Study: As neonatal cholestasis is a common infant problem with more than 50 possible differential diagnoses, fast and comprehensive, cost effective and ideally non-invasive diagnosis is desirable to initiate timely therapy to improve patient outcome. Also for other hepatopathies, especially those manifesting in acute liver failure, quick diagnosis is important, as they could constitute contraindication to liver transplantation or can be treated with specific curative therapies. We developed a next generation sequencing (NGS) panel of 21 genes associated with acute and chronic hepatopathies. The panel includes familial cholestasis syndromes, Niemann–Pick disease type C, Alagille syndrome, Congenital Bile Acid Synthesis Defects, Crigler-Najjar Syndrome, Wilson disease, Mitochondrial DNA depletion syndromes, Deoxyguanosine kinase deficiency, DNA helicase deficiency, Hereditary fructose intolerance and Transaldolase deficiency.

Methods: A TruSeq Custom Amplicon (TSCA) panel of 21 genes related to paediatric or juvenile hepatopathies was designed for targeted resequencing on the MiSeq sequencing device (Illumina). Data analysis is performed using Sequence Pilot 4.1 2 software (JSI medical systems GmbH).

For library preparation, this sequencing technology uses an extension-ligation step to add adapter-oligonucleotides to the target genes. Indexed sequencing primers hybridizing to the adapters generate a patient specific label to allow simultaneous sequencing of multiple patients in one flow cell. The flow cell immobilizes patient’s DNA by hybridizing with the adapters. Bridge amplification generates clusters of every amplicon which were analyzed by means of sequencing by synthesis (SBS) technology.

Pathogenic and potential pathogenic mutations are confirmed by Sanger Sequencing.

Results: The designed panel includes 525 amplicons with a length of 250 bp and spans exonic regions with 25 bp intron padding. By sequencing 16 patients in one run a coverage of 3700x can be reached on average. Due to a repetitive region, 51 bp of one target gene (ABCB4) cannot be covered by the NGS approach.

An assay performing time of 2 days and measuring on the MiSeq device taking additional two days allows a generation of results within one week.

Conclusion: Our NGS based analysis of 21 genes potentially represents a fast and comprehensive tool to diagnose genetically determined paediatric hepatopathies. As a result, next to shortening the hospital stay by reduction of examinations and reduced patient’s burden because of smaller required blood volumes, fast and specific initiation of therapy enables a better prognosis.
Disclosure of Interest: None Declared
**Hepatology**

**Hepatology**

PO-H-0278

**PREDICTORS OF DISEASE REMISSION IN CHILDREN WITH AUTOIMMUNE HEPATITIS**

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**Objectives and Study:** Despite advances in understanding pathogenesis of autoimmune hepatitis (AIH), treatment decisions are complicated by diversity of clinical presentation as well as lack of prognostic criteria to stratify high risk patients. We conducted this study to assess outcome of medical management and predictors of response in children with autoimmune hepatitis.

**Methods:** Prospective data collected between June 2012-October 2014 of patients diagnosed with AIH at a single centre was analysed. Diagnosis was based on revised IAIHG (International Autoimmune Hepatitis Group) score. Data collected for clinical features, laboratory tests (including IgG levels, autoimmune markers, viral serology), liver biopsy, imaging and endoscopy findings at diagnosis along with evolution of clinical parameters during follow-up. Primary outcome was biochemical remission (AST/ALT <1.5 upper limit of normal) at 6 months after starting immunosuppressive therapy. Patients were categorized as group 1 (disease remission) and group 2 (no disease remission).

**Results:** 39 children (22 boys, 56%) were diagnosed with autoimmune hepatitis with median age of 9.5 yrs (range 1.3-18 yrs). Type 1 AIH was present in 20/39 (51%), type 2 AIH in 7/39 (18%), whereas the remaining 31% were seronegative autoimmune hepatitis. Acute hepatitis like presentation seen in 15/39(38%) while 17/39 (44%) had decompensation with ascites or encephalopathy. Associated autoimmune disorder was present in 17/39 (43%) cases including autoimmune hemolytic anemia (25%), celiac disease (11%), ulcerative colitis(5%). Liver biopsy showed typical features of AIH in all cases with additional biliary features in 36%. Five patients were excluded due to death/liver transplant(n=3) or inadequate follow-up(n=2). Median follow-up in remaining 34 patients was 9 months (range 3-27 mths). Biochemical disease remission at 6 months was achieved in 20/34 (59%, group 1) on first line immunosuppression. Biochemical parameters including liver function tests, IgG level and PELD score were similar in the two group.

Predictors of disease remission on univariate analysis included acute hepatitis-like presentation (p=0.03) while lack of disease remission was associated with autoimmune hemolysis (p=0.02), Type 2 AIH (p=0.01) and histological evidence of necrosis (p=0.02). On multivariate analysis, histological evidence of necrosis was the only significant predictor of lack of disease remission. Presence of decompensation, PELD score and presence of overlap syndrome were not significantly associated with disease remission.

**Conclusion:** Histological evidence of necrosis at diagnosis is a significant predictor of lack of disease remission in children with autoimmune hepatitis and may warrant more aggressive immunosuppressive treatment.
Disclosure of Interest: None Declared
Efficacy of Probiotics for Treatment of Pediatric Obesity with Nonalcoholic Steatohepatitis

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Objectives and Study: Nonalcoholic fatty liver disease is nowadays the most frequent cause of chronic liver disease in obese children. Many studies have suggested that perturbations in gut microflora are linked to extraintestinal diseases, including nonalcoholic steatohepatitis (NASH). Tumor necrosis factor-alpha (TNF-α), a proinflammatory adipokine, plays a role in the pathogenesis of NASH. The aim of this study was to evaluate the effect of probiotics for treatment of NASH in obese children.

Methods: Thirty-three obese children (M:F=27:6) with NASH were enrolled with the median age of 11 (10,14.5) years. NASH was diagnosed by the presence of either serum aspartate aminotransferase (AST) or alanine aminotransferase (ALT) level greater than 40 U/L, bright echo pattern of liver by ultrasonography, and exclusion of other liver diseases. Subjects were double-blind randomized to receive probiotics (Lyophilized live Lactobacillus acidophilus min 1,000 million, Bifidobacterium bifidum min 1,000 million /capsule) or placebo, both orally 1 capsule thrice daily for six months. Recommendation of weight loss and lifestyle changes was provided to all subjects. Anthropometric (body weight, height, body mass index), liver function (AST, ALT, gamma glutamyltranspeptidase; GGT), liver stiffness (FibroScan®) parameters and serum TNF-α level before and after six months of treatment were analyzed.

Results: There were 17 (M:F=13:4) and 16 (M:F=14:2) in probiotics and placebo groups, respectively. In probiotics group, only AST marginally decreased (p=0.049) at 6 months whereas other parameters remained unchanged. In placebo group, body weight z-score (p=0.02), AST (p<0.001), ALT (p<0.001), and GGT (p=0.01) decreased significantly but other parameters remained steady. At the end of treatment, both groups were comparable in terms of anthropometric, liver function, liver stiffness, and serum TNF-α level.

Conclusion: The present study was unable to demonstrate the beneficial effect of probiotics on anthropometric and liver function parameters as well as the inflammatory marker in obese children with NASH.

Disclosure of Interest: None Declared
**Objectives and Study:** There are several pharmacotherapeutic options for Wilson disease, however neither was compared to each other in randomized controlled trial in children. Zinc seems to be effective in neurological presentation of Wilson disease but there are very limited data on its effects in patients presenting with hepatic symptoms.

The aim of the study was to compare effects of initial treatment with zinc vs. penicillamine in a retrospective analysis of newly diagnosed pediatric patients with Wilson disease and liver presentation.

**Methods:** 88 patients with mild presentation of Wilson disease were included in this study (acute and fulminant liver failure excluded). Diagnosis was based according to the Ferenci et al. scoring system and/or by mutation analysis.

61 patients aged 11±3.4yrs started therapy with zinc and 27 pts with penicillamine aged 12.3±4yrs. Liver function tests were analyzed before, after 6 months and 1 year of treatment.

**Results:** At baseline all the patients presented with increased transaminases ALT 182.6±140 U/I, AST 105±69 U/I, while INR, bilirubin, albumins and haemoglobin were within normal limits.

In the zinc treated patients ALT levels decreased significantly from the baseline 143(80-207) U/I after 6 months 53.5(46.5-95) (p<0.05) and tended to further decrease at12 months of treatment to 47(33-63) U/I [median(Q1-Q3)].

Similarly in patients on penicillamine baseline ALT 183,5(61-269) U/I markedly decreased after 6 months 62.5(46.5-97) (p<0.05) and tended to further decrease at 12 months of treatment 40(36-61) U/I..

During 12 months of observation 7 pts initially treated with Zinc were switched to penicillamine due to adverse events as nausea and abdominal pain after a few months, whereas 2 pts on penicillamine changed to zinc.

**Conclusion:** Both zinc and penicillamine seem effective in the initial treatment of presymtomatic patients and mild liver presentation of Wilson disease in children.

Side effects of zinc usually appear sooner, in the first months of treatment, and may necessitate change of therapy.

**Disclosure of Interest:** None Declared
PELD VERSUS PRISM-III SCORES FOR PROGNOSTICATION IN PALF – ARE DYNAMIC SCORES BETTER?
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Objectives and Study: Pediatric end-stage liver disease (PELD) and Pediatric risk of mortality (PRISM III) scores are routinely used for prognostication in the setting of end-stage chronic liver disease and pediatric intensive care setting, respectively. These scores need to be validated in the setting of Pediatric acute liver failure (PALF). The present study evaluated the prognostic utility of King’s college criteria (KCC), PELD and PRISM III scores for prediction of mortality or need for LTx in PALF in a living donor liver transplant centre.

Methods: All children aged 0-18 years fulfilling the PALF study group (PALFSG) definition were included. KCC, PELD (or MELD for above 12 years of age) and PRISMIII scores were calculated at admission and at 72 hours. AUROC curves were obtained and binary logistic regression analysis was done with regard to poor outcome (mortality or need for LTx at Day 30 of admission).

Results: There were 79 children (51 males). Overall, 40 (51%) had poor outcome (29 deaths and 11 LTx - 18 within 72 hours of admission). KCC, PELD and PELD72 scores had significantly higher AUROCs (0.940, 0.936 and 0.886, respectively; p< 0.001) than PRISMIII (p=NS) or PRISM72 (p=0.001). KCC>3, PELD>29 and PELD72>26 had a sensitivity of 83.3%, 80% and 87.5%, specificity of 86.4%, 90.9% and 95.5% and positive likelihood ratio of 6.1, 8.8 and 19.4, respectively. A positive increase in PELD value by >5 or a static or increasing PRISMIII also predicted poor outcome. On multivariate analysis, admission values of KCC and PELD, whereas 72 hours value of PELD72 as well as change in PRISMIII(>0) determine poor outcome (p< 0.001).

Conclusion: KCC, PELD and PELD72 better predict poor outcome than PRISMIII score in PALF, however the dynamicity of latter is more helpful than of PELD score. Frequent monitor of vital signs, neurological status and biochemical values is a useful guide for prognostication in PALF.

Disclosure of Interest: None Declared
Objectives and Study: Very little information is available on whether treatment with n-3 long-chain polyunsaturated fatty acids have a beneficial effect on liver fat content and cardiovascular disease (CVD) risk factors in children with nonalcoholic fatty liver disease (NAFLD). To examine in a parallel randomized double-blind placebo-controlled trial whether six months treatment with docosahexaenoic acid(DHA) improves hepatic steatosis and associated CVD risk factors including left ventricular(LV) dysfunction in children with biopsy-proven NAFLD.

Methods: Of 58 randomised children, 51 (25 DHA and 26 placebo) completed the study. The main outcome was the change in hepatic fat content (% HFF) as detected by magnetic resonance imaging. Secondary outcomes were the changes in visceral adipose tissue (VAT), epicardial adipose tissue (EAT) and LV function, as well as in insulin sensitivity, alanine aminotransferase (ALT), triglycerides and body mass index-standard deviation score (BMI-SD score).

Results: Blood DHA significantly increased in the DHA group (P<0.0001), compared to placebo. Within both groups, we found a significant decrease in BMI-SD score. In the DHA group, we also found a significant decrease in ALT, triglycerides, fasting insulin and HOMA-IR. However, compared to placebo, only the changes in fasting insulin (P<0.05) and triglycerides (P<0.05) were significant. DHA treatment significantly decreased HFF when compared with baseline (P< 0.05) or placebo (P<0.05). VAT and EAT also significantly decreased when compared with baseline (P<0.05 and P<0.05,respectively) or placebo (P<0.05 and P<0.05,respectively). Systolic and diastolic LV function did not improve after DHA treatment.

Conclusion: A 6-month DHA supplementation decreases liver steatosis, VAT and EAT in children with NAFLD.

Disclosure of Interest: None Declared
**Hepatology**

**Hepatology**

PO-H-0283

**EARLY ONSET OF WILSON DISEASE - DIFFICULTIES IN THE DIAGNOSIS**

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**Objectives and Study:** Wilson's disease (WD) may present symptomatically at any age, although the majority presents between ages 5 and 35. Making early diagnosis can be difficult based on biochemical tests and there are only case reports of Wilsonian pts. in very young age. The aim of our study was to analyze clinical presentations, diagnostic tests and therapies of early onset Wilson disease <5 y of age.

**Methods:** We retrospectively analyzed data of 130 patients with confirmed diagnosis of WD treated in our center since 1996 and identified these with clinical suspicion <5 y of age.

**Results:** Eleven patients (5 M, 6 F) had first symptoms or abnormal liver function tests ≤ the age of 5 y, in that group 5 pts. presented with liver dysfunction at the age of ≤ 2 y. 4 patients had family history of Wilson disease. In 3 cases hepatomegaly was observed. The diagnosis of WD was confirmed in 5 cases before the age of 5 y. At baseline alanine transaminase (ALT) levels were significantly increased [279±147 (70-488) U/l; mean±SD (min-max)] and aspartate transaminase (AST) levels were also high [156,9±89,6 (48-361) U/l]. In 9 cases caeruloplasmin serum level was <20 mg/dl. Urinary copper excretion was tested in 7 pts. and in 4 pts. the levels were between 50 and 100 mcg/day, only 3 pts. had levels > 100 regarded to be diagnostic for Wilson disease. Liver copper was tested in 3 cases, all values were higher than 250 µg/gm of dry weight, mean 1187±580,5 (604,5-1766). The most common mutation was p.H1069Q mutation (compound heterozygote -4 pts, homozygote -3 pts., one chromosome mutation- 2 pts.). 7 patients were treated with zinc compounds, in 4 cases penicilamine therapy was started. Both therapies were effective. No serious side effects were noticed. The mean ALT after 3, 6 and 12 month of therapy was 117±112 (37-367); 82,2±55,9(36-216); 38±10,6 (21-55) retrospectively.

**Conclusion:** Wilson disease can present at early age with significantly increased transaminases and hepatomegaly. Diagnostic approach is challenging as urinary copper excretion is difficult to perform in children ≤ 2 years old and most of all that may not be highly increased. Zinc and D-pen seem to be effective therapies.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Insulin resistance is regarded to be the major complication of obesity leading to liver steatosis and fibrosis. The golden standard of insulin resistance measurement is glucose challenge test. The aim of our study was to assess insulin resistance in children with NAFLD with prolonged glucose challenge test and to look for correlations with other insulin resistance markers, adipokines, lipids and liver function parameters.

**Methods:** We analyzed metabolic and biochemical parameters as well as selected endocrine markers in 75 children (64 males and 11 females; aged 13.3+/−4.11 years) with NAFLD diagnosed based on combination of ultrasound and increased transaminase activity. Prolonged oral-glucose tolerance testing (OGTT) was performed for 240 min (measurements in 30 minute-periods).

**Results:** Impaired fasting glucose (IFG) and impaired glucose tolerance (IGT) were defined as a fasting plasma glucose (FPG) level of 100−126 mg/dl, and a 2-h post-load glucose on the OGTT of 140−200 mg/dl respectively. IncAUCins / incAUCglu levels were 410,0±61,6 / 346,2±154,4 (mean+/−SD) and were abnormal in 28/24 patients. HOMA-IR as a simple indicator of insulin resistance (>2.5) was increased in 64 pts (mean 4,89±2,5). We found linear correlation between AUC of glucose and GGTP (r=0,33, p<0,02), leptin (r=0,50, p<0,006), Lp(a) (r=0,5, p<0,006) and fasted glucose.

Furthermore, we found the linear correlation between the area under the curve for insulin and the following parameters: insulin (r=0.65, p<0.00), HOMA-IR (r=0.63, p<0.00), adiponectin (r=0.44, p<0.02), ghrelin (r=0.47, p<0.013), Lp(a) (r=0.50, p<0.008) and plasma phospholipid trans fatty acid (r=0.28, p<0.045). We found no correlation between ALT and AUCglu and AUCins. Hyperinsulinemia expressed as elevated fasting insulin levels (>16 µIU/mL) was observed in 64 children (80%), and impaired glucose tolerance was observed in six children (7.5%).

**Conclusion:** Conclusion: Lipoprotein (a), adiponectin, leptin and trans fatty acid are strictly correlated with insulin resistance which is not the case for liver function tests. HOMA-IR can be used as a screening test of insulin resistance, still it seems not to be very specific.
Glucose intolerance is not very common when tested with incAUCglu in children with NAFLD but can pick up those with normal fasted glucose levels.

**Disclosure of Interest:** None Declared
SERONEGATIVE HEPATITIS IN CHILDREN IS IT AN AUTOIMMUNE DISORDER?

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Objectives and Study: Besides well-defined hepatitides of viral or autoimmune origin, there are children in whom the cause of hepatitis is not found; the presentation, management and outcome of such seronegative hepatitides are not well known. The aim of this study was to characterize the clinical, biochemical and follow-up features of children with this “so called” seronegative hepatitis with acute or chronic onset.

Methods: From 1988 to 2010, 38 children were investigated for an acute or chronic hepatitis of unknown origin and were included in this study according to the following criteria: 1. exclusion by appropriate tests, depending on the acute or chronic presentation, of hepatotropic virus infection (A,B,C,E,EBV,CMV,HSV) and in selected patients HHV6 (26 pts), Parvovirus B 19 (21 pts), adenovirus (12 pts) and enterovirus (11 pts) by negative blood PCRs; 2. absence of any of the organ and non-organ specific auto-antibodies characterizing children with autoimmune hepatitis: ANA, SMA, LKM, LC1 AMA and SLA (29 pts) by indirect immunofluorescence on rat organ slices; 3. exclusion of other causes of liver disease; 4. liver histology availability.

Results: Four groups were identified: 1) 12 children with increased serum gammaglobulins concentrations; 2) 10 children with normal or low serum gammaglobulins and no combined blood disease; 3) 10 children with combined aplastic anemia: in 7 presenting after a median interval of 1 month after the diagnosis of acute hepatitis and in 3 children, including the one who underwent liver transplantation with an onset contemnoraneous of the hepatitis. 4) 6 children with peripheral blood cytopenia, which was diagnosed simultaneously with hepatitis in 5 of them and appeared 10 months later in the other. Anti-platelets antibodies were detected in 3 of the 4 thrombocytopenic children studied, and anti-neutrophils antibodies were present in one additional patient. An extrahepatic autoimmune disorder was present in 16 families and in 23 children. Liver histology displayed in all portal fibrosis, interface hepatitis and/or inflammatory centrilobular necrosis of variable degree. Immunosuppressive treatment was associated with normalization of aminotransferases in all but one child who required liver transplantation. Relapses were observed in 10 children in groups 1 and 2. Lymphocytopenia (<1000/mm³) was found in 12 children in groups 3 and 4 and in 1 child of group 2. All children are alive after follow-ups of 4 to 17 year and 18 are still under immunosuppression.

Conclusion: Childhood seronegative hepatitis is likely of autoimmune origin. Early liver histology is recommended as well as immunosuppressive treatment. Lymphocytopenia at the time of hepatitis should alert to the possibility of a hematological complication.

Disclosure of Interest: None Declared
A CAUSE OF CHOLESTASIS AND HEPATIC FAILURE IN CHILDREN: NEONATAL INTRAHEPATIC CHOLESTASIS CAUSE BY CITRIN DEFICIENCY

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Objectives and Study: Neonatal intrahepatic cholestasis caused by citrin deficiency (NICCD) is rare disease. It is a novel metabolism disease which caused by deficiency of citrin, a liver-type mitochondrial aspartate-glutamate carrier encoded by the SLC25A13 gene. Its deficiency causes not only NICCD but also adult-onset type II citrullinemia (CTLN2) with severe hepatic-neurology syndrome. Aims of study: Present some clinical features, laboratory finding, results molecular analysis and following processes of NICCD patients

Methods: Method: Prospective description study. 236 patients, who had hepatic troubles and were diagnosed SLC25A13 mutations by PCR/PCR-RFLP enrolled in this study

Results: Results: The patients manifested variable features included prolonged cholestasis jaundice unknown the cause, bleeding diathesis, edema, chubby face, hypoproteinemia, abnormal liver enzymes, coagulation disorder, hyperammonemia, elevated alpha-feto protein, amino acid…. There were 96 in 236 patients were diagnosed NICCD by molecular analysis. Some NICCD clinical manifestations include: Jaundice (95,8%), hepatomegaly (31,3%), steatorrhea (89,6%), chubby face (88,5%), splenomegaly (29,4%), faint (2,1%). Laboratory finding: Hyperbilirubinemia (95,8%), increase AST (100%), ALT (88,5%), AST/ALT ratio > 2.5 (89,6%), coagulation disorder (87,5%), hypoproteinemia (82,3%), hypoalbuminemia (84,4%), hyperammonemia (92,7%), 100% patients had elevation of AFP and 70,8% had increase of citrullin. DNA analysis of SLC25A13 revealed combinations of 851del4, 1638ins23, IVS6+5G>A and IVS16ins3kb with 5 genotypes, 86 homozygous and 6 compound heterozygous. No relation between phenotype and genotype has been found. With supportive treatment and nutritional manipulation most of patients in group recovered completely by the age 18 months. However, there were 8 patients had died of uncompensative hepatic failure

Conclusion: Conclusions: NICCD should be considered in the differential diagnosis of cholestatic and hepatic failure infants. Phenotype of NICCD is very polymorphic and not always benign

Disclosure of Interest: None Declared
THE FREQUENT PNPLA3 P.I148M POLYMORPHISM MAY MODULATE THE SEVERITY OF WILSON’S DISEASE IN PAEDIATRIC PATIENTS

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Objectives and Study: The common patatin-like phospholipase domain containing 3 (PNPLA3) polymorphism p. I148M (rs738409) is associated with non-alcoholic fatty liver disease and cirrhosis in chronic liver diseases (Krawczyk/Lammert Semin Liv Dis 2013). Wilson’s disease (WD) may have a variable course and present with fatty liver, hepatitis, chronic cirrhosis or acute liver failure (ALF), which is not fully explained by ATP7B mutations. Neurological presentation in children with WD is very rare. The aim of the study was to evaluate the PNPLA3 distribution in paediatric patients with Wilson’s disease with variable clinical presentation.

Methods: Clinical and biochemical data was obtained from 44 children with WD (age range 3 – 17 years, 23 boys) diagnosed according to the Ferenci score. In all patients, DNA genomic was isolated and the PNPLA3 polymorphism (rs738409) was genotyped using a PCR-based assay with 5’-nuclease and fluorescence detection. We correlated PNPLA3 genotypes with clinical traits, including results from liver biopsies.

Results: In the group of 36 WD children presenting with hepatitis – 11 patients (30%) carried the PNPLA3 genotype [IM] and 25 patients (70%) had genotype [II]. Among five ALF patients – two patients carried genotype [II], two were heterozygous and one child – was an homozygote. Four of them underwent liver transplantation. Two patients had neurological presentation of WD and both of them carried genotype [MM]. Two patients presented with chronic cirrhosis, all of them were homozygous mutation carriers.

Conclusion: The [MM] genotype of the PNPLA3 p.I148M variant seems to be associated with neurological presentation and cirrhosis in children with Wilson’s disease. There is no clear correlation of the acute liver failure and PNPLA3 genotype. Analysis of larger cohorts of patients with WD is urgently recommended to delineate the role of the PNPLA3 rs738409 polymorphism in manifestation and progression of hepatic and neurological phenotypes.

Disclosure of Interest: None Declared
**Hepatology**

**SPECTRUM OF DRUG-INDUCED LIVER INJURY IN CHILDREN – APPLICATION OF HY’S LAW & PROGNOSIS**

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**Objectives and Study:** Drug-induced liver injury (DILI) is defined as a liver injury caused by various medications, herbs, or xenobiotics, leading to liver dysfunction with the exclusion of other common etiologies. There is limited pediatric data on DILI and the application of Hy’s law in pediatric age-group has not been studied. To study the spectrum of DILI in children as per Hy’s law and their clinical presentation and outcome.

**Methods:** From January 2011 to September 2014 children below 18 years of age presenting with liver dysfunction with a history of drug intake were included. Causality was established as per Roussel-Uclaf causality assessment method (RUCAM). DILI was classified biochemically as per Hy’s law into hepatocellular, cholestatic or mixed. Clinical presentation and course were recorded.

**Results:** There were 25 cases of DILI - 17 (68%) were males with median age of 8.9 years (3 months to 17 years). Causality assessment was highly probable in 5 (20%), probable in 8 (32%), possible in 11 (44%) and unlikely in 1 (4%). The commonest incriminating drugs were antitubercular (36%), complementary and alternative medicines (32%) and antiepileptics (16%). Hepatocellular, mixed and cholestatic patterns of DILI were seen in 8, 8 and 9 cases, with a median time from drug initiation to symptom onset of 10, 34 and 90 days, respectively. DILI was responsible for acute liver failure (ALF) in 10, acute hepatitis in 8, acute-on-chronic liver failure (ACLF) in 3, chronic liver disease with portal hypertension in 3 and hepatic venous outflow tract obstruction in 1. Of the ALF, acute hepatitis and ACLF patients, 21 (90.5%) cases improved with a median time taken for normalization of bilirubin and ALT of 65 (7-165) and 60 (5-195) days, respectively.

**Conclusion:** DILI in children needs a high index of suspicion, especially with usage of antitubercular, complementary and alternative medicines and antiepileptic drugs. Most of the DILI cases resolve with discontinuation of incriminating drug. Chronicity is seen in 16% of cases.

**Disclosure of Interest:** None Declared
INFLUENCE OF EBV-ASSOCIATED ACUTE ACALCULOUS CHOLECYSTITIS ON CLINICAL COURSE AND PROGNOSIS OF EBV INFECTION IN CHILDREN

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Objectives and Study: Acute acalculous cholecystitis (AAC) is a rare disease in the children and because of its low incidence, AAC was not considered as priority in pediatric patients with gastrointestinal symptoms in the past. However, the incidence of AAC increased gradually because of the development of better diagnostic tools such as abdominal ultrasonography. Though Ebstein-barr virus (EBV) infection is not rare disease among etiology of AAC, only few cases of AAC caused by EBV infection have been reported. This study aimed to analyze and evaluate the influence of EBV-associated acute acalculous cholecystitis on clinical course and prognosis of EBV infection in children.

Methods: The retrospective study was performed at Seoul National University Bundang Hospital between March 2004 and January 2013. A total of 287 EBV infected participants were identified during the study period. For total 94 patients were performed abdominal ultrasonography among these, clinical manifestations, laboratory data, and ultrasonographic findings were retrospectively reviewed and analyzed.

Results: Of the 94 children with EBV infection (mean age, 7.1 ± 4.3 years; 47 boys, 47 girls) who underwent ultrasonography during the acute phase of disease, gallbladder wall thickness was present in 24 (25.3%) and was included to AAC group. Pericholecystic fluid was present in 2 among these patients. There was no significant difference in age and gender between AAC group and non-AAC group with EBV infection \( (P = 0.813 \text{ & } P = 0.478) \). Platelet count among laboratory factors were significantly lower in the AAC group than in the non-AAC group \( (p = 0.004) \), and direct bilirubin, alanine aminotransferase and γ-glutamyl transferase were significantly higher in the AAC group \( (P = 0.000 \text{ & } P = 0.041 \text{ & } P = 0.001, \text{ respectively}) \). The duration of hospitalization was longer in patients with AAC \( (P = 0.043) \).

Conclusion: The results of this study describes that abnormalities of the gallbladder related with primary EBV infection was more frequent complication than previously known. For avoiding to unnecessary surgical operation, it is necessary that EBV infection should be considered for the differential diagnosis. In particularly, EBV associated AAC patients require a longer hospital stay than those who don't. Thus AAC in association with EBV infection suggest a poor clinical course. Furthermore, early use of abdominal sonography to EBV infected patients with elevated direct bilirubin, alanine aminotransferase and γ-glutamyl transferase and low blood platelet counts may lead to early diagnosis and treatment of AAC. Early decision making can significantly improve clinical outcomes as well as therapeutic strategy in AAC.
Disclosure of Interest: None Declared
REVIEW OF PAEDIATRIC ACUTE LIVER FAILURE IN THE LAST 10 YEARS. EXPERIENCE 2 TERTIARY CENTRES.

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Objectives and Study: Acute liver failure (ALF) is a rare but devastating syndrome with a high rate of mortality. It is a medical emergency requiring the establishment of specific treatment as early as it is diagnosed. The etiology and prognostic in childhood differs from adults and the prognostic criteria are not well established. The aim of the study was to retrospectively review the etiology, evolution, prognostic indicators and treatment of ALF in pediatric patients.

Methods: We performed a retrospective review of data in all patients who presented an ALF between January 2004 to December 2013 at Vall d’Hebron and Sant Joan de Déu Hospitals in Barcelona. ALF was diagnosed using the definition of the Pediatric ALF Study Group. Irreversible liver damage (ILD) was defined as patient death or need for liver transplantation (LT). ALF prognosis was assessed by four different scores: King’s College criteria, Clichy’s criteria, Pediatric End-Stage Liver Disease (PELD) score and Indocyanine green plasma disappearance (ICG-PDR) test. Sensitivity, specificity, positive and negative predictive values were calculated to describe the predictive and discriminative values of survival predictors.

Results: A total of 75 children with ALF were collected and analyzed. The most frequent identifiable etiology was toxic followed by viral hepatitis (21.4% and 10.7%, respectively). Spontaneous recovery was registered in 41 patients (54.7%). Twenty out of 34 patients who suffered ILD were listed. Ten underwent LT and 10 died on the waiting list. The 14 patients with ILD not listed had contraindications for the LT. There was no difference in outcome between different etiologies. Hepatic Encephalopathy (HE) was detected in 48 (64%) of the patients, having a worse outcome compared with the group without HE (56.2% vs 25.9% developed irreversible liver damage; p 0.062). International Normalized Ratio value on admission was significantly higher in patients with ILD (4.37 vs 3.2; P < 0.001).

Patients treated with N-acetylcysteine (31/75, 41.3%) had a similar pattern to those who didn’t receive (ILD of 48.4% vs 41.2%) respectively. The median ICG-PDR was significantly lower in patients who suffered ILD (median 4.8%/min; range 4-5.3) compared to those who survived with medical treatment (median 14%/min; range 8.35-25.95; P < 0.001), being ICG-PDR the one with greater sensitivity, specificity and predictive values.

Conclusion: In our sample the INR and ICG-PDR values were significantly associated with ILD. HE tended to be associated with a worse prognosis. Treatment with NAC has not demonstrated improved outcomes in our sample. ICG-use PDR can be very useful, in combination with other scores, to enhance the categorization of patients with ALF.

Disclosure of Interest: None Declared
CHALLENGES IN THE MANAGEMENT OF PAEDIATRIC NON-ALCOHOLIC FATTY LIVER DISEASE: A LONGITUDINAL FOLLOW-UP STUDY

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Objectives and Study: Non-alcoholic fatty liver disease (NAFLD) affects up to 10% of children in the western world, and in conjunction with obesity is becoming a public health concern. Despite this, the natural history of paediatric NAFLD is unclear due to a lack of longitudinal studies. In the UK, there are no established guidelines to identify those at risk of progressive liver disease (non-alcoholic steatohepatitis (NASH)) and that require transition to adult hepatology services.

Methods: We performed a retrospective review of children consecutively diagnosed with NAFLD at a tertiary referral hepatology service in the UK, between 2003 and 2014. Patients had been referred from either primary care physicians or general paediatricians with incidental, asymptomatic, abnormal liver function tests (LFTs) and/or fatty liver on ultrasound scan (USS). Patient characteristics, metabolic features and complications of liver disease were recorded at baseline and follow-up.

Results: 100 patients with primary NAFLD were followed-up for a mean 2.5±2.1 years. 77% (77/100) were male and mean age at presentation was 12±2.8 years. 59% were Caucasian and 41% were Asian. 67% were referred due to abnormal LFTs and 28% due to an abnormal ultrasound. On presentation, median BMI standard deviations (SDs) was 1.9 (range 0.45-3.0, 98th centile), ALT 71.5 (range 5-421) IU/L, cholesterol 4.3 (range 1.3-6.2) mmol/L, and bilirubin 8 (range 2-44) µmol/L. 12% (13/100) had type 2 diabetes confirmed by oral glucose tolerance test or HbA1c. 20/100 patients had undergone biopsy. 65% (13/20) of patients had biopsy-proven NASH and 25% (5/20) had moderate-severe fibrosis.

At the end of follow-up, there was a trend towards increasing severity of the metabolic syndrome. 65% of patients had an increase in HbA1c (mean increase 9±23 mmol/mol) and 56% had an increase in cholesterol (mean increase 0.4±0.4 mmol/L), but these changes were not statistically significant. There were no liver related complications during follow-up. At the end of follow-up, 66/100 patients had been discharged from the paediatric clinic. 79% (52/66) were under the care of their primary care practitioner, including 9 patients with NASH and fibrosis on biopsy. Only 3% (2/66) had transitioned to the care of an adult hepatologist, with the remaining 18% (12/66) under another secondary care specialist.

Conclusion: There is a need for validated non-invasive scoring systems to help identify children who require liver biopsy and long-term follow-up. With the collaboration of adult colleagues, those with NASH ± fibrosis should undergo long-term follow-up to aid our understanding of disease progression. However, this will require additional resources in adult hepatology.
Disclosure of Interest: None Declared
THE EFFECT OF NITISINONE ON HEPATIC FIBROSIS IN HEREDITARY TYROSINAEMIA TYPE I
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Objectives and Study: Nitisinone has transformed the management of Hereditary Tyrosinaemia type 1 (HT1). Treatment following early diagnosis (ED) seems to prevent the development of liver failure and hepatocellular cancer in childhood, while later treatment following clinical presentation (CP) is less effective. However the effect on liver fibrosis, which can develop before birth, is unknown. The Enhanced Liver Fibrosis (ELF) test has demonstrated validity as a non-invasive marker for liver fibrosis in a range of childhood diseases.

Aim. To estimate the degree of hepatic fibrosis by ELF in a stable group of children with HT1 treated with Nitisinone and to determine if age at treatment has an effect. Results expressed as median and range.

Methods: ELF was measured in 11 children with HT1 at age 7.2 (0.6-15.6). Six were ED and were treated in the first month of life. Five presented clinically and were treated at 4 months of age (3 months – 3 years).

Results: All children were clinically well with no evidence of portal hypertension. ELF suggested no significant fibrosis in 9/11 cases with one having moderate and one severe fibrosis. Repeat ELF after two years in the child with initially severe fibrosis was normal. Both of the children with fibrosis were in the ED group. There was no difference in ELF between the ED and CP groups (8.73 (8.12-10.89) vs 8.56 (8.44-8.78)).

Conclusion: Hepatic fibrosis is rare in children with HT1 treated with Nitisinone. Where hepatic fibrosis does occur, it may resolve with time. Children with HT1 treated with Nitisinone are unlikely to develop chronic liver disease.

Disclosure of Interest: P. McKiernan Conflict with: Alnylam Pharmaceuticals, Conflict with: Synageva, M. A. Preece: None Declared, S. Santra: None Declared
Hepatology

HEPATITIS C SPECIFIC T-CELL RESPONSES IN CHILDREN OF INFECTED MOTHERS
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Objectives and Study: The risk of vertical transmission of hepatitis C virus (HCV) infection from mother to child is reported to be around 5 % (1). Previous studies have shown that uninfected children (age 1-4 years) of HCV positive mothers develop HCV specific T-cell responses (2). The aim of this study was to investigate if an HCV specific T-cell response was detectable in uninfected children of HCV infected mothers and if so, how it developed over time from birth and onwards.

Methods: Blood samples from 15 HCV RNA positive mothers (tested at 0-7 months postpartum), 27 HCV-RNA negative children of infected mothers (tested consecutively at 0-2, 6, and 18 months of age) and 9 vertically infected children/adolescents (ages 1 month-19 years) were collected. HCV specific immune responses were measured by interferon-gamma (IFN-γ) enzyme-linked immunospot (ELISpot) assay and 3H-thymidine incorporation (proliferation) assay using cultures of peripheral blood mononuclear cells (PBMCs) stimulated in vitro with HCV proteins and peptides.

Results: HCV specific T-cell responses were observed in 73% (11/15) of the HCV-positive mothers, 39 % (12/31) of the HCV-negative children and 44% (4/9) of the HCV vertically infected children determined by ELISpot and proliferation assays. We were able to detect HCV-specific T-cell responses in children at 2, 6, and 18 months of age, but not at birth. The strongest T cell response was seen around 6 months of age in the uninfected children and around 0-3 months postpartum in the HCV-infected mothers.

Conclusion: Our results indicate that vertical exposure induced an HCV specific T-cell response in around 40 % of the uninfected children. T-cell responses were detectable from 2 months of age, suggesting that the most probable time point of viral exposure was around the time of birth.


Disclosure of Interest: None Declared
THE PROTECTIVE EFFECT OF CAPPARIS OVATA IN ACUTE HEPATOTOXICITY INDUCED BY PARACETAMOL

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Objectives and Study: Paracetamol, a commonly used antipyretic and analgesic drug worldwide is the most common cause of liver failure for which a sufficiently safe and effective treatment has not yet been found. Therefore, the present study was designed to investigate the efficiency of Capparis ovata, as a protective agent, against acute paracetamol toxicity of the liver.

Methods: Female Wistar-Albino rats, were divided into 4 groups as: 1) paracetamol, 2) Capparis ovata +paracetamol, 3) Capparis ovata and 4) control. Groups 2 and 3 were given 1.5 cc.day$^{-1}$ Capparis ovata, and groups 1 and 4, 1.5 cc.day$^{-1}$ distilled water for 8 days. On day 8, 3000 mg.kg$^{-1}$ paracetamol was administered orally to groups 1 and 2. All rats were sacrificed on day 9 and blood and liver tissue samples were taken. AST, ALT, total bilirubin, direct bilirubin, GGT, ALP levels were assessed. A lipid peroxidation marker, thiobarbituric acid reactive substance (TBARS) levels were measured in blood and liver. Liver tissues were evaluated histologically and scored for degenerative findings.

Results: AST, ALT and total bilirubin levels were lower in group 2 than in group 1 (Table 1, p<0.05). TBARS levels were lower in group 2, 3 and group 4 than in group 1 (p<0.05). Histopathological change scores were lower in the Capparis ovata +paracetamol group than in the paracetamol group (p<0.05).

Table 1. Serum AST and ALT levels.

<table>
<thead>
<tr>
<th>Group</th>
<th>AST (U/L)</th>
<th>ALT (U/L)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 (PS)</td>
<td>189.5±39.7*</td>
<td>112.1±20*</td>
</tr>
<tr>
<td>2 (PS+CAP)</td>
<td>108.1±4.3**</td>
<td>64.9±2.8**</td>
</tr>
<tr>
<td>3 (CAP)</td>
<td>113.7±5.4</td>
<td>52±2.9</td>
</tr>
<tr>
<td>4 (C)</td>
<td>109±7.3</td>
<td>48.1±2.1</td>
</tr>
</tbody>
</table>

Data are expressed as means ± SD, PS: Paracetamol, CAP: Capparis ovata, C: Control

*Group 1 is compared with group 3 and 4: p<0.05, **Group 2 compared with group 1: p<0.05

Conclusion: The results of this study have proven that Capparis ovata has antioxidant and hepatoprotective activities. It is concluded that Capparis ovata has a protective effect on the liver, both histopathologically and biochemically, against paracetamol-induced liver injury.

Disclosure of Interest: None Declared
**Hepatology**

**Hepatology**

PO-H-0295

THE V444A POLYMORPHISM IN BILE SALT EXPORT PUMP PREDISPOSES TO INFECTION-ASSOCIATED AND PARANEOPLASTIC HIGH-GGT CHOLESTASIS

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**Objectives and Study:** Transient cholestasis may occur in paediatric patients with Epstein-Barr virus (EBV) infection, cholecystolithiasis, or acute lymphoblastic leukaemia (ALL). In analogy to recent findings in intrahepatic cholestasis of pregnancy (IHC) and drug-induced liver injury (DILI), we hypothesize a correlation between such cholestasis and the V444A polymorphism in bile salt export pump (BSEP), encoded by *ABCB11*. We suggest that an abnormal pro-inflammatory cytokine milieu may lead to diminished BSEP expression on the hepatocyte canalicular membrane in individuals who harbour the V444A mutation and thereby to icteric cholestasis.

**Methods:** Children and adolescents (0 - 18 years) without previously identified hepatobiliary disease in whom hyperbilirubinaemia, elevated alkaline phosphatase activity (AP), and elevated gamma-glutamyl transferase activity (GGT) were observed were assessed for the c.1331T>C single-nucleotide polymorphism in *ABCB11* (predicted to yield in BSEP the V444A polymorphism) and were classed by genotype as homozygous C (CC), heterozygous (CT), or homozygous T (TT), the “normal” genotype without a disease correlation. Biomarker values (bilirubin, AP, GGT, LDH) were compared among the groups.

**Results:** Nineteen patients with EBV infection (n=8), cholecystolithiasis (n=8), or ALL (n=3) were included. Most were in the heterozygote CT group (n=8), followed by the homozygote CC group (n=7). Only 4 patients had the TT genotype. The CC genotype was correlated with the highest mean values for bilirubin (9.84 ± 7.72 mg/dl), GGT (389 ± 869 U/l), and LDH (421 ± 297 U/l).

**Conclusion:** The V444A polymorphism, in homozygous or heterozygous state, seems to predispose to bouts of transient infection-associated and paraneoplastic cholestasis. To identify the c.1331C>T polymorphism in *ABCB11* may help to explain icteric episodes and may prevent unneeded investigations. Whilst chronic BSEP deficiency is associated with normal-range serum GGT, GGT values rose in our patients with acute-onset icterus and the V444A polymorphism, including those without cholelithiasis. This may offer insights into mechanisms of GGT fluctuations in cholestasis.

**Disclosure of Interest:** None Declared
RELATIONSHIP THE DEGREE OF THE LIVER DYSFUNCTION AND ITS MORPHOLOGIC CHANGES IN CHRONIC HEPATITIS C IN CHILDREN

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Objectives and Study: Identify the relationship of morphological changes of the liver tissue and the degree of liver dysfunction in children with chronic hepatitis C (CHC).

Methods: Analyzed retrospective data from the morphological study of biopsies of the liver tissue of 86 patients aged 1 to 17 years (mean age 8.3±4.1) with CHC. Evaluated histological activity index by Knodell, the degree of fibrosis or cirrhosis by Desmet, the nature of the inflammatory infiltrate, the nature of degeneration and necrosis of hepatocytes. Assessment of the degree of liver dysfunction was carried out on a total evaluation of each indicator reflecting the involvement of the liver in the metabolism of proteins, fats and carbohydrates, on a 5-point scale: albumin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, cholesterol, glucose, lactate, ammonia, urea, transferrin, ceruloplasmin, prothrombin, fibrinogen.

Results: Morphological signs of dystrophy of hepatocytes were present in 49 of the 86 cases (57.0%) and were characterized by various combinations of structural failure of hepatocytes: fatty degeneration - in 10.5% of cases acidophilic degeneration - 14.0%, ballooning degeneration - 9.5%. The inflammatory infiltrate was detected in 98.8% of cases and was presented by lymphocytes in 83.7% of cases, 55.8% - histiocytes. Hepatocyte necrosis of varying severity was detected in 19 of 86 cases (22.1%). Histological activity index was 3.1±2.1 points and in 65.1% of cases was presented minimal activity in 31.4% - mild, 3.5% - moderate. Severe histological activity was not detected in any case. In 96.5% of cases revealed fibrosis: mild fibrosis – in 56.9%, moderate - in 31.5%, severe - 8.2% of cases. Cirrhosis was not detected in any case. The degree of liver dysfunction in children with CHC was reduced to 19.1 ± 7.8%, and in 25.0% of cases corresponded to moderate violations, and in 75.0% of cases - minor violations of liver function. Liver function in children in the absence of fibrosis or mild fibrosis was reduced to 16.8±7.7%, and in children with moderate and severe liver fibrosis - at 26.0±7.4% (p=0.038).

Conclusion: In children with CHC morphologically determined inflammatory infiltration in 98.8% of cases, degeneration of hepatocytes - for 57.0% of the hepatocyte necrosis - 22.1%, fibrosis - 96.5%. Cirrhosis of the liver in children with chronic hepatitis C has not been identified. Liver dysfunction was more pronounced at moderate to severe fibrosis than in its absence or mild fibrosis.

Disclosure of Interest: None Declared
NORMAL VALUES OF SERUM BILE ACIDS IN NEONATES
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Objectives and Study: Serum bile acids (BA) are high in neonates and gradually fall, reaching adult values by age 11 (Jahnel et al. 2014, unpublished data). BA are mostly conjugated to glycine; however - since taurine is abundant in breast milk and supplemented in infant formulas - in neonates BA are mostly conjugated to taurine. We aimed to measure BA composition in healthy neonates to determine standard values for this age group.

Methods: Serum total BA (tBA) concentrations were measured in 16 healthy term neonates without cholestasis on the third day after birth. Neonates were divided into two groups: Fasted (n=5) and fed (n=11). Using high-performance liquid chromatography – high-resolution mass spectrometry to analyse 10 µl of serum, we created 15-BA profiles including unconjugated and taurine- or glycine-conjugated BA.

Results: In fed neonates tBA values (16.3 ± 5.8 µmol/l) were higher than in fasted neonates (5.4 ± 3.3 µmol/l). In fed vs. fasted neonates taurine-conjugated BA (10.2 ± 2.8 µmol/l vs. 2.3 ± 0.6 µmol/l) were clearly more abundant than glycine-conjugated BA (5.8 ± 0.5 µmol/l vs. 2.1 ± 0.5 µmol/l). Primary taurocholic acid, taurochenodeoxycholic acid, and glycocholic acid were the most abundant BA, whereas levels of all secondary BA were <0.1 µmol/l. No differences in tBA profiles were visible between breast-milk-fed and formula-fed neonates.

Conclusion: This study confirms that taurine-conjugated BA are the predominant BA species in neonates. Since BA may serve as non-invasive biomarkers in hepatic and gastrointestinal disorders, to determine age-specific normal fed and fasted BA value ranges in neonates is essential.

Disclosure of Interest: None Declared
ETHNIC DIFFERENCES IN PAEDIATRIC NON-ALCOHOLIC FATTY LIVER DISEASE

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Objectives and Study: Non-alcoholic fatty liver disease (NAFLD) is now the most common cause of liver disease in children, with an estimated prevalence of 5-10%. The majority of published data has involved Caucasians. Data is lacking regarding the phenotypic differences of NAFLD in children of Asian origin.

Methods: We performed a retrospective review of children consecutively diagnosed with NAFLD at a tertiary referral hepatology service in the UK, between 2003 and 2014. Patients had been referred from either primary care physicians or general paediatricians with incidental asymptomatic abnormal liver function tests (LFTs) and/or fatty liver on ultrasound scan (USS). Patients with inadequate data or with secondary fatty liver disease were excluded. Patients were divided by ethnicity into Asian and Caucasian. All values are (±SD), unless stated.

Results: 100 patients with primary NAFLD were identified. 59/100 were Caucasian and 41/100 were of Asian origin, of whom, 73% (30/41) were Pakistani. There was male predominance in both groups, 73% (43/59) in Caucasian and 78% (32/41) in Asians. Mean ages at presentation were 12.6±2.5 and 11.7±2.8 years in Caucasian and Asian groups, respectively.

Asian patients had a significantly lower body mass index (BMI) centile than Caucasian (91.2±9.5 vs. 96.1±5.1, p< 0.05). There were no differences in LFTs between Asian and Caucasian patients, ALT (87.8±60.9 vs. 94.3±84.5 IU/L) and bilirubin (9.4±7.6 vs. 9±6.5 µmol/L). 61% (25/41) Asian patients had an elevated gamma glutamyl transferase, compared to 60% (35/59) Caucasian patients. Markers of the metabolic syndrome were similar in both groups: total cholesterol 4.4±1 vs. 4.4±1 mg/L, triglycerides 2.0±1.4 vs. 2.2±1.4 mg/L, and HbA1c 38.6 vs. 39.1±7.4mmol/mol.

20 patients had undergone biopsy. 33% (2/6) demonstrated moderate-severe fibrosis in Asian patients, compared to 21% (3/14) Caucasian patients (p=0.61).

Conclusion: Asian children with NAFLD have similar disease severity as their Caucasian counterparts, despite a significantly lower BMI centile at presentation. Referring clinicians and risk stratification scores require a greater awareness of ethnic differences in adiposity in paediatric NAFLD.

Disclosure of Interest: None Declared
**Objectives and Study:** Intrahepatic duct dilatation and common hepatic duct dilatation are not rare findings in pediatric abdominal ultrasonography. However, the clinical significance has not yet been established and there are only a few studies on pediatric populations with a dilated bile duct. This study aims to investigate the natural course and clinical significance of intrahepatic duct dilatation and common hepatic duct dilatation in pediatric patients.

**Methods:** From November 2005 to March 2014, 119 pediatric patients (range 1 day old to 17 years old) in whom intrahepatic duct dilatation or common hepatic duct dilatation was detected by abdominal ultrasonography in Severance Children's Hospital were retrospectively enrolled.

**Results:** A total of 119 pediatric patients were enrolled and they were divided into 2 groups. Forty-four subjects, without definite cause of bile duct dilatation and did not need treatment were assigned as the first group and the other 75 subjects, with definite cause of bile duct dilatation or underlying bile disease requiring treatment were assigned as the second group. Among the first group, 25 patients (56.8%) showed spontaneous resolution of bile duct dilatation, 17 patients (38.6%) showed no interval change and 2 patients (4.5%) did not come for subsequent studies. The second group is composed of 28 patients who were diagnosed as having choledochal cyst and 47 patients whose biliary tract dilatations were due to secondary causes such as gallbladder stone/sludge, hepatitis, post operation status and malignancy.

**Conclusion:** Primary biliary tract dilatation without definite cause in pediatric patients showed relatively benign clinical courses. More than half of this biliary tract dilatation spontaneously resolved, and there was no case of aggravation or progression to other disease at later. Additional investigations are needed to evaluate long-term prognosis and to compare clinically relevant findings in patients with similar findings in ERCP or MRCP.

**Disclosure of Interest:** None Declared
INFECTIONOUS COMPLICATIONS IN BILIARY ATRESIA; A SINGLE CENTRE EXPERIENCE
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Objectives and Study: To evaluate incidence, timing and bacterial aetiology of cholangitis and spontaneous bacterial peritonitis (SBP) in Biliary Atresia (BA), after Kasai Porto-enterostomy (KP), prior to liver transplantation (LT).

Methods: A single-centre retrospective analysis, comprising 78 patients who underwent KP between 2008-2010

Results: 78 patients (36M:42F) who underwent KP (BA; Type III 90%; syndromic 10%) comprised our study group. Cholangitis followed in 38/78 (48%) patients; median number of episodes 2 (range: 1, 5). Median age for first episode was 5.6 months (2, 72.5). Six patients showed dilated biliary radicles on ultrasound. Organisms were isolated from blood cultures in six patients; E-coli (n=2), Staphylococcus Aureus, Klebsiella, Streptococcus Pneumonia and Pseudomonas. 27/38 (71%) patients with cholangitis underwent LT, 10 are alive with their native liver and one died (decompensated liver disease, variceal bleed).

Ascites developed in 29/78 (37%) patients, at median age 6.5 months (3.1, 66). Ascitic taps were performed in 41% (12/29), due to respiratory distress with fever (5/12) or without fever (7/12) at median age 7.4 months (3.2, 22.8). 16/17 patients that did not have ascitic taps underwent LT at a median age 17.2 months (7.4, 79.7) and one died whilst listed for LT. Timing of tap was at the onset of ascites in six patients and at a median time of 2 months (0.1, 4.6) from onset of ascites in the remaining six patients. Four patients fulfilled criteria for SBP diagnosis; 3 culture-negative (wcc > 250mm), one bacteri-ascites (wcc < 250mm; mixed gram-positive cocci and gram-negative rods). No culture-positive SBP was identified. One culture-negative SBP was positive for Streptococcus Pneumoniae in blood culture. Five patients that underwent ascitic taps previously had cholangitis. Antibiotics were already commenced in 8/12 patients pre-tap. Raised plasma wcc (>17 mm) was identified in SBP (3/4) and non-SBP (3/8) patients. All SBP patients underwent LT at a median age 10.5 months (7.1, 16.1). Non-SBP patients underwent LT (n=4), are alive with native liver (n=1) or died (n=3). The 3 patients that died were listed for LT.

Conclusion: Cholangitis and SBP occurred in 48% and 5% of BA patients respectively, with cholangitis episodes presenting earlier. Few cases revealed positive bacterial cultures, in particular in ascitic fluid, which may be attributed to antibiotic use pre-tap. The definition of SBP in children needs to be considered cautiously to account for antibiotic use and new molecular techniques should be sought to aid diagnosis. LT is a successful outcome for cholangitis, SBP and non-SBP ascites.

Disclosure of Interest: None Declared
COINCIDENCE OF HYPERAMINOTRANSFERAZEMIA AND CHRONIC NEUTROPAENIA IS HIGHLY SUGGESTIVE OF SHWACHMAN-DIAMOND SYNDROME IN CHILDREN.

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Objectives and Study: The aim of the study was to describe the incidence of clinical symptoms and laboratory abnormalities in patients with Shwachman-Diamond syndrome (SDS) confirmed by molecular diagnostics.

Methods: We present 13 patients (9 girls, 4 boys), aged from 6 months to 7 years (at first visit); follow-up period varied from 1 to 9 years. In all children we excluded viral infections, cystic fibrosis, coeliac disease, α-1-antitrypsin deficiency, inborn errors of metabolism, primary immunodeficiency. We analyzed the results of liver enzymes activity, 72-hour fecal fat balance, peripheral blood and bone marrow smears, serum immunoglobulins, thoracic X-ray, abdominal ultrasound and anthropometric measurements. Three patients underwent liver biopsy; one had colonoscopy.

Results: The children have been admitted to our department due to chronic diarrhea, failure to thrive and/or hyperaminotransferazemia. All developed one or more severe infections (sepsis, bacterial pneumonia), had recurrent upper respiratory tract infections, 5 had chronic diarrhea. All presented with short stature and low weight; 3 had narrow thoracic cage. Elevated aminotransferazem has been observed in all patients, with highest values of AST reaching 600 U/l and ALT up to 450 U/l noted between 2 and 3 yo, with normal activity of GGTP. The patients (8/13) currently older than 5, have normalized activity of aminotransferazem before 5 yo. 72-hour faecal fat balance was abnormal in 3 cases of 12 tested. Abdominal ultrasound showed hyperechogenic pancreas in 7 patients. Thoracic X-ray showed narrow thoracic cage and abnormal ribs in 3 patients. All children had absolute neutrophil count below 1500 cells/μl- if tested between infections, 2 developed thrombocytopenia, 1 had severe anaemia, 1 pancytopenia. Bone marrow aspiration, performed in 9 patients, revealed normal marrow cellularity and left-shifted granulocytic series in 7 cases, 2 children had hypoplastic bone marrow. Six patients had low serum IgM concentration. Neutropaenia, was at first overlooked in 4 patients, resulting in performing liver biopsy (described as hepatitis chronica) or colonoscopy with biopsy (both were normal).

Conclusion: 1. Children with increased activity of aminotransferazem should be carefully tested towards chronic or recurrent neutropaenia.
2. Coincidence of hyperaminotransferazemia and neutropaenia and/or short stature should become an indication for molecular diagnostics towards SDS.
3. Hyperaminotransferazemia and short stature should be included in diagnostic criteria of SDS in children.
Disclosure of Interest: None Declared
FOUR POLISH PATIENTS WITH NEW TYPE OF SRD5A3-CDG

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Objectives and Study: Congenital disorders of glycosylation (CDG) are genetic diseases with an extremely broad spectrum of clinical symptoms. SRD5A3, encoding steroid 5α reductase 3 which takes part in dolichol phosphate biosynthesis, is responsible for a new CDG, SRD5A3-CDG. 15 children and 4 adults with this syndrome have been described so far, mostly Turkish, Baluchi and 3 Polish patients. The aim of the study was to analyze the typical symptoms of the disease in all Polish patients based on a single center experience.

Methods: We reviewed retrospectively four Polish children with SRD5A3-CDG, three of whom were earlier described. They have been diagnosed and treated in our Institute since 2000. In all the children isoelectric focusing of serum transferrin and the screening for SRD5A3 mutations were performed.

Results: Two sisters and two unrelated boys aged 0.7(0.3-8) years [median(min-max)] at diagnosis were followed-up for 12.3(4.5-12.7) y.

All patients suffered from psychomotor retardation, muscle hypotonia, visual impairment due to variable eye malformations (optic nerve hypoplasia/atrophy, chorio-retinal coloboma) and nystagmus, and had elevated liver enzymes, coagulopathy and low levels of low density lipoprotein cholesterol. In all but one patient craniofacial dysmorphia features and mostly transient microcytic anemia were observed. Ichthiosiform skin lesions, cerebellar vermis atrophy in MRI and stereotypic movements were found in two out of four patients. One child was fed by gastrostomy because of malnutrition with improvement, one was obese.

Conclusion: The new SRD5A3-CDG should be considered in patients with combination of delayed psychomotor development, skin lesions, visual impairment and hepatitis with coagulopathy when glycosylation studies are positive. Sequencing of SRD5A3 is required to confirm the diagnosis.

References: Morava et al. A novel cerebello-ocular syndrome with abnormal glycosylation due to abnormalities in dolichol metabolism. Brain 2010:133;3210-3220

Disclosure of Interest: None Declared
Hepatology

PO-H-0303

EARLY IDENTIFICATION OF TYPE C2 NIEMANN-PICK DISEASE BY URINARY BILE ACID PROFILE DETERMINATION IN A NEWBORN: POTENTIAL OF TANDEM MASS SPECTROMETRY FOR THE DIFFERENTIAL DIAGNOSIS OF NEONATAL CHOLESTASIS

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Objectives and Study: Background. Neonatal cholestasis (NC) is a rare but potentially life-threatening condition. It can be determined by primary hepatobiliary diseases as well as by endocrinological, genetic, infectious and metabolic disorders. Early recognition of the underlying cause is essential to ensure rapid treatment and optimal prognosis. Even in specialized centers, however, a prompt diagnosis may be hampered by the wide overlap among diseases causing NC and by the complexity of many diagnostic tests.

Aim. To report the case of an early diagnosis of Niemann-Pick disease type C2 (NPC2) in a child presenting with NC through tandem mass spectrometric analysis of urinary bile acids, and to demonstrate that a non invasive urine test may hold great potential in determining the etiology of NC.

Methods: Urinary bile acid excretion was determined by tandem mass spectrometry (MS/MS) and by liquid chromatography in high-resolution mass spectrometry (LC-MS).

Results: A 20 days old boy, born from consanguineous parents, was referred for prolonged jaundice and pale stools. Mild axial-limb hypotonia and enlarged spleen were detected on physical examination. Blood tests revealed low GGT (38U/L), cholestasis (direct bilirubin 117umol/L, bile salts >50umol/L), ALT elevation (202U/L) and impaired liver function (albumin 2.8 g%, INR 1.47). An abdominal US confirmed the presence of splenomegaly and showed a normal liver. A cherry red spot was bilaterally detected by fundus examination. Abnormal amounts of unusual bile acids were identified by MS/MS and LC-MS in the urine; the increased excretion of sulphated and additionally conjugated forms of 3 beta-hydroxy-, 3 beta-hydroxy-7-oxo-, and 3beta, 7 alfa/beta-dihydroxy-5-cholenoic acids suggested NPC2. The diagnosis was subsequently confirmed by genetic analysis of the NPC2 gene.

Conclusion: During cholestasis urine becomes the major route for bile acid excretion. MS/MS analysis of urinary bile acids is a rapid, sensitive and not invasive analytical method to establish bile acid excretion profiles both qualitatively and quantitatively. We have demonstrated that it may indicate the presence of NPC, a rare lysosomal lipid storage disorder, even at a very early stage. Urinary bile acid profile should be always determined during the evaluation of undiagnosed cases of NC in specialized centers of pediatric hepatology.
Disclosure of Interest: None Declared
SERUM CONCENTRATION OF IL-18 IN CHILDREN WITH NONALCOHOLIC FATTY LIVER DISEASE

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Objectives and Study: Interleukin-18 (IL-18) is a proinflammatory cytokine associated with metabolic syndrome (MS). Nonalcoholic fatty liver disease (NAFLD) can be regarded as a feature of MS. Therefore, we evaluated serum IL-18 concentration in obese children with NAFLD.

Methods: The study comprised 108 obese children (age range 7-17, mean – 13 years) with the initially suspected liver disease (hepatomegaly and/or increased ALT activity and/or liver steatosis in ultrasound). Viral hepatitis (HCV, HBV, CMV), autoimmune (AIH) and metabolic liver diseases (Wilson’s disease, alfa-1-antitrypsin deficiency, cystic fibrosis) were excluded. The fasting serum IL-18 concentration was determined (MBL, ELISA). The degree of liver steatosis in ultrasound (USG) was graded according to Saverymuttu scale. Advanced liver steatosis was defined as a score >1. The total intrahepatic lipid content was assessed by magnetic resonance proton spectroscopy (1HMR). Receiver operating characteristics (ROC) analysis was used to calculate the power of the assay to detect advanced liver steatosis and presence of fatty liver in 1HMR.

Results: Fatty liver in ultrasound was confirmed in 89 children and in 72 in 1HMR; 39 of them also presented elevated ALT level (NAFLD). IL-18 concentration was significantly higher in examined patients than in controls (n=15) (p=0.038). The significant IL-18 correlations with ALT (r=0.2), GGT (r=0.23), triglycerides (r=0.21), hsCRP (r=0.36) and the degree of liver steatosis (USG) (r=0.2) were found. NAFLD children had significantly higher IL-18 level as well as ALT, GGT, HOMA-IR, waist circumferences and total amount of lipids in 1HMR compared to other obese children. IL-18 level was also significantly higher in hepatopathic obese children with advanced liver steatosis (n=42) than in children without steatosis (n=19) (p=0.035). The ability of serum IL-18 (cut-off >326.8pg/ml, Se=60%, Sp=75%, NPV=34%, PPV=90%) to differentiate children with fatty liver in 1HMR from those without steatosis was significant (AUC=0.68; p=0.006).

Conclusion: Elevated serum concentration of IL-18 and its significant correlation with hepatocyte injury, systemic inflammation and degree of liver steatosis indicate the role of this cytokine in pathomechanism of NAFLD. IL-18 seems to be a suitable non-invasive biomarker in predicting advanced liver steatosis and fatty liver in obese children.

Disclosure of Interest: None Declared
**Objectives and Study:** Cystic fibrosis (CF) may affect the liver. We investigated changes in serum bile acid (BA) levels in different ages in CF patients with the aim to evaluate BA as a serum marker for CF-associated liver disease.

**Methods:** Serum concentrations of BA were measured by liquid-chromatography-tandem mass spectrometry in patients suffering from CF (3 age groups, subdivided into groups with and without ursodeoxycholic acid (UDCA) treatment). BA levels were correlated with values for biomarkers of hepatobiliary injury such as bilirubin, alkaline phosphatase activity (AP), gamma-glutamyl transferase activity (GGT), and serum transaminase activity (AST, ALT).

**Results:** BA levels were measured in 49 patients. Most patients were receiving continuous UDCA-treatment (n=36) and showed BA values significantly above reference ranges: < 11 years, 11.7 ± 6.2 µmol/l (3.61 – 6.41 µmol/l, p<0.01; n=7); 12 – 19 years, 6.3 ± 7.8 (3.09 – 4.12; p<0.01; n=15); > 19 years, 7.9 ± 4 (3.09 – 4.12; n=14). The group without UDCA treatment also showed serum BA concentrations higher than reference ranges, albeit without statistical significance: < 11 years, 5.1 ± 4.8 (n=2); 12 – 19 years, 5.77 ± 0.96 (n=3); > 19 years: 4.4 ± 4 (n=8). In no group were biomarker-value changes (AP, GGT, AST, and ALT levels) significant compared to healthy controls; however, average values of AST, ALT, and GGT in the group without UDCA treatment were higher than the average values in the group with UDCA treatment.

**Conclusion:** Increases in serum BA values in our CF patients were principally due to UDCA treatment, but some increase independent of UDCA effect also was present. BA values in serum seem not to be an early marker for progressive liver disease in CF. However, BA measurements could be used to test CF patients’ compliance with regular UDCA ingestion.

**Disclosure of Interest:** None Declared
ETIOLOGY, OUTCOME AND PROGNOSTIC FACTORS OF CHILDHOOD ACUTE LIVER FAILURE IN A METROPOLITAN AREA OF GERMANY

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Objectives and Study: Pediatric acute liver failure (PALF) is a rapidly progressive, potentially fatal clinical syndrome occurring in previously healthy children. Aim of our study was to detect the current leading causes of PALF in a single center in Germany, and to identify possible prognostic clinical and biochemical markers.

Methods: From January 2010 until December 2013, 37 pediatric patients with PALF were included in our study. Medical records were reviewed for demographic, laboratory and clinical data. Laboratory results on admission as well as peak values (ALT, AST, creatinine, bilirubin, INR, albumin, ammonia) as well as PELD and MELD score on admission were assessed and analyzed.

Results: Fifteen (41%) patients recovered spontaneously, 14 (38%) patients died without transplantation, and 8 (21%) patients received a liver transplant. Patients who survived were significantly older than patients who died (p=0.039). Specific causes of PALF could be identified as infectious diseases (16%), metabolic diseases (14%), toxic liver injury (11%), immunologic diseases (8%), or vascular diseases (8%). Causes of PALF remained indeterminate in 16 patients (43%). High ammonia levels (p=0.047), low albumin levels (p=0.011) and low ALT levels (p=0.007) on admission were associated with worse outcome. Further predictor of worse outcome were high peak ammonia levels (p=0.030).

Conclusion: Infectious diseases are the most common known cause of PALF. However, in a large proportion of patients the cause for PALF remains cryptic. Ammonia levels may be of prognostic value to predict outcome.

5. Narkewicz MR, Dell Olio D, Karpen SJ, et al. Pattern of diagnostic evaluation for the causes of

Disclosure of Interest: None Declared
THE SPECTRUM OF SICKLE CELL ASSOCIATED LIVER DISEASE IN CHILDREN – KING’S COLLEGE HOSPITAL EXPERIENCE

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Objectives and Study: Children with sickle cell disease may have liver involvement, not only during crises but may also develop chronic liver disease. There are perceived risks with liver biopsy in the condition so the spectrum of liver disease is not well defined and optimal investigation and management are not clear. We set out to describe our experience with children presenting with sickle cell associated liver disease to better inform practice.

Methods: Children with sickle cell disease who presented to a tertiary care paediatric liver service over the past 5 years were identified from a departmental database. Data were collected from clinical notes, laboratory, radiological and histological reports. SPSS v 21.0 was used for analysis.

Results: During the study period 58 children with sickle cell disease and liver involvement were referred to the service. The median age at presentation was 11.3 yrs (IQR 8.3, 13.8) (34 male). 9 were on blood transfusion programs, 8 undergoing chelation with desferroxamine. At presentation median bilirubin was 89umol/L, only 6 had a normal bilirubin. Median conjugated bilirubin was 82umol/l. Transaminases were abnormal in 35(60%) and gGT in 41(71%). Synthetic function was preserved in all and there was no evidence of hypersplenism. Examination revealed hepatomegaly in 24(41%) and splenomegaly in 28(48%). Ultrasound reported dilated ducts in 22(38%), heterogenous liver in 3(5%). 27(47%) patients underwent MRCP, in 5 this was described as a cholangiopathy without obstruction, in 12 gallstones were seen and in 7 obstruction from stricture. 15(26%) patients underwent ERCP, in 3 this demonstrated a cholangiopathy, in 5 gallstones and other abnormalities including stricture in 6. Liver biopsy was undertaken in 9(16%); this showed a cholangiopathy in 3, 1 of which was cirrhotic, hepatitis in 4 with periportal fibrosis in 3, cirrhotic transformation in the remaining 2. Overall diagnosis was biliary obstruction due to stone or inspissated bile in 30(52%), autoimmune liver disease in 12(21%), sickle cholangiopathy in 4(7%), sickle hepatopathy in 5(9%) and miscellaneous including viral hepatitis in 7(12%). Children with autoimmune disease had a higher AST (p<0.005) but not ALT, GGT or bilirubin. They also had higher immunoglobulins and positive autoantibodies (p<0.001). All children were managed with ursodeoxycholic acid and those with symptomatic gallstones were referred for cholecystectomy. Autoimmune liver disease was treated with immunosuppression.

Conclusion: Liver involvement in sickle cell disease is not uncommon, the most common presentation is with biliary obstruction, though there are significant number of children with autoimmune liver disease in addition to cholangiopathy/hepatopathy of uncertain aetiology.

Disclosure of Interest: None Declared
Objectives and Study: Identify the relationship of morphological changes of the liver tissue and the degree of liver dysfunction in children with autoimmune hepatitis (AIH).

Methods: Analyzed data from the morphological study of biopsies of the liver tissue of 40 patients aged 1 to 17 years (mean age 11.1±3.0) with AIH. Evaluated histological activity index (HAI) by Knodell, the degree of fibrosis or cirrhosis by Desmet, the nature of the inflammatory infiltrate, the nature of degeneration and necrosis of hepatocytes. Assessment of the degree of liver dysfunction was carried out on a total evaluation of each indicator reflecting the involvement of the liver in the metabolism of proteins, fats and carbohydrates, on a 5-point scale: albumin, alanine aminotransferase, aspartate aminotransferase, total bilirubin, cholesterol, glucose, lactate, ammonia, urea, transferrin, ceruloplasmin, prothrombin, fibrinogen.

Results: Morphological signs of dystrophy of hepatocytes were present in 31 of the 40 cases (77.5%) and were characterized by various combinations of structural failure of hepatocytes: fatty degeneration - in 12.5% of cases acidophilic degeneration - 7.5%, ballooning degeneration - 17.5%. Hepatocyte necrosis of varying severity was detected in 72.5% of cases. Rosette formation was determined in 52.5% of cases. The inflammatory infiltrate was detected in all specimens and presented by lymphocytes in 100.0%, plasma cells - in 45.0%, histiocytes - in 35.0% of cases. Cirrhosis was detected in 27.5% of cases. In 72.5% of cases revealed fibrosis: mild fibrosis - in 7.5%, moderate - in 20.0%, severe - 45.0%. In children who are not receiving immunosuppressive therapy was 10.7±4.3 points in children receiving immunosuppressive therapy >2 weeks HAI was significantly lower and was 6.9±3.4 points (p=0.031). In children who are not receiving immunosuppressive therapy the liver function was reduced by 42.6±11.2%, and in children receiving immunosuppressive therapy >2 weeks, the liver function was reduced by 25.0±10.5% (p<0.001). The degree of liver dysfunction is more pronounced at moderate and severe histological activity (37.8±14.5%), than at the minimal and mild histological activity (27.2±13.2%) (p=0.003). The degree of liver dysfunction was more pronounced in the liver fibrosis score of 3-4 on Desmet - at 40.3±13.0%, than in fibrosis score of 0-2 on Desmet - at 32.6±10.9% (p=0.015).

Conclusion: In children with AIH morphologically determined inflammatory infiltration in 100.0% of cases, degeneration of hepatocytes - for 77.5% of the hepatocyte necrosis - 72.5%, fibrosis - 72.5%, cirrhosis - 27.5%. The more pronounced the level of histological activity and / or fibrosis or cirrhosis, the more significantly impaired liver function.
Disclosure of Interest: None Declared
ACUTE LIVER FAILURE IN CHILDREN: ETIOLOGY, OUTCOME AND PROGNOSTIC FACTORS

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Objectives and Study: The objectives of the study were: 1) To describe the evolution of patients admitted for acute liver failure (ALF) and its causes 2) To identify prognostic factors for liver transplantation-free survival at 21 days after admission.

Methods: Diagnosis of ALF following current criteria (PALF Study Group) was made in 95 children between 1999 and 2014. Patients were excluded for active oncologic disease and recent cardiac surgery. Data in children who survived without liver transplantation (LT) were compared with those in children who underwent LT or died. King’s College’s criteria (KCC), Liver Injury Units (LIU) and Admission Liver Injury Units (aLIU) scores were calculated retrospectively.

Results: Median age was 14 months; 58% male. Distribution by age was: newborn (19%), 1-12 months old (26%), 13-36 months old (19%) and >3 years old (36%). ALF causes were metabolic (19%), indeterminate (14%), autoimmune (14%), viral (13%), Wilson (6%), neonatal alloimmune disease (6%), haemophagocytic lymphohistiocytosis (5%), ischaemic (4%), toxic (4%) and others (15%). The most frequent causes by age were: 1) Newborns (18%): neonatal alloimmune (33%), galactosemia (22%), viral (11%) and others (33%); 2) 1-36 months: metabolic (30%), autoimmune (18%), unknown (18%), viral (7%); 3) >3 years old (34%): viral (20%), Wilson (17%), autoimmune (15%), unknown (12%), hemophagocytic syndrome (12%), toxic (9%) and others (15%). At 21 days after admission, 43% had survived with native liver, 35% had undergone LT and 22% had died without LT. Transplant-free survival depended on etiology, being lower for alloimmune disease and unknown etiology. A better prognosis was observed in conditions amenable to therapy. Clinical factors related with a worse prognosis were jaundice, ascites, gastrointestinal bleeding, encephalopathy (especially grade 3-4) at admission and a need for mechanical ventilation or renal replacement therapy. Biochemical factors: peak levels of bilirubin, INR, lactic and ammonia were higher and platelets lower in the non-survivors with native liver group. 80% of those fulfilling KCC and 37% of those who did not, either died or required LT. 77% of those with LIU > 370 and 75% of those with aLIU > 310 did not survive with their native liver and 76% of those with LIUs > 209 and 63% with aLIU < 160 survived without LT.

Conclusion: ALF etiology was varied and differed by age. The most frequent cause in our series was metabolic disease; a cause was not identified in 14% of children. At 21 days after admission, 43% survived with their native liver, 35% had undergone LT and 22% had died. Identifying patients who will survive without LT remains a challenge. While helpful, the present scoring systems are not
definitive. An indication for LT should be based on the combination of clinical, etiological and biochemical factors.

**Disclosure of Interest:** None Declared
IS LIVER BIOPSY ESSENTIAL FOR DIAGNOSIS IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE AND ABNORMAL LIVER TESTS?

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Objectives and Study: Liver disease is a recognized extra-intestinal manifestation of inflammatory bowel disease (IBD). The aims of the study are to describe characteristics of patients with abnormal liver tests at the time of initial diagnosis of IBD in a single tertiary centre over the last 11 years and to evaluate the role of liver biopsy.

Methods: Patients were identified from the departmental endoscopy register and the electronic patient administration system using ICD-10 classification. Retrospective data was collected from patient notes. Patients underwent standard blood tests for IBD, autoantibodies, immunoglobulins, hepatitis screen, and alpha-1-antitrypsin deficiency. All patients underwent liver ultrasound (USS) +/- magnetic resonance cholangiopancreatography (MRCP). Some patients underwent liver biopsy.

Results: 16 patients were identified (9 females). 12 had ulcerative colitis, 3 indeterminate colitis and 1 Crohn’s disease. Eleven patients were diagnosed with sclerosing cholangitis (SC). 5 patients were positive for smooth muscle antibody (SMA positive). 10/12 patients had bile duct abnormalities identified at USS and/or MRCP and were diagnosed with SC. 2/10 patients had advanced liver disease with splenomegaly and fibrosis/cirrhosis on USS. One of these 2 patients underwent liver transplant 7 years later. 8/10 patients, underwent liver biopsy confirming a histological diagnosis of SC in keeping with changes seen on imaging. One patient with normal imaging, except calculi (SMA positive) was diagnosed with SC following liver biopsy. One patient (SMA positive) was presumed to have SC, despite normal imaging and did not undergo liver biopsy initially. She was maintained on a small dose of steroid and ursodeoxycholic acid but underwent liver biopsy 6 years later despite normal LFT’s because of thrombocytopenia after restarting azathioprine and was found to have liver fibrosis. The remaining 4 patients had transient transaminitis, one had pancreatitis (SMA positive) and another was diagnosed with Coeliac disease at the same time as IBD. No other autoantibodies were positive in any of the patients.

Conclusion: In patients with IBD, the diagnosis of SC based on abnormal imaging (USS +/- MRCP) was not altered by liver biopsy.

Disclosure of Interest: None Declared
Objectives and Study: Glycogen storage disease (GSD) are group of rare genetic diseases, characterized with glycogen accumulation in tissues (muscle or liver).

Methods: We examined 54 children with hepatic form of GSD at age from 1 to 17 years: 19—children with type- I, 16—type-III, 19—type-VI. Children were observed in the dynamics, that allowed us to identify age-dependent deviations in T-cells immunity. Lymphocytes subsets was measured by flow cytometry.

Results: Number of T-cells corresponds reference intervals differed in children depending from age:0-2 years-90%; 2-5 years- 60%; > 6 years- only 35% of cases. We revealed changes in the peripheral lymphocytes subsets balance depended on GSD type. The most pronounced changes were revealed in type I: 45% of children was observed an increased content of T-lymphocytes, but only if I and III types were observed decrease in T-lymphocyte ratio in 23% and 7%, respectively. Index CD4/CD8 was increased in all types of GSD. The number of regulatory T-cells (Treg) and Th17-lymphocytes was increased in all types GSD compared with the reference intervals: Treg (107,9±6,5cells/ml vs 62,3±3,1cells/ml), Th17-lymphocytes (280,4±12,8 cells/ml vs 156,3±4,2 cells/ml); (р<0,001). That indicated increased autoimmune diseases risk in patients with GSD.

Conclusion: The obtained data connected with increased infectious disease rate in children with GSD. It's necessary to carry out regular investigation of T-cell immunity status in patients with GSD for timely prevention and treatment of intercurrent diseases.

Disclosure of Interest: None Declared
AZATHIOPRINE SAFETY IN PAEDIATRIC PATIENTS WITH AUTOIMMUNE LIVER DISEASE: A RETROSPECTIVE OBSERVATIONAL STUDY

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Objectives and Study: Azathioprine (AZA), along with corticosteroids, represents a fundamental drug in the treatment of autoimmune liver disease (AILD). Adverse drug reactions associated with AZA have been reported in some population studies conducted mainly in adults with inflammatory bowel disease (IBD). However, studies among pediatric population with AILD are scarce. Therefore, the aim of this study was to evaluate adverse events associated with AZA in children and adolescents with AILD such as autoimmune hepatitis (AIH) type 1 and 2 (AIH-1, AIH-2) and seronegative, autoimmune sclerosing cholangitis (ASC), small duct sclerosing cholangitis (SDSC) and overlap syndrome. Moreover, this study analyzed the role of the underlying disease and of the possible association with IBD in the development of adverse events.

Methods: Medical records of 52 patients (18 males and 34 females) with AILD (17 patients AIH-1; 12 AIH-2; 3 seronegative AIH; 5 ASC; 3 SDSC and 12 overlap syndrome) who were treated with AZA for at least 6 months between January 1993 and December 2013 were retrospectively reviewed. Mean age at the beginning of AZA was 8.9 years (range 1.8 to 17.9 years). Mean duration of treatment with AZA was 8.2 years (range 0.6 to 22.6 years). 13 patients also had IBD. When AZA was first administered all patients were simultaneously treated with other immunosuppressive drugs (prednisone and/or cyclosporine).

Results: Twenty seven (52%) of the 52 patients experienced one or more adverse reactions to AZA. Treatment discontinuation however was necessary in only 2 patients (4%) who experienced severe leuco/lymphocytopenia and heartburn respectively. In both cases the adverse events completely regressed after AZA withdrawal.

Nearly all of the adverse events were hematologic in nature (96%), consisting of lymphocytopenia, anemia, macrocytosis, thrombocytopenia and neutropenia. In more than 95% of cases, the hematologic adverse events were defined as mild/moderate. These events were transient in half of the cases, of which more than 70% resolved spontaneously. Other adverse events that occurred were gastrointestinal disturbance (4%), infection (4%) and hair loss (8%). No cases of pancreatitis, hepatotoxicity, arthralgia, skin rash, or sepsis were reported in our patients.

The type of AILD does not appear to be a risk factor for the development of adverse events, whereas the association with IBD, although not reaching statistical significance, defines a subgroup of patients with an apparent greater tendency to drug-toxicity (62% vs. 49%, p=0.5).
**Conclusion:** The use of AZA in the treatment of AILD in pediatric patients demonstrated a high safety profile. Further studies are needed to confirm these findings in order to better guide treatment decisions.

**Disclosure of Interest:** None Declared
Hepatology
PO-H-0313

PARENTERAL NUTRITION ASSOCIATED CHOLESTASIS IN EXTREMELY LOW BIRTH WEIGHT INFANTS
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Objectives and Study: To assess risk factors and prognosis of very low birth weight infants with parenteral nutrition associated cholestasis.

Methods: 43 extremely low birth weight infants were included as study group, they all are hospitalized on the first day of birth, the liver function was normal before parenteral nutrition beginning. All of them had used parenteral nutrition more than 14days. 48 extremely low birth weight infants without PNAC be involved in as control group. The index include the therapy of these infants, complications, the time of beginning and end of PN, the cumulative amount of amino acids, the highest amount of amino acids, the cumulative amount of fat emulsion, the highest amount of fat emulsion, weight, calorie, liver function, electrolyte, blood fat, ultrasound etc. All infants were treated with early minimal enteral feeding. Infants of PNAC group were treated with ursodesoxycholic acid. All infants followed up to 1 years of age.

Results: There are not statistical difference in gender, age and complications between two groups(\(p>0.05\)). In study group, D-Bil was 47.8±6.7\(\mu\)mol/L when PNAC appeared. The time for diagnosis of PNAC was 5.6±1.2 week after birth. Peak value of D-Bil was 80.9±10.8\(\mu\)mol/L, it appeared in 7.8±1.4 week after birth. The increase of parenteral nutrition amount showed positive correlation with D-Bil increase. The time for oral feeding tolerance set up, the time for PN, the time of beginning and end of PN, the cumulative amount of amino acids, the highest amount of amino acids, the cumulative amount of fat emulsion, the highest amount of fat emulsion and calorie of 14 days of PN were statistical difference between two groups. 43 infants with PNAC were cured. The longest duration of PNAC was 121 days. logistic regression analysis showed the time for PN, the time of beginning of oral feeding and combined infection were the risk facts of PNAC.

Conclusion: The prognosis for PNAC is not so bad in our study. the time for PN, the time of beginning of oral feeding and combined infection were the risk facts of PNAC.

Disclosure of Interest: None Declared
**URINE COPPER LEVEL IN DIAGNOSIS OF WILSON’S DISEASE IN CHILDREN**

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**Objectives and Study:** In Wilson's disease, a diagnostic level of urine copper in children have not been reported. Herein, we evaluated 24-hour urine copper levels of children with Wilson's disease to compare with chronic liver disease or, healthy children.

**Methods:** One hundred and fifty four children were enrolled in this study. We retrospectively reviewed 24-hour urine copper levels of children at diagnosis with Wilson's disease and chronic liver disease or, healthy children whom were searched for Wilson's disease due to an affected sibling or preliminary diagnosis.

**Results:** Sixty six (42.9%) children with Wilson’s disease and, 88 children (57.1%) with chronic liver disease or, healthy children were compared. Half of the patients were male (n = 77) and the mean age was 10.09 ± 3.79. Prothrombin time/international normalized ratio (PT/INR), both basal and D-penicillamine induced urinary copper excretion, serum copper levels, liver copper contents were significantly higher and ceruloplasmin levels were significantly lower in the Wilson’s disease group compared with chronic liver disease or, healthy children. If the copper levels in the 24-hour urine accepted as 70mcg to discriminate Wilson’s disease, the area under the Receiver Operating Characteristic (ROC) curve 0.894 (p <0.0001) (95% confidence interval; 0.841-0.947) and the sensitivity 81.82%, specificity was found to be 89.77%. If the diagnostic value accepted as above 100mcg, sensitivity 69.7% and, specificity was found to be 92.05%. If the ceruloplasmin levels <20 mg/dL and, 24-hour urine copper level is >70mcg, sensitivity 75.76%, specificity 97.73%, positive predictive value was found to be 96.15 for the diagnosis of Wilson's disease.

<table>
<thead>
<tr>
<th></th>
<th>24-hour urine copper level &gt;70mcgr</th>
<th>24-hour urine copper level &gt;100mcgr</th>
<th>Ceruloplasmin &lt;20mg/dl + 24-hour urine copper level &gt;70mcgr</th>
<th>Ceruloplasmin &lt;20mg/dl + 24-hour urine copper level &gt;100mcgr</th>
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<tbody>
<tr>
<td>Sensitivity</td>
<td>81.82</td>
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<td>75.76</td>
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<tr>
<td>Specificity</td>
<td>89.77</td>
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<td>Positive Likelihood Ratio</td>
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<td>Negative Likelihood Ratio</td>
<td>0.2</td>
<td>0.33</td>
<td>0.25</td>
<td>0.36</td>
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<tr>
<td>Positive predictive</td>
<td>85.71</td>
<td>86.79</td>
<td>96.15</td>
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</tbody>
</table>
Conclusion: Ceruloplasmin levels <20 mg/dL and, 24-hour urine copper level >70mcg are suggestive of Wilson's disease in children.


Disclosure of Interest: None Declared
RELATIONSHIP BETWEEN NON-ALCOHOLIC FATTY LIVER DISEASE AND MEDITERRANEAN DIET IN CHILDREN

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Objectives and Study: The aim of this study was to investigate the association between non-alcoholic fatty liver disease (NAFLD) and consumption of the Mediterranean diet in children.

Methods: Patients with NAFLD were included to the study (n=106, 66 boys, 12.46 ± 2.62 years). Children’s anthropometric measurements (including total body fat by bioimpedance) and laboratory data were recorded. Age and sex matched 106 children without any known chronic diseases were included as control group. Compliance with the Mediterranean diet was assessed using the Mediterranean Diet Quality Index (KIDMED index) (1).

Results: Ultrasonography revealed stage 1 hepatosteatosis in 59.0% (n=62) of children, stage 2 in 36.2% (n=38) and stage 3 in 5.8% (n=5). Mean KIDMED index in the children with NAFLD was 2.69 ± 2.46, compared to 5.24 ± 2.11 in the control group (p<0.001). KIDMED index was low (≤3) in 71 (66.9%) of the children with NAFLD, moderate (4-7) in 30 (28.3%) and good (≥8) in 5 (4.8%). In the control group, KIDMED index were low in 16 children (19.4%), moderate in 70 (67.3%) and good in 18 (17.3%) (p<0.05). KIDMED index was not correlated with total body fat level, waist/height ratio, BMI or HOMA-IR. In addition, no correlation was determined between KIDMED index and ALT, HDL, LDL, triglyceride, total cholesterol or stage of hepatosteatosis.

Conclusion: This study shows an association between NAFLD and consumption with the Mediterranean diet in children. With its many beneficial properties, the Mediterranean diet may prevent the development of NAFLD and together with a change in lifestyle may exhibit therapeutic effects in subjects with NAFLD.


Disclosure of Interest: None Declared
INTENSIVE LIFESTYLE TREATMENT FOR NON-ALCOHOLIC FATTY LIVER DISEASE IN SEVERELY OBESE CHILDREN: INPATIENT VERSUS AMBULATORY TREATMENT

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Objectives and Study: Lifestyle intervention is the only established therapy for non-alcoholic fatty liver disease (NAFLD). The optimal treatment schedule and predictors of response of this treatment have not been established in children. In addition, therapy resistant severely obese children are rarely studied. We aimed to compare the efficacy of an inpatient intensive lifestyle intervention versus ambulatory intensive lifestyle intervention versus usual care for treating NAFLD in therapy resistant severely obese children.

Methods: A cohort study of 51 severely obese non-diabetic children (mean age 14.7 (±2.4) years; BMI z-score 3.5(±0.5)) with liver steatosis were non-randomly allocated to 6 months of inpatient or ambulatory treatment in a tertiary obesity centre or usual care. Proton Magnetic Resonance Spectroscopy determined liver steatosis and serum ALT were the primary outcome measures. Baseline variables were evaluated as predictors of treatment response.

Results: Liver fat content normalized in 43%, 29% and 22% and serum ALT normalized in 41%, 33% and 6% at the end of 6 months inpatient, ambulatory or usual care treatment, respectively. Comparing among treatment groups, only the proportion of ALT normalization at the end of 6 months inpatient and ambulatory treatment compared to usual care were significant higher (p=0.005 and p=0.002, respectively). However, this study was only powered to detect differences over 25%. Treatment effects of inpatient and ambulatory treatment were sustained at 1.5 years follow-up. Improvement in BMI z-score and insulin sensitivity during treatment were the parameters related to treatment effect. No baseline characteristic, including PNPLA3 polymorphism or leptin, was consistently predictive for treatment response.

Conclusion: A 6-months intensive inpatient and ambulatory lifestyle treatment in severely obese children reverses NAFLD in a minority of patients. This study suggests that inpatient compared to ambulatory intensive treatment only slightly increases treatment success. Further efforts to optimize and individualize lifestyle interventions and additional treatments options are needed particular for severely obese children resistant to conventional lifestyle interventions.

Disclosure of Interest: None Declared
MICROBIOTA AND GUT-LIVER AXIS IN OBESITY RELATED LIVER DISEASE: A PAEDIATRIC PILOT STUDY

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Objectives and Study: It increasingly appears that Gut Microbiota (GM) and gut-liver axis malfunction modulate body fat excess and its comorbidities. Here we investigated roles of GM and intestinal permeability in obese children w/wo hepatometabolic comorbidities as compared to normal weight (NW) individuals.

Methods: 15 otherwise healthy children (7-14 yo) after profiling for obesity risk factors (SDSC scale for Sleep Disorders, KIDMED scale for Mediterranean Diet adhesion), clinical, auxologic, laboratoristic and ultrasonographic parameters, were allocated in 3 groups: NW, Obese with [St(+)] and without [St(-)] hepatic steatosis. GM communities were studied by 16SrRNA high-throughput sequencing (ILLUMINA Miseq, SanDiego). Intestinal permeability (lactulose/mannitol ratio) was assessed by HPLC.

Results: 1. OBESITY. Obese children had lower GM α-diversity and lower levels of anti-obesogenic phylum Verru microbia. Fecal γ-Proteobacteria instead correlated with BMI and daily calories (r=0,70; p=0,01 and r=0,54; p=0,04, respectively). Synergistetes and Chloroflexy correlated with Sleep Disorders (r=0,53;P=0,04) and adhesion to Mediterranean Diet (r=-0,67; p<0,05) respectively.

2. OBESITY RELATED FATTY LIVER.
   a. Obese had higher levels of fecal ε- and γ-Proteobacteria, (p=0,04 and p=0,01, respectively), i.e. two genera belonging to a Gram [-] phylum comprising abundant alcohol-producing bacteria involved in augmented intestinal permeability and fatty liver. In our series this mirrored more frequent abnormal intestinal permeability in [St(+)] (4/5 vs 1/5) (p= 0,045).
   b. [St(+)] characteristically also expressed H2 utilizing-methanogenic bacteria (Archaea-Methanobrevibacter Smithii), and correlated with H2-producing bacteria Bacteroidetes-Prevotella (r=0,49 ;p <0,05)

Conclusion: Here we confirmed several murine/human preliminary literature data suggesting a peculiar GM dysbiosis and low diversity in obesity and NAFLD. Coexistence also in our series of H2-producing bacteria and H2-utilizing methanogenic bacteria suggests that H2 transfer between
bacterial and archaeal species reflects increased energy harvesting and may serve as a target in studies with tailored probiotics.

Disclosure of Interest: None Declared
Objectives and Study: The aim of this study is to define clinical features and course of patients with portal hypertension (PH).

Methods: Eighty patients with PH who underwent oesophagogastroduodenoscopy (OGD) during 2009-2013 were enrolled. OGD findings and demographic features, diagnoses, medications, laboratory and ultrasonographic (US) findings were retrospectively analysed.

Results: Of 80 patients, 33 (41.3%) were female. The mean ages at the diagnosis of primary disease and at time of endoscopy were 5.1±4.4 and 8.7±4.6 years, respectively. 18 (22.5%) patients had extrahepatic portal vein obstruction (EHPVO) and 62 (77.5%) had various chronic liver diseases (CLD) (Table). Ratios of prematurity and umbilical venous catheterization, and levels of aminotransferases and prothrombin time were statistically higher in EHPVO group than CLD group. 59 (73.8%) patients had oesophageal varices (OV), bleeding was the first symptom in 18 (30.5%), and 6 bled before the treatment. OV were classified as grade 4 (G4), G3, G2 and G1 in 16 (27.1%), 27 (45.8%), 10 (16.9%) and 6 (10.2%) patients. Red sign on varices, gastric varices, portal gastropathy and portal duodenopathy were determined in 14 (23.7%), 30 (50%), 40 (67.8%) and 5 (8.9%) patients, respectively. 30 patients were given primary (PP) and 22 patients were given secondary (n=22) prophylaxis (SP). Prophylaxis included beta blocker therapy (BBT) combined with endoscopic therapy or not. Twenty four patients were given only BBT. 7 patients were not on BBT because of bronchoconstriction. Mean duration of BBT was 40 months. OV bleeding during follow-up was determined 4 of 30 (13.3%) patients in primary and 10 of 22 (45.5%) patients in secondary prophylaxis group.

Bleeding rate was higher in patients with high grade varices (p<0.01), gastric varices (p=0.02) and positive red sign (p<0.01). No bleeding occurred in G1 group.

There were no difference of gender, presence of splenomegaly, mean portal and splenic venous diameter, white blood cell and platelet counts, mean platelet volume and prothrombin time between groups with varices and no varices. One patient had liver transplantation and all of the patients were alive. Improvement in varices size was observed in 62.2% patients. Medical plus endoscopic therapy had higher improvement rate than medical therapy alone but not statistically significant.

TABLE. Etiologies

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<th>Diagnoses</th>
<th>Varices (n=59)</th>
<th>No varices (n=21)</th>
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<tr>
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### Table

<table>
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<th>Condition</th>
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<tr>
<td>Wilson disease</td>
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</tr>
<tr>
<td>GSD (type 3 and 4)</td>
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<td>3</td>
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<td>Ductal plate malformation</td>
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<td>1</td>
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<tr>
<td>PFIC</td>
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<tr>
<td>Other</td>
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</tbody>
</table>

**Conclusion:** In this study, we demonstrated that the most common cause of PH was EHPVO and grade of varices, presence of gastric varices and red sign were correlated with OV bleeding. Medical plus endoscopic therapy may help resolution of varices.

**Disclosure of Interest:** None Declared
Hepatology

PO-H-0319

ADVANCED LIVER DISEASE CORRELATES WITH LOW SERUM LYSOSOMAL ACID LIPASE ACTIVITY

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1 Saare Zedek Medical Center, 2 Hadassah Medical Center, Jerusalem, Israel

Objectives and Study: Deficiency of lysosomal acid lipase (LAL) causes Wolman disease (WD) and cholesteryl ester storage disease (CESD) due to organ infiltration by macrophages filled with cholesteryl esters and triglycerides. Decreased LAL in various degrees may be asymptomatic, cause fatty liver or even cirrhosis. Replacement enzyme therapy is currently available in clinical trials. Aims: to study LAL levels in patients with Non Alcoholic Fatty Liver Disease (NAFLD)

Methods: Medical records of patients aged 1 year to 65 years that underwent liver biopsy from the years 2006 to 2012 were screened. Patients with biopsies showing cryptogenic cirrhosis, microvesicular steatosis or metabolic syndrome related macrovesicular steatosis, were screened for LAL activity using the new method of dried blood spots specific assay (Synageva Inc.). Clinical, laboratory, imaging and pathological data was collected and analyzed.

Results: of those patients screened 4 had cryptogenic cirrhosis, 9 had microvesicular steatosis and 9 had macrovesicular steatosis. The mean age was 32.4±23.3 (ranges 2.9 – 71.8) years. Mean LAL activity was 0.74 (median 0.8, ±0.28) nmol/punch/hour. Three cases had LAL<0.37 (carriers) but none of the 22 cases had LAL<0.03 (diagnostic for WD & CESD). However, threshold of LAL activity <0.6 (as compared to 0.4 and 0.5), in seven of the 22 cases allocated severity markers of liver disease: low serum calcium, hypoalbuminemia, low total protein and prolonged INR due to synthetic dysfunction, low platelets due to hypersplenism and portal hypertension, high serum uric acid a result of low blood volume, and impaired glucose and HbA1c levels suggesting insulin resistance.

Conclusion: LAL activity <0.6 is associated with severe liver injury in patients with fatty liver and cirrhosis. Although our pilot study is small and had biases the results are in-line with other reports suggesting lysosomal alterations in NAFLD. Further larger studies are warranted to define the relation of LAL levels to the severity of liver disease and the need for replacement therapy in those cases.

Disclosure of Interest: None Declared
GLYCOGENIC HEPATOPATHY IN TYPE 1 DIABETES: AN ACUTE COMPLICATION?
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Objectives and Study: Glycogenic hepatopathy (GH) key feature is glycogen accumulation in the liver causing hepatomegaly and raised serum transaminases in patients with type 1 diabetes (DM1) and poor glycemic control. Wide fluctuations in both glucose and insulin levels are held responsible for its occurrence which may happen at any age and anytime during the course of the disease. We present 4 patients with GH.

Methods: Liver biopsy specimens were obtained from patients and histologic features of large hepatocytes with pale cytoplasm and periodic acid Schiff (PAS) positive staining were observed.

Results: A 12-year old female with 1 year history of poorly regulated DM1 presented with diabetic ketoacidosis (DKA) and severe abdominal pain. Besides hepatomegaly her physical examination was unremarkable. Elevated liver enzymes were noted (AST 630 U/L, ALT 548 U/L, GGT 87 U/L). Coagulation studies, protein electrophoresis and abdominal ultrasound (US) were normal. EBV and CMV serology were negative. Transaminase level normalized during following 2 weeks. Two months later she had new episode of abdominal pain and elevated liver enzymes (10xULN). Alpha-1 AT deficiency, Wilson disease, autoimmune and viral hepatitis (CMV, EBV, hepatitis B,C, parvoB19, adenovirus) were excluded. US revealed moderate hepatomegaly. Liver biopsy showed normal liver architecture, with no evidence of inflammation or fibrosis. Hepatocytes were large with pale cytoplasm. PAS staining showed abundant glycogen accumulation. 20% of hepatocytes showed macrovesicular steatosis. The diagnosis of GH was made. The remaining 3 patients were long-time diabetics who had at least one episode of severe DKA, and had developed the same clinical symptoms. The increase in transaminases was 10-30xULN. They had the same diagnostic procedure performed as the first patient. Important differences were detected in their liver tissue specimens. The first of them (15 years, 10 years duration of DM1, Graves' disease) had a typical GH pathohistological finding. Another (23 years, 4 years duration of DM1) additionally showed significant fibrosis. The third patient (16 years, 13 years duration of DM1, hyperlipidemia) had typical GH and perportal fibrosis and steatosis resembling non-alcoholic steatohepatitis (NASH). Improvement of glycemic control within subsequent weeks led to normalisation of transaminases in all 4 patients.

Conclusion: Although GH appears as acute and fully reversible complication of DM1 at least in our patients, we lack sufficient data for that conclusion. GH may also be the first step in possible subclinical progression and development of chronic liver disease. Therefore we need to actively search for this complication and develop strategies for its long-term follow up.

Disclosure of Interest: None Declared
A CHILD WITH HEPATITIS C VIRUS – AUTOIMMUNE HEPATITIS OVERLAP SYNDROME

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Objectives and Study: A link between infection and autoimmunity is well known and extensively documented for the hepatitis C virus (HCV). Overlap syndrome of hepatitis C virus and autoimmune hepatitis (AIH) is characterized not only by the presence of auto-antibodies during the HCV infection, but above all by the presence of histological features of both disease at the same time. This syndrome is a distinct entity, which is mainly defined in adult patients, but a very few cases are described in children.

Methods: We report on a new paediatric case of HCV-AIH overlap syndrome.

Results: Sefora is an adopted newborn who was referred to our Institute from the age of 4 months because of chronic hepatitis C virus. She was born in September 2002 by drug addicted mother. She presented with hepatosplenomegaly, aspartate (AST)/alanine (ALT) aminotransferases 138 U/L/127 U/L, HCV-RNA genotype 1a positivity. Follow-up showed stability of transaminases level and normal γ-globulin. In November 2004 LKM antibodies (never done previously) turned out positive with titre of 1:2560. Other antibodies (ANA, ASMA, AMA, ANCA, LC1, SAL/LP, dsDNA) and HLA B51 were negative. After four years, she presented a significant increase in transaminase values (AST/ALT 913/1578). Liver biopsy showed chronic hepatitis, mild to moderate activity with moderate porto-septal and focally bridging fibrosis, mild to moderate interface activity. It was started combined therapy with peg-interferon (1.5 mcg/kg once a week subcutaneous) and ribavirin (15 mg/kg/day). She had a quick normalization of liver enzymes, with undetectable HCV-RNA, but on 18th week of treatment she presented a new severe elevation in transaminases (AST/ALT 2190/2235) with persisting elevated LKM, likely consistent with AIH flare. Prednisone 2 mg/kg/day was started in conjunction with azathioprine 0.5 mg/kg/day up to 2 mg/kg/day, achieving biochemical remission. Prednisone was tapered down to 5mg/day. During the follow-up, persisting normal liver function tests were associated to improvement of histological findings (a lower degree of activity and fibrosis), despite HCV-RNA reactivation.

Conclusion: Actually there are no defining diagnostic criteria for HCV-AIH overlap syndrome and no univocal treatment approach is standardized. The risk of exacerbation of one entity during the treatment of the other one it is a well known possibility. We decided to treat HCV primarily, achieving normalization of liver function tests and HCV-RNA after 4 months of treatment, and starting successfully treatment for AIH during a new exacerbation. HCV-RNA positivity will be tightly monitored in the follow-up and the infection will be treated in case of disease relapse.

Disclosure of Interest: None Declared
THE PREVALENCE OF HEPATITIS B VIRUS INFECTION IN NIGERIAN CHILDREN PRIOR TO VACCINE INTRODUCTION INTO THE NATIONAL PROGRAMME ON IMMUNISATION SCHEDULE

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Objectives and Study: Hepatitis B virus infection is a major global health problem with public health importance. The infection which is commonly acquired in childhood often progresses to chronic liver disease which could lead to death in adulthood. In a bid to control the infection, the Nigerian government in 2004 introduced hepatitis B vaccine into the National Program on Immunization. There are no studies on the prevalence of hepatitis B in children prior to the 2004 when the vaccine was introduced. The prevalence of the infection prior to 2004 will serve as a baseline for evaluating the effect of the vaccine in the prevention of the infection. The objective of the study was to determine the seroprevalence and predictors of viral Hepatitis B in Nigerian children aged 11-18 years.

Methods: This was a cross sectional analytical study conducted in July 2014 among 749 secondary school children in Calabar, Nigeria. The children were selected from six secondary schools using a multi-staged sampling technique. Ethical clearance was obtained from the Cross River State Medical Ethical Committee. A validated structured interviewer administered questionnaire was used to obtain information related to hepatitis B from participants following parental consent. Blood sample was obtained for qualitative detection of Hepatitis B surface antigen using rapid chromatographic immunoassays with test kits from ABON(China)having sensitivity, specificity and accuracy of >99%, 97% and 98.5% respectively for the virus. Data was analyzed using SPSS version 20.2

Results: Nine of the 749 students screened were positive for HBsAg. The overall prevalence of HBV infection was 1.2 % while the sex specific prevalence was 0.8% for males and 1.8% for females. After multivariate analysis, age was the only predictor of hepatitis B infection (OR 3.92; 95% CI 1.22-12.63; p-value 0.02).

Conclusion: The prevalence of hepatitis B virus infection in children prior to the introduction of its vaccine in 2004 was quite low. Despite the low prevalence, the introduction of the vaccine is justifiable in view of the public health importance of the infection.

Disclosure of Interest: None Declared
**ZINC METABOLISM PARAMETERS IN WILSON DISEASE PATIENTS WITH A MILD LIVER DISEASE**

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**Objectives and Study:** Wilson’s disease (WD) is due to an inherited disorder which affects hepatic copper (Cu) excretion into the bile. In recent decades, also zinc (Zn) has been linked with WD, especially in the field of treatment. So far, less emphasis Zn has received from a pathogenetic and diagnostic point of view. Cu and Zn have competing roles in a way, where Cu overload leads to Zn deficiency1. Significant decrease in serum plasma Zn was previously described in a cohort of 18 WD children (3–13 y with a mean of 10.5±2.5 y). In this population, all WD children had hepatic and neurological complications and presented abnormal Cu accumulation in liver and ventricular enlargement. Authors did not specify if the patients were on therapy at the time of the evaluation. The aim of our study was to evaluate Zn metabolism parameters at diagnosis of WD in patients with mild liver disease.

**Methods:** Fifty WD patients (32 males; mean age at diagnosis 7.9 years, range: 1-26 years) were retrospectively evaluated. Patients were eligible for the study if: 1) the diagnosis was confirmed by molecular analysis or liver copper content>250 µg/g dry tissue or both; and 2) data were available about copper and zinc parameters at diagnosis. Linear regression analysis was applied to assess dependence of Zn parameters on age and Cu metabolism parameters, and the Pearson correlation coefficient (r) was defined.

**Results:** We have analysed basal serum and urinary Zn in a subgroup of 14 WD children (8 males) diagnosed at a median age of 71 months (range 13-166 months) who were symptom-free and had elevated aminotransferases. Mean basal serum plasma Zn level at diagnosis was 163.3+/−32.59 mcg/dl (normal values 64-124 µg/dl3); mean urinary Zn 381.7+/−68.3 mcg/24 h. As for other Cu metabolism parameters, we found: total serum Cu 40.85+/−9.36 mcg/dl, urinary Cu 108.07+/−51.52 mcg/24 h, ceruloplasmin 7.53+/−4.5 mg/dl, liver copper content 860.75+/−355.25 mcg/g dry weight. Serum and urinary Zn levels were not correlated (r=0.59; P=0.15, P NS). Serum Zn level did not correlate with age at diagnosis (r=0.15; P=0.59, NS), urinary Cu (r=0.23, P=0.45, NS), serum Cu (r=0.10, P=0.71, NS) and liver Cu content (r=0.53; P=0.13, NS). No correlation was found also for urinary Zn excretion.

**Conclusion:** Our results suggest that in WD patients with a mild liver disease Zn serum levels are normal or high. Differently from Cu urinary levels, that in a previous study of ours resulted directly related to age at diagnosis of WD4-5, Zn urinary levels are not related to age at diagnosis of WD patients. Further studies to clarify the role of Zn in WD pathogenesis and clinical phenotype are required.

**References:**


Disclosure of Interest: None Declared
Objective and Study: Pediatric Non-Alcoholic Fatty Liver Disease (NAFLD) is a leading cause for chronic liver disease in children and adolescents. The Enhanced Liver Fibrosis (ELF) test has demonstrated validity as a non-invasive marker for liver fibrosis in paediatric NAFLD. There is limited data regarding the natural history of paediatric NAFLD.

Objective: Investigate serial ELF measurements in a cohort with paediatric NAFLD.

Methods: Serial ELF measurements were collected prospectively in a cohort of children with NAFLD. ELF scores were calculated using a validated algorithm and compared to anthropometry, biochemistry, and PELD/MELD scores measured at diagnosis and follow-up. The diagnosis of NAFLD was based on liver histology or the triad of obesity, deranged liver function tests, and suggestive ultrasound findings. Patients were provided consistent dietary and lifestyle advice.

Results: 22 children (9M, 13F), median age 12 years (range 4 -17 years) and BMI 29 (range 20-41kgs), were diagnosed with NAFLD. Median duration of follow-up was 2.1 years (range: 1-5 years). Mean ELF at diagnosis was 9.06 (mild n=3, moderate, n=1, severe n=3), and on follow-up 8.76 (mild n=1, moderate n=1, severe n=2 ≥stage3 fibrosis) (P=0.13). Mean BMI-Z score at assessment was 2.04 and follow-up 2.07 (P=0.7). Mean PELD/MELD score was 7 and 7.2 at diagnosis and follow-up, respectively (P=0.15).

Conclusion: Serial ELF scores and PELD suggest there is no significant progression of chronic liver disease in children with NAFLD over a 2-year period. Further long-term follow-up studies are required to validate ELF as a monitoring tool.


Disclosure of Interest: None Declared
DIAGNOSIS OF LIVER STEATOSIS AND FIBROSIS USING TRANSIENT ELASTOGRAPHY IN CHILDREN WITH NON-ALCOHOLIC FATTY LIVER DISEASE

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Objectives and Study: Nonalcoholic fatty liver disease (NAFLD) has become one of the most common chronic liver diseases worldwide. Transient elastography (Fibroscan®) was validated and proven to be a valuable technique in the assessment of liver fibrosis and Controlled Attenuation Parameter (CAP) appeared to be accurate in evaluation of liver steatosis in chronic liver diseases. The aim of this study was to evaluate the relationship of anthropometric parameters, liver function tests and lipid metabolism markers with the liver stiffness measurement (LSM) and Controlled Attenuation Parameter (CAP) using transient elastography Fibroscan® to find further evidence for the role of obesity and metabolic disturbances in fatty liver disease in children.

Methods: 125 overweight/obese children aged 14±2.8yrs with NAFLD, who presented with mildly increased ALT 26 (17-45), AST 23 (20-32), GGTP 19 (14-31) U/l [median, Q1-Q3], underwent liver stiffness (LSM) and steatosis (CAP) measurements using Fibroscan® as well as liver function tests and lipid profile markers. In addition detailed anthropometric measurements including weight, height, BMI, waist circumference, abdominal, triceps and subscapular skinfolds were performed and their respective z-scores were calculated. Correlations between studied parameters were tested by linear regression analysis.

Results: Liver stiffness [kPA] was strictly related to ALT (r=0.46), AST (r=0.43), GGTP (r=0.22), TG (r=0.31), z-score BMI (r=0.39), z-score waist (r=0.3) and z-score for skinfolds. Controlled Attenuation Parameter [dB/m] correlated significantly with ALT (r=0.58), AST (r=0.49), GGTP (r=0.32), TG (r=0.24), z-score BMI (r=0.38) and z-score for skinfolds. Multiple regression analysis model showed that, among anthropometric parameters, best sub-set predictors for both liver stiffness (LSM) and steatosis (CAP) were z-score BMI and z-score triceps skinfolds. Laboratory tests that best predicted liver stiffness were total cholesterol, triglycerides and ALT while for liver steatosis they were triglycerides, LDL-cholesterol and ALT.

Conclusion: 1. Liver fat content measured by CAP and liver stiffness correlate strongly with liver function tests, triglycerides and age- and gender-related anthropometric parameters in children with NAFLD.
2. BMI and triceps skinfolds seem to be the best predictors of fibrosis and steatosis when measured by transient elastography.
3. Total cholesterol, triglycerides and ALT seem to be the best predictors of fibrosis whereas triglycerides, LDL-cholesterol and ALT are the best predictors of liver steatosis.
Disclosure of Interest: None Declared
PARTICULARITIES OF CHRONIC HBV INFECTION IN A PAEDIATRIC POPULATION FROM WEST OF ROMANIA

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Objectives and Study: Introduction: Natural history studies show that the risk of development chronic HBV infection is inversely proportional with age of acquisition: 25% of children infected at <5 years develop chronic infection, versus <10% adults. In Romania, treatment of HBV infection in children was limited to lamivudine (until 2011) and alpha2b standard interferon. Treatment of all children with chronic B hepatitis must be tempered by studying the natural history in children. Spontaneous HBeAg clearance is influenced by mode of transmission, viral load, necroinflammatory activity, immunocompetence, genotype. Aim: To investigate the rate of HBe/HBsAg seroconversion during childhood, spontaneous and after antiviral treatment.

Methods: We retrospectively studied 176 children with chronic HBV infection and +HBeAg. The route of transmission was vertical in 92 and parenteral/unknown in 84 children. The mean age at diagnosis was 7.5 years (6 months-16 years). In the lot with vertical transmission, 64 children emerged from +HBeAg mothers with high viral load and 28 from -HBe/+HBsAg mothers with low viral load. 112 children were diagnosed in the first 4 years of life. HBV markers, viral load, clinical and liver function were tested at least once every 6 months.

Results: 24 (21%) of the 112 infected infants seroconvert in “e” system before 4 years without treatment. 3 (12%) infants with spontaneous HBeAg seroconversion emerged from +HBeAg mothers compared to 6 (25%) from -HBe/+HBsAg mothers with low viral load. 15 (63%) from noninfected mothers (p<0.005). No spontaneous “s system” seroconversion was detected. 58 children older than 4 years (+HBsAg/+HBeAg, hypertransaminasemia, detectable viral load, necroinflammatory activity) started antiviral treatment. HBeAg seroconversion and virusologic respond rate were 48% after 12 months of Interferon and 24%, respectively 45% after 12 months, respectively 24 months of Lamivudine (p<0.005 at one year). HBsAg clearance was obtained in 2 cases (3%) after one year of Interferon and in 1 case (1.7%) after 2 years of Lamivudine.

Conclusion: Maternal carrier status is very important: children of HBeAg seropositive mothers have lower rates of HBeAg seroconversion. Due to the possibility of spontaneous HBeAg seroconversion, antiviral treatment shouldn’t be initiated in the first 4 years of life. HBsAg clearance rate was higher but not statistic significant in children who had anti-HBeAb achieved under Interferon treatment.

Disclosure of Interest: None Declared
THE ROLE OF SMALL INTESTINAL BACTERIAL OVERGROWTH IN DEVELOPMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE IN OBESE CHILDREN

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Objectives and Study: Small intestinal bacterial overgrowth was proposed to contribute to the development of non-alcoholic fatty liver disease (NAFLD) probably by increasing intestinal permeability and absorption of endotoxin and other bacterial products. In this study, we aimed to determine the role of small intestinal bacterial overgrowth in development of non-alcoholic fatty liver disease in obese children.

Methods: Six to 17 year-old obese children were included in the study. Body mass index z-scores, fasting serum glucose, insulin, total cholesterol, high density lipoprotein (HDL), low-density lipoprotein (LDL), triglyceride, alanine aminotransferase (ALT) levels were determined. Hepatosteatosis was assessed by the same radiologist. Small intestinal bacterial overgrowth was determined by lactulose hydrogen breath test (Gastro Gastrolyser, Bedfont Scientific Ltd, England) in all patients.

Results: In total, 137 obese children (62 female, 45.3%) were included in the study. Mean age and body mass index z-scores were 11.6±2.45 years and 2.09±0.31 respectively. Seventy two children (52.6%) had hepatosteatosis. Insulin resistance has been determined in 65 of 103 (63.1%) patients. Lactulose breath test was positive in 21 (15.3%) children. The age, gender distribution and body weight z-scores were similar in children with or without NAFLD. Small intestinal bacterial overgrowth was determined in 10 (15.4%) patients with NAFLD and in 11 (15.3%) patients without NAFLD (p=0.986). In patients with NAFLD, ALT and HOMA-IR values were higher than obese patients without NAFLD (p=0.005 and p=0.012 respectively).

Conclusion: Overweight children with NAFLD don’t have increased frequency of small intestinal bacterial overgrowth compared to ones without NAFLD. So, small intestinal bacterial overgrowth does not seem to contribute to development of NAFLD.

Disclosure of Interest: None Declared
**Hepatology**

**PO-H-0328**

**BLAUSYNDROME: A RARE CAUSE OF HEPATOSPLENOMEGALY**

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1 Bill Griffiths 3

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**Objectives and Study:** Blau syndrome (BS) is a rare granulomatous inflammatory condition first described in 1985. BS presents with a recognized classic triad of arthritis, skin rash and uveitis. It is caused by mutations in the nucleotide-binding oligomerization domain containing 2 (NOD2) gene located on chromosome 16. Mutations are sporadic or inherited in an autosomal dominant fashion.

We present a 5 year-old girl referred to our department for investigation of hepatosplenomegaly. She was diagnosed with juvenile idiopathic arthritis (JIA) a year prior following a 6-month history of general malaise, lethargy and joint swelling. Clinically, she had hepatosplenomegaly with tenosynovitis of her wrists and ankles. Her liver function tests were normal. Her inflammatory markers including erythrocyte sedimentation rate and serum amyloid A were elevated. She was treated with corticosteroids and methotrexate.

**Methods:** We performed a complete full liver work-up including serum autoantibodies, immunoglobulins, caeruloplasmin, urinary penicillamine challenge, viral serology and liver biopsy. The only positive findings were of a mildly raised angiotensin converting enzyme, positive anti-SLA antibodies and elevated complement C3 levels. The liver biopsy revealed portal granuloma with mild inflammation.

Her father was diagnosed with JIA aged 6 and remains on treatment. He developed liver disease aged 22. Liver biopsy revealed portal granulomas with fibrosis. A diagnosis of Sarcoidosis was made. He was treated with corticosteroids. 5 years later; his liver disease has progressed with severe portal hypertension with variceal bleeding and cholestatis. Repeat biopsy demonstrates an obliteratorive venopathy with granulomatous cholangiopathy.

**Results:** Given the similiarities in presentation and the presence of granuloma in his liver biopsy, we suspected BS as a cause of her hepatosplenomegaly. Genetic analysis was performed and she has 2 pathogenic variants in her NOD2 gene confirming BS. Her Father’s genetic results are awaited.

**Conclusion:** To date, there is no evidence for the effective treatment of BS. Patients have been managed with various combinations of corticosteroids, methotrexate and monoclonal antibodies to tumour necrosis factor and interleukin-1. Our patient has not suffered a rash or uveitis, the commonest and most significant cause of morbidity in BS. The progression of liver disease in her father is worrying and poses difficult questions for her future immunosuppressive management.

In conclusion, a diagnosis of BS should be suspected in children with evidence of arthritis, systemic granuloma with or without hepatosplenomegaly.

Disclosure of Interest: None Declared
ABSOLUTE PROTEIN QUANTIFICATION REVEALS MATURATION OF HUMAN HEPATIC TRANSPORTER PROTEINS DURING EARLY CHILDHOOD

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Objectives and Study: Transporter proteins are membrane-bound proteins that mediate the cellular uptake or efflux of endogenous (e.g., bile salts, bilirubin, steroid hormones) and exogenous compounds (e.g., drugs, toxins). These transporter proteins are highly expressed in tissues such as liver, intestine and kidney and play important roles in the absorption, disposition and elimination of their substrates. For example, reduced expression of liver uptake and/or efflux transporters has been associated with disorders in bilirubin metabolism, such as Dubin-Johnson syndrome and Rotor syndrome. In addition, many clinically relevant food-drug interactions at the level of transporter proteins have been described. In order to better determine accurate drug doses for children and to study the impact of nutrition on this, knowledge about the maturation of these proteins during different neonatal developmental stages and in young children is important. Currently, the available information is very limited, mainly due to major ethical issues regarding obtaining and studying neonatal samples. The aim of the current study was to assess age-related differences in absolute expression levels of transporter proteins in neonatal and adult liver samples.

Methods: Neonatal and paediatric post-mortem livers were studied in relation to adult livers. Absolute quantification of a large set of transporter proteins (including MDR1 [P-glycoprotein], BCRP, MRP1-3, BSEP, OATP1B1, and OATP2B1) was performed using an Ultra Performance Liquid Chromatography tandem Mass Spectrometry (UPLC-MS-MS) method. Stable isotope-labelled peptides were used as internal standard. Neonatal data were compared to adult data.

Results: Clear differences in absolute expression levels of important liver-associated transporter proteins were observed during neonatal maturation and shortly after birth. Absolute expression of BCRP and GLUT1 was, respectively, ~2-fold and ~45-fold higher in neonatal liver samples compared to adult liver samples. Expression of MDR1 and OATP2B1 was comparable between neonatal and adult liver, whereas absolute expression of MRP2 (~1.5-fold), MRP3 (~1.6-fold), BSEP (~2-fold) and OATP1B1 (~1.7-fold) was significantly lower in neonatal liver samples compared to adult.

Conclusion: Our data show age-dependent differences in hepatic transporter expression. Especially for the glucose transporter GLUT1 remarkable differences between neonatal and adult livers were observed. This suggests that significant deviations in drug absorption and food-drug interactions, caused by age-related differences in transporter expression levels, may be expected and should be taken into account when dosing drugs to babies and children.

Disclosure of Interest: None Declared
QUALITY OF LIFE IN CHILDREN WITH WILSON DISEASE – THE MEANING OF THE PSYCHOLOGICAL RESOURCES

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Objectives and Study: In the present study we focused on the psychological resources which are assisting keeping the psychological balance and competence in overcoming life problems. In the child illness a correctly functioning family is one of these important resources. Poor life quality may results with poor compliance with therapy which seems to be a major problem in effective treatment of Wilson disease. The aim of the study was to predict the effect of the mental health of parents on the quality of life of children with Wilson disease.

Methods: 50 children with Wilson disease (23 girls and 27 boys) ages 7 to 18 years (12.4 ± 3.15) with normal liver function or slightly increased transaminases under long-term therapy and their 50 parents (41 women and 9 men) ages 31 to 51 years (39.56 ± 5.24) participated in the study. Children completed questionnaire on quality of life containing: “physical well-being”, “psychological well-being”, “social relationship” and “everyday functioning” using the KINDLR. Children emotional and behavioral problems was assessed for Child Behavior Checklist/4-18 (CBCL) and Youth Self-Report (YSR). Both is made up of eight syndrome scales: withdrawn, somatic complaints, anxious/depressed, social problems, thought problems, attention problems, rule-breaking behavior and aggressive behavior. To identified parents mental health disorders (somatic symptoms, anxiety and insomnia, social dysfunction and severe depression) was used General Health Questionnaire 28.

Results: In the statistical analysis the Pearson’s correlation coefficient was calculated.

<table>
<thead>
<tr>
<th>KINDLR</th>
<th>Psychological well-being</th>
<th>Physical state</th>
<th>Social relationship</th>
<th>Functional in everyday life</th>
</tr>
</thead>
<tbody>
<tr>
<td>GHQ 28</td>
<td></td>
<td></td>
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<tr>
<td>somatic symptoms</td>
<td>-0.424(**</td>
<td>-0.488(**</td>
<td>n.s.</td>
<td>-0.463(**</td>
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<tr>
<td>anxiety and insomnia</td>
<td>n.s.</td>
<td>-0.405(**</td>
<td>-0.294(*)</td>
<td>-0.481(**</td>
</tr>
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<td>social dysfunction</td>
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<td>-0.450(**</td>
<td>n.s.</td>
<td>-0.539(**</td>
</tr>
<tr>
<td>severe depression</td>
<td>n.s.</td>
<td>n.s.</td>
<td>n.s.</td>
<td>0.425(**</td>
</tr>
</tbody>
</table>

** p<0.01 ; * p< 0.05

Conclusion: 1. The mental balance of parents is an important resource protecting from adverse effects of a chronic illness, improving the psychological welfare in dealing with illness what is finding expression in qualities of life of the child. 2. It should provide the psychological support for the family which will let keep or improve the psychological condition of parents.

Disclosure of Interest: None Declared
**Objectives and Study:** Patients after liver transplantation are potentially at increased risk of cardiovascular complications due to long-term immunosuppression. In adults this is an important cause of morbidity and mortality. The aim of this study was to estimate the risk of cardiac events in long-term pediatric liver transplant recipients with special focus on subclinical atherosclerosis.

**Methods:** In 25 patients at the median age of 16 years (range 12-18) and at least 8 years (range 8-16) after LTx, with stable graft function and no significant post-transplant complications for at least 6 months we measured carotid intima-media thickness (cIMT), relative wall thickness (RWT), left ventricular mass index (LVMI), 24h arterial blood pressure monitoring (ABPM). Laboratory assessment comprised: lipid profiles (triglycerides, cholesterol, LDL, HDL, VLDL, apolipoproteins: ApoAI, ApoB, ApoE), lipoprotein a Lp(a), lecithin-cholesterol acyltransferase (LCAT), oxidative stress parameters: glutathione (GSH), glutathione peroxidase (GPx), atherosclerosis markers: asymmetric dimethylarginine (ADMA) and oxidized-LDL (oxyLDL). These parameters were compared with age matched healthy controls: n=33, median age 15.5 years (12-18).

**Results:** BMI Z-scores did not differ between groups however 90th percentile was exceeded in 5 patients after LTx. cIMT was normal in all patients according to age percentiles, median 0.4 (range 0.35-0.42). Median RWT was 0.35 (0.22-0.54) and was abnormal in 5 patients (20%). Median LVMI-S was 28.1 (18.5-40.6), abnormal in 2 (8%). All patients were normotensive according to ABPM. Lipids were not significantly disturbed in the study group: cholesterol 136 ± 22 mg/dl, triglycerides 84±47 mg/dl, HDL 44±11 mg/dl, LDL 78±19 mg/dl, VLDL 12,6±4,8 but oxidative stress markers showed decreased GSH 756 ±49 vs 782 ±52 mol/ml (p=0.08) and GPx 31.9 ±2.0 vs. 34.7 ±2,5 U/gHb (p<0.01). Concurrently two important biochemical markers of atherosclerosis were not increased: ADMA 0,56±0.36 vs 0,61±0.34 mol/l (p=0.69), oxyLDL 229±155 vs. 217±103 mU/ml (p=0.84). Interestingly, apolipoprotein E (ApoE), which may have preventive role against atherosclerosis, was higher in the study group 13,7±3,2 vs 9,8±4,2 g/l (p<0.01). Other parameters were not disturbed: ApoB 0.64 g/l ±0.28 vs 0.73 ± 0.19 (p=0.13), Lp(a) 13,8 ±4,8 vs 13,9 ±11,1 mg/dl (p=0.18), ApoAI 1,28±0,32 vs 1,41±0,21 (p=0.14), LCAT 119±25 vs 146±58 (p=0.11).
**Conclusion:** Although markers of atherosclerosis are not significantly disturbed, children after liver transplantation present with higher risk of cardiovascular complications and cardiac follow-up is mandatory especially in adolescence before transition to adult care.

**Disclosure of Interest:** None Declared
Objectives and Study: Cardiovascular risk is elevated in adult liver transplant recipients. To date, no conclusive data are available in children after liver transplantation (pLTx). However, pediatric liver transplant patients have been reported to have increased incidence of hypertension. In addition, calcineurin inhibitor nephrotoxicity occurs and might contribute to increased cardiovascular risk. We therefore hypothesize that indicators of increased cardiovascular risk might be found in children after liver transplantation.

Methods: In an ongoing study on cardiovascular risk factors after pLTx, we have currently investigated 26 pediatric liver transplant recipients aged 10.5 (6.6-17.8) years. Patients were between 1.5 and 15 (median 6.5) years after transplantation. We assessed casual blood pressure (BP), aortal pulse wave velocity (PWV) and carotid intima-media thickness (IMT). In 17 patients, we also performed and ambulatory BP measurements (ABPM). All values were normalized for age and expressed as SDS values.

Results: None of the patients was hypertensive (> 95. percentile for gender, age height) based on casual BP measurements at time of the investigation. This was confirmed in all but one patient by ABPM. Four patients received antihypertensive therapy using an ACE inhibitor. Mean PWV was 0.34 ± 1.04 SDS adjusted for age; 2 patients showed PWV values elevated > 95. percentile. Mean IMT was 1.91 ± 1.01 SDS adjusted for age; 16 patients (62%) showed IMT values > 95. percentile.

Conclusion: In our cohort BP was well controlled with only a small proportion receiving antihypertensive treatment. Despite normal BP values IMT was increased reflecting a high amount of atherosclerosis in these patients. The reasons for these changes are subject to further analysis.

Disclosure of Interest: I. Goldschmidt: None Declared, D. Kracht Conflict with: grant by the German Ministry for Education and Research, E. D. Pfister: None Declared, U. Baumann: None Declared, A. Melk: None Declared
CHRONICITY OF LIVER DISEASE IS AN IMPORTANT FACTOR IN PREDICTING LONG TERM COGNITIVE OUTCOMES AND NEUROCHEMISTRY WITH AND WITHOUT LIVER TRANSPLANTATION.

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Objectives and Study: Children with a history of liver disease have increased risk of long-term deficits in cognitive skills. The aim of this study was to observe a set of neurocognitive mechanisms that may contribute to long-term outcomes of children with different forms of compromised liver function.

Methods: 3 groups of children with different types of liver disease, who either did or did not have Liver Transplantation (LTx), were compared across cognitive (Wechsler Intelligence scales) and neurological domains using proton magnetic resonance spectroscopy (1H-MRS) to measure neurometabolites relative to the creatine (Cr) standard.

Results: Volumetric measures of standard neuro-metabolites were not significantly different between groups except the SLD group, who had not yet been transplanted, had significantly lower myo-inositol concentrations, relative to the creatine standard. Duration of symptomatic liver disease was strongly correlated with lower IQ scores across the entire patient cohort (FSIQ, r s =-0.75, p<0.01) and intellectual ability was lowest in the CLD group which contrasted with the ALF group who performed in the normal range.
| Glutamate/glutamine/Cr | Control= .72 (sd 0.7) | 2.06 (.30) | 1.87 (.20) | 1.68 (.14) |

*Illness duration defined by presence of jaundice, pruritis, growth failure, ascites, hypo-albuminaemia, prolonged prothrombin time*

**Conclusion:** Disease history and duration of symptomatic liver disease rather than LTx itself, has the greater impact on long-term cognitive performance. Neurochemistry stabilises to normal after LTx, but $^1$H-MRS has the capacity to detect subclinical problems in children with stable liver function before LTx, particularly those who had reduced ml concentrations, previously associated with sub-hepatic encephalopathy (Long LL et al Exp Biol Med 2009;234:1075).

**Disclosure of Interest:** None Declared
AUDIT OF LONG TERM HISTOLOGICAL OUTCOMES AFTER LIVER TRANSPLANTATION IN CHILDREN WITH CONTINUING PARENTERAL NUTRITION REQUIREMENTS

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Objectives and Study: There are only a few reports of isolated liver transplantation (iLTx) for intestinal failure associated liver disease (IFALD) in children who develop catastrophic deterioration in liver function during weaning from parenteral nutrition (PN). The indications of iLTx have been described [Dell Olio JPGN 2009; Botha Liver Transpl. 2006], but there are concerns that short bowel syndrome might contribute to long term allograft dysfunction via malabsorption of bile acids / bacterial overgrowth and that post LTx exposure to PN combined with immune-suppression may lead to chronic inflammation. We compared histology of children who had liver transplantation (LTx) for extra-hepatic biliary atresia (EHBA) with a cohort of 6 patients who survived >10yrs after iLTx.

Methods: A retrospective audit of all patients transplanted between 2000-2003 identified 6 children with IFALD who had iLTx (3 = gastroschisis; 3 = necrotising enterocolitis) and 15 consecutive age matched EHBA patients. The following data were obtained: age of donor; type of graft; liver histology; liver function; renal function; duration of exposure to PN after transplant. The histology slides were anonymised and scored by two pathologists using the Ishak score for fibrosis.

Results: Age at transplant and donor age were similar: iLTx 9.66 mons EHBA 8.96mons; donor age = 23.34 mons and 26.52 months respectively. One patient was recovering from chickenpox in the iLTx group at the time of the 10yr review. There were no differences in frequency of rejection episodes between iLTx and EHBA and similar low scores for fibrosis and inflammation was seen in both groups. Even though duration of PN exposure post iLTx was variable (up to 4.5yrs) and iLTx patients were significantly smaller - there was no correlation between duration of PN, length of bowel and fibrosis scores.

<table>
<thead>
<tr>
<th></th>
<th>iLTx 10yrs after LTx</th>
<th>EHBA 10 yrs after LTx</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean height and weight z scores [sd]</td>
<td>-1.89[1.22] -1.41 [1.29]</td>
<td>-0.43 [1.93] 0.25 [1.45]</td>
</tr>
<tr>
<td>Median Bilirubin mmol/L and range ()</td>
<td>11 (8-203)</td>
<td>6 (5-34)</td>
</tr>
<tr>
<td>PN exposure in days median &amp; (range)</td>
<td>428 (100-1668)</td>
<td>0</td>
</tr>
<tr>
<td>Ishak inflam score (0-18) mean &amp; [sd]</td>
<td>0.92 [1.16]</td>
<td>1.23 [1.72]</td>
</tr>
<tr>
<td>Ishak fibrosis score (0-6) mean &amp; [sd]</td>
<td>2.08 [1.16]</td>
<td>1.17 [1.24]</td>
</tr>
</tbody>
</table>

Conclusion: Exposure to PN after LTx does not appear to cause additional fibrosis or inflammatory changes in liver allograft and short bowel syndrome is not a risk factor for hepatic fibrosis. Isolated
liver transplant is an important option that should be considered in children who develop liver failure when weaning from PN.

Disclosure of Interest: None Declared
**Hepatology Transplantation**
PO-H-0335

**RAPAMICYN-BASED IMMUNOSUPPRESSION FOR LIVER TRANSPLANTED CHILDREN**
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**Objectives and Study:** m-TORs inhibitors are often used as complementary treatment after solid organ transplantation. Experience with rapamicyn (RP) as main immunosuppressant drug in pediatric liver transplantation is very limited and poorly documented. We reviewed our recent experience.

**Methods:** retrospective review of patients who undergone change of immunosuppression from tacrolimus to RP in the last 5 years. Patients without liver histology at baseline or at follow up were excluded. Biopsies were reviewed as for activity and fibrosis (Ishak score). Central fibrosis (CF), perisinusoidal fibrosis (PF), ductular proliferation (DP) and ductular atrophy (DA) or ductopenia were also evaluated with a semiquantitative score. Side effects and reason of treatment withdrawal were also noted.

**Results:** we studied 12 patients. Median age at liver transplantation (LT) was 23.5 months (6-176), indication to LT was biliary atresia in 6 patients, hepatoblastoma in 2, autoimmune disease in 2, acute liver failure and PFIC in 1 case each. Median age at start of RP was 87 months (57-250) after a median of 66 months from LT (43-130), indication was polyclonal PTLD in 9 and chronic renal injury in 3. RP blood level were targeted to 4-6 ng/ml. Last biopsy was after a median of 36.5 months (23-67) from start of RP. Median duration of therapy at last follow up was 46 months (23-77).

Baseline histology showed a mean staging value of 1.4 (±0.8), mean grading value of 2.4 (±2.2). Three patients had mild CF, 1 PF, 9 some degree of DP, 1 mild ductopenia. At last follow-up biopsy, mean staging degree was 1.4 (±1.2), mean grading 1.4 (±1.1). CF was noted in 8 patients (7 mild, 1 moderate), PF in 2, DP in 10, mild DA in 3 and mild ductopenia in 1.

As for staging, it was stable in 5 patients, improved in 4 and progressed in 3 at last follow up; grading improved in all. All patients but one are still on RP at the end of follow-up. In one case tacrolimus was restarted because of progression of fibrosis. RP was well tolerated with no major adverse events. Only one child had oral ulcers successfully treated with topic steroids.

**Conclusion:** Overall, RP-based immunosuppression was safe and well tolerated after a medium term follow-up. No significative worsening of liver histology emerged from our revaluation. Even if we observed progression of fibrosis in 3 cases, 2 of them presented a remarkable staging degree (2 and 3) already at baseline and in one progression was negligible (from 0 to 1). Even so, Ishak score do not take into account central fibrosis that appeared at last biopsy in the majority of patients. Whether or not this finding could be referred to RP therapy remains to be clarified.

**Disclosure of Interest:** None Declared
Hepatitis E Virus Seroprevalence in Children After Liver Transplantation

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Objectives and Study: Hepatitis E virus (HEV) infection is a significant cause of acute and chronic graft hepatitis in liver transplant recipients. Recent reports showed that HEV seroprevalence is declining in western countries, but high HEV antibody prevalence was described in adults after solid organ transplantation. Seroprevalence in children after liver transplantation is unknown. This study aims at describing HEV antibody prevalence and seroconversion rate in Canadian children after liver transplantation.

Methods: Children who underwent a liver transplantation between 1995 and 2013 at Sainte-Justine Hospital were enrolled in the study. Sera were collected before transplantation and every year following transplantation until adulthood. All available patients’ sera were tested for anti-HEV IgG by a reported in-house ELISA technique using a recombinant HEV peptide made of 12 immunodominant regions (Recombinant Hepatitis E Virus Mosaic, ProSpec-Tany TechnoGene Ltd., Ness Ziona, Israël). Validation of the in-house ELISA against a widely used commercial assay (Wantai, Bio-Pharm) in a subset of samples showed positive and negative predictive values of 88.2% and 55.6%, respectively. Results are shown as mean ± standard deviation or median and interquartile range.

Results: Overall 161 children underwent liver transplantation between January 1995 and June 2013. Median age at transplantation was 2.4 years (range 1-5.9). Immunosuppression was based either on tacrolimus or cyclosporine in 68% and 32% of children, respectively. HEV IgG seroprevalence before transplantation was 10.8%, comparable to 6.9% in healthy children at our institution. Children were followed up for 7.4 ± 5.1 years. Median age at last follow-up was 12.3 years (range 6.6-16.6). HEV IgG seroprevalence at last follow-up was 36.9%. Fifty-eight percent of the patients had at least a positive test for HEV IgG during the duration of follow-up. Seroconversion occurred 2.9 years (range 1.3-4.5) after liver transplantation. ELISA for IgM seroprevalence and qPCR for viral RNA detection are ongoing for each serum sample.

Conclusion: HEV IgG seroprevalence strikingly increased in children after liver transplantation, with seroconversion occurring early during follow-up. Such a finding suggests that immunosuppression plays a major role in HEV infection. Clinical, biochemical and histological signs associated to HEV infection in this population, as well as the consequences of such an infection, are currently being studied.

Disclosure of Interest: None Declared
UNUSUAL MALIGNANCIES POST SMALL BOWEL TRANSPLANT IN CHILDREN: SINGLE CENTRE EXPERIENCE

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Objectives and Study: Post transplant lymphoproliferative disease is a known complication in post small bowel transplant recipients seropositive for Epstein-Barr infection. **Objective:** To evaluate the incidence of unusual malignancies in children post small bowel transplantation.

Methods: Retrospective analysis of children who underwent small bowel transplantation for primary digestive disorders between January 2000 to December 2014 at the Birmingham Children’s Hospital, Liver and Small Bowel Transplantation Unit.

Results: Sixty-seven small bowel transplants were performed on children (37 male, 30 females) with an underlying primary digestive disorder. Median age was 3.5 years and weight 14kgs at time of transplant. We identified four cases of unusual malignancies and rare site of presentation. Two patients were diagnosed with smooth muscle tumours, with one located at the stomal orifice and the other in cervicothoracic paravertebral area. Patient 3 developed a retroperitoneal angiosarcoma and patient 4 developed brain PTLD. Patient outcomes were poor in all but one child who currently survives with Cytotoxic T cell therapy.

Conclusion: Unusual malignancies occur in around 5% of children post small bowel transplantation. High index of suspicion is required to make timely diagnosis, as they are often difficult to treat and carry a poor prognosis.
Disclosure of Interest: None Declared
Hepatology Transplantation
PO-H-0338

INTESTINAL EXPLANT MODEL TO STUDY THE DIRECT EFFECT OF IMMUNOSUPPRESSIVE DRUGS ON THE GUT

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Objectives and Study: De novo food allergy occurs frequently after pediatric liver transplantation. The use of FK506 and young age at transplantation are risk factors. We found an increase in serum Immunoglobulin (Ig) A and serum markers of mucosal IgA in food allergic liver transplant patients suggestive for defective intestinal IgA secretion (1). The effect of immunosuppressive drugs (IS) on intestinal mucosal immune homeostasis is unknown. To gain insight in the direct effect of IS on cytokine and local Ig production at gut level, we developed an intestinal explant model.

Methods: Small intestinal transmural biopsies were collected in 15 immunologically healthy children (median age 6 months; range 1-120) undergoing abdominal surgery. Homogenised tissue was suspended in tissue culture medium (TCM) and plated in 48-well plates. The suspension was pretreated for 1 hour with methylprednisolone, FK506 (both 10^{-9}, 10^{-8}, 10^{-7} M) or cyclosporine (0, 1, 10 μg/ml) and then stimulated for 24 hours with TCM (negative control) or staphylococcus enterotoxin B (SEB) (0.5 μg/ml). After 24 hours tissue pellets and supernatants (SN) were collected. SN were analysed by Multiplex for pro-inflammatory and T cell related cytokines (INF-γ, IL-1β, IL-2, IL-4, IL-5, IL-6, IL-10, IL-17, TGF-β) and by ELISA for IgA, E and G production. Kruskall-Wallis and Mann-Whitney U test were used to compare groups and subgroups mutually (p<0.05 statistically significant).

Results: SEB stimulation of intestinal tissue resulted in polyclonal immune activation. Cyclosporine and FK506 caused a dose-dependent inhibition of IL-2 secretion. A dose-dependent decrease in IL-17 and INF-γ was seen with all IS. There was no significant effect on Ig, IL-1β, TGF-β, IL-4, IL-5, IL-6 and IL-10 secretion.

Conclusion: This intestinal explant model provides us with an excellent tool to study the net effect of IS on the gut immune response. Besides the expected decrease in IL-2 by calcineurin inhibitors, we found a significant decrease in IL-17 and INF-γ. Since IL-17 is known to promote intestinal IgA translocation via induction of the polymeric Ig receptor (plgR), this might explain the observed increase in serum IgA.

References: (1) Raised IgA and circulating T follicular helper cells are linked to the development of food allergy in pediatric liver transplant patients. R De Bruyne et al. Submitted to CEA October 2014. (2) Th17 cells upregulate polymeric Ig receptor and intestinal IgA and contribute to intestinal homeostasis. A T Cao et al. J Immunol 2012; 189:4666-73.

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Vol. 60, Supplement 1, May 2015
Disclosure of Interest: None Declared
OUTCOME OF LIVER TRANSPLANTATION FOR PROPIONIC ACIDEMIA – GERMAN EXPERIENCE AND REVIEW OF THE LITERATURE

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Objectives and Study: Propionic acidemia (PA) is a rare autosomal recessive inherited disorder of branched chain amino acid metabolism. Despite improvements in conventional medical management, the neurologic outcome is often poor. Liver transplantation (LT) is proposed as a suitable option to improve the metabolic situation, longterm outcome and quality of life. As the metabolic defect affects different tissues besides the liver, the potential for the development of metabolic complications seems not completely be eliminated. We aimed to summarize the actual experience with LT in propionacidemia in order to provide an update on outcomes and derive recommendations for affected families.

Methods: We describe the clinical course of 5 patients transplanted at german transplant centers so far. Moreover, a systematic search of the current literature was performed to identify and evaluate all reported LT in PA. These were another 24 children. The patients were evaluated regarding time of onset of metabolic decompensation, reason for LT, therapy and outcome after LT.

Results: Twenty-six patients (90%) showed early postnatal metabolic decompensation. Another 3 patients developed first symptoms later in life (5, 8 and 12 months, respectively). The median age at LT was 4.5 months (range: 7 months to 18 years). The type of LT was living-related in 10/29 patients (34%), and deceased donation in 19/29 (66%). The indication for LT was poor metabolic control with potential or evident neurologic impairment in 26/29 patients. Three patients were transplanted after cardiac complications (heart failure, cardiac shock). The 1-year patient survival was excellent with 93%, the two-year patient survival 90%. Three patients died of LT-related complications. One patient intraoperatively experienced cardiac complications. About 21% (6/29) developed surgical complications (intestinal perforation n=1, hepatic artery thrombosis n=3, venous outflow obstruction n=1, hypoperfusion n=1). Two of the surviving 26 patients (7%) suffered from metabolic decompensation after LT. Nearly 50% of the transplanted patients are described to perform normal after LT.

Conclusion: LT for PA showed a good short- and long-term survival with a high rate of early surgical complications possibly attributed to early age at transplant. The neurologic development improved or remained normal in a high percentage of patients. Nevertheless, there is still a risk of metabolic decompensation in other tissues such as the brain with severe neurological sequelae.

Disclosure of Interest: None Declared
COMPLICATIONS AFTER LIVER TRANSPLANTATION IN PROPIONIC ACIDEMIA

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Objectives and Study: Propionic acidemia (PA) is a severe metabolic disorder with severe cardiac and neurologic complications and a poor quality of life(1, 2). Liver transplantation (LT) was thus proposed in PA to increase enzyme activity. We studied retrospectively LT in PA in two European centers, over twenty years, in order to better delineate the indications and complication, and discuss the possible optimization of the procedure in timing and management.

Methods: The medical files of patients who underwent LT in Birmingham Children Hospital and Necker Enfants-Malades Hospital since 1984 were reviewed.

Results: Twelve patients underwent 17 LT between 1991 and 2013, with a median follow-up of 17 years. The median age at first transplantation was 3.2 years. The graft survival rate was at 60% at 5 years. Seven of the 12 patients died (58%) within the first year after LT. Death occurred from 2 to 253 days. Contrary to the previous reports(3, 4), patients developed severe, unusual and unexpected complications (75%). Renal failure was strikingly present in half of the patients before LT and worsened in all of them. When present, the cardiomyopathy resolved. Among surviving patients, the quality of life was substantially increased with no acute metabolic decompensation despite dietary relaxation.

Conclusion: The survival rate after LT in PA is poor because of severe complications. Among them, the more frequent are hepatic artery thrombosis, acute respiratory distress syndrome, heart failure and renal dysfunction. Based on our experience, we recommend to carefully assess cardiac and renal functions before and after LT, and to use renal sparing immunosuppressive protocols as we feel like renal disease after LT for PA is probably not only drug-related. We suggest that earlier LT may carry a more acceptable risk in younger patients who have experienced fewer metabolic consequences. As kidney transplantation has been performed successfully in methylmalonic acidemia(5), a metabolic disease in the same biochemical pathway, we raise the question of which organ should be transplanted (liver versus kidney), in order to provide adequate enzyme activity with an acceptable risk.

References:
Disclosure of Interest: None Declared
OUTCOME OF LIVE VERSUS DECEASED DONOR LIVER TRANSPLANTATION IN INFANTS WITH BILIARY ATRESIA

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Objectives and Study: Biliary atresia (BA) is the most common indication for liver transplantation (LT) in infants. Surgical advances have led to live donor (LD) as well as deceased donor (DD) LT being possible options. Our programme commenced DDLT in 2000 and introduced LDLT in 2007. The aim of this study is to compare outcome of DD and LDLT in infants with BA listed for LT at age < 1 year.

Methods: All infants with BA listed for LT between 2000 and 2013 were studied. From 2007, families were counselled regarding the possible option of LDLT. All infants were on DD waiting list until time of LT, irrespective of whether LD was being considered. Outcome data was entered prospectively into unit database for national audit purposes.

Results: 50 infants (M1:F1) were listed for LT at median age 190 (62-351) days, 18 in Pre-LD era. 7 had BASM, and 7 had no previous Kasai. 3 died awaiting DDLT (1 in Pre-LRD era) and 47 underwent LT (33 DD 14LD). Patient and graft survival 1 year post LT was 45/47 (96%) and 41/47 (87%), and long term (median FU 6y 4m) was 45/47 (96%) and 38/47 (81%).

Comparing DDLT and LDLT, median time from listing to LT was for DDLT 36 (43-176) and LDLT 76 (20-216) days. Post-LT admission duration for DDLT was 23.5 (16-128) and LDLT 22 (15-59) days. Primary non-function (PNF) occurred in 4/33 (12%) following DDLT, (all underwent re-LT) and 0/14 after LDLT. After 1yr FU, patient / graft survival are 97% (32/33) / 85% (28/33) for DD and 93% (13/14) / 93%(13/14) for LD recipients. Two children died, one (DD) due to PNF and sepsis after re-LT, the second (LD) due to hepatic artery (HAT) and portal vein thrombosis (PVT) recurring after re-LT.

Excluding 4 who lost grafts to PNF, complications at 1 yr FU in 29 DD and 14 LD recipients were compared. HAT (5) or stenosis (1) occurred in 3/29 (10%) DD and 3/14 (21%) LD recipients (p=0.18). Of these, 1 (LD) underwent re-LT, 4 (2 DD: 2 LD) thrombectomy and revision and 1 (DD) angioplasty. PVT or stenosis occurred in 3/29 (10.3%) DD and 6/14 (43%) LD recipients (p=0.01). Of these, 5 (4 LD) had PV stenosis treated by angiographic venoplasty. Biliary complications occurred in 4/29 (14%) DD and 5/14 (56%) LD recipients (p=0.1). Acute rejection requiring treatment occurred in 9/27 (33%) DD and 5/14 (36%) LD recipients (p=0.65).

Conclusion: LT for infants with BA has a good outcome with 96% 1 yr survival being maintained during FU. Although LDLT led to a higher incidence of vascular complications requiring intervention, particularly portal vein stenosis requiring angiographic venoplasty, likelihood of PNF or re-
transplantation was reduced. Overall mortality of 3/50 on waiting list was not seen in those in whom LD was possible

**Disclosure of Interest:** None Declared
PAEDIATRIC LIVER TRANSPLANTATION FOR CYSTIC FIBROSIS RELATED LIVER CIRRHOSIS (CFLC) — A SINGLE CENTRE REPORT.

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Objectives and Study: CF related liver cirrhosis (CFLC) is the third most common source of death after lung disease and complications due to organ transplantation in about 2-4 % of CF patients [1]. Long-term follow-up of different cohorts of CF patients carefully monitored for hepatic involvement indicates a cumulative incidence of liver disease ranging between 27% and 35%, without incident cases after the age of 18 years [2, 3]. Especially the prognosis of children CFLC is poor. Liver transplantation (LTx) offers the only potentially curative treatment for portal hypertension and its complications. Most centers do not accept patients with CF for isolated LTx due to the systemic nature of the disease (reduced pulmonary function, chronic pulmonary infection, malnutrition, and malabsorption).

Methods: Retrospective data analysis of all paediatric liver transplantation for CFLC. We analyzed the data with regard to the specific problems leading to the indication for liver transplantation, operating procedures (kinds of anastomoses, kinds of immunosuppression as well as the follow up investigations with focus on both paraclinical data including laboratory values, lung function tests and developmental parameters. All statistical investigations were performed with IBM SPSS (version 19, SPSS Statistics/IBM Corp, Chicago IL, USA)

Results: We report here our series of 30 paediatric patients with CFLC from 1998 to 2014. Overall we transplanted 23 paediatric patients, 7 patients died on waiting list for LTx. The mean age at transplantation was 13.78 (range 8.67-17.42) years. The mean of follow up time was 4.5 years (range: 30 days to 9.8 years). In almost all patients a cure of hepatic CF manifestations as well as a positive influence on nutritional status and overall a increase in quality in life was achieved. 2 patients died after LTx (35 and 43 month after LTx) due to infectious complications. 7 more patients are still on waiting list for LTx.

Conclusion: We report here our series of 23 paediatric liver transplantations in long time follow up. We demonstrate, that isolated LTx cure hepatic manifestation of CF with well subsequent improvement of abdominal, extra-abdominal comorbidities, nutritional status and quality of life.

References: 1. Siano et al. Digestive and liver disease 2010

Disclosure of Interest: None Declared
CONTRAST ENHANCED ULTRASONOGRAPHY IN PAEDIATRIC LIVER TRANSPLANTATION RECIPIENTS

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Objectives and Study: Early vascular complications, in particular hepatic artery thrombosis (HAT) are feared complications after pediatric liver transplantation (Ltx). Contrast enhanced ultrasonography (CEUS) is a very useful method to detect blood flow in adult patients. However, none of the contrast agents available on the market have been authorized for patients below 18 years of age. On the other hand, off label use is known to occur, but outcome data are scarce (1). The aim of the present single centre study was to describe the diagnostic yield and possible side effects of CEUS after pediatric Ltx.

Methods: Patients below 18 years who underwent Ltx 2005-14 and were subjected to CEUS, using the contrast agent sulphur hexafluoride (SonoVue®), were retrospectively reviewed through the hospital chart system. Hexafluoride was given intravenously at a dose of 0.1 ml/kg body weight, maximum 2.4 ml.

Results: CEUS was performed in the postoperative period on 52 occasions in 24 patients (median age 5.1 years, range 0.6-15.7) who underwent 29 transplantations. The most common pretransplant diagnoses were biliary atresia (n=8), other cholestatic disorders (8), acute fulminant liver failure (2). Nineteen recipients received grafts from deceased donors (segment 2+3 in 10, left lobe in 3, right lobe in 2, whole liver in 4) and 5 from live donors (segment 2+3 in 4 and left lobe in 1). CEUS could detect HAT in 4 out of 24 patients, 3 of whom were subsequently subjected to surgery without any preceding computerized tomography (CT) angiography. In the fourth patient HAT was further verified by CT angiography, but no operation was performed and at a later ultrasonography investigation the hepatic artery had been recanalized. The examination could verify normal arterial flow in 18 of 24 patients. No obvious side effects, such as allergic reactions or cardiovascular events could be attributed to any of the CEUS investigations.

Conclusion: CEUS is useful in detecting HAT and can minimize the need for radiation intensive and potentially nephrotoxic investigations such as CT angiography. Although no side effects were noted in this retrospective chart review, this needs to be confirmed in larger prospective studies. Such trials might be performed in collaboration with regulatory authorities with the aim to make the contrast agent legally available for all pediatric patients.


Disclosure of Interest: None Declared
MANAGEMENT OF HEPATOCELLULAR CARCINOMA IN CHILDREN IN LIVER TRANSPLANTATION SET-UP IN INDIA

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Objectives and Study: Hepatocellular carcinoma (HCC) is a rare tumor in children. HCC has a poor outcome. We studied the outcome of children with HCC undergoing the liver transplantation in India.

Methods: Over a period of three years, all children (age 0-18 years) who underwent liver transplantation were evaluated. Children with HCC diagnosed on 4 phase contrast enhanced computed tomogram (CECT) scan of abdomen or explanted liver were evaluated and followed-up.

Results: Among the 107 children who underwent liver transplantation, HCC was seen in 5.7% children with median age of 5 years (21 months to 11.5 years). Three had tyrosinaemia, one case of progressive familial intrahepatic cholestasis-2, congenital hepatic fibrosis and biliary atresia each. HCC was detected by CECT abdomen in all children except one. Three children with tyrosinaemia had multifocal HCC. None of the patients had metastasis. In one patient with tyrosinaemia, HCC was an incidental finding detected on histopathology of explanted liver. Immunohistochemistry from the explanted liver confirmed presence of HCC. Largest tumor size was 60 mm in diameter. On histopathological studies, HCC was moderately differentiated in 3 and well-differentiated in 2. One patient with congenital hepatic fibrosis had fibro-lamellar variant of HCC. One child with biliary atresia died due to primary graft dysfunction on 5th day of transplantation. Rest all were surviving without recurrence at median follow up of 15 months (10-17 months).

<table>
<thead>
<tr>
<th>Table 1: Hepatocellular carcinoma in children</th>
</tr>
</thead>
<tbody>
<tr>
<td>S no</td>
</tr>
<tr>
<td>------</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
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<tr>
<td>3</td>
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<tr>
<td>4</td>
</tr>
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<td>5</td>
</tr>
</tbody>
</table>
Conclusion: Multifocal HCC was seen in children with HT, HCC at early stages in children can be cured with liver transplantation. Liver transplantation offered 80% survival at 15 months in children with early HCC.

Disclosure of Interest: None Declared
**Hepatology**

**Transplantation**

**PO-H-0345**

**CIRRHOTIC CARDIOMYOPATHY IN CHILDREN WITH END STAGE LIVER DISEASE: RETROSPECTIVE SINGLE CENTRE EVALUATION.**

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**Objectives and Study:** Prevalence and clinical impact of cirrhotic cardiomyopathy [CCM] in children with end stage liver disease is unknown. Preliminary adult data suggest significant impact of CCM on post transplantation outcome. We aim to evaluate the prevalence of cardiac changes identified on echocardiography and ECG in children before liver transplantation and the correlation of such findings with the stage of hepatic fibrosis in the explanted livers.

**Methods:** Patients [pts] below the age of 19 years liver transplanted in our center between 2002-2012 were included. Children with congenital heart disease, primary portal-vein thrombosis or metabolic conditions associated with cardiomyopathy were excluded. Fibrosis of the explanted livers was staged according to ISHAK [FS] and correlated to ECG and echocardiography findings done between 0 and 49 month median 4 months prior to liver transplantation [LT]. As marker for CCM we used Z-Scores of end-diastolic left ventricular diameter [LVIDd] and end-diastolic left ventricular posterior wall thickness [LVPWd] as well as QTc time from ECGs and echocardiography studies. Statistical analysis was performed by SPSS with Fisher Exact Test.

**Results:**

<table>
<thead>
<tr>
<th>Diagnosis (diseases with n=&gt;1)</th>
<th>n</th>
<th>Z-Score LVIDd (median)</th>
<th>Z-Score LVPWd (median)</th>
<th>QTc (ms) (median)</th>
<th>FS (median)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Neonatal hemochromatosis</td>
<td>2</td>
<td>0.66</td>
<td>0.75</td>
<td>441</td>
<td>F6 (6)</td>
</tr>
<tr>
<td>Biliary atresia and other bilary anomalies</td>
<td>9/7</td>
<td>1.09</td>
<td>0.33</td>
<td>412</td>
<td>F0-6 (6)</td>
</tr>
<tr>
<td>ALF</td>
<td>1/3</td>
<td>-0.8</td>
<td>0.0</td>
<td>448</td>
<td>F0-6 (3)</td>
</tr>
<tr>
<td>autoimmune liver disease</td>
<td>1/4</td>
<td>0.5</td>
<td>0.6</td>
<td>408</td>
<td>F4-6 (6)</td>
</tr>
<tr>
<td>LBMD (incl. CF)</td>
<td>3/5</td>
<td>0.57</td>
<td>0.21</td>
<td>417</td>
<td>F0-6 (6)</td>
</tr>
<tr>
<td>PFIC1/2, MDR3</td>
<td>1/3</td>
<td>1.55</td>
<td>0.98</td>
<td>416</td>
<td>F3-6 (6)</td>
</tr>
<tr>
<td>Tumor</td>
<td>9</td>
<td>0.67</td>
<td>-0.38</td>
<td>417</td>
<td>F0,2,6 (0)</td>
</tr>
<tr>
<td>ARPKD</td>
<td>8</td>
<td>0.68</td>
<td>0.74</td>
<td>411</td>
<td>F0,4,5,6 (5)</td>
</tr>
</tbody>
</table>
Of 258 consecutive pts that met inclusion criteria sufficient data was available for 193 pts aged 4.3y (0.2-18y). Explanted livers from 17 pts had a FS of F0, F1=1pts, F2= 4pts, F3= 6pts, F4= 5pts, F5= 32pts, F6= 128pts. A significant correlation of higher LVIDd Z-Scores to higher FS (p=0.036; average Z Score in FS F6 group 1.0) was detected, but not for LVPWd and FS (p=0.55). In contrast to other studies no association between QTc and FS was found, paradoxical the lowest average QTc (381sec) was detected in the FS F6 group.

**Conclusion:** Z-Scores of LVIDd increase with grade of liver cirrhosis. The average Z-Score of LVIDd though remains within the normal range. The clinical relevance of such subtle changes needs to be determined. The results of our retrospective analysis of QTc are in contrast to previously published results. In summary our results emphasize the need for larger prospective trials to better understand CCM.


**Disclosure of Interest:** None Declared
Hepatology
Transplantation
PO-H-0346

LARGE ASCITES AS A MARKER OF EARLY PORTAL HYPERTENSION DUE TO GRAFT DYSFUNCTION AFTER PAEDIATRIC LIVER TRANSPLANTATION

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Objectives and Study: Noninvasive markers of early graft dysfunction after liver transplantation (LTX) are lacking and, in centers not performing protocol biopsies, subtle complications may be overlooked. We speculated that the amount of ascites produced early after LTX was a reliable sign of portal hypertension (PH), and therefore a putative marker of early LTX complications. We also evaluated the relationship between ascites and pre- and post-LTX donors' and recipients' features.

Methods: The medical charts of patients transplanted consecutively between 2011-2014 were analysed. A mean amount of ascitic fluid loss collected from the abdominal drainage ≥20 ml/kg/day in the first 15 days was considered abnormal and was correlated with graft dysfunction, defined as abnormal liver function tests accompanied by rejection or other abnormal patterns at histology. The drain losses were also correlated with surgical complications, pre-transplant PH, native and graft liver size, graft to recipient body weight ratio and graft to native liver weight ratio as markers of possible “small for size” syndrome.

Results: 84 LTXs (66 left lateral segments, 10 whole livers, 8 right lobes) in 72 patients (M/F 38/34, mean age 4.3 years) affected by biliary atresia (35, 49%), metabolic disorders (8, 11%), acute liver failure (6, 8%), sclerosing cholangitis (5, 7%), other biliary cirrhosis (5, 7%), liver tumors (5, 7%), Alagille syndrome (3, 4%) miscellaneous (5, 7%) were analysed. Twelve patients underwent retransplantation. Thirty-two (38%) LTX were complicated by graft dysfunction and 27 (37.5%) by surgical complications. At statistical analysis pre-LTX PH and graft/donor features were not correlated with large amounts of ascites, that instead was associated with low body weight at LTX (p= 0.029), histological graft dysfunction (p= 0.026), and surgical complications (p=0.05. Pearson correlation).

Conclusion: Younger recipients tend to have relatively larger fluid losses after LTX. An ascitic fluid drainage ≥20 ml/kg/day is associated with histological features of graft dysfunction and can be used as a marker of early complications in this setting.

Disclosure of Interest: None Declared
LIVER TRANSPLANTATION IN CITRULLINAEMIA; A SINGLE CENTRE EXPERIENCE

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Objectives and Study: Citrullinaemia or arginosuccinate synthetase (ASS) deficiency, a urea cycle defect, classically presents in the neonatal period with poor feeding, vomiting, hyperammonaemia and encephalopathy. Acute management includes prompt treatment of the hyperammonaemia, while protein-restricted diet with ammonia-lowering agents are required lifelong. Despite medical management, long-term neurocognitive outcomes remain suboptimal.

Methods: A retrospective review of all patients with ASS deficiency referred to a tertiary paediatric liver centre in the UK.

Results: Eight children were identified (6 male, median age at referral 1.5 years, range 0.5 – 5.3 years). All presented in the neonatal period with hyperammonaemia (median 1131 mmol / L, range 350 – 1702) including one with a family history of neonatal death. All were treated with protein-restriction, sodium benzoate and sodium phenylbutyrate. Six had developmental delay and required gastrostomy feeding. Indications for liver transplantation (LT) were: frequent metabolic decompensations (5), acute liver failure (1) and elective (2).

Six children were transplanted, while two are awaiting surgery. Median age at LT was 1.55 years; range 1.3 – 5.9 years. Five children received 6 left lateral segment grafts while one received a living-related left lateral segment as an auxiliary graft. Post-LT complications included aspiration pneumonia, post-transplant lymphoproliferative disease (2), subclavian vein thrombosis (1) and hepatic artery thrombosis (1). One graft was lost due to HA thrombosis, re-transplant within 2 weeks. Graft and patient survival was 93% and 100%, respectively. Median follow up post-transplant is 1.6 years, range 0.8 – 2.9 years. All children are off ammonia-lowering agents and protein restricted diet. Tacrolimus and prednisolone in 5 and prednisolone only in 1. Ammonia post–LT is < 50 mmol / L in all and median citrulline is 242 μmol / L, range 204 – 820, normal range 8 – 57 μmol / L. Feeding, developmental skills and subjective quality of life have improved in all of the children following LT.

Conclusion: LT is an effective mode of management for early onset ASS deficiency and should be considered in the management of individual cases.
Disclosure of Interest: None Declared
CHOLANGITIS AFTER HEPATIC PORTOENTEROSTOMY FOR BILIARY ATRESIA: ASSOCIATED RISK FACTORS AND IMPACT ON OUTCOME.

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Objectives and Study: Cholangitis (CO) are one of the most important complications after hepatic portoenterostomy (PE) in patients with biliary atresia. They are considered one of the major determinants of transplant free survival after successful PE, being responsible of progressive cirrhosis, portal hypertension and sepsis. The aim of the study was to retrospectively assess the risk factors of CO after PE in patients with Biliary Atresia and to evaluate its impact in outcome.

Methods: We performed a retrospective review of data in all patients who underwent a PE at the Vall d’Hebron Hospital of Barcelona from September 1994 to August 2014. Patients whose initial operations were performed elsewhere and who were referred later to our hospital were excluded from analysis. They received intravenous antibiotic prophylaxis for a minimum period of 7 days after the surgery followed by oral antibiotics according to clinical criteria. CO was defined as the sudden onset of jaundice with elevated transaminases and bilirubin and laboratory parameters suggestive of infection. Early CO was defined as a CO that occurred during the first six months post-PE. Partial flow restoration was defined as bilirubin > 2 mg/dL six months after surgery.

Results: Sixty-two patients (32 boys, 30 girls) were included in the study with a median age at PE of 57 days (r: 21-159). Fifteen out of 62 patients (24.2%) did not restore biliary flow after surgery, 31 (50.0%) had partial recovery and 16 complete flow restoration (25.8%). Forty-four patients (70.9%) reported at least one CO in the follow up with a total CO of 89. Patients with partial or without restoration of the biliary flow presented a higher risk of CO compared with patients with complete flow restoration (0.8 and 0.65 vs 0.18 col / pac / year, P <0.001). Patients who had early CO had increased risk of late CO (OR: 5.71; 95% CI 1.8-14.3.). Transplant-free survival was significantly lower in patients who had early CO (25.9 vs 39 months P> 0.05). The use of prophylactic antibiotic over six months did not decrease the risk of CO increasing the risk of colonization by multiresistant bacteria (0.6 vs 0.25%, respectively, P> 0.05).

Conclusion: Partial restoration of flow could predispose to post-PE CO. The early CO may have a negative impact on patient outcomes (shorter time of transplant free survival and increased susceptibility to successive CO). Antibiotic prophylaxis beyond six months after PE, is not related with a protective effect on CO however may increase the presence of multi-resistant germs. Prospective trials are needed to confirm these preliminary results.

Disclosure of Interest: None Declared
POST- TRANSPLANT MALIGNENCIES IN PAEDIATRIC LIVER TRANSPLANT RECIPIENTS

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Objectives and Study: Liver transplantation is the treatment of choice for patients with end stage liver diseases. It mostly results in long term survival. However, de novo cancer is one of the most serious complications. The main cause for the occurrence of this complication is the use of chronic immunosuppressive therapy that is needed after transplantation to prevent rejection. Development of some tumors are associated with viral agents such as Epstein-Barr virus with lymphoma or HHV-8 with Kaposi's sarcoma. The aim of this study is to evaluate types of malignancies and clinical course in post-transplant pediatric patients.

Methods: A total of 185 patients without a previous diagnosis of cancer (including hepatocellular carcinoma) underwent deceased donor OLT from 1997-2013 at the Liver Transplantation Center of Ege University. The analysis was made in the form of a retrospective chart review.

Results: De novo cancers were diagnosed in 11 patients. Cancer types diagnosed in these patients were post-transplant lymphoproliferative disorder (n=7, % 63,6), Kaposi's sarcoma (n=1, % 9.09), lymphoma (n=2, %18,1 ) and liver sarcoma (n=1, %9,09). Primary diagnoses were biliary atresia, PFIC, tyrosinemia, autoimmune hepatitis and fulminant hepatic failure. The mean time for diagnosis of malignancies was 30 months after the liver transplantation. Seven patients were given tacrolimus, whereas the remaining four were given sirolimus. EBV DNA was isolated from seven patients, and three of them developed PTLD. Three patients were diagnosed with lymphoma; and one patient was diagnosed with primary liver sarcoma.

Conclusion: This study aimed to reveal the incidence of malignancy in pediatric patients after liver transplantation. There are a lot of studies on this subject conducted on adults, whereas only a few studies have been published by pediatric departments. Liver transplantation is a life-saving treatment. Immunosuppressive therapy is unavoidable after transplantation, and malignancies are inevitable. However, the incidence of de novo cancer due to transplantation can be reduced with regular screening and close follow-up.


**Disclosure of Interest:** None Declared
Nutrition
Basic Science
PO-N-0350

PREVALENCE OF IGE-MEDIATED HAZELNUT ALLERGY AND CLINICAL FEATURES IN CHILDHOOD

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Objectives and Study: It was aimed to determine the prevalence and clinical characteristics of hazelnut allergy in childhood.

Methods: This cross-sectional study is recruited 20800 randomly selected 6-18-years-old children. A self-administered questionnaire was completed by parents and children. Any child who reported any allergy history to hazelnut were invited for skin prick tests (SPT), prick-to-prick (PTP), double blind placebo controlled food challenge (DBPCFC), and oral food challenges (OFC), respectively. SPT and PTP were applied to all children suspected of hazelnut allergy. DBPCFC was applied to SPT and/or PTP positive children.

Results: The questionnaires were completed by 15783 children, which was a response rate of 75.9%. The number of children who had parental-reported hazelnut allergy was 36. Informed consent to participate in further evaluation was obtained from 33 of the children suspected of hazelnut allergy. SPT and PTP were applied to all of 33 children. DBPCFC tests were applied to those who positive for SPT and/or PTP of 15 children. Seven were positive, and eight were negative in DBPCFC. Only one child was OFC positive in which DBPCFC negative 8 children. The proven IgE-mediated hazelnut allergy was found in 8 patients. The prevalence was found to be 0.051% (95% CI, 0.000219-0.000998).

Table 1. Characteristics of the patients with hazelnut allergy

<table>
<thead>
<tr>
<th>Pt.No</th>
<th>Age/sex</th>
<th>SPT</th>
<th>PTP</th>
<th>DBPCFC</th>
<th>OC</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>9/M</td>
<td>Hazelnut, D1, D2, grass, brich pollen</td>
<td>Hazelnut</td>
<td>Urticeria</td>
<td>-</td>
</tr>
<tr>
<td>2</td>
<td>16/M</td>
<td>D1, D2</td>
<td>Hazelnut</td>
<td>OAS, rash, breathing difficulties</td>
<td>-</td>
</tr>
<tr>
<td>3</td>
<td>15/M</td>
<td>Neg</td>
<td>Hazelnut</td>
<td>Neg</td>
<td>Hazelnut anaphylaxis</td>
</tr>
<tr>
<td>4</td>
<td>12/M</td>
<td>Hazelnut</td>
<td>Neg</td>
<td>Rash, sneezing, nasal congestion</td>
<td>-</td>
</tr>
<tr>
<td>5</td>
<td>9/M</td>
<td>D1, D2, brich pollen, mould</td>
<td>Hazelnut</td>
<td>Hoarseness, nausea, vomiting, cough</td>
<td>-</td>
</tr>
<tr>
<td>6</td>
<td>13/M</td>
<td>Neg</td>
<td>Hazelnut</td>
<td>Rash, itching, diarrhea</td>
<td>-</td>
</tr>
<tr>
<td>7</td>
<td>13/M</td>
<td>Hazelnut, D1, D2, egg</td>
<td>Hazelnut</td>
<td>Puriritis, sneezing, itching,</td>
<td>-</td>
</tr>
</tbody>
</table>

**Conclusion:** The results of this study showed that the prevalence of IgE-mediated hazelnut allergy was extremely low. Anaphylaxis due to hazelnut allergy may rarely occur. Therefore, it should be kept in mind that such these conditions may cause hazelnut, with patients in food allergy.

**Disclosure of Interest:** None Declared
INTRODUCTION OF FORMULA FEEDING INDUCES SUBCLINICAL INFLAMMATION AND ALTERED CHROMATIN STRUCTURE IN THE INTESTINE OF PRETERM PIGS PREDISPOSING TO NECROTISING ENTEROCOLITIS

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Objectives and Study: To analyze how enteral food introduction affects intestinal gene regulation and chromatin structure in preterm neonates, potentially predisposing to necrotizing enterocolitis (NEC).

Methods: Preterm piglets were fed total parenteral nutrition (TPN) or PN plus slowly increasing volumes of enteral nutrition (0-64 mL/kg/d formula or bovine colostrum). Intestinal gene expression profiles, CpG signaling and chromatin structure were analyzed five days after birth. Chromatin structure changes and inflammatory response genes were investigated in CaCo-2 cells.

Results: Enteral feeding led to differential up-regulation of several inflammatory and pattern recognition receptor genes, including IL8 and TLR4. This correlated with mild mucosal lesions and more open chromatin configurations particularly in formula-fed pigs. Colostrum-fed pigs were only minimally affected and also showed elevated IL10 mRNA levels. In CaCo-2 cells, treatment with a histone deacetylase inhibitor led to marked increase in TLR4 mRNA and more pronounced IL8 mRNA expression upon stimulation with lipopolysaccharide.

Conclusion: Initiation of enteral feeding, particularly with formula, induces subclinical inflammatory lesions in the premature intestine and a more open chromatin structure in key inflammatory genes. This may predispose to later intestinal dysfunction and NEC. Consequently, it is critical to optimize the time, amount and diet of the first enteral feeds for preterm infants.

Disclosure of Interest: None Declared
Parentreral Nutrition up-regulates the expression of CUGBP1: An RNA binding protein that represses enterocyte proliferation in vitro

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Objectives and Study: Total parenteral nutrition (TPN) support results in intestinal mucosal atrophy and the exact mechanisms remain unclear. CUGBP1 was discovered up-regulated in the intestine tissue of TPN rats, but its contribution needs to be further studied. This study aimed to investigate the effect of CUGBP1 on enterocyte proliferation, and to assess its expression pattern with respect to parenteral nutrition in vitro.

Methods: HCT116 and Caco-2 cells were applied as in vitro models. The impact of CUGBP1 on enterocyte proliferation was detected by RTCA (Real Time Cellular Analysis). Apoptosis and cell cycle were evaluated using flow cytometry. Time-lapse fluorescence microscopy was introduced to dynamically observe the hallmark events of cell growth that may be influenced by CUGBP1. The effect of parenteral nutrition (PN) solution on the expression of CUGBP1 was assessed.

Results: The proliferation of Caco-2 cells was repressed by ectopic expression of CUGBP1, and promoted by CUGBP1 silencing. RTCA analysis revealed the doubling time of control cells, CUGBP1 overexpression cells and CUGBP1 knockdown cells were 21.1±0.4 hours, 28.5±0.6 hours (p<0.05) and 15.5±0.5 hours (p<0.05), respectively. Flow cytometric analysis revealed that CUGBP1 overexpression promoted apoptosis while CUGBP1 knockdown prevented cells from apoptosis. The rate of apoptosis was 5.1% (control), 10.2% (CUGBP1 overexpression, p<0.05) and 4.4% (CUGBP1 knockdown, p>0.05). Following UV irradiation, the rate of apoptosis was 23.1% (control), 32.4% (CUGBP1 overexpression, p<0.05) and 13.8% (CUGBP1 knockdown, p<0.05). Cell cycle assay revealed that CUGBP1 overexpression induced G2/M phase arrest in HCT116 cells, and the expression of cell cycle regulation proteins was changed correspondingly. Notably, time-lapse imaging tracked one individual cell expressing CUGBP1-RFP, indicating that robust CUGBP1 may lead to a failure in cell division. The expression of CUGBP1 in both HCT116 cells and Caco-2 cells was up regulated by PN solution in a dose-dependent manner. 1%, 3% and 5% PN increased CUGBP1 expression levels by ~ 1.1, 2.8 (p<0.05) and 3.2 (p<0.01) folds, respectively. In terms of the main constitutions, 1% lipid emulsion (equivalent to the amount in 5% PN solution) increased CUGBP1 expression levels by ~ 2.2 folds (p<0.05), and 1.5% amino acid mixture (equivalent to the amount in 5% PN solution) increased CUGBP1 expression levels by ~ 1.6 folds (p<0.05). Particularly, the effect of 5% PN solution was partly abolished by the addition of choline (~ 50% off, p<0.05).

Conclusion: CUGBP1 represses enterocyte proliferation in vitro and its expression is regulated by parenteral nutrition.

Disclosure of Interest: None Declared
**THE ANTI-INFLAMMATORY POTENCY OF AMINO ACID BASED FORMULA (AAF)**

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**Objectives and Study:** Amino acid-based formulas (AAF) are used for the dietary management of cow’s milk allergy and multiple food protein intolerances. This is a validated and accepted concept based on allergen avoidance. However, a recent study showed that intake of AAF, in addition to a milk-, egg-, wheat- and soy-free diet, led to a reduced colonic inflammatory status in paediatric patients (≤ 5 years of age)\(^1\). The present study aimed to evaluate the immune modulating effect of an AAF (Neocate) and its pure total amino acid fraction.

**Methods:** The immune modulating effects of Neocate, its amino acid fraction and individual amino acids were studied using three different *in vitro* experimental models. 1.) Human peripheral blood mononuclear cells (PBMCs) were stimulated for 20 hours with lipopolysaccharide (LPS) followed by measurement of cytokine levels in the culture supernatants. 2.) Rat basophil leukemia (RBL) cells were activated by IgE crosslinking as a model for the allergic effector response. Degranulation and cytokine levels were detected 30 minutes and 20 hours after activation, respectively. 3.) CXCL8-induced human neutrophil chemotaxis was measured using Boyden chambers.

**Results:** Neocate, its amino acid fraction and glycine inhibited the LPS-induced TNF\(\alpha\) production in a concentration dependent manner. The combination of glycine and glutamine inhibited the TNF\(\alpha\) production in a synergistic way (glutamine by itself did not affect the LPS-induced TNF\(\alpha\) production).

In the RBL cell-based assay, glycine did not affect degranulation while both TNF\(\alpha\) and IL-4 production were inhibited in a concentration dependent manner. CXCL8-induced neutrophil chemotaxis was inhibited by the amino acids fraction and glycine, but not by the complete amino acid-based formula.

**Conclusion:** The present study demonstrates that the amino acids in Neocate are able to dampen both pro-inflammatory, as well as, Th2 responses. The immune modulating effects of AAF as detected in biopsies of allergic children\(^1\), might be mediated through specific amino acids or combinations thereof, including glycine and glutamine. Both mechanistic and clinical studies are required to evaluate in more detail how amino acid combinations influence inflammatory processes, immune homeostasis and tolerance induction and what their potential impact and therapeutic relevance can be.

**References:** 1. Immunomodulatory Effects of Amino Acid Based Formulæ (AAF) in Gastrointestinal Non-IgE mediated Food Allergy, H.E. Jones et al., ESPGHAN 2015

**Disclosure of Interest:** A. Hartog Conflict with: Nutricia Research, N. Buurman Conflict with: Nutricia Research, L. F. Harthoorn Conflict with: Nutricia Research, H. E. Jones: None Declared, M. Bajaj-
Elliott: None Declared, A. P. Vos Conflict with: Nutricia Research, J. Garssen Conflict with: Nutricia Research
HIGH-PROTEIN DIET DURING GESTATION PROMOTES ADIPOSY AND FOOD INTAKE IN FEMALE RAT PUPS IN THE LONGER TERM

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Objectives and Study: During the perinatal period, starting from the beginning of gestation, environment and especially nutrition has a programming effect on health of the offspring in adulthood (Gluckman et al, 2008; Hallam et al, 2013). Suboptimal nutritional intake during gestation, especially energy or protein deficiency, is associated with disease susceptibility of the child (Han et al, 2012). Protein is an important nutritional factor for later life metabolic health and disease risk. Whether dietary protein quantity has a differential effect depending on the critical window of development, e.g. during gestation or lactation, is at present unknown.

The aim of this study is to determine the effect of maternal high-protein (HP) diet during gestation or lactation on offspring metabolic response to a western diet challenge after weaning.

Methods: Three groups of Wistar rat dams received either control diet (C, 20% proteins) during gestation and lactation (C group), HP diet (55% proteins) during gestation (HPgest group), or HP diet during lactation (HPlact group). From weaning until the age of 10 weeks, female pups were exposed to C or western diet (W, 42% fat, 19% sucrose, 20% proteins). Each pup group was composed of 8 females. Results were analyzed using a mixed model with the MIXED procedure of SAS.

Results: Maternal gestation diet has no effect on birth weight. Regardless of the maternal diet, W diet after weaning increases triglyceride quantity in liver of all groups at 10 weeks (p<0.0001). HPgest pups have less visceral adipose tissue (AT) at weaning (p=0.02) and more subcutaneous AT at 10 weeks (p=0.02). At 10 weeks-old, HPgest pups have more adipocytes than C and HPlact (p=0.007).

In addition, W diet specifically induces in HPgest pups, when compared to C and HPlact pups, a higher weight gain (gestation diet*diet after weaning*time effect: p<0.0001), an increased food intake (gestation diet*diet after weaning effect: p=0.01) and a higher adiposity at 10 weeks (gestation diet*diet after weaning effect: p=0.006 in absolute weight and p=0.02 in % body weight).

Conclusion: These results show that maternal HP diet during gestation, but not lactation, leads to a higher sensitivity of female pups after weaning to obesity under a western diet. The programming effect seems to be mediated by adipose tissue as HP diet during gestation enhances differentiation and/or proliferation of adipocytes, thus increases the capacity of pups to store fat.

Disclosure of Interest: C. Desclée De Maredsous Conflict with: Danone Nutricia Research, A. Oosting Conflict with: Danone Nutricia Research, C. Delteil: None Declared, F. Blachier: None Declared, P.
Barbillon: None Declared, T. Mary-Huard: None Declared, D. Tomé: None Declared, R. Oozeer
Conflict with: Danone Nutricia Research, A.-M. Davila: None Declared
APICAL EXPOSURE TO DIETARY NON-DIGESTIBLE OLGOSACCHARIDES AND BACTERIAL CGP DNA SUPPRESSES TH2 TYPE CHEMOKINE RELEASE BY ACTIVATED INTESTINAL EPITHELIAL CELLS

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Objectives and Study: Dietary short chain galacto- and long chain fructo-oligosaccharides (scGOS/lcFOS) and TLR9 ligand CpG DNA affect intestinal epithelial cell (IEC) function. Epithelial derived IL-1α is known to contribute to allergic sensitization in the lung. To study the effect of IL-1α on Th2 polarizing chemokine release by IEC and the modulatory effect of scGOS/lcFOS and CpG DNA in presence or absence of monocyte derived dendritic cells (moDC).

Methods: HT-29 cells (IEC) cultured in transwells were pre-incubated basolaterally with IL-1α ± IFNγ/TNFα and apically with scGOS/lcFOS ± CpG DNA for 6 hours, washed and basolaterally exposed to immature moDC or medium while apically exposed to scGOS/lcFOS ± CpG for 24-48 hours. Th2 driving IL-25, CCL2, CCL22 and regulatory galectin-9 and TGF were measured in basolateral supernatants. After 48h of co-culture, moDC were added to allogenic naïve T-cells for 6 days (MLR) and cytokines were measured.

Results: Combined IFNγ/TNFα activation induced the release of CCL2 and CCL22 by IEC, which was further enhanced by IL-1α. IFNγ/TNFα ± IL-1α activation also increased galectin-9 and TGF (24h). Exposure to scGOS/lcFOS ± CpG DNA reduced CCL2 and CCL22, while galectin-9 and TGF remained high. In the 48h supernatants of IEC/moDC co-cultures, scGOS/lcFOS enhanced galectin-9 in presence or absence of CpG DNA. scGOS/lcFOS plus CpG DNA reduced IL-25 in co-cultures pre-exposed to IFNγ/TNFα/IL-1α while increasing IFNγ concentrations in the MLR.

Conclusion: IL-1α enhances Th2 polarizing chemokine release by IFNγ/TNFα activated IEC. Combined exposure to dietary scGOS/lcFOS plus CpG DNA suppresses this response skewing away from the allergic phenotype.

This study was performed within the framework of Dutch Top Institute Pharma (T1.501).

Disclosure of Interest: None Declared
RED CELL DISTRIBUTION WIDTH IN IRON DEFICIENT CHILDREN AGED 0.5 – 3 YEARS

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Objectives and Study: Early detection of iron deficiency (ID) and iron deficiency anemia (IDA) in young children is important to prevent impaired neurodevelopment. Unfortunately, many biomarkers of ID are influenced by infection/inflammation thus limiting their usefulness. Red cell distribution width (RDW), an index of variation in red blood cell size, might be a promising indicator of ID since it is increased in iron deficient patients (1-3) and reported not to be influenced by infection (4). The aim of this study was to investigate the value of RDW for detecting ID(A) among otherwise healthy children.

Methods: A multi-center observational study was conducted in the Netherlands in 2011-2012 to investigate the prevalence of ID(A) in 400 healthy children aged 0.5 – 3 years. ID was defined as a serum ferritin (SF) concentration <12 µg/L in the absence of infection (CRP <5 mg/l) and IDA as a hemoglobin concentration <110 g/L combined with ID according to the criteria of the World Health Organisation.

Results: RDW was inversely correlated with SF (correlation coefficient -0.191, p=0.000) and not associated with CRP (elevated in 12.5%, p=0.342). ID and IDA were both associated with higher RDW levels. Calculated cut-off values for RDW to detect ID and IDA gave a relatively low sensitivity (52.6% and 56.5%, respectively) and specificity (65.4% and 74.4%, respectively). Anemic children with a RDW > 14.4% had a 3.9 higher odds (95% CI 1.4-10.7, p=0.008) to be iron deficient, compared to anemic children with a RDW <14.4%.

Conclusion: RDW can be helpful for identifying ID as the cause of anemia in 0.5 – 3 year old children, but not as primary biomarker for ID or IDA. RDW values are not influenced by the presence of infection.


Disclosure of Interest: None Declared
BUTYRATE ENHANCES THE CAPACITY TO DRIVE IMMUNE TOLERANCE IN THE GUT BY SUPPORTING EPITHELIAL PRODUCTION OF RETINOIC ACID

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Objectives and Study: Objectives and study
Dietary Vitamin A is required in various biological processes including reproduction, growth, cellular differentiation/proliferation, lipid metabolism, and specific immune functions such as tolerance induction. Reduced levels of the short chain fatty acid (SCFA) butyrate have been associated with microbial dysbiosis and disease development. Butyrate serves as main energy source in colonocytes, and is purported to exert anti-inflammatory effects. Using novel enteroid culture systems for primary intestinal epithelia, we aimed to study the effect of butyrate on the production of the Vitamin A metabolite retinoic acid (RA). This is relevant because intestinal epithelia dictate homeostasis and immune tolerance by stimulating tolerogenic CD103+DCs through the release of RA. In this regard the retinal dehydrogenases aldha1a1 and aldha1a3 are key restricting enzymes for retinoic acid production and activity.

Methods: Methods
Mouse CMT93, human CACO-2 cell lines, and mouse crypt-derived intestinal enteroid cultures were incubated with SCFA and analysed for RA metabolic enzyme expression, stemness, and maturation markers. Functional RA conversion was analysed by Aldefluor activity assays. Since RA is an important signalling molecule exerting its effect through specific retinoic acid receptors (RAR) the effect of butyrate on RAR expression was also investigated by qPCR.

Results: Results
Butyrate (0-5mM) dose dependently induced aldha1a1 and -3 expression in human CACO-2 and mouse CMT93 epithelial cells (up to 10-30 fold at 5mM for aldha1a1 and -3 resp.). Using Aldefluor assays, we further validated that butyrate increased the functional conversion to RA. These data were replicated in primary “mini-guts” grown as enteroids. In enteroids, butyrate (2-5mM) up regulated aldha1a3 expression (50 fold over control), whereas aldha1a1 was unaffected. RA receptor alpha was up regulated two-fold, indicating enhanced RA signalling. Butyrate (2-5mM) reduced stemness marker (LGR5, OLMF4) expression but up regulated Wnt target genes (CD44, ASCL2, CDKN1), indicating that enhanced RA conversion did not solely reflect epithelial cell dedifferentiation.

Conclusion: Conclusion
We conclude butyrate can support epithelial conversion of dietary retinoic acid thereby enhancing the capacity to generate tolerogenic DCs and drive immune tolerance in the gut.
EARLY SUPPLEMENTATION WITH 2'-FUCOSYLLACTOSE DURING LACTATION ENHANCES MEMORY AND LEARNING PROCESSES LATER IN LIFE IN RATS

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Objectives and Study: Human milk oligosaccharides (HMOs) have been proposed to exert beneficial effects on brain development. During the last decades, most of the studies have focused on the evaluation of sialylated structures but recent experiments have also tested fucosylated oligosaccharides, i.e. 2'-fucosyllactose (2'-FL). The present study is aimed to determine whether 2'-FL has an effect on the development of newborn brain, contributing to enhanced cognitive skills later in life.

Methods: Rat pups received an oral supplementation of 2'-FL (2'-FL group) or water (control group) during the lactation period. Thereafter, animals were maintained with a solid standard diet. Rats (n=12 rats/group) were evaluated twice, at 4-6 weeks old and again at 1 year old, using a battery of behavioral tests (Morris water maze [MWM], Y maze and novel object recognition [NOR]). In vivo long term potentiation (LTP) was also performed at the stated ages (n=10 rats/group).

Results: Both groups showed similar behavior when the animals were assessed just after weaning (4-6 weeks of age), although the 2'-FL group seemed to perform slightly better in MWM. At 1 year of age, 2'-FL rats performed significantly better in the NOR and Y maze paradigms, when compared to the controls. In addition, in vivo LTP was more intense and longer lasting in the rats supplemented with 2'-FL than in control animals both at 4-6 weeks and at 1 year of age.

Conclusion: The oral administration of 2'-FL during the lactation period improved the cognitive status of rats at different stages of life.

Objectives and Study: Breast milk is considered a protective factor against food allergy. The major short chain fatty acids, butyrate produced by gut microbiota exerts positive effect on immune system. We aimed to see whether butyrate concentration in human milk is able to prevent food allergy in animal model.

Methods: We determined by gas chromatography butyrate concentration in 40 samples of mature breast milk collected from lactating women (aged 21-42 years), receiving a mean content of 12.2 g (SD±3.45)/d of dietary fiber). 4-week-old female C3H/HeOuJ mice were sensitized by oral route with b-lactoglobulin (BLG) plus cholera toxin (CT) as an adjuvant in the presence or absence of butyrate. Acute allergic skin response, anaphylactic symptom score, body temperature, intestinal permeability, anti-BLG IgE, IL-4 and IL-10 production were assessed soon after oral food challenge.

Results: Mean butyrate concentration in breast milk was 0.47 mM (SD±0.15). This means that a breastfed infant receives a daily dose of butyrate of about 20 mg/Kg body weight. The same concentration was able to significantly prevents CMA in the animal model, as suggested by a dramatic inhibition of acute allergic skin response, anaphylactic symptom score, body temperature decrease, intestinal permeability increase, anti-BLG IgE, IL-4 and IL-10 production (p<.05).

Conclusion: Our data support the role of butyrate as effective human milk component able to prevent food allergy.

Disclosure of Interest: None Declared
DIRECT EFFECTS OF FERMENTED COW'S MILK WITH LACTOBACILLUS PARACASEI CBA L74 ON HUMAN ENTEROCYTES.

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Objectives and Study: Fermented cow's milk with *Lactobacillus paracasei* CBA L74 (FM-CBAL74) exerts a preventive effect against childhood infectious diseases. We evaluated if this effect is at least in part related to a direct interaction with human enterocytes.

Methods: Human enterocytes (Caco-2) were stimulated for 48 hours with FM-CBAL74 at different concentrations. Cell growth was assessed by colorimetric assay (MTT (3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide); innate immunity peptides synthesis, beta-defensin-2 (HBD-2) and cathelicidin (LL-37), by ELISA. Cell differentiation, tight junction proteins (zonulin and occludin), HBD-2 pathway, and anti-inflammatory modulation were analyzed by Real Time PCR using enterocytes RNA.

Results: FM-CBAL74 stimulates in a dose-dependent manner cell growth (+600%, p<.05), HBD-2 (+1018%, p<.05), LL-37 (+3400%, p<.05) synthesis; and lactase (+65%, p<.05), zonulin (+167%, p<.05) and occludin (+177%, p<.008) expression with maximal effective doses between 11.5 and 115 mg/ml. Same effective FM-CBAL74 doses stimulate expression of toll like receptor-2 (+170%, p=.007) and transcription factor NF-kB, (+333%, p<.05); and down-regulate *inflammatory* mediators expression (COX-2, -48%; iNOS, -37%, p<.05). The effects of FM-CBAL74 are dependent on a thermo-stable component/s.

Conclusion: Through a direct interaction with the enterocytes FM-CBAL74 regulates cell growth and differentiation, innate immunity, and inflammatory mediators expression. These actions are responsible at least in part for the positive effect observed in children.

Disclosure of Interest: L. Paparo: None Declared, R. Aitoro: None Declared, R. Nocerino: None Declared, Y. Maddalena: None Declared, V. Pezzella: None Declared, A. Amoroso: None Declared, C. Di Scala: None Declared, E. Siciliano: None Declared, B. Buono: None Declared, R. Berni Canani: None Declared
FEEDING INFANT FORMULA SUPPLEMENTED WITH THE PROBIOTIC BACTERIA BIFIDOBACTERIUM LONGUM SUBSP. INFANTIS CECT7210 PRODUCE BENEFICIAL CHANGES IN GASTROINTESTINAL MICROBIAL COMMUNITIES: A METAGENOMIC APPROACH.

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Objectives and Study: The present metagenomic study aimed at monitoring the colonization of microbial communities in the gastrointestinal tract in two different infant groups fed infant formula with probiotic Bifidobacterium longum subsp. infantis CECT7210 (treated group) or without the probiotic bacteria (control group).

Methods: V3-V5 region of the 16S rRNA gene was amplified by PCR using key-tagged eubacterial primers and metagenomic DNA from fecal samples. Unidirectional pyrosequencing was carried out on a 454 Life Sciences GS FLX+ instrument (Roche) following the Roche Amplicon Lib-L protocol. FASTA files were BLAST against NCBI 16s rRNA database using blastn. Statistical analysis were performed using R.

Results: Microbial biodiversity was increased in the group fed infant formula containing CECT7210 in comparison with the control group, ratio Phylum Bacteroidetes/Firmicutes at the end of the nutritional intervention with probiotic CECT7210 was lower in the treated group than in the control group (0.0017±0.0064 versus 0.0054 ± 0.0138). Presence of Bifidobacterium species and Bifidobacterium longum species were significantly increased in the treated group at the end of the study compared with the control group (p ≤ 0.026 and p ≤ 0.0023 respectively). Presence of pathogens (Escherichia, Clostridium, Salmonella and Yersinia) was lower in the treated group compared with control group but this difference was not statistically significant. In spite of global pathogen reduction was not significant, presence of Escherichia coli in the treated group was statistically lower than in the control group (p ≤ 0.024).

Conclusion: Results allow concluding that consumption of infant formula with probiotic bacteria CECT7210 can promote healthier microbiota in babies and play a positive role in the gastrointestinal tract of infant.

EFFECT OF EXCLUSIVE ENTERAL NUTRITION ON DENDRITIC CELL PHENOTYPE IN CHILDREN WITH CROHN'S DISEASE

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Objectives and Study: In childhood Crohn's disease (CD), exclusive enteral nutrition (EN) is as effective as steroids in inducing remission in active CD. Studies in CD suggest a key role for dendritic cells (DC) in initiating intestinal inflammation, particularly enhanced expression of activation marker CD40, and bacterial pattern recognition markers TLR2 and TLR4 on intestinal DC. In addition, there is increased expression of gut homing molecule β7 on blood DC in active CD. The phenotype of DC in children with CD is unknown and the mechanism of action of EN in inducing remission and mucosal healing remains unclear, but may involve modulation of mucosal immunity. The objective was to establish the DC profile in CD children before & after EN.

Methods: Blood (10ml) was collected at diagnosis of CD in 18 children before EN and 8 healthy children. Blood was also collected after 6 weeks of EN in children with CD. Peripheral blood mononuclear cells (PBMC) were obtained by centrifugation of blood. PBMC were labelled with monoclonal antibodies and acquired on a flow cytometer. DC were identified as HLA-DR+ lineage− cells and further identified as myeloid (CD11c+), and putative plasmacytoid (CD11c−). Expression of homing markers β7 (gut), CLA (skin), CCR9 (small bowel), CCR7 (lymph node), pattern recognition markers (TLR2 &4) and activation & maturation (CD40 & 86) markers were studied in mDC and pDC. Statistical analyses were carried out using GrapPad Prism software.

Results: Healthy children (n=8) were compared with children with active treatment-naïve CD (n=18). The median age was 13 years (range 9-15 years). 11 CD children were male. The Montreal classification was A1L2B1 in 12 patients. The PCDAI at diagnosis was a median of 55 (range 25-65). 14 children entered remission. Compared with healthy children, the children with treatment-naïve active CD had a greater proportion (%) of blood myeloid DC expressing the activation markers (Mean ± (SD) Standard deviation) - CD40 (55±9 v/s 10±2) and CD86 (80±18 v/s 14±11), the TLR2 (81±17 v/s 7±6) and TLR4 (50±11 v/s 4±3) and the gut homing molecule β7 (55%±7 v/s 6±1) (p<0.05). After EN, blood myeloid DC from children with CD displayed a decreased expression of CD40 (p=0.04), CD86 (p=0.04), TLR2 (p=0.005), TLR4 (p=0.003) and β7 (p=0.001). Post EN, the levels of the DC markers approached those found in healthy children.

Conclusion: Children with treatment-naïve active CD display an activated DC profile, particularly to bacterial products and an enhanced gut homing phenotype, which is restored with EN to a profile similar to that found in healthy children.

Disclosure of Interest: R. Vora Conflict with: Supported by MSD to attend ECCO, D. Bernardo: None Declared, H. O. Al-Hassi: None Declared, S. C. Knight: None Declared, J. Fell: None Declared, A. Hart: None Declared
DIETARY GALACTO-OLIGOSACCHARIDES REDUCE AIRWAY EOSINOPHILIA AND ENHANCE THE TH2 SUPPRESSIVE EFFECT OF BUDESONIDE IN HOUSE DUST MITE-INDUCED ASTHMA IN MICE

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Objectives and Study: In house dust mite (HDM) allergic asthma, symptoms occur due to airway eosinophilia and Th2 cell activation. Budesonide is used to treat airway inflammation and hyper-responsiveness. We showed that dietary non-digestible galacto-oligosaccharides (GOS) suppress symptoms in a murine model for HDM-induced asthma. We aimed to study combined dietary GOS and budesonide treatment on allergic asthma in mice.

Methods: BALB/c mice were intranasally (i.n.) sensitized with PBS in presence or absence of 1µg HDM and challenged i.n. with PBS or 10µg HDM on days 7 till 11 while being fed a diet containing 0, 1 or 2.5 v/w% GOS. On day 7, 9, 11, and 13 budesonide was either or not instilled oropharyngeally. On day 14, airway resistance to metacholine and inflammation were determined. Leukocyte subtypes were analyzed in the broncho-alveolar lavage (BAL) and in lung cell suspensions. Mucosal mast cell protease-1 (mmcp-1) was measured in serum and cytokines in lung homogenates.

Results: HDM allergy significantly increased airway responsiveness and BAL leukocyte numbers. Budesonide treatment suppressed this, which reached significance in mice fed GOS. Budesonide reduced the number of lymphocytes and eosinophils in the BAL. Feeding GOS in absence of budesonide treatment reduced the number of eosinophils as well. In addition, both GOS as well as budesonide reduced mmcp-1 serum concentrations. Interestingly, only in the GOS fed mice, budesonide treatment reduced IL-33 and IL-13 concentrations and the frequency of Th2 cells in the lung.

Conclusion: Dietary intervention using GOS may be a novel way to improve effectiveness of anti-inflammatory drug therapy in asthma.

References: This study was performed within the framework of Carbohydrate Competence Center (WP25).

Disclosure of Interest: L. Willemsen: None Declared, K. Verheijden: None Declared, A. Kraneveld: None Declared, J. Garssen Conflict with: also employed at Nutricia Research BV, G. Folkerts: None Declared
ABSORPTION OF THE HUMAN MILK OLIGOSACCHARIDE 2'-FUCOSYLLACTOSE IN RAT PUPS

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Objectives and Study: Human milk contains all the nutrients necessary to support infant growth and development, including a rich repertoire of human milk oligosaccharides (HMOs). The HMO fraction is unique regarding its diversity, quantity and complexity. 2'-fucosyllactose (2'-FL) is the most abundant HMO in the majority of human milk. In contrast, trace amounts of oligosaccharides are present in mature bovine milk and in milk-based infant formula. Although the prebiotic effects of HMOs have been established in vitro, HMOs may have systemic effects. Recent findings described the presence of HMOs in the plasma and urine of breast-fed infants providing evidence that HMOs reach the circulation. Furthermore, systemic levels of 2'FL correlate with levels present in human milk. Consequently, HMOs have the potential to impact health beyond the intestine.

Aim: To investigate the time-course of 2'-FL absorption from the intestine to the blood stream as well as its excretion in the urine compartment after an oral gavage at increasing doses in rat pups.

Methods: Four hour-fasted Sprague Dawley rat pups (1-12 day old) were given a unique oral gavage of 2'-FL at several doses (1, 2.5, 5 and 10 g/L). Pups were sacrificed (n=8) at different times after the gavage (0, 30, 60, 90, 120, 180 and 240 min) and serum and urine samples were collected. Samples were analyzed by UHPLC-MS/MS for the quantification of HMOs.

Results: After the oral bolus, 2'-FL was quickly taken up from the intestine to the plasma compartment. The appearance of circulating 2'-FL as well as the excretion of 2'-FL in urine after an oral bolus was dose-dependent. At the doses tested, no saturation effect was noticed regarding the absorption of 2'-FL from the intestine to the blood stream.

Conclusion: In rat pups, orally-given 2'-FL is effectively absorbed from the intestine to the circulation in a dose-dependent manner. This result confirms observations in breast fed infants, and suggests systemic effects of HMOs in support of health and development.

COMBINATION OF DHA WITH BIOACTIVE WHEY PROTEIN, NATURAL BOVINE COMPLEX LIPIDS ACCELERATES FUNCTIONAL MATURATION OF NEURONAL NETWORKS IN VITRO

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Objectives and Study: Adequate nutrition early in life is important for healthy growth and development. Studies have shown that docosahexaenoic acid (DHA), for example, plays an important role in infant brain development. DHA is located in plasma membranes of neurons and glia cells and supports processes such as neuronal signal transmission. Since the capacity for endogenous DHA synthesis in the brain does not meet requirements for optimal brain growth and function, DHA has been added to infant formula. In the current study, we asked whether the beneficial effects of DHA can be increased by supplementation of additional membrane components, natural bovine complex lipids, and a bioactive whey protein (BWP).

Methods: We used neuronal cell cultures from mice which form actively communicating networks when growing on micro electrode arrays (MEA). We used the MEA technology in combination with multi-parametric data analysis methods to follow functional neuronal maturation from neurons of embryonic status to mature neuronal cells for 4 weeks in vitro.

Results: The results show that DHA alone accelerates functional neuronal maturation between 14 and 21 days in vitro (DIV). Combination of DHA and BWP accelerates maturation compared to DHA alone between 7 and 14 DIV but wanes after 21 DIV. Combining DHA, BWP and natural bovine complex lipids together accelerates functional neuronal maturation above all other combinations and does not exhibit the late decline shown for the single components.

Conclusion: In conclusion, we show for the first time that the combination of DHA with natural bovine complex lipids as well as BWP significantly accelerates functional neuronal maturation in vitro. Future research should explore whether these findings translate into functional benefits.

A CONCEPT INFANT FORMULA WITH LARGE, PHOSPHOLIPID COATED, DROPLETS
DEMONSTRATES SLOW IN VITRO GASTRIC LIPOLYSIS AS COMPARED TO A REGULAR
INFANT FORMULA

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Objectives and Study: Protection against obesity later in life has been suggested to be one of several
health benefits of breastfeeding. We developed a concept infant milk formula (IMF) with large,
phospholipid coated, lipid droplets (Nuturis®). This concept formula reduced fat accumulation and
improved the metabolic profile in adulthood in a murine programming model [1, 2]. It is anticipated
that differences in lipid digestion kinetic may have contributed to this sustained, protective effect. In
this study, lipid digestion kinetic was evaluated in an in vitro model closely mimicking the digestive
conditions of young infants.

Methods: Concept IMF and an isolipidic, regular IMF were subjected to gastric and intestinal
conditions. Gastric digestion was mimicked by a gradual pH decrease over 120 minutes to pH 4.3
upon addition of hydrochloric acid, alpha-amylase, porcine pepsin, and fungal lipase. Subsequently,
intestinal digestion was mimicked over 120 minutes by pH increase to a pH of 7.2 upon addition of
sodium hydroxide/sodium carbonate, porcine trypsin, pancreatin and bile extract. Samples were taken
at different time points and free fatty acids (FFA) were quantified by gas chromatography. Structural
analysis of the samples was done by microscopy and particle size distribution measurements.
Experiments were performed in triplicate and results shown as means ± SEM. Differences in lipolysis
were analyzed by independent samples T-test with equal variances and considered significant at
P<0.05.

Results: The average gastric lipolysis was slower for Concept IMF compared to regular IMF: 37 ± 5
vs. 62 ± 2 µg FFA/min (P=0.002). The average intestinal lipolysis was comparable: 62 ± 8 vs. 63 ± 15
µg FFA/min (P=0.105). During gastric digestion, microscopic images and particle size distribution
were markedly different. In regular IMF the specific surface area and volume weighted average
diameter changed profoundly due to formation of large protein aggregates. For Concept IMF protein
aggregate formation was far less and intact large lipid droplets remained present, with less profound
changes in particle size distribution.

Conclusion: The in vitro gastric lipolysis of Concept IMF was slower compared to regular IMF. These
differences in gastric lipolysis may also impact gastric emptying rate, lipid metabolism, and the
postprandial response. How this is mechanistically linked to the preclinical observed long term effects
of the Concept IMF remains to be further elucidated.

THE EFFECTS OF SHORT CHAIN GALACTO- AND LONG CHAIN FRUCTO-Oligosaccharides Treatment on Social, Anxiety-Like and Stereotypic Behaviour in Healthy Male Balb/c Mice

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Objectives and Study: An increasing amount of studies show that the gut microbiota is involved in behavioral development. Most studies have been performed in germ-free mice or via antibiotic-induced alteration of the microbiota composition1. Non-digestible oligosaccharides, so-called prebiotics, can modulate the microbiota in a favourable way, increasing the amount of bifidobacteria and lactobacilli2. We conducted a dietary intervention study with short-chain galacto- and long-chain fructo-oligosaccharides (scGOS/lcFOS) to examine the effects of early life changes in microbiota activity on behavioral development in healthy male Balb/cByJ mice.

Methods: Male mice (n=10 per group) were exposed to control diet or 3% GOS/FOS diet during lactation and after weaning throughout the experiment. On P10, we examined ultrasonic vocalizations (UVs) emitted by male pups after 3 minutes of maternal separation. During prepubescence, pubescence and adulthood, social interaction, anxiety-like behaviour (marble burying), and stereotypic behaviors (self-grooming) were assessed. In addition, levels of ceacal short chain (SCFA) and branched chain (BCFA) fatty acids were measured.

Results: Mice that were exposed 3% scGOS/lcFOS through lactation showed a significant reduction in the amount of emitted UVs, compared to mice fed the control diet (P=0.04). Furthermore, male mice fed 3% scGOS/lcFOS buried significantly fewer marbles than control mice (prepubescent, P=0.003; pubescent, P<0.001; adult, P=0.003). scGOS/lcFOS also resulted in reduced stereotypic self-grooming behaviour (pubescent, P=0.07; adult, P=0.006). Mice fed the scGOS/lcFOS diet showed an increased social interest during adulthood compared to control animals (P=0.01). Analysis of ceecal samples revealed that 3% scGOS/lcFOS resulted in increased levels of butyric acid and decreased levels of valeric acid and BCFA (iso-butyric and iso-valeric acid).

Conclusion: Overall supplementation of scGOS/lcFOS during lactation and after weaning point to a reduction of anxiety-like and repetitive/compulsive behaviour in male mice from prepubescence to adulthood. In addition, an increased social interest of the adult male after scGOS/lcFOS supplementation was observed. The behavioral improvement was associated with a scGOS/lcFOS-induced increased sacharolytic and decreased proteolytic fermentation by the adult gut microbiota.

OBJECTIVES AND STUDY: It has been reported that breast-feeding during the first six months of an infants’ life is associated with lower incidences of infections compared to formula-feeding. Recent evidence suggests that oligosaccharides in breast milk may be involved in promoting infants’ health through biological activities such as prebiotic, anti-pathogenic and immunomodulatory. In an attempt to mimic the functions of human milk oligosaccharides, Galacto-oligosaccharides (GOS) have been developed as functional ingredients to modulate and maintain the intestinal micro flora of infants. Research has previously focused on the “bifidogenic” effect of GOS. As a prebiotic, GOS aids in the establishment of a balanced intestinal micro flora, thereby reducing the colonising potential of pathogenic bacteria. In this study the potential of GOS to inhibit the adhesion of a number of pathogenic genera used in this study included *Listeria*, *Escherichia coli*, *Salmonella* and *Cronobacter*, pathogens commonly associated with gastrointestinal infections of infants. It was also determined if any observed anti-adhesive effect of GOS was strain specific, employing additional strains of *E. coli* and *Cronobacter*.

METHODS: The four pathogens listed above were incubated in the presence of GOS at a concentration of 20 mg/mL. After 1 h incubation at 37 °C, the bacteria were introduced to the human colorectal adenocarcinoma cell line HT-29 and incubated at 37 ºC for 2 h. The total number of adhering bacteria was determined by treating the cell line with 0.1 % triton X-100 and plating on brain heart infusion agar.

RESULTS: It was determined that GOS significantly inhibited the adhesion of both *Escherichia coli* 12500 (49%) and *Cronobacter* 6531 (68%), but not *Listeria* or *Salmonella* species. This anti-adhesive effect was determined to be strain specific, as it did not inhibit the adhesion of additional strains of *E. coli* or *Cronobacter*.

CONCLUSION: The anti-adhesive effect of GOS may inhibit the adhesion of pathogenic bacteria, while the previously reported prebiotic effects of GOS would allow for the colonisation of the digestive tract by commensal bacteria thereby contributing to the overall intestinal well-being of the infant. This study demonstrates the multifunctional activity of GOS and highlights their potential alternative bio-functionalities as anti-pathogenic agents. However, the results do serve as a reminder that the observed *in vitro* anti-adhesive activity is strain specific and this should be considered in any future applications of GOS.

Disclosure of Interest: None Declared
Increase of CUGBP1 induced by lipopolysaccharide represses the translation of occludin and E-cadherin and damages intestinal barrier function

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Objectives and Study: Lipopolysaccharide damages the intestinal barrier function, but its exact molecular mechanisms remain incomplete. The effectiveness and stability of the intestinal epithelial barrier depend on the apical junctional complex (AJC), including tight junctions (TJs) and adherens junctions (AJs). Given the truth that CUG-binding protein 1 (CUGBP1) binds to GU-rich elements located in the 3'-untranslated regions (UTRs) of occludin and E-cadherin and regulates their translation, this study sought to determine if Lipopolysaccharide (LPS) damages intestinal barrier function through CUGBP1.

Methods: BALB/c mice and Caco-2 cells were treated with LPS. The binding of CUGBP1 with E-cadherin and occludin mRNAs was examined by ribonucleoprotein/IP analysis. The expression of CUGBP1, E-cadherin and occludin was examined by immunohistochemical staining and Western Blotting. The translation of their mRNA was examined by chimeric luciferase reporter assays. CUGBP1 function was investigated by its gene silencing. Barrier function was detected by paracellular tracer flux assay and transepithelial electricity resistance.

Results: LPS treatment increased the paracellular tracer flux of Caco-2 monolayers through decreasing E-cadherin and occludin protein levels, which is associated with increased expression of CUGBP1. LPS didn’t affect E-cadherin and occludin mRNA level obviously but enhanced the binding of occludin and E-cadherin mRNA with CUGBP1 and repressed their translation significantly as indicated by chimeric luciferase reporter assays. Notably, silencing CUGBP1 eliminated the decreases of occludin and E-cadherin induced by LPS through reversing the elevation of CUGBP1 protein level thus restoring the barrier function. In vivo, CUGBP1 expression increased while in mouse intestinal mucosa after LPS treatment. Consistently, CUGBP1/occludin mRNA and CUGBP1/E-cadherin mRNA complexes also increased, which was associated with a reduction in occludin and E-cadherin expression and barrier dysfunction.

Conclusion: These results indicate: increase of CUGBP1 induced by Lipopolysaccharide represses the translation of occludin and E-cadherin mRNA thus damaging intestinal barrier function.

Disclosure of Interest: None Declared
Objectives and Study: Preterm infants are at risk for iron deficiency (ID) and iron deficiency anemia (IDA) during the first months of life. Several parameters are used to predict later ID and IDA. Zinc protoporphyrin/heme ratio (ZPP/h) in cord blood has been described as an useful indicator of iron available for erythropoiesis at birth. The objective of the study was to establish the value of ZPP/h in early detection of ID and IDA in healthy late preterm infants in the first months of life.

Methods: In a prospective cohort study we analyzed the iron status in 141 healthy preterm infants born between 32+0 and 36+6 weeks of gestational age (GA) not receiving iron supplementation. ZPP/h, haemoglobin (Hb), ferritin and C-reactive protein (CRP) were analyzed at the postnatal age of 1 week, 6 weeks and 4 months. At 4 months of age ID was defined as a ferritin level < 20 µg/L in infants with a CRP ≤ 5 mg/L. IDA was defined as Hb < 105 g/L in combination with ID according to WHO criteria.

Results: At 4 months of age ID and IDA were present in 27 (19,1%) and 11 (7,8%) infants, respectively. ZPP/h levels were significant higher at 1 week (p < 0.001) and 6 weeks (p = 0.042) of age in infants who develop ID compared to those without ID at 4 months of age. ZPP/h levels were not different at the age of 4 months. Infants with IDA at 4 months of age had higher ZPP/h levels at the age of 6 weeks (p = 0.005) and 4 months (p < 0.001) than infants without IDA. In this study population ZPP/h was negatively correlated to ferritin at the age of 1 week (β = -0.400, p < 0.001) and 6 weeks (β = -0.282, p < 0.001) and to Hb at 6 weeks (β = -0.260, p = 0.001) and 4 months of age (β = -0.198, p = 0.013). After correction for factors that may influence ZPP/h values in early life the correlation between ZPP/h and ferritin remained only at 1 week of age. Confounding factors did not influence the correlation of ZPP/h and Hb at 6 weeks and 4 months of age.

Conclusion: High ZPP/h levels reflects iron deficient erythropoiesis only at the age of 1 week. ZPP/h is of no value to detect iron deficiency after the first week of life in healthy late preterm infants.

Disclosure of Interest: None Declared
A QUANTIFICATION OF TOTAL PROTEIN IN HUMAN MILK FROM THREE GLOBAL COHORTS THROUGH THE FIRST YEAR OF LACTATION: A GEHM STUDY

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Objectives and Study: The quantity of protein in human milk is believed to be unreservedly important for growth and development of breastfed infants. This study, in support of the Global Exploration of Human Milk (GEHM) project, provides a longitudinal assessment of total protein in human milk and investigates if total protein concentration is influenced by temporal or geographical factors.

Methods: This study reports total protein concentration as a weight-to-weight percentage based on Dumas combustion in longitudinal samples collected from three global populations (Mexico City, Mexico, Shanghai, China, and Cincinnati, United States) at 4, 13, 26, and 52 weeks lactation. Since some components of human milk, including protein, are known to vary throughout the day, all samples for the GEHM study were collected identically in the morning by emptying an entire breast via electric pump. Additionally, commercially available human milk standards and NIST Standard Reference Material (SRM) 1849a were incorporated into analyses to further verify the accuracy of Dumas combustion for determination of total protein in human milk. The human milk standards analyzed by combustion all fell within protein certified ranges determined by Kjeldahl methodology. A diluted solution of SRM 1849a was analyzed before, during, and after each analytical run to ensure accuracy and consistency of all results.

Results: The average total protein decreased rapidly from 4 to 13 weeks of lactation (1.40 ± 0.14% to 1.16 ± 0.16%) and then remained relatively stable to 52 weeks (1.17 ± 0.13%), with very similar temporal changes demonstrated in the milk from mothers in each geographical region.

Conclusion: Similar trends have been reported and are further strengthened by data generated from these samples collected using standardized techniques. By incorporating additional assessments of accuracy, as well as the integration of samples from different geographical populations across multiple points of lactation, the foundation of knowledge into total protein concentration in human milk is strengthened.

FORMULA CARBOHYDRATE CONTENT DIFFERENTIALLY SHAPES THE MICROBIAL COMMUNITY PATTERNS AND NEC INCIDENCE IN PREMATURE PIGS

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Objectives and Study: Major risk factors for necrotizing enterocolitis (NEC) include premature birth, formula feeding, and microbial colonization of the gastrointestinal tract (GIT). Microbial colonization is thought to begin at birth and is strongly influenced by diet carbohydrate content. We previously showed that feeding formula composed of lactose vs. maltodextrin protects against NEC in preterm pigs, yet the impact on the abundance and diversity of the gut microbiome was unknown. The aim of this study was to use 16S rRNA gene sequencing to quantify the GIT microbial communities in preterm piglet at birth and after feeding formulas containing either lactose or corn syrup solids and correlate these findings with NEC phenotype.

Methods: Preterm piglets delivered by cesarean-section at 103 d gestation were sampled within 4-6 hr birth (NB) or given total parenteral nutrition for 2 d followed by gradual introduction of enteral formula feeding from 3-7 d. Pigs were fed formulas matched in nutrient content but containing either lactose (L), corn syrup solids (CS) or 1:1 mix (MIX). DNA was isolated from ileal and colonic mucosa as well as stomach, ileum, and colon contents, the V4 region of the 16S rRNA gene was sequenced and analyzed using QIIME and R. Total bacterial DNA load was measured by qPCR.

Results: Bacterial DNA was detected but in relative low abundance throughout the GIT of NB vs formula fed pigs (10² vs. 10⁴ 16S/ng DNA). However, the 16S DNA abundance was not different between either the diet groups or healthy vs. NEC groups. The NB microbiome displayed greater diversity than all formula-fed pigs, based on number of observed OTUs. NEC vs. healthy phenotype and CS vs. L formula both showed decreased diversity. These differences in diversity were greater in mucosal-associated vs. luminal DNA samples. The dominant orders among all groups were bacilli, clostridia, and gammaproteobacteria. The Clostridium and Escherichia-Shigella represented ~50% of the observed genera. The abundance of Clostridium was increased, whereas that of Escherichia-Shigella was decreased in CS vs. L and NEC vs healthy pigs, respectively.

Conclusion: We conclude that the newborn, cesarean-derived preterm pig GIT contains 16S rDNA in low abundance with a diverse microbiome signature dominated by bacilli, clostridia, and gammaproteobacteria. Our results in piglets are consistent with recent reports in human preterm...
infants. Feeding formula containing lactose vs. corn syrup solids selects for greater microbiota diversity and is associated with lower NEC incidence.

Disclosure of Interest: D. Burrin Conflict with: Mead Johnson, Fresenius Kabi, Lucta, L. Call: None Declared, B. Stoll: None Declared, A. Akinkuotu: None Declared, O. Olutoye: None Declared, N. Ajami: None Declared, J. Petrosino: None Declared, A. Wittke Conflict with: Mead Johnson
THE TOTAL AMINO ACID PROFILE OF HUMAN MILK IS STABLE THROUGH THE FIRST YEAR OF LACTATION AND CONSISTENT ACROSS GEOGRAPHICAL POPULATIONS: A GEHM STUDY

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Objectives and Study: Development of breastfed infants is thought to be considerably influenced by the amino acid composition of human milk. This study investigates the maternal provisioning of amino acids by characterizing the free and total amino acids profiles in human milk from three globally distinct populations through the first year of lactation.

Methods: Part of the Global Exploration of Human Milk (GEHM) study examines amino acid content of breast milk as well as variability in amino acid profiles over the course of lactation, both between individual mothers and across geographical populations. Total and free amino acid profiles, determined using specialized ion exchange chromatography followed by post column derivitization, are reported for milk samples collected from ten mothers in each of three global cohorts (Mexico City, Mexico, Shanghai, China, and Cincinnati, United States) at 4, 13, 26, and 52 weeks lactation. All samples for the GEHM study were collected identically in the morning by emptying an entire breast via electric pump. This study utilized meticulous sample handling techniques as well as statistically monitored process control during analyses to ensure the accuracy of generated results.

Results: These findings demonstrate that free amino acid profiles exhibit higher variability amongst individuals while total amino acid profiles remain notably consistent even when investigated in distinct locations, amongst multiple donors, and across lactation. This characteristic pattern, observed in all amino acids, can be illustrated by the essential amino acid Threonine (Thr), which has a variability of 55% for free Thr and 4% for total Thr.

Conclusion: This work highlights a remarkable stability in the total amino acid profile of human milk independent of geographical and temporal changes. These observations, strengthened by rigorously controlled sample collection and handling as well as utilization of multiple control measures during analyses, provide additional insights into amino acids in human milk.

**Nutrition**
**Basic Science**

PO-N-0374

**TYPE OF FEEDING AND SLEEP IN INFANCY: A COMPARISON BETWEEN BREASTFED AND FORMULA-FED INFANTS USING ACTIGRAPHY.**

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**Objectives and Study:** Actigraphy has been reported as a new, non-invasive and reliable method for the assessment of sleep in early infancy, showing a high reliability in correctly recognizing sleep time and awakenings. Parental diary reliability is questionable, while polysomnography cannot be easily performed. Data concerning the relationship between sleep and type of feeding in early infancy are scanty. In this study we evaluated sleep duration and number of awakenings in breastfed and formula fed infants using actigraphy.

**Methods:** We enrolled 39 infants 1-12 months old, 19 were exclusively or predominantly breastfed while 20 were exclusively or predominantly formula fed (in weaned infants we considered the type of milk associated to weaning meals), hospitalized in “Pediatria 1 Lattanti” University Division - Regina Margherita Children’s Hospital, Città della Salute e della Scienza di Torino, Turin, Italy. They were monitored with a wrist-placed actigraph during night (from midnight to 6 am) during hospitalization. A subgroup (14 breastfed infants and 14 formula fed ones) performed the monitoring for 24 hours. We evaluated sleep time and number of awakenings in order to understand if there are significant differences between breastfed subjects and formula fed ones. Data from the actigraph were obtained using Sadeh’s algorithm for infancy. Statistical analysis was performed using Wilcoxon–Mann–Whitney test (tests were two-tailed with a significance level of 5%).

**Results:** Data are reported in the table as mean ± standard deviation.

<table>
<thead>
<tr>
<th></th>
<th>Breastfed (n=19)</th>
<th>Formula fed (n=20)</th>
<th>Difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nocturnal sleep time (min)</td>
<td>284.53 ± 46.59</td>
<td>293.60 ± 54.91</td>
<td>-9.07 ± 47.96</td>
<td>0.37</td>
</tr>
<tr>
<td>Nocturnal awakenings (n)</td>
<td>4.63 ± 2.62</td>
<td>3.70 ± 2.03</td>
<td>0.93 ± 2.43</td>
<td>0.32</td>
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</tbody>
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<table>
<thead>
<tr>
<th></th>
<th>Breastfed (n=14)</th>
<th>Formula fed (n=14)</th>
<th>Difference</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep time in 24 h (min)</td>
<td>656.93 ± 87.39</td>
<td>648.21 ± 122.89</td>
<td>8.72 ± 95.86</td>
<td>0.60</td>
</tr>
<tr>
<td>Awakenings in 24 h (n)</td>
<td>15.21 ± 6.21</td>
<td>14.00 ± 5.99</td>
<td>1.21 ± 6.15</td>
<td>0.61</td>
</tr>
</tbody>
</table>

**Conclusion:** According to our data, no significant differences concerning sleep time and number of awakenings were found between breastfed and formula fed infants. However, further evaluations involving more subjects are needed in order to better clarify this issue. The use of an objective and reliable tool for sleep evaluation, such as the actigraph, could provide reliable and comparable data.


**Disclosure of Interest:** None Declared
**MODE OF DELIVERY AFFECTS SPECIFIC PROTEIN ABUNDANCE IN HUMAN COLOSTRUM**

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**Objectives and Study:** Human colostrum is the most important source of nutritional, anti-infective, and immunological factors as well as metabolic enzymes produced during the first days of lactation. On the other hand, mode of delivery has been previously described as a factor that influences human milk microbiota content which could also be reflected on the final protein content. The aim of this work is to study the influence of the mode of delivery on the protein content in human colostrum by grouping the samples into 3 mode of delivery groups (vaginal delivery, elective and non-elective C-section) and mass spectrometry (MS) techniques.

**Methods:** The study design includes three different groups of human colostrum obtained from patients giving birth by vaginal delivery, cesarean delivery, and programmed cesarean. Protease inhibitors were added to the whey fraction of colostrum and minor proteins were enriched by the ProteoMiner kit. Extracted proteins were separated by SDS-PAGE gel electrophoresis and subsequently digested using trypsin enzyme. The generated fragments were analysed by nESI-LC-MS/MS using an Amazon quadrupole-ion trap mass spectrometer in tandem from Bruker. Data analysis for spectral processing, peak list generation, database search and identification, alignment of the spectra, normalization, and relative quantitation, was done using Mascot Distiller software.

**Results:** A total of seven proteins have been identified and quantified using a label-free quantitation methodology. Lactoferrin (TRFL), clusterin (CLUS), Lactadherin (MFGM), Immunoglobulin α-2 chain (IGHA2), and α-lactalbumin (LALBA) content showed significant differences ($p<0.05$) between the three different modes of delivery. Non-significant differences were detected in the polymeric immunoglobulin receptor (PIGR) protein whereas immunoglobulin α-1 chain (IGHA1) protein showed significant differences ($p<0.05$) in cesarean delivery. The Principal Component Analysis (PCA) showed the variance among the protein content and demonstrate that the protein concentration of colostrum when analyzing the studied proteins changed depending on the mode of delivery. The analysis of the PCA loading plot revealed that MFGM and CLUS proteins have comparable importance for the description of the first component and thus responsible for influencing the clustering.

**Conclusion:** Our results indicate that mode of delivery influences protein content in human colostrum. Further studies should be done in order to quantify a bigger group of minor proteins and correlate its content with milk microbiome.

**Disclosure of Interest:** None Declared
THE IMPACT OF CASEIN AND WHEY PROTEINS ON GUT MICROBIOTA DURING CATCH UP GROWTH

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Objectives and Study: Recent studies have shown that gut microbiota is associated with certain diseases. Milk oligosaccharides were shown to affect the composition of gut microbiota, increasing the abundance of *Clostridium* (*Firmicutes* phylum), that produce butyrate and other short chain fatty acid. Objectives: As milk is an important stimulator of growth, and as infant’s formula and human milk differ in their protein composition we examined if milk proteins affect the composition of gut microbiota during nutritional induced catch up (CU) growth.

Methods: Young Sprague Dawley rats were either allowed free access to food (control group; AL) or subjected to 40% food restriction for 36 days. Following the restriction period, one group was kept restricted (RES), the other three groups were re-fed with no restriction for additional 24 days with the following diets: 1- regular rat chow containing only proteins from grains (CU); 2- Chow in which the sole source of protein was cow’s casein (Cas) or 3- cow’s whey (Whey).

Results: The average body weight of all re-fed animals was significantly lower compared to the AL group and higher than the RES group. Bioinformatics analysis of fecal microbiota showed that the ratio between the main bacterial phyla (*Firmicutes* and *Bacteroidetes*) was significantly higher in the AL compared to the RES group. Interestingly, re-feeding with the normal chow increased the ratio similar to that of the AL group. Specifically, we found a significant increase in the AL and CU groups in the level of the families *Clostridiaceae* and *Lactobacillaceae* (*Firmicutes* phylum), both short chain fatty acid-producing microbiota. On the other hand, there was a significant decrease in the *Bacteroidaceae* family (*Bacteroidetes phylum*) compared the RES group. Although bioinformatics analysis showed that the gut microbiome of the Whey and Cas groups were clustered together and was significantly different from chow fed animals, indicating the significant effect of protein source (plant vs animal), the whey formulated diet resulted in significant increase in the *Bacteroidaceae* family (*Bacteroidetes phylum*) as well as *Lactobacillaceae* family (*Firmicutes phylum*) and decreased *Prevotellaceae* family (*Bacteroidetes phylum*) (a changes reported to be enriched in obese individuals) compared to Cas group. This may be associated with the fact that animals in the Whey group showed a significantly reduced body weight gain compared to the CU and Cas groups.
Conclusion: These results indicate that the quantity of the food and the protein identity affect gut microbiota, even when using adequate amounts of high quality proteins.

Disclosure of Interest: None Declared
DESATURASE INDICES FOR SATURATED FATTY ACIDS SUGGEST LOWER ACTIVITY THAN FOR ELONGASES IN THE PREMATURE INFANTS NEONATALLY.

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1 Dept of Biosciences and nutrition, Karolinska Institutet, Stockholm, 2 Borås Children Hospital, South Älvsborg’s Hospital, 3 Borås Children Hospital, South Älvsborg’s Hospital, Borås, Sweden

Objectives and Study: Long-chain monounsaturated fatty acids are of importance for myelination, rapidly developing in late gestation up to 2 yrs of age. Donor human milk has low concentration of long saturated and monounsaturated fatty acids compared to premature milk (PLEFA 2012) and the concentrations in formula is low. We investigated premature infants from birth to 1 month corrected age and their developmental pattern of nervonic (NA, 24:1w9), lignoceric (LiA, 24:0) and oleic (OA, 18:1w7/9) acids, all synthesized from stearic acid (SA, 18:0).

Methods: Forty-five infants born after 29-36 w gestation (57% late premature) were examined at 1 week and at time of expected birth (40 weeks) and 1 m corrected age (44 weeks) for fatty acid pattern in plasma phospholipids and in breast milk at 1 w. Fatty acid pattern was determined with GLC and extensive data of the cohort has been reported (Lipid Health Dis 2009).

Results: NA decreased from 1 w to 1 m corrected age, but LiA and OA did not change significantly. SA increased markedly to 40 weeks. Similarly the ratio NA/OA, NA/LiA and NA/SA decreased. There was a strong correlation between NA and OA (r=0.43, p=0.006) and NA and LiA (r=0.74, p<0.001) at 1 w but at 1 m the correlation between NA and OA had changed (r=-0.49, p=0.001) but was still positive between NA and LiA (r=0.40, p=0.007). Similar results were shown for the ratios. The steaeryl-CoA-desaturase (SCD) index determined by the ratio OA/SA and palmitoleic/palmitic (16:1/16:0) acids decreased but elongase index (SA/PA) increased during the same time. Arachidonic acid and docosahexaenoic acid, known to inhibit SCD, were strongly negatively correlated to OA. The decreasing SCD indices suggest that the changed correlation between NA and OA was not due to consumption of OA. In multiple regression analyses, including all other significant correlations, the beta-coefficient for NA to LiA/SA was 0.66 (1w) and 0.69 (40 w) (p<0.000) explaining 43-48% of the variability of NA, but at 1 m corresponding value was 0.53 (p<0.000) including the OA/SA ratio with beta-coefficient -0.52, together explaining 34% of the variability of the NA concentration. The data suggest that NA might develop from LiA and not from OA as expected.

Conclusion: Our analyses of the early pattern of long chain saturated and monounsaturated fatty acids important for myelination suggest that NA might be synthesized from LiA by desaturation and not exclusively from OA as expected. This result might be related to the high levels of LCPUFA neonatally interfering with SCD, and may be exclusively to ascertain the early development of white matter.
Disclosure of Interest: None Declared
CONSUMPTION OF DIET CONTAINING A PREBIOTIC BLEND AND BIOACTIVE WHEY PROTEIN FRACTIONS INCREASED DENDRITIC SPINE DENSITY OF RAT HIPPOCAMPAL NEURONS

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Objectives and Study: Research increasingly demonstrates the important role specific dietary factors have on certain aspects of brain function. In general neuroscience research, cognitive benefits have been shown to result from interventions that modulate dendritic spine density in medial prefrontal cortex (mPFC) or dentate gyrus (DG) of animals. However, it is presently unknown to what extent early dietary interventions can alter the dendritic spine profile of animals. The aim of this study was to determine if a diet containing a prebiotic blend of polydextrose and galactooligosaccharides with bioactive whey protein fractions (TEST) alters dendritic spine morphology compared to a control (CONT) diet.

Methods: Weanling Long Evans rats received CONT or TEST diets for 40 days. Brains were perfused, sectioned, and target neurons labeled using ballistic dye labeling. Individual spines were measured on medial prefrontal cortex (mPFC) and hippocampal dentate gyrus (DG) neurons manually for head diameter, length, and neck diameter using the Afraxis ESP platform.

Results: While total spine density did not differ between diets on mPFC neurons, TEST diet produced a significant increase in total dendritic spines in DG neurons in the hippocampus. Similar changes in spine density have been reported in association with cognitive benefits from environmental enrichment and exercise in rodents. In-depth analysis further revealed that the increase in spine density was largely driven by increases in the immature-type spine phenotypes, including filopodia-like spines.

Conclusion: The present results demonstrate that providing rodents with a diet containing prebiotic blend and bioactive whey protein fractions early in life modulates dendritic spine density in hippocampal dentate gyrus. Further research is warranted to determine if functional effects produced by TEST diet are associated with DG-related functions of the hippocampus.

3P- PRESCHOOL PREVENTION PROGRAM: A MODEL FOR AN EARLY OBESITY PREVENTION

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Objectives and Study: Pediatric overweight (OW)/obesity (OB) is a major public health problem, highly recalcitrant to late prevention and therapies. We performed a controlled and measurable study to test a pilot university-municipality agreed obesity preventive multi-compartment intervention, promoting knowledge and preferences about Mediterranean Diet (MD) and healthy physical activity in 3-6 y.o. preschoolers children.

Methods: 115 Italian preschoolers allocated into an intervention (n=80) and a control group (n=35), were physically characterized. Family questionnaires on obesogenic risk factors (KidMed, MedDiet, Neophobia scores), photo-panels based game-interviews on children knowledge/preferences, coloring/(in)formative depliants focusing on MD and healthy physical activities, seminars, plain-yogurts & fresh fruits snackings, and daily physical activity sessions under professional Italian National Olympic Committee expert supervision. Controls were exposed only to anthropometrics, family questionnaires, and game-interviews.

Results: OW/OB prevalence was 36.6% (18.3% OW; 18.3% OB). Visceral adiposity (Waist-to-Height ratio >1SD) was already present in OW/OB (64%) and also in Normal Weight (NW) (26%). Blood pressure correlated with anthropometric measurements (r=0.4;p<0.05) and its mean percentiles were higher in OW/OB than in NW (p<0.001). Parents’ low schooling (r=-0.3; p<0.01), younger age (r=-0.3; p<0.01), higher BMI (r=0.2; p<0.05), body weight misperception (r=0.7; p<0.001), and preschoolers’ high screen-time (r=0.2; p=0.03), car-time (r=0.3; p<0.05), birth weight (r=0.5; p<0.05), portion sizes (r=0.4; p<0.005), and low MD adherence (r=-0.4; p<0.05) correlated with children body weight. At a 7-month follow-up evaluation anthropometric values did not change in both groups, but the intervention group showed significantly improved healthy foods and physical-activities knowledge/preferences (p<0.001), along with increased not-sedentary activities (p<0.05) and variety of vegetables consumed (p<0.05), reduced food-neophobia (p<0.05) and sweetened beverages intake (p<0.05). Control group on the contrary showed an even higher screen-time (p<0.05).

Conclusion: Obesity and its related metabolic complications start already during preschool age. An early multi-compartment prevention program involving preschoolers, parents, teachers and institutions appears to improve eating and lifestyle habits and warrants larger and further appraisal.

Disclosure of Interest: None Declared
THE POSSIBILITY OF CREATING THE FIRST HUMAN MILK BANK IN RUSSIA. PUBLIC OPINION POLL

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Objectives and Study: Mother’s own milk is the best form of nutrition for all neonates including preterm infants. When mother’s own milk it is not available or not sufficient, donor human milk is a valid alternative. Abundant evidence has confirmed substantial benefits of the use of donor human milk not only for preterm infants but for infants with severe digestive, renal or allergic disease. The aim of our study was to analyze the public opinion regarding the possibility and the need of creating the first human milk bank in Russia. 91 participants were included in our study, which were devoted into three groups: mothers (n=31), fathers (n=30), healthcare professionals (physicians and nurses, n=30). The average age of the participants was 31±10 y (mothers), 35±15 y (fathers), 43±19 y (healthcare professionals).

Methods: The method of polling was used in the study. All women were asked to fill in the questionnaire containing 17 questions. To analyze the results, the statistical program SPSS Statistics 19.0 (SPSS Inc., USA) was used.

Results: 80% of healthcare professionals, 60% of fathers and 41.9% of mothers think that donor milk is useful for infants when mother’s milk is not available. Only 38.7% of mothers, 30% of fathers and 47% of healthcare professionals are ready to use donor milk for their own children if mother’s own milk is not available. Only one third of parents and 46.7% of healthcare professionals believe that donor milk is safe. Almost one third of all respondents do not believe that donor milk is safe. Our study showed that if the respondents were confident in safety of donor milk most of them (67%) would use it in feeding their own children. The majority of participants (67%) believes that breast milk preserves its unique properties after pasteurization. Healthcare professionals were more informed regarding the question of whether they heard about human milk banks or not: 76.7% of healthcare professionals and only 32.3% of mothers and 26.7% of fathers answered this question in the affirmative. Half of all respondents think that it is necessary to create the donor milk bank in Russia. Moreover, the proportion of those who believes it is necessary to create this bank is higher among those who have heard about donor milk banks (70.7% vs. 34% respectively). Also our investigation showed that 77% of mothers are ready to become a donor of breast milk and 77% of fathers would advise their wives to become a donor of breast milk in case of surplus amount of it.

Conclusion: Our study revealed low public awareness of usefulness and safety of donor milk. To promote the donation of breast milk in Russia comprehensive measures that raise public awareness of donor milk should be taken.

Disclosure of Interest: None Declared
ANALYSES OF THE HUMAN MILK PEPTIDOME BY NANO-ESI-LC-MS AND MALDI-MS UTILISING DIFFERENT EXTRACTION STRATEGIES

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Objectives and Study: It is known that peptides in human milk have various important biological functions and thus contribute to the benefits of human milk [1, 2]. These endogenous peptides show a wide diversity much lower concentration compared to carbohydrates, lipids or proteins. To gain a deeper insight into the human milk peptidome mass spectrometry is the most promising analytical approach if combined with more suitable peptide extractions procedures prior MS.

Methods: We qualitatively compared, modified and combined known sample clean-up techniques like centrifugation, ultra-filtration (UF) [2], TCA precipitation, liquid-liquid extraction (LLE) [3] and solid phase extraction (SPE). That involves sample preparation protocols, including removal of lipids, carbohydrate and proteins as well as enrichment of native peptides. These protocols were adapted to the different demands of two complementary MS systems (MALDI- and nano-ESI-LC-MS).

Results: We show that, SPE is still necessary as the final step in all tested sample preparation protocols in order to eliminate carbohydrates and to enrich for peptides. In the case of MALDI-MS, ultra-filtration (UF) seems to be the most advantageous method, yet easiest clean-up strategy for higher mass peptides (m/z 2000-6000). A liquid-liquid-peptide extraction according to Wessel & Fluegge [3] yields promising results but also some residual human milk proteins are co-extracted. Nevertheless, both approaches are a considerable improvement compared to other attempts. In contrast, defatting by centrifugation and subsequent TCA protein precipitation is preferred for the lower working mass range (m/z 300-2000) as typically employed in ESI-MS.

Conclusion: Taken together, the improved strategies described above are suitable to facilitate either nano-ESI- or MALDI-LC-MS-analysis of the human milk. By combining the two approaches we achieved deeper insights into the diversity of native human milk peptides covering a mass-range between 200-6000 Da. The established methods will be used to identify functional endogenous human milk peptides e.g. in human milk specimen from clinical observation studies or in physiological assays.

WHOSE CRITERIA FOR EXCLUSIVE BREASTFEEDING: INFORMATION AND REALITY
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Objectives and Study: to obtain the prevalence of breastfeeding and exclusive breastfeeding until 6 months of life. Assess the knowledge of mothers about the benefits of breastfeeding and exclusive until 6 months; assess the impact of information in relation to the desire to breastfeed and the reasons for WHO recommendations failure.

Methods: Questionnaires were applied to the recent given birth women in a tertiary Hospital maternity, divided into case-group (providing information about breastfeeding advantages/recommendation of exclusive breastfeeding up to 6 months) and control-group (not informed by the authors). At 6 months of age, implementation of telephone questionnaire about continuity, or not, and if exclusive breastfeeding. For statistical analyses were used frequency tables and McNemar test.

Results: Answer to the questionnaire 242 mothers, 239 had intended to breastfeed, 54.0% of which exclusively until 6 months. In the 2nd survey, of 192 responded mothers, 63.5% were breastfeeding. Exclusively until 6 months, 35.4%. In case-group, 56.7% of respondents planned to breastfeed exclusively until 6 months and 39.2% did so; control group 50.5% planned it and 31.6% did so. In case-group 89.7% say they intend to breastfeeding in the next son and in control group 52.6%, p <0.001. Of the 54 mothers who did not breastfeed exclusively, 46.3% was invoked labor laws as the reason for diversification and 36.0% professional advice. The reason given to abandon breastfeeding was “agalactia” in 78.6%.

Conclusion: There were statistically significant differences in behavioral intention, but not in attitude, between the case group and the control group, after information. The labor law was the reason to give age not recommended diversification in most surveyed. Complied with the recommendations 1 in 3 infants. This is a prevalence near to the best results in the world, but still a minority of infants.

Disclosure of Interest: None Declared
INFLUENCE OF SPORTS IN THE NUTRITIONAL STATUS, OXIDATIVE STRESS AND NEUROTHROPHIC FACTORS OF CHILDREN

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Objectives and Study: Beneficial effects of physical exercise are well known. However, exercise can lead to alterations in oxidative balance in animals and adults. Few studies have been conducted in children on this topic. Improvement in memory and cognition is described in trained children but the mechanism is not clear. BDNF (Brain Derived Neurothrophic Factor) and IGF-1 (Insulin Growth Factor) are neurotrophic proteins which increase with exercise and could be considered as mediators of this effect. Our objective was to evaluate the effect of competitive sport in nutritional status, oxidative stress and peripheral levels of neurotrophic factors in children.

Methods: A team of cyclists (n=39), aged 13.2 ± 1.6 was studied, before training and competition season (preseason) and in the middle of the competition (season). They were compared with a matched control (n=27) group in age (13.2 ± 2.2) and sex. This group only did the school exercise. We determined clinical and anthropometric assessment, dietary intake, oxidative stress parameters (malondialdehyde (MDA), oxidized proteins and the glutathione ratio) and plasma BDNF and IGF-1 levels.

Results: Both groups were well nourished. Body mass index, arm circumference, triceps and subscapular skinfold were higher in controls than in cyclists at preseason, and even higher compared to cyclist in season period (p>0.05). All the groups consumed less percentage of carbohydrates, fibre and vitamins D and E, and consumed higher percentage of protein and fat than recommended. MDA levels were significantly lower in controls compared to cyclists in preseason (p<0.05). But cyclists in preseason reached values significantly higher compared to cyclists in season (p<0.05). The trend of oxidized proteins and GSSH/GSH was similar to MDA in the sportive children. At baseline, these showed the higher values of BDNF, with statistically significant differences with the other groups. The IGF-1 values followed the same trend. However, during season, cyclists suffered significant decrease in the both levels.

Conclusion: Sportive children exhibit anthropometric parameters and body composition more suitable than sedentary children. Regulated exercise is an antioxidant itself. However, during no controlled exercise, we found an increase in oxidative stress parameters. Cyclists have levels of BDNF and IGF-1 significantly higher than their sedentary peers, which could justify the better school performance described in the literature in trained children. Our results emphasize the impact of exercise in the childhood, a time of intellectual and psychological development of great significance. However both the duration and intensity of exercise should be considered.
Disclosure of Interest: None Declared
THE IMPACT OF PAEDIATRIC HOME PARENTERAL NUTRITION (HPN) SERVICE ON THE
CLINICAL OUTCOME AND HEALTH CARE COSTS IN QATAR

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Objectives and Study: Total Parenteral Nutrition (TPN) is used to preserve life and growth when oral/enteral nutrition cannot provide protein-energy needs. When a child does not require hospitalization but depends on long-term PN, HPN is the best option for improving the quality of life of those children and their families within the constraints of the disease (Koletzko et al, 2005). Before starting HPN in Qatar, children with intestinal failure (IF) were kept as in-patients to receive TPN until either their bowel recovered or they underwent intestinal transplantation. This was associated with a high rate of morbidity and mortality. In the developed countries, private Homecare companies usually run the HPN service. Since there were no such private companies available in Qatar, an innovative approach had to be developed to allow the provision of such service.

Objectives:
1. To describe how HPN service was developed in Qatar
2. To describe the impact of HPN service on the patients and the health service in Qatar

Methods: This is a retrospective study done at Hamad Medical Corporation (HMC) in Qatar. The medical files of all the pediatric patients who needed TPN for more than 3 months between 2007 – October 2014 were reviewed to find out the impact before and after introduction of HPN service.

Results: 10/11 (91%) long-term TPN patients were successfully discharged on HPN. Significant reduction in the rate of CVL sepsis was demonstrated in 9/10 (90%). In the 4 years period prior to starting HPN, 14/14 (100%) patients traveled abroad for intestinal rehabilitation and/or transplant assessment; 5 of them (36%) underwent intestinal transplantation. Post-HPN service, no patient (0%) traveled abroad or had intestinal transplantation done (p < 0.0001). Before HPN, 4/14 (28%) patients passed away compared to 2/10 (20%) post-HPN.

Cost comparison

<table>
<thead>
<tr>
<th></th>
<th>Cost</th>
<th>Comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isolated intestinal transplant</td>
<td>$1,206,800.00</td>
<td>Average stay 3 yrs</td>
</tr>
<tr>
<td>Living cost in USA</td>
<td>$11,000/month</td>
<td>average stay is 6 months if no transplantation done</td>
</tr>
<tr>
<td>Clinic visit in USA</td>
<td>$1200/visit</td>
<td>1-2 visits/month</td>
</tr>
<tr>
<td>Receiving PN in hospital in Qatar</td>
<td>$1200/day</td>
<td></td>
</tr>
<tr>
<td>Receiving HPN in Qatar</td>
<td>$400/day</td>
<td></td>
</tr>
</tbody>
</table>
**Conclusion:** HPN service in Qatar has proved to be successful and cost-effective. It proves that, even in a small country, it is possible to establish and run a successful HPN service using the local resources available.


**Disclosure of Interest:** None Declared
INFLUENCE OF THE MOTHERS’ DIET AND BREASTFEEDING ON THE SWEET FOOD PREFERENCES OF THEIR CHILDREN AT 3.5 YEARS

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Objectives and Study: A series of breastmilk flavours are transmitting from the amniotic fluid to the foetus, these could influence the later food preferences of their children. To analyse the associations between the mothers’ intake at pregnancy and at 6 months postpartum, with the intake of their children at 3.5y, according to the feeding type at 3 months of life.

Methods: The study was performed in a selected group of mother-child pairs (n:49) participating in the PREOBE study (www.proyectopreobe.com www.ClinicalTrials.gov NCT01634464). Mothers’ dietary assessment was performed by a food frequency questionnaire (FFQ) at 24 weeks of pregnancy and 24 weeks postpartum; the nutrient intake was analysed according to the dietary recommendations for pregnant women of the United States Department of Agriculture. In the same way, dietary assessment in their children at 3.5y was performed using a 3-days food diary and was analysed using the DIAL software for assessing diets and food calculations. ANOVA test, non-parametric tests and multiple linear regression models were applied for data analysis using SPSS vs 21.0. The percentage of total energy value (%TEV) from sugar in children’s diet was considered the dependent variable, and sugar intake by mothers during pregnancy and postpartum plus the infant feeding type at 3 months of life were considered as independent variables.

Results: At 3.5y, the children born to mothers that ate more sugars during pregnancy and postpartum period, which received breastfeeding or mixed-breastfeeding at 3 months of age, had a higher %TEV intake from sugar [3.3 (3.4)] than those children who received infant formula feeding [0.3 (1.3)] (R²=0.227; b=2.052; P=0.043).

Conclusion: Mothers’ intake during pregnancy and postpartum, and infant feeding type at 3 months of age, seems to be related to the sweet food preference during childhood at 3.5y. These results could be explained because infant feeding type at 3 months of age would have certain influence in the taste receptors development. The exposure to breastmilk during the first months of life seems to increase the preference for sweet foods at 3.5y as mothers’ intake of sugars are higher, probably determining a sweeter breast milk respect to infant formula. This study has been supported by the Andalusian
Objectives and Study: Malnutrition at an early age can result in severe consequences such as short stature, delayed cognitive development and impaired immunity. Impaired immunity leads to increased risk of infections which can further reduce food intake and deteriorate nutritional status. The aim of this study was to analyze the impact of nutritional status on the incidence of nosocomial infections in children hospitalized at a pediatric tertiary medical center.

Methods: This was a prospective cohort study which included children hospitalized at four Pediatric Departments (Gastroenterology, Neurology, Pulmology and Nephrology) during a period of 12 months. In all children standardized anthropometry was performed within the first 24 hours after admission and on hospital discharge. Malnutrition was defined as the Body Mass Index (BMI) and weight for height of <−2 standard deviation scores (SDS, WHO reference). Malnourished children were compared to non-malnourished patients in relation to: weight change during hospital stay, frequency of nosocomial infections and length of hospital stay (LOS).

Results: During a period of one year altogether 365 of children were included into the study (male: 171 / 46.8%); mean age 7.26 years, (range: 1 m-18 y). At hospital admission overall 50 patients (13.7%) were malnourished; moderate malnutrition (BMI −2 to −3 SDS) was present in 29 (7.9%) patients and severe malnutrition (BMI <−3 SDS) in 21 (5.7%) patients. In respect to the weight change during the hospital stay, at the time of discharge significantly lower number of children were severely malnourished (decrease from 5.7% to 2.7%, p<0.001). Altogether 21 child (5.7%) experienced nosocomial infection; malnourished children acquired nosocomial infections significantly more often in comparison to other patients (8/50 vs 13/315, p=0.001). Lastly, the LOS was significantly longer in children who were malnourished (10.5 vs. 8.3 days, respectively; p =0.04). Binary logistic regression showed that odds of acquiring nosocomial infections was 3.9 times higher (OR 95% CI 1.398-10.869) in children who were malnourished, moreover, risk increased with prolonged hospital stay (OR 1.176; 95% CI 1.087-1.273).

Conclusion: Paediatric patients who were malnourished on admission had significantly prolonged LOS and increased risk of acquiring nosocomial infections.

Disclosure of Interest: None Declared
**Nutrition**

*Clinical Nutrition*

PO-N-0387

**DETECTING UNDER-NUTRITION ON HOSPITAL ADMISSION - SCREENING TOOL VERSUS WHO CRITERIA**

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1 Zagreb School of Medicine, 2 University Hospital Centre Zagreb, Zagreb, Croatia

**Objectives and Study:** The purpose of this study is to describe the current prevalence of malnutrition on hospital admission to a paediatric gastroenterology hospital unit and compare the value and feasibility of Screening Tool Risk on Nutritional status and Growth (*STRONGkids*) scoring system versus anthropometric WHO criteria in identifying children at risk of developing malnutrition during hospital stay.

**Methods:** Prospective observational study. A total of 124 children (age 0.08-17.91 yrs; median 10.35 yrs, 67 male) were evaluated on admission to the Division of Paediatric Gastroenterology, University Hospital Centre Zagreb in the period January-April in 2013 and in 2014. The *STRONGkids* based on 4 items: (1) subjective clinical assessment, (2) high risk disease, (3) nutritional intake, (4) weight loss was applied and measurements of weight and length were performed. Main outcome measures: *STRONGkids* score 1-3 and 4-5 indicated moderate and high risk for malnutrition, respectively. SD-scores < -2 BMI and height-for-age were considered to indicate acute and chronic malnutrition respectively. SD scores between -1 -2 were considered to indicate borderline under-nutrition. Data analysis: descriptive statistics, Kruskal-Wallis (KW) test, Fisher’s exact (FE) test.

**Results:** Anthropometry indentified 18.5% acutely and/or chronically malnourished children on admission and altogether 50/124 patients with nutritional risk (malnourished and borderline nourished). *STRONGkids* identified considerably more children prone to developing malnutrition: 94/124 (80 moderate, 14 high risk). The *STRONG* scoring system was in accordance with anthropometric measurements: a significant difference in BMI values among patients distributed in 3 *STRONGkids* risk groups was observed (KW test, CHI² = 62.7; p<0.0001). Median duration of hospitalisation was 6.5 days (2-64 days). Children with higher risk for malnutrition stayed longer in hospital (KW test, CHI² 19.05; p < 0.0001). Patients that lost weight during hospitalisation (33.1%) were further analysed: 8/41 were not detected to be at risk by either method, 11/41 were identified by *STRONGkids* and anthropometry, and 22/41 were detected only by *STRONGkids* (Fisher's exact test p=0,08).

**Conclusion:** This study confirmed the serious issue of malnutrition among children hospitalized due to gastroenterological diseases. *STRONGkids* was superior to anthropometry in recognizing in-patients prone to developing malnutrition. Using this tool, a significant relationship was found between having a “high risk” score, a negative SD-score in BMI and a prolonged hospital stay. The results support routine nutritional screening in order to forestall hospital-acquired malnutrition.

**References:** *Clin Nutr 2010 ;29:106-11.*
Disclosure of Interest: None Declared
NUTRIENT AND ENERGY INTAKES VARY DEPENDING ON THE PREDOMINANT TYPE OF MILK FED TO CHILDREN AGED 12-18 MONTHS IN THE UNITED KINGDOM: SECONDARY ANALYSIS OF DATA FROM THE DIET AND NUTRITION SURVEY OF INFANTS AND YOUNG CHILDREN (DNSIYC)

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Objectives and Study: Good nutrition in the early years of life is important as this is a period of rapid growth and development. Since milk is a major food for infants and young children, this study evaluated the impact of the type of milk fed on nutrient intake and status.

Methods: Data from the UK-based Diet and Nutrition Survey of Infants and Young Children were used to investigate the intakes of key nutrients, and iron and vitamin D status, of children aged 12–18 months who were not breastfed, and were either consuming >400ml/d whole cow's milk (n=404) or >400ml/d of fortified milk (including follow-on milk and growing up milk; n=139). Haemoglobin and/or serum ferritin, and serum 25(OH) D concentrations were available for about 20% of children. Unpaired Mann-Whitney tests were conducted to compare nutrient intakes (assessed using a 4-day food and drink diary) and serum markers between consumers of fortified and cow's milk. To compare average intakes between the two milk consumer groups all statistical tests used weightings to account for the fact that the participants in the sample data may represent unequal proportions of participants in the total population.

Results: Mean daily intakes of iron, zinc, vitamin A and vitamin D were significantly higher in the fortified milk group. Mean daily intakes of energy, protein and calcium were significantly higher in the cow's milk group. Haemoglobin was not significantly different between groups, but the fortified milk group had significantly higher serum ferritin (p=0.049) and serum 25(OH) D (p=0.014).

Table 1. Weighted daily mean intakes of nutrients for fortified milk (>400ml/d) and cow's milk (>400ml/d) consumers.

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Fortified Milk Consumers: Weighted Mean Intake</th>
<th>Cow's Milk Consumers: Weighted Mean Intake</th>
<th>Unpaired Mann-Whitney test p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy kcal/d</td>
<td>983</td>
<td>1046</td>
<td>0.00182</td>
</tr>
<tr>
<td>Protein g/d</td>
<td>33.8</td>
<td>44.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Calcium mg/d</td>
<td>795</td>
<td>996</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Iron mg/d</td>
<td>10.4</td>
<td>5.1</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Zinc mg/d</td>
<td>7.3</td>
<td>5.4</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td></td>
<td>Vitamin A μg/d</td>
<td>Vitamin D μg/d</td>
<td></td>
</tr>
<tr>
<td>---------------------</td>
<td>---------------</td>
<td>---------------</td>
<td>-----</td>
</tr>
<tr>
<td>Consumption of milk</td>
<td>992</td>
<td>669</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Whole cow's milk</td>
<td>10.5</td>
<td>1.9</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

**Conclusion:** This analysis demonstrates significantly different intakes and status between infants consuming fortified milk versus those consuming whole cow's milk. Given the insufficiency of vitamin D and iron in particular in UK young children's diets, these results should be considered by those responsible for ensuring adequate nutrient intakes of young children.

**Disclosure of Interest:** A. Sidnell Conflict with: Employed by Nestle Nutrition, S. Pigat Conflict with: Consultancy service provided., R. O'Connor Conflict with: Consultancy service provided., A. Connolly Conflict with: Consultancy service provided., A. Stephen Conflict with: Consultancy service provided.
Nutrition
Clinical Nutrition
PO-N-0389
LOW IRON INTAKE AND IRON STATUS OF 6- AND 12- MONTHS OLD POLISH INFANTS ARE LINKED WITH MILK FEEDING PRACTICES
Anna Stolarczyk 1 Fanny Krumholz 2 Simone R.B.M Eussen 2 Katarzyna Szott 1 Aldona Wierzbicka 3 Piotr Socha 1
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Objectives and Study: Iron intake and status have been assessed in only a few European studies, most of which have not been performed on a randomly selected sample of the population. Our objective was to assess the iron intake, iron status and prevalence of iron deficiency in a representative sample of 6- and 12-month old infants from Poland. In addition, we aimed to determine the impact of the milk feeding practices on iron intake and status.

Methods: Cross-sectional study of iron intake and status from a randomly selected sample of 6- and 12-month old Polish infants (ID numbers selected proportionally to the number of residents and degree of urbanisation, n=317). Nutrient intake was assessed based on a 24h food record. Iron status was measured by serum ferritin (SF) and haemoglobin (Hb) concentrations. Iron deficiency was defined as SF<12 ug/L, and iron deficiency anaemia was defined as iron deficiency combined with Hb<11 g/dL. Iron intake results are given as mean ± SD mg/d.

Results: The iron intake of our infant population (5.9 ± 3.0 mg/d) was below the Polish Estimated Average Requirements (EAR) of 7 mg/d. A total of 68% of the 6-month old and 56% of the 12-month old infants had intakes below the EAR. Of all infants, 11% were iron depleted and 5% had iron deficiency anaemia. Although breastfed infants had a low estimated mean iron intake (3.2 ± 2.0 mg/d), they did not show higher incidence of iron deficiency nor anaemia than non-breastfed infants. However, infants consuming cow’s milk had low iron intake (2.5 ± 1.3 mg/d) and showed higher incidence of iron deficiency than non-cow’s milk consumers (30% versus 9%, p<0.01).

Conclusion: More than half of the Polish infants had lower iron intake than the EAR. Breastfeeding provides a high bioavailable and most optimal source of iron to the infants, which contributes to healthy iron status. In non-breastfed infants, the type of milk consumed highly influenced the iron intake and status. Overall, we confirmed that appropriate milk and complementary feeding during the first year of life is of major importance to maintain a healthy iron status in Polish infants aged 6 and 12 months.

Disclosure of Interest: A. Stolarczyk: None Declared, F. Krumholz Conflict with: Danone Nutricia Research, S. R. Eussen Conflict with: Danone Nutricia Research, K. Szott: None Declared, A. Wierzbicka: None Declared, P. Socha: None Declared
Objectives and Study: Parenteral Nutrition (PN) has been used in paediatric practice for more than forty years and is given to children with a non functioning gut or to those who cannot meet their nutritional requirements with enteral feeds alone. Although a well established technique PN is by far no panacea and the risk of potentially fatal complications should be balanced against the true benefit of the patient. The aim of this study was to establish if the indications for PN prescribing in a large tertiary referral children’s hospital were appropriate and to compare the results to those published by the National Confidential Enquiry into patient outcome and death (NCEPOD) in 2010 (1).

Methods: All children and newborns receiving inpatient PN between October 2013 and March 2014 were entered into the study. Data was collected prospectively from PN prescriptions issued by the hospital pharmacy, case notes and dietetic records. The appropriate indications for the use of PN was based on the 2005 guidelines by the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) (2)

Results: A total of 303 children (67 newborns) were identified. The median age at the start of PN was 38 months (range from 0 to 223). Patients were referred from various departments across the hospital including medical specialities (34 %), surgery (35%) and intensive care (31%). The mean duration of PN was 18 days (1-160 days). Indications for PN prescribing were critical illness (66/303), pre and post surgery nutritional support (63/303) and bone marrow transplantation (28/303). The ESPGHAN recommendations for the use of PN were followed in 91.7 % of cases (95.5 % of newborns, 90.8 % children). Our results were similar to those reported by NCEPOD ( 92.4 % newborns, 88.6 % children). PN was considered inappropriate in 12/303 patients and equivocal in 13/303.

Conclusion: Although the indications for inpatient PN in children is mostly justified, there is still a proportion of patients who is receiving PN unnecessarily. Our results are similar to those published by the NCEPOD audit and highlight the need for more PN training and better access to nutritional support teams.

References: 1. NCEPOD report on parenteral nutrition: A mixed bag:
http://www.ncepod.org.uk/2010pn.htm
Disclosure of Interest: None Declared
IRON STATUS OF VEGETARIAN INFANTS AND CHILDREN COMPARED WITH OMNIVORES - SYSTEMATIC REVIEW OF LITERATURE AND META-ANALYSIS

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Objectives and Study: For the last two decades we are observing an increased interest in vegetarian diets worldwide. Concerns are raised with respect to vegetarian infants and children, pointing towards an increased risk of nutritional deficiencies, especially with regard to iron. The aim of the study was to evaluate the risk of developing iron deficiency anaemia among infants and children on vegetarian diets compared with omnivores.

Methods: We included observational and intervention studies assessing the prevalence of iron deficiency anaemia among healthy vegetarian infants and children compared with those on traditional diets. We performed a literature search of trials using MEDLINE, EMBASE, CENTRAL and EBSCO published through April 2014 in English or Polish language. Additional papers were identified through reference lists of the included articles and position statements of dietetic and paediatric associations. Vegetarian diet was defined as one that completely excludes meat or fish. We included studies where subjects were following vegetarian diet for at least 6 months.

Results: Out of all retrieved references only 6 studies matched the inclusion criteria, whereas 5 had enough data for meta-analysis. Studies regarding macrobiotic or semivegetarian diets, without control group or with invalid definition of vegetarian diet where excluded. Overall 311 participants (185 vegetarians vs. 126 omnivores) aged 6mo.-18yrs. from 6 different countries were evaluated. Out of 6 studies, 2 were conducted among vegans. Both qualitative analysis and meta-analysis reported no statistically significant differences (p>0.5) with respect to developing iron deficiency anaemia between vegetarian and omnivorous children (RR: 1.16; 95% CI: 0.74:1.82).

Conclusion: Although the study was conducted in an evidence-based manner and suggests no increased risk of developing iron deficiency anaemia, the count of subjects is too small to give a definitive conclusions. The findings may act as a helpful tool for planning further research.

Disclosure of Interest: None Declared
**Objectives and Study:** In critically ill children hospitalized in pediatric intensive care, an optimal nutrition support, and particularly an adequate energy and protein intake, is associated with improved outcomes. However, both the prescription of nutrition support and its administration are complex and limited by several barriers. The aims of this pilot study were to determine the amount of nutrition prescribed and delivered to critically ill children in comparison with their requirements.

**Methods:** In this prospective pilot study, critically ill children hospitalized for >24 hours in pediatric intensive care unit and without oral nutritional intake at admission were consecutively included. The amount of energy and protein that were prescribed and delivered were recorded daily until the 10th day of hospitalization, discharge or death. Energy and protein requirements were calculated with the Schofield equation and the guidelines of the American Society for Parenteral and Enteral Nutrition, respectively. The ratios prescriptions/requirements and delivery/requirements were calculated daily.

**Results:** We included 64 children with a median age of 2.7 years [IQR 0.4-5.7] and a length of stay of 7 days [IQR 4-10]. Nutrition support was used in 88% of children and introduced within 22 hours [IQR 13-29] after admission. Enteral nutrition was used in 81% of patients. For the entire stay, the ratio prescriptions/requirements was 88±50% for energy and 52±39% for protein. On day 7, this ratio reached 120±56% for energy and 88±43% for protein. When looking for the ratio delivery/requirements for the entire stay, the results were 76±52% for energy and 47±35% for protein. This ratio reached 105±49% for energy and 80±37% on day 7. Younger children were more likely to have higher ratios than older children.

**Conclusion:** This pilot study shows that prescriptions and delivery of calories in critically ill children are close to their estimated requirements. In contrast, the protein requirements are far to be satisfied. The main reason is a protein prescription strongly lower than the recommendations. Older children are more at risk of not reaching their energy and protein requirements.

**Disclosure of Interest:** None Declared
AUTOANTIBODIES AGAINST APPETITE-REGULATING PEPTIDES INFLUENCE ON GHRELIN LEVEL IN SHORT CHILDREN EXPOSED TO CANDIDA ALBICANS COLONISATION AND HELICOBACTER PYLORI INFECTION.

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Objectives and Study: Peptide hormones synthesized in gastrointestinal tract (GI) in addition to neuropeptides, regulate growth and body weight in children. The GI microflora (i.e. Candida albicans – CA and Helicobacter pylori – HP) is an antigenic source. Based on the molecular mimicry hypothesis, intestinal microbe-derived antigens may trigger the production of autoantibodies cross-reacting with regulatory peptides. The aim of the study was to assess whether in short children with CA colonisation and HP infection the autoantibodies anti selected neuropeptides (Ab anti-NP) are more prevalent than in the control group.

Methods: Material and methods: The study group comprised 77 short (height below -2.0 SD), children (28 girls and 49 boys), mean age: 10.2±3.6 SD years). The control group comprised 14 children with normal height (9 girls and 5 boys), mean age: 11.9±3.8 SD years). In every child, serology to detect HP (anti-HP IgG and IgA) was performed and stool samples were cultured for CA. Among short children without CA and/or HP infections, anti-NP Abs were detected in 3 cases only (out of 35) – 8.5%, while in the control group they were not found. Moreover, the prevalence of anti-ghrelin, anti-leptin, anti-alfaMSH and anti-orexinA Ab was assessed.

Results: Results: In 42 out of 77 short children CA and/or HP infections were confirmed. In 15 of them (35.7%) anti-NP Abs were found. In 7 out of 14 children from the control group CA and/or HP infections were confirmed and in 2 of them (28.6%) anti-NP Abs were found. Among short children without CA and/or HP infections, anti-NP Abs were detected in 3 cases only (out of 35) – 8.5%, while in the control group they were not found. We found that ghrelin concentrations is significantly lower in children with Aba anti-NP.

Conclusion: In short children with C. albicans colonisation and/or H. pylori infection the incidence of antibodies against neuropeptides is elevated, which may be connected with the molecular mimicry phenomenon. It may be a reason of worse high velocity in these children due to disorders in neuropeptides activity. However, further studies are necessary to elucidate this issue.

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Disclosure of Interest: None Declared
Objectives and Study: We aimed to identify the different relationships between the infant feeding type in the first 6 months of life, total protein intake and meat intake at pre-school age.

Methods: 203 children participating in the PREOBE project (www.ClinicalTrials.gov NCT01634464) were studied in the present analysis. Feeding type was enquired to the mothers at 3 and 6 months of life in the offspring, and it was classified in 3 groups: Exclusive breastfeeding (EBF) n=90, infant formula feeding (IFF) n=45, and mixed feeding (MF) n=68, when the babies received both types of feeding. Dietary assessment in children aged 3.6±0.42 (no group differences p<0.07) was performed using 3-day food diaries, protein intake g/Kg/day and the percentage of total energy value (%TEV) from meat, were analysed using the DIAL software for assessing diets and food calculations. ANOVA test and Bonferroni post-hoc correction was performed for data analysis using IBM SPSS Statistics 21.0.

Results: It was seen that at 3 and 6 months, 44% and 17% received EBF; 22% and 52% received IFF; and 34% and 31% received MF respectively. The protein Recommended Dietary Allowance (RDA) for children between 1-3y is 1.05g/Kg/day and 4-8y is 0.95g/Kg/day. There were not statistically significant differences between the total protein intake at pre-school age (EBF 3.5±0.7; IFF 4.0±0.7 and MF 3.7±1.1g/Kg/day) and feeding type received at 3 mo (p=0.435) and 6 mo (p=0.839). However, the children who received IFF at 3 mo, showed higher %TEV intake from meat (18.9±2.2%) at 3.6y versus those who received EBF (12.5±4.1%) or MF (12.1±4.5%) (p=0.001), although this association was not demonstrated with the type of feeding received at 6 mo. Nevertheless, BMI z-score at 3.6y did not show significant differences between groups 0.62±0.75 (p=0.340).

Conclusion: This work suggests a potential protective role of human milk against the development of obesity, which could be related to the programming of taste and eating behaviour, owing to low content of protein and saturated fat. The infants born from obese women will have a higher risk to develop obesity in later ages through this eating behaviour mechanism. The intake of protein in all pre-school children was higher than the recommendations, regardless of the type of feeding received in the first 6 mo of life. The higher energy intake from meat at pre-school age seems to be related to

TRAVEL BEHAVIOUR OF CHILDREN WITH INTESTINAL FAILURE ON HOME PARENTERAL NUTRITION

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Objectives and Study: Home parenteral nutrition (HPN) is a well established practice in children with prolonged or irreversible intestinal failure (IF). Although their quality of life is considered better than in patients receiving hospital PN, normal childhood activities can be restricted. Holidays away from home have been identified as one factor contributing to physical and mental well being. We aimed to identify socio-demographic or illness-specific factors influencing travel behaviour in HPN children and their families.

Methods: A standardised questionnaire was sent to all HPN patients attending the IF clinic at Great Ormond Street Hospital London. Age, gender, underlying disease, time in months spent on HPN, daily infusion hours and concomitant enteral feeds given were documented and the frequency and mode of travelling away from home, destination, problems encountered in planning the holiday and during the actual stay recorded. Parents were asked to judge the overall experience.

Results: A total of 30/40 (75%) children consented to participate, 20/30 (66.6%) went on one or more holidays of which 5/30 (16.6%) more than one per year. Most patients travelled abroad (14/30, 70%). Spending time away from home was positively correlated with the duration in months since starting HPN (traveller: mean 58.6 months, non travellers: mean: 28.6 months, p 0.022). The daily infusion time, tolerance of enteral feeds or age of the child did not influence travelling behaviour. The majority (11/20) rated the experience of going on holiday as good, 19/20 (95%) families expressed the wish to travel again. Reasons given for deciding against going away from home were fear of possible difficulties en route and in the resort and the child’s unstable underlying medical condition. A minority had financial difficulties. The volume, size and weight of the HPN bags and the extra luggage required were the most common practical problems described.

Conclusion: The majority of our families with children on HPN chose to go on holiday. The longer the child has been on HPN the more likely it was that time was spent away from home. The experience was considered positive in most.

Disclosure of Interest: None Declared
EVALUATION OF MALNUTRITION AND METABOLIC BONE DISEASE IN CHILDREN WITH BRONCHIECTASIS

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Objectives and Study: Bronchiectasis is an important chronic suppurative pulmonary disease. Malnutrition, hipovitaminosis D and decrease in bone mineral density (BMD) are common problems in the setting of chronic inflammatory conditions. Therefore, we aimed to evaluate prevalence of malnutrition, vitamin D status and BMD in children with bronchiectasis.

Methods: In this descriptive study, we evaluated 65 children with bronchiectasis. Body weight and height z-scores, hemoglobin, calcium, phosphate, alkaline phosphatase, 25-hydroxyvitamin-D levels and bone mineral densities are measured. Patients were classified as vitamin D deficient (serum 25-hydroxyvitamin-D <20 ng/ml), insufficient (20 ng/ml-29 ng/ml) or sufficient (≥30 ng/ml). Metabolic bone disease is classified as osteopenia (BMD z-scores between -1 and -2 SDS) or osteoporosis (BMD z-scores ≤-2 SDS).

Results: We studied 39 girls (60%), 26 boys (40%), with an average age of 11.37 ± 3.69 years. Mean body weight and height z-scores were -0.34 ± 1.13 and -0.52 ± 1.30 respectively. In total, 7 (10.7%) children had short stature and 19 (29.2%) had malnutrition. The mean concentration of vitamin D in patients was 17.49 ± 6.26 ng/mL. Sixty seven percent of all patients had vitamin D deficiency, 30% had vitamin D insufficiency. Only in 3% of patients vitamin D levels were above 30 ng/ml. The mean BMD z-score was -1.18±0.91. Osteopenia and osteoporosis was documented in 40% and 17% of patients respectively. There were no differences in BMD z-scores and vitamin D levels between patients with or without malnutrition (p=0.57 and p=0.81 respectively).

Conclusion: Malnutrition, vitamin D deficiency and metabolic bone disease are common problems of children with bronchiectasis. So, we recommend not to forget to pay more attention to non-pulmonary problems of these children.

Disclosure of Interest: None Declared
USE OF BONE MINERAL DENSITOMETRY FOLLOWING ALUMINUM CHELATION IN CHILDREN ON LONG TERM PARENTERAL NUTRITION

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Objectives and Study: Patients on long term total parenteral nutrition (TPN) are at risk of Aluminum (Al) toxicity, a condition that was first demonstrated in patients on hemodialysis. Al toxicity may induce osteomalacia, encephalopathy and anemia. We aimed to study the value of bone densitometry following aluminum chelation using Desferrioxamine in children receiving long term TPN.

Methods: Saudi Arabia, were reviewed. Long term TPN was defined as being on TPN for > 3 weeks duration. The hospital pharmacy prepared all the TPN solutions from premade components that were purchased from external manufacturer. Only patients who had a bone mineral densitometry (BMD) examination were included. The files of all children on long term TPN at King Faisal Specialist Hospital & Research Center, Riyadh, were reviewed. The Z score of the lumbar spine was used as a marker of the level of bone mineral density. A measurement of the level of calcium, magnesium, phosphorus, and vitamin D were done.

Results: We had a total of 8 patients on cyclic TPN. Their diagnosis were: microvillus inclusion disease (3), tufting enteropathy (2), syndromic diarrhea (1), severe combined immunodeficiency (1), short gut syndrome (1). Only five patients had BMD examination. The other 3 were excluded. The mean age of was 108 months (6 to 13 years) with a mean TPN duration of 21 months. A mean Al level of 1.61 micro-mol/L (<0.4 micromol/L). Measurement of bone disease markers showed a mean of 2.25 mmol/l, 0.80 mmol/l, 1.48 mmol/l and 44.6 nmol/l for calcium, magnesium, phosphorus, and vitamin D respectively. The mean Z-score of the lumbar bone of the included patients was -2.2. Only 1 patient had a high Al level (Al = 4.39 micro-mol/L, Al = 0.157 micro-mol/L/Kg) and received Desferrioxamine at a dose of 4.2 mg/kg then 1 year later it was increased to 10.7 mg/kg. His BMD pre chelation showed a Z-score (of the lumber spine) = -4.2, while the post chelation BMD showed a Z-score = -3.2.

Conclusion: To our knowledge, this is the first report of the response to Desferrioxamine therapy using BMD. The improvement in the z-score of our patient supports the use of BMD as a routine method of evaluating such patients. However, a larger study is needed.

Disclosure of Interest: None Declared
SYSTEMATIC REVIEW: BODY COMPOSITION IN CHILDREN AND ADOLESCENTS WITH INFLAMMATORY BOWEL DISEASE

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Objectives and Study: Pediatric inflammatory bowel disease (IBD) is associated with chronic inflammation, weight loss, growth restriction and malnutrition, alterations in body composition reflect the end point of these processes. Bone mass deficits are well described in this population, but little is known about other body composition compartments.

The aim of this systematic review was to define the alterations in the non-bone tissue compartments in children and adolescents with IBD, and explore the effects of demographic and disease related parameters.

Methods: A systematic review of studies reporting whole body compositional changes in children and adolescents, aged ≤25 (in keeping with North American age criteria for adolescents), with either Crohn's disease or ulcerative colitis (UC) was undertaken in line with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines, protocol registration number CRD42013004180 (1). A systematic search of PubMed (www.ncbi.nlm.nih.gov/pubmed) and Web of Science databases was carried out on 23 May 2014 and 24 May 2014 respectively.

Results: 22 studies were included in this systematic review, reporting on a total of 1102 children with IBD (821 Crohn's, 201 UC), pooled mean age 14.4±3.3 years, and 38.5% female. Data were highly heterogeneous, in terms of methodology and subjects. Most studies reported body composition based on the three compartment model; lean mass, fat mass and bone mass. The commonest methodology employed was whole body dual X-ray absorptiometry, n=728. Deficits in protein related compartments were reported: lean mass deficits were documented in 93.6% of Crohn's and 47.7% of UC subjects when compared with healthy control populations. There were associations with disease activity and gender. Fat related compartment findings were inconsistent.

Conclusion: Despite the between-study heterogeneity, there is consistent evidence from the literature identified to suggest deficits in protein-related compartments (lean mass and fat free mass) are common in the paediatric IBD population. Firm conclusions cannot be reached about changes in fat components. Deficits in lean mass are associated with worse prognosis in other chronic inflammatory diseases in adults (2). Further studies are needed to identify in which tissues these deficits lie and describe fat distribution to understand what impact this has on tissue function, and disease in children with IBD.
References:


Disclosure of Interest: None Declared
Objectives and Study: Assessment of dietary intake is essential in the care of patients with inflammatory bowel disease (IBD). We aimed to study nutritional intake in children with IBD in order to evaluate the role of dietary intake on disease activity and nutritional status in these children.

Methods: The study investigated prospectively the nutritional status of 90 children and adolescents with IBD. Outpatient visits included medical evaluation, nutritional assessment (3 days dietary records) and laboratory investigations. Assessment of food intake was performed using “Tzameret” (Ministry of Health, Israel), a national validated computer program for dietary food intake assessment. Results: Three days dietary records were provided by 68 children, seven on exclusive enteral nutrition (EEN), eleven on usual diets with different polymeric formulas supplements and 50 subjects on usual diet. All children were supplemented with iron and multivitamins. Forty eight percent of children on usual diet had energy intake below 80% RDA for age and gender. Magnesium, phosphate, iron and zinc intake were below 80% EAR (estimated average requirement) in 84%, 46%, 44% and 52% respectively. In 72% of children calcium intake was even lower than 50% AI (adequate intake). Vitamin C, B1, B2, folic acid, B6, B12, A and E were below 80% EAR in 54%, 46%, 44%, 14%, 54%, 24%, 14%, 60% and 82% respectively. Children on EEN or supplemented with formulas had all nutrients' intake above 80% of recommendations for age and gender with the exception with calcium intake which was below 80% EAR in 30% even in these groups. Supplementation of the diet with formulas was positively and significantly correlated with anthropometry (weight (p<0.001), height (p=0.21), BMI z-scores (0.003), % mid arm circumference (p=0.013), biochemistry: albumin (p<0.001), C-reactive protein (p<0.001, ESR (p<0.001), ferritin (p=0.008), vitamin B12 (p=0.022), vitamin D (p=0.012) and dietary intake of carbohydrates (p=0.005), calcium, magnesium, iron, zinc, vitamin A, B1, B2, B6, B12, A, E (p<0.001), folic acid (p=0.005) and negative significant with fiber intake (p<0.001). Anthropometry, biochemistry and food intake were not significantly associated with disease status (remission or relapse).

Conclusion: In the absence of diet complementation with formula supplements, food intake is inadequate for many nutrients in a large proportion of children with IBD. Supplementation of usual diets with nutritional formulas is associated with better nutritional status in children with IBD.
Disclosure of Interest: None Declared
REDUCED RISK OF PULMONARY EMBOLI IN CHILDREN TREATED WITH LONG-TERM PARENTERAL NUTRITION

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Objectives and Study: Pulmonary embolism (PE) is a life-threatening complication of long-term parenteral nutrition (PN) with a prevalence of 35% in children. In 2003 new intravenous lipid emulsions (ILEs) with MCT, olive and/or fish oil in addition to soybean oil were first introduced. The aim was to compare the incidence of PE and risk factors before and after the introduction of the new ILEs.

Methods: 327 surveillance ventilation-perfusion (V/Q) scintigraphies from 68 children aged 0.3-15 years, treated with PN at home from 1993-2010, were retrospectively reviewed. Rate of PE/1000 central venous catheter (CVC) days, number of children that experienced at least one PE pre- and post-introduction of new ILEs were compared. Multivariate analyses were performed to compare risk factors.

Results: Twenty-two (32%) children (19/42 before 2003 and 3/26 after 2003, p=0.007) had at least one episode of PE. Thirty seven (11%) episodes of PE were detected accounting for a mean of 0.2/1000 CVC days prior to 2003 and 0.05/1000 CVC days after 2003, p=0.04. Regression analysis indicated that a higher content of ILE/infusion (p=0.045) and frequency of ILE infusion of >three nights/week were associated with higher PE risk (p=0.001). Treatment with new ILE was associated with lower risk (p=0.003).

Conclusion: Although there was a four-fold fall in PE incidence with new/mixed ILE containing less soybean, PE remains a complication. We recommend 12-18 monthly surveillance with lung perfusion scan, as well as anticoagulant treatment once a PE has been diagnosed.

Disclosure of Interest: None Declared
EATING AND SLEEPING PATTERNS DIFFERENCES BETWEEN IDIOPATHIC SHORT STATURE AND LEAN PREPUBERTAL CHILDREN AND CHILDREN WITH NORMAL HEIGHT AND BODY WEIGHT

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Objectives and Study: To investigate the dietary and sleeping patterns in healthy children with idiopathic short stature (ISS) and low proportion between weight percentile and height percentile in comparison to children with normal height and weight.

Methods: Eighty six pre-pubertal healthy children were recruited: Cases (n=43) height below 3rd percentile, weight percentile ≤ height percentile; Controls (n=43) height above 25th percentile, BMI between 5th and 85th percentile. Patterns were assessed by food diaries, child eating behavior, quality of life, physical activity and the sleep assessment questionnaires.

Results: The absolute daily average energy, protein and carbohydrates intake was significantly lower (P<0.05) in cases than in controls. However, when calculated those variables as kcal or grams per body surface area (BSA) unit, there were no significant differences between the two groups. Micronutrients intake (iron, zinc, calcium, vitamin A and vitamin C, calculated as percentage from RDA recommendations) was significantly lower (P<0.05) in cases than in controls. Cases were characterized as slower eaters, having a higher sensitivity to satiety, having a lower responsiveness to food and lower enjoyment from food according to the child eating behavior questionnaire and lower physical functioning according to the quality of life questionnaire. Physical activity level and sleeping patterns were similar in cases and controls. According to the regression analysis, cases were characterized as having different eating patterns: slower eaters and having a lower responsiveness to food, and lower intake of vitamin A as percentage from RDA.

Conclusion: We have shown that ISS and lean children have a lower dietary quality, and lower micronutrient intake, with similar energy and macronutrients intake per BSA. In addition ISS and lean children have poor eating patterns. Understanding the differences in dietary intake and eating behaviors may be beneficial in the development of targeted nutritional intervention for ISS and lean children, thus enabling the achievement of the full growth potential in these children.

Disclosure of Interest: None Declared
**Nutrition**

**Clinical Nutrition**

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**WAIST TO HEIGHT RATIO: A SIMPLE TOOL IN RECOGNISING CHILDREN AT INCREASED RISK FOR METABOLIC SYNDROME**

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Objectives and Study: Metabolic Syndrome (MS) is one of the most important comorbidity linked to obesity, also in children. Visceral adiposity is part of MS cluster, so that measurement of Waist Circumference (WC) is an essential step for screening MS in adulthood and in childhood. Up today, valid cut-off percentiles for WC are not available for the whole pediatric population, arising some difficulties to diagnose the syndrome. **AIM OF THE STUDY:** To individuate a simple clinical diagnostic tool for screening obese children at high risk for MS

Methods: We enrolled in the study 803 subjects (395 girls and 408 boys, mean age 9.43±2.5 ys, median age 9.5 ys) whose mean BMI z-score was 2.2±0.53. The entire cohort was screened for MS, defined according to modified American Heart Association Criteria. For each patient we measured WC and calculate Waist to Height ratio (WHtR) according to: WC (cm)/Height (cm). We used Receiver Operating Characteristic (ROC) curve and Youden Index for detecting the usefulness of this parameter.

Results: The prevalence rate of MS in our population was 13.07% (105 pts). Children with MS had mean WHtR of 0.65±0.09. Children without MS presented mean WHtR equal to 0.62±0.06, this difference was statistically significative (p<0.001). The Area Under ROC curve (AUC) was 0.690 for WHtR (CI 95%: 0.637-0.743, p<0.001) in detecting MS. Particularly, WHtR cut-off value equal to 0.62 showed a sensibility of 80.8% and a specificity of 55.2% in identifying obese children affected by MS.

Conclusion: WHtR is strongly related to MS and it seems to be a simple, non invasive and practical tool in detecting Paediatric MS: a cut-off value of 0.62 should suggest second-level examinations in ambulatory medical practice.

Disclosure of Interest: None Declared
MICROTRACERS IN PAEDIATRIC FOOD RESEARCH: A NOVEL TOOL TO ESTABLISH ABSORPTION, METABOLISM AND EXCRETION OF NUTRIENTS OR INGREDIENTS

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¹TNO, Zeist, ²Erasmus MC, Rotterdam, Netherlands

Objectives and Study: In the Netherlands, non-therapeutic intervention studies with children are only considered ethical if the risk and the burden of the study is minimal to the child. Our objective was to investigate the possibilities of a new strategy to obtain absorbance, metabolism, and excretion data of relevant compounds in young children. Therefore, we explored the use of an intervention of an extremely low oral dose paracetamol (ng/kg range) combined with a radioactive tracer, necessary for ultrasensitive AMS detection, in the pediatric population (0-6 y).

Methods: A study protocol was submitted to the Dutch CCMO for medical ethical approval. The pediatric study was designed with a microtracer of 14C labelled paracetamol (dose 3 ng/kg, 60 Bq/kg) in children that were in the PICU. An important inclusion criterion was the presence of an indwelling catheter to enable collecting small blood samples. These small blood volumes combined with low dosing regimes required bioanalytical analysis with AMS.

Results: Current study was approved for conduct in The Netherlands. Over 20 children have been recruited (>40% consent rate from parents) between 0-6 years old. AMS shows to be sufficiently sensitive to establish the pharmacokinetics of paracetamol and its’ metabolites.

Conclusion: In current study, risk of participation in the study was minimal because the intervention consisted of only a microdose of paracetamol, while the burden was considered minimal because of the use of an indwelling catheter. Radiological risk of 60 Bq/kg 14C paracetamol as the lowest possible risk category of the ICRP, was considered to be justified.

The use of microtracers (limicrodose of 14C labelled substances) in clinical studies in adults was shown before to provide useful pharmacokinetic data. A labelled microtracer enables to distinguish the ingredient of a formulated product from the endogenously present substance. Possibilities of using a microtracer in infant formula development to improve infant nutrition, will be discussed in relation to the ethical and logistic challenges that we have experienced in current study.


Disclosure of Interest: W. Vaes Conflict with: TNO conducts microtracer studies and AMS analysis, M. Mooij Conflict with: Employed by Erasmus Medical Center for research on the use of pediatric
microdosing to establish the ontogeny of drug metabolism, S. de Wildt Conflict with: Grant holder of ZonMW grant on the use of microdosing to establish the ontogeny of drug metabolism
**Nutrition**

**Clinical Nutrition**

PO-N-0404

**ASSESSMENT OF DELIVERY AND INTERRUPTIONS OF NUTRITIONAL SUPPORT IN CRITICALLY ILL CHILDREN**

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Jacques Cotting 2

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2 Pediatric Intensive Care Unit, University Hospital, Lausanne, Switzerland

**Objectives and Study:** In pediatric intensive care unit, nutritional support is an integral part of the treatment. An adequate energy and protein intake can improve nutritional outcomes and decrease the appearance of protein-energy malnutrition. However, nutritional support is frequently delayed or interrupted. The aims of this pilot study were: to compare the amount of nutrition delivered to critically ill children with the amount prescribed by physicians, to determine the interruptions of nutritional support and to identify the barriers impeding adequate intake.

**Methods:** In this prospective pilot study, critically ill children hospitalized for >24 hours in pediatric intensive care unit and without oral nutritional intake at admission were consecutively included. The amounts of energy and protein from nutritional support that were prescribed by physicians and delivered to the patients were recorded daily until the 10th day of hospitalization, discharge or death. A ratio delivered/prescribed intake of 100±10% was considered as adequate. The interruptions of nutritional support were collected using medical charts and expressed in frequency and hours.

**Results:** We included 64 children with a median age of 2.7 years [IQR 0.4-5.7]. Nutritional support was introduced in 88% of patients, within 22 hours [IQR 13-29] after admission. For the entire stay, energy and protein intakes were significantly lower than the prescriptions with a mean ratio of 90±16% and 95±19% (p <.001), respectively. Children aged ≤12 months had the highest ratios, with 93±21% for energy and 99±25% for protein. Nutritional support was interrupted in 75% of patients for a median of 10 hours [IQR 5-19]. Nursing/physiotherapy and extubation were the barriers that interrupted nutritional support, the most frequently and for the longest duration.

**Conclusion:** In critically ill children, energy and protein intake are lower than the prescriptions. The results obtained in infants were better than in older children. By reducing the number and duration of interruptions and by quickly compensating, the intake administered is close to the amount prescribed by physicians.

**Disclosure of Interest:** None Declared
A SINGLE-BLINDED STUDY ON THE EFFECT OF SACCHAROMYCES BOULARDII CNCM I-745 ON GROWTH AND DEVELOPMENT IN PRETERM INFANTS

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Objectives and Study: Immature gastrointestinal functions increase the risk of poor growth, as well as nosocomial infections and necrotizing enterocolitis (NEC) in the preterm infant. The effects of probiotics on growth and development in premature infants have been poorly investigated poorly. *Saccharomyces boulardii* CNCM I-745 (*S. boulardii*) is a non-pathogenic probiotic yeast. The aim of this study was to evaluate if feeding supplemented with *S. boulardii* can improve growth and clinical outcomes in preterm and small for gestational age infants.

Methods: A prospective, randomized, case–controlled trial was conducted in infants with a gestational age of 30 to 37 weeks and a birth weight between 1500 to 2500 g. The study group received *S. boulardii* supplementation, 50 mg/kg twice daily, compared to a non-intervention group (control group). The primary outcomes were short term growth parameters including weight gain, linear growth, head and chest circumference increase, and secondary outcomes were clinical outcomes, feeding in intolerance and complications.

Results: A total of 125 infants were enrolled in the study, 63 in the treatment and 62 in the control group. *S. boulardii* was administered for the first time at 2.63 days after birth (1 day to 6 days, 46 within 3 days, only 5 between 4 and 6 days). The total number of days of *S. boulardii* administration was on average 25.3 days (range: 9 to 28 days). Weight gain (16.14 ± 1.96 g/kg/d) vs. 10.73 ± 1.77 g/kg/d; p <0.05) and formula intake at maximal enteral feeding (128.44 ± 6.67 ml/kg/d) vs. 112.29 ±7.24 ml/kg/d, p <0.05) were significantly higher in the study group. There was a non-significant but strong trend for a decrease of sepsis and gastro-intestinal symptoms in the *S. boulardii* group (p 0.058 and 0.052, respectively). Hospital stay in the *S. boulardii* group was shorter (p=0.035). There was no significant difference in linear growth, head and chest circumference increase, incidence of abdominal distension, incidence of sepsis, as well as days of parenteral nutrition. No adverse effects related to *S. boulardii* were observed.

Conclusion: Prophylactic supplementation of *S. boulardii* at a dose of 50 mg/kg twice a day appeared to bring preterm infants weight gain closer to that of intra-uterine growth rate, reduce feeding intolerance, and had no adverse effects.

Disclosure of Interest: L. Xu: None Declared, Y. Wang: None Declared, Y. Wang: None Declared, J. Fu: None Declared, M. Sun: None Declared, Z. Mao: None Declared, Y. Vandenplas Conflict with: Biocodex and United Pharmaceuticals
A CORRELATION STUDY OF DOCOSAHEXAENOIC ACID INTAKE WITH ITS LEVELS IN PLASMA IN CHINESE PREGNANT AND LACTATING WOMEN

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Institute of Reproductive and Child Health/Ministry of Health Key Laboratory of Reproductive Health, School of Public Health, Peking University Health Science Center, Beijing, Wyeth Nutrition Science Center, Shanghai, China

Objectives and Study: Dietary docosahexaenoic acid (DHA) has been documented to correlate with plasma DHA in some settings but not in China. We aimed to assess the relationship of DHA intake in a recent month assessed by a tailored iPad-based electronic food frequency questionnaire (FFQ) with plasma DHA levels in women residing in coastland (Weihai), lakeland (Yueyang) and inland (Baotou) of China.

Methods: In this cross-sectional study, a total of 407 mid-pregnancy (17±2 wks), 397 late pregnancy (39±2 wks) and 406 lactating (42±7 d postpartum) women were recruited equally from the three regions during May and July 2014. The FFQ comprised three parts: seafood (75 items), freshwater food (38 items), and DHA milk powder and supplements (68 items). Trained health professionals interviewed all participants to complete the FFQ via laptop computers, where all food pictures with estimated net sizes were provided. Total fatty acid in plasma was determined with capillary gas chromatography. DHA levels were provided as a percentage by weight of total fatty acids.

Results: The median DHA intakes in coastland, Lakeland and inland region were 27.8 (IQR: 12.4–60.6), 19.4 (9.4–40.6) and 9.0 (2.8–22.2) mg/d, respectively. The corresponding mean DHA percentages were 2.7±0.8, 2.2±0.5 and 1.9±0.5. The crude and the region- and group-adjusted Spearman correlation coefficients between the dietary DHA intake and plasma DHA levels were 0.34 and 0.25 (p values<0.001). The participant group-adjusted coefficient for coastland was 0.36, for lakeland 0.19 and for inland 0.19 (all p values<0.001). The region-adjusted coefficient was 0.19 for mid-pregnancy, 0.25 for late pregnancy and 0.30 for lactating women (all p values<0.001). The region- and group-specific Spearman correlation coefficients were provided in Table.

<table>
<thead>
<tr>
<th>Region</th>
<th>Participant group</th>
<th>mid-pregnancy</th>
<th>late pregnancy</th>
<th>lactating</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weihai</td>
<td></td>
<td>0.39</td>
<td>0.24</td>
<td>0.44</td>
</tr>
<tr>
<td>Yueyang</td>
<td></td>
<td>0.02</td>
<td>0.33</td>
<td>0.23</td>
</tr>
<tr>
<td>Baotou</td>
<td></td>
<td>0.19</td>
<td>0.16</td>
<td>0.20</td>
</tr>
</tbody>
</table>

Conclusion: The DHA intake is moderately correlated with plasma DHA levels, indicating a possibility for using the FFQ to estimate DHA intake in Chinese pregnant and lactating women.

BREASTFEEDING AND INTRODUCTION TO COMPLEMENTARY FEEDING IN A PROSPECTIVE DANISH BIRTH COHORT

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Objectives and Study: The objective of this study was to obtain precise, prospective data on breastfeeding, the use of infant formula, and introduction to complementary feeding in a Danish birth cohort. Preliminary results were presented at the 46th Annual Meeting of ESPGHAN in London in 2013.

Methods: The Odense Child Cohort is a birth cohort consisting of children born in the municipality of Odense from January 2010 to December 2013. Approximately 2500 children constitute the cohort. The results presented in this abstract are based on births from the 8th of April 2012 to the 31st of October 2012 and data collected in weeks 1-34 after birth.
Weekly SMS-questions were used as the data collection method. The mothers received from three to five questions every week from day three after birth. The questions were identical from week to week, and preferably ongoing until the infant was no longer breastfed.

The study was approved by The Regional Scientific Ethical Committees for Southern Denmark and The Danish Data Protection Agency.

Results: During the study period a total of 499 women gave birth to a single, term, liveborn infant.
Response rates as well as breastfeeding rates are presented in the following table:

<table>
<thead>
<tr>
<th>Time after birth</th>
<th>3 days</th>
<th>10 days</th>
<th>8 weeks</th>
<th>17 weeks</th>
<th>26 weeks</th>
<th>34 weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Response rate*</td>
<td>98.2 %</td>
<td>97.2 %</td>
<td>92.0 %</td>
<td>91.2 %</td>
<td>89.6 %</td>
<td>89.8 %</td>
</tr>
<tr>
<td>Any breastfeeding</td>
<td>96.7 %</td>
<td>93.6 %</td>
<td>82.6 %</td>
<td>73.0 %</td>
<td>60.2 %</td>
<td>48.7 %</td>
</tr>
<tr>
<td></td>
<td>(474/490)</td>
<td>(454/485)</td>
<td>(379/459)</td>
<td>(332/455)</td>
<td>(269/447)</td>
<td>(218/448)</td>
</tr>
<tr>
<td>Exclusive breastfeeding</td>
<td>61.2 %</td>
<td>74.6 %</td>
<td>62.3 %</td>
<td>48.6 %</td>
<td>1.3 %</td>
<td>0 %</td>
</tr>
<tr>
<td></td>
<td>(300/490)</td>
<td>(362/485)</td>
<td>(286/459)</td>
<td>(221/455)</td>
<td>(6/447)</td>
<td>(0/448)</td>
</tr>
<tr>
<td>Partial breastfeeding</td>
<td>30.2 %</td>
<td>14.0 %</td>
<td>15.7 %</td>
<td>21.3 %</td>
<td>57.9 %</td>
<td>48.7 %</td>
</tr>
<tr>
<td></td>
<td>(148/490)</td>
<td>(68/485)</td>
<td>(72/459)</td>
<td>(97/455)</td>
<td>(259/447)</td>
<td>(218/448)</td>
</tr>
<tr>
<td>Unknown if formula</td>
<td>5.3 %</td>
<td>4.9 %</td>
<td>4.6 %</td>
<td>3.1 %</td>
<td>2.7 %</td>
<td>4.0 %</td>
</tr>
<tr>
<td></td>
<td>(26/490)</td>
<td>(24/485)</td>
<td>(21/459)</td>
<td>(14/455)</td>
<td>(12/447)</td>
<td>(18/448)</td>
</tr>
<tr>
<td>--------------------------------------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
<td>----------</td>
</tr>
<tr>
<td>Introduced to solid foods</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>7.2 %</td>
<td>85.8 %</td>
<td>88.4 %</td>
</tr>
<tr>
<td></td>
<td>(36/499)</td>
<td>(428/499)</td>
<td>(441/499)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Not introduced to solid foods</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>78.4 %</td>
<td>1.8 %</td>
<td>0 %</td>
</tr>
<tr>
<td></td>
<td>(391/499)</td>
<td>(9/499)</td>
<td>(0/499)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unknown if introduced to solid foods</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>14.4 %</td>
<td>12.4 %</td>
<td>11.6 %</td>
</tr>
<tr>
<td></td>
<td>(72/499)</td>
<td>(62/499)</td>
<td>(58/499)</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*) Regarding question number one

**Conclusion:** The breastfeeding initiation rate was very high (> 95 %), although almost one third (30.2 %) supplemented with infant formula within the first few days after birth. Two weeks after birth supplementation declined to 14.0 %. Seventeen and 26 weeks after birth, 48.6 % and 1.3 % respectively were exclusively breastfeeding. All infants had been introduced to solid foods 29 weeks after birth. The use of SMS-questions resulted in very high response rates to all times.

**Disclosure of Interest:** None Declared
VITAMIN D DEFICIENCY IN CHILDREN WITH SHORT BOWEL SYNDROME

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Objectives and Study: Patients with short bowel syndrome (SBS) during and after weaning off parenteral nutrition (PN) are at high risk of nutritional deficiencies, including vitamin deficiencies. The pleiotropic actions of vitamin D and its influence on health are well-known. Assessment of 25-OHD concentration in paediatric patients with SBS receiving PN and weaned off PN was the aim of the study.

Methods: 47 patients (23 females and 24 males) with SBS aged 0.5 - 18.1 years (median: 7.4 years) were selected for the study. The median duration of PN was 6 years 7 months. 8 patients were already weaned off PN. 23 patients (49%) had extended small intestine resection (remnant small intestine <40 cm). 21 patients (45%) had additionally resection of large intestine. Chemiluminescence immunoassay (CLIA) was used to estimate concentration of 25-OHD. Nutrition status and growth were evaluated based on anthropometric measurements. The student’s t-test and Pearson’s correlation test was used to analyze the results.

Results: Mean concentration of vitamin 25 OH D in the research sample was 24.9 µg/ml. 12 patients (25%) were described as deficient in 25-OHD (25-OHD concentration <20 ng/ml). 20 patients (43%) had insufficient concentration of 25-OHD (20-29 ng/ml) and only 15 children (32%) had optimal 25-OHD concentration (≥30 ng/ml). Almost all patients (45) were additionally orally supplemented with vitamin D. Medium oral vitamin D supplementation in whole research sample was 2095 IU per day; 106.29 IU/kg/day. The 25-OHD concentration was negatively correlated with oral vitamin D supplementation (r=-0.5791). In whole research sample the 25-OHD concentration was not seasonally dependent. Extension of resection had no evident influence on concentration of 25-OHD. There was no statistically significant correlation between concentration of 25OHD and nutritional status assessed by anthropological measurements (SDS body weight, SDS body height). 25 OHD concentration was not correlated with number of days of PN.

Conclusion: SBS may be related to suboptimal 25-OHD concentration. The routine surveillance of serum vitamin concentration and consideration of modifying parenteral vitamin supplementation is indicated in children with SBS.

Disclosure of Interest: None Declared
Objectives and Study: Vitamin D deficiency is a major public health problem in the United Kingdom and in many other parts of the world. Children with special needs are at greater risk due to factors such as decreased mobility and outdoor play, concomitant medications that increase catabolism of vitamin D, reduced nutritional intake and low body weight. Gastrostomy-fed children receiving a nutritionally complete formula may still be at risk of vitamin D deficiency due to the above factors. The objective of this study is to assess the vitamin D status of special needs children receiving full or partial nutrition via gastrostomy.

Methods: Thirty-two children (24 male) aged 5-16 years, from 7 special schools in Manchester receiving gastrostomy feeds took part in the study. Blood samples were obtained in March 2014 (end of winter) to evaluate serum levels of 25hydroxyvitamin D (25OHD), calcium (Ca), phosphorus (P), alkaline phosphatase (ALP) and parathyroid hormone (PTH). In addition, carers were interviewed to obtain a dietary history and assess the subjects' exposure to sunlight.

Results: All children had complex medical conditions. 26 were non-ambulatory and 18 were taking anti-epileptic drugs. Nineteen children (59%) had a Fitzpatrick skin type score of III or higher (South Asian or Black African ethnicity). The children had little or no sunshine exposure in the 3 months prior to data collection. Thirty results were obtained for serum 25OHD. The mean serum 25OHD was 71.1nmol/L (±21.4nmol/L). One child was found to be vitamin D deficient (serum 25OHD 24.6nmol/L) and 4 children were vitamin D insufficient (serum 25OHD range 29.9-47.9nmol/L). 2/25 children (8%) had an elevated PTH (serum PTH 75ng/L and 110ng/L). All children had normal serum P, Ca and ALP.

Thirteen children received less than 10ug of vitamin D per day from their feed (range 3.5-9.2μg/day). None of the children were taking vitamin supplements.

Dietary calcium intake met the recommended intake for age and gender in all but one subject.

Conclusion: From our results we conclude that nutritionally complete gastrostomy feeds may be protective against vitamin D deficiency in gastrostomy-fed children with special needs.

Disclosure of Interest: H. Kuter Conflict with: This study was funded by Danone UK, G. Das Conflict with: This study was funded by Danone UK, M. Mughal Conflict with: This study was funded by Danone UK
PORTUGUESE NATIONAL SURVEY USING THE STRONG KIDS NUTRITIONAL RISK SCREENING TOOL IN HOSPITALISED CHILDREN

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Objectives and Study: Nutritional screening in pediatric hospitalized children is very important, since children have a higher risk of developing malnutrition, due to their growth needs. The aim of this study was to establish the level of malnutrition risk of children at Portuguese hospitals, using STRONGkids screening tool and to assess its practical application in a clinical setting.

Methods: A prospective observational multi-centre study was performed in 5 of the main Portuguese hospitals, to achieve a representative sample of the paediatric population (nationwide). The STRONGkids screening tool was used to determine “risk” of developing malnutrition on admission. In addition, measurements of weight, length and mid-arm circumference (MUAC) were performed at admission and discharge. A SD-scores < -2 for weight-for-height for children up to 60 months (or body mass index thereafter) and height-for-age were considered to indicate acute and chronic malnutrition respectively.

Results: A total of 419 children were evaluated. Median age was 4,0 years and median length of hospital stay (LOS) was 4 days. Approximately 57% (56,7%) of the children were classified as moderate or high risk of developing malnutrition by the STRONGkids tool. Children classified as moderate and high risk had significantly lower SD-scores for weight-for-height, and the high risk group had a significantly longer LOS compared to children with low and moderate nutritional risk (12 days versus 4 days, respectively). Eighty-nine percent of those classified as low risk did not have malnutrition (using the WHO criteria) while 39,1 % of those classified as high risk were malnourished (using the WHO criteria). Weight and MUAC variation between admission and discharge were not statistically significant between nutritional risk groups.

Conclusion: Using the nutritional risk screening tool STRONGkids, a significant relationship was found between having a high risk score, a lower SD-score weight-for height and a longer LOS. Thus, this tool seems to be a feasible and simple tool for identifying children at risk of developing malnutrition in hospitals.

References:


**Disclosure of Interest:** None Declared
Objectives and Study: Nutritional support provided should be geared towards adequate calorie intake, prevention and treatment of macro and micro-nutrient deficiencies. The dose of the nutrients intake needs to be compatible with the existing metabolism to avoid unwanted complications. Nutritional support of the critical ill children remains a controversial topic within our PICUs, with no clear guidelines as to the timing, mode and type of nutrition in infants and children. This study is aimed at ascertaining the stumbling block towards a good nutritional practice.

Objectives
To review the provision of nutritional care to the critically ill children in PICU in a tertiary care hospital in Kenya.
To identify the risk factors associated with inadequate provision of nutritional support.

Methods: Caloric and protein intake and nutritional parameters were reviewed in 183 children in the PICU over a six month period. Risk factors of an inadequacy and delay to achieve a sustained optimal caloric intake were identified using a multivariate analysis.

Results: Calories prescribed to the PICU patients were noted to be inadequate in 59%. The time to initiation of feeds were noted to be more than six hours in 78%. A combination of enteral and parenteral regimen was administered in 72% of patients. Adequate delivery of the amount of calories prescribed was noted in 82%. Parenteral nutrition delivered more amount of the prescribed calories when compared with enteral nutrition, which was significantly lower (p<0.001). Nasogastric feedings were the most common mode (96%) of enteral feeds. Significant interruption to the delivery of enterally administered nutrition was noted and these were attributed to feed intolerance, vomiting, and abdominal distension and PICU procedures. Commercial feeds were used to feed 91% of the different disease conditions.

Conclusion: Inadequate nutritional support is very common in PICU, with an increased incidence of complications. A lack of clear feeding protocols, improper distribution of limited resources, poor staffing and lack of knowledge about the importance of good nutritional practices form the basis of an inadequate nutritional support.


Disclosure of Interest: R. Kumar Conflict with: None, R. Musoke Conflict with: None
Nutrition
Clinical Nutrition
PO-N-0412

DOCOSAHEXAENOIC ACID STATUS IN CHINESE PREGNANT AND LACTATING WOMEN
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Objectives and Study: Data concerning docosahexaenoic acid (DHA) in Chinese pregnant and lactating women are sparse. We aimed to assess DHA nutritional status as well as its intake patterns in pregnant and lactating women from coastland (Weihai), lakeland (Yueyang) and inland (Baotou) of China.

Methods: A cross-sectional study was conducted in the three regions from May to July 2014. 407 mid-pregnancy (17±2 wks), 397 late pregnancy (39±2 wks) and 406 lactating women (42±7 d postpartum) were recruited equally from three regions. Dietary DHA was assessed via a tailored iPad-based food frequency questionnaire. Fasting venous blood samples were collected. Fatty acid profiles in plasma and erythrocyte were assayed with capillary gas chromatography; DHA levels were expressed as a percentage by weight of total fatty acids.

Results: The overall median DHA intake was 17.5 (IQR: 7.0-41.8) mg/d; the patterns of DHA intakes across the three participant groups varied considerably in different regions. In coastland, the intake was significantly higher in late pregnancy women (median=42.0 mg/d) than in both mid-pregnancy women (24.5 mg/d) and lactating mothers (24.6 mg/d) (p values <0.05), whereas in lakeland, the intake for mid-pregnancy (22.1 mg/d) and late pregnancy (21.6 mg/d) women were significantly higher than that for lactating mothers (14.7 mg/d) (p values <0.05); however, the intake did not substantially differ among the three groups of participating women who lived in the inland (median=10.4, 7.6 and 9.0 for mid-pregnancy, late pregnancy and lactating women, respectively) (p=0.24). The overall mean plasma DHA level was 2.24±0.69; the mean level for women during mid-pregnancy (2.63) was higher than that for late pregnancy (2.04) and lactating women (2.06) (p values <0.05). The overall mean erythrocyte DHA level was 6.17±1.49; the mean level for women during mid-pregnancy (6.59) was also higher than that for late pregnancy (6.10) and lactating women (5.82) (p values <0.05). Further analyses stratified by the region showed similar patterns of both plasma and erythrocyte DHA levels across the participant groups.

Conclusion: Dietary DHA intake is substantially inadequate even for women residing in coastland. The intake patterns across the three typical stages vary by regions, likely indicating different fish-consuming habits during pregnancy/lactating period, while the patterns of blood DHA variations are quite consistent in three regions, further indicating a need to investigate on other factors affecting DHA nutritional status.
Disclosure of Interest: Y.-B. Zhou: None Declared, Y.-L. Zhang: None Declared, Y. Li: None Declared, G.-S. Xu: None Declared, H.-T. Li: None Declared, J.-M. Liu Conflict with: Wyeth Nutrition
ASSOCIATION BETWEEN PREMATURITY AND CHILDHOOD OBESITY/CO-MORBID CONDITIONS IN THE CHILDREN'S HOSPITAL HEROES PATIENT POPULATION

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1 UNMC, 2 Creighton, Omaha, United States

Objectives and Study: Very low birth weight infants with rapid weight gain have been shown to have a greater risk of adult obesity, cardiovascular disease, and diabetes than term peers. The highest prevalence of obesity (11.2% age 8) occurred in preterm infants with BW 2001-2500 grams. Preterm infants in the Infant Health and Developmental Program had faster linear growth and improved cognition with a greater risk of overweight/obesity at 8 and 18 years. Our objective is to determine if prematurity status effects BMI and co-morbid factors including asthma, diabetes, obstructive sleep apnea, and hypertension in children enrolled at a child obesity clinic (HEROES).

Methods: A retrospective IRB approved review of 357 patients enrolled in HEROES clinic. Descriptive statistics were used to summarize data. Fisher's exact test was used to evaluate association of co-morbidities and prematurity status.

Results: 357 patients were evaluated, 62 (17%) were premature (< 37 weeks). Current age was similar among the two groups (11.7 yrs p=0.51). 30.6% of obese children born preterm had asthma, compared to 24.4% of obese children that were not born preterm (p=0.34). 5.3% of all subjects had a diagnosis of diabetes (3 preterm [4.8%], 16 term [5.4%], p=1). Insulin resistance was documented in 10 preterm and 44 term obese children (p=0.81). 52 patients were diagnosed with Obstructive Sleep Apnea (7 or 11.2% preterm, 45 or 15.2% term, p=0.55). Our data did not show a statistically significant difference in the incidence of hypercholesterolemia, hypertriglyceridemia, or hypertension between preterm and term obese children. There were 22 preterm children with elevated cholesterol levels (35.4%), compared to 120 term children (40.6%) (p=0.48). Hypertriglyceridemia was documented in 26 preterm children (41.9%), and 113 term children (38.3%) (p=0.67). An elevated blood pressure and/or a diagnosis of hypertension was documented in 8 preterm and 46 term obese children (p=0.7). None of the evaluated co-morbidities was statistically significantly associated with prematurity status.

Conclusion: Prematurity has been associated with higher rates of obesity and co-morbid conditions, an outcome of concern when determining nutrition plan of care for these high risk infants. In our cohort of obese patients, there was no statistically significant association between prematurity status and 8 common co-morbid conditions of obesity.

Disclosure of Interest: A. Anderson Berry Conflict with: Grant Funding Of other research, Conflict with: Present my research in educational settings, L. Ruybal: None Declared, C. Fernandez: None Declared, E. Lyden: None Declared, C. Hanson: None Declared
COMPARISON OF TWO PROBIOTICS IN FOLLOW-ON FORMULAE IN CHINESE INFANTS: BIFIDOBACTERIUM ANIMALIS SUBSP. LACTIS HN019 PROTECTED AGAINST RESPIRATORY TRACT INFECTIONS

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Objectives and Study: A double-blind, placebo-controlled clinical trial was conducted in urban China to investigate the health benefits of probiotic bacteria in human infants.

Methods: The study was conducted in Fuyang, Anhui Province, China, and enrolled 192 healthy infants aged 6 to 12 months. Infants received one of three premium follow-on formulae daily for 12 weeks during the Chinese winter (December 2012 – March 2013). One group of infants (n=64) received a follow-on formula supplemented with $10^6$ CFU/g *Bifidobacterium animalis* subsp. *lactis* HN019, the second group (n=64) received a formulae with $10^6$ CFU/g *Lactobacillus rhamnosus* HN001, while the third group (n=64) received formula without added probiotics (control). The primary endpoint was physician-confirmed bacterial or viral respiratory infections during the 12 week treatment period. Secondary endpoints included antiviral or antibiotic treatments, hospitalization, stool frequency and consistency, and parentally-reported (i.e. unconfirmed) infections.

Results: According to intention-to-treat criteria, confirmed respiratory tract infections were observed in 9.4% of the control group, compared to 3.1% in the HN001 group (p = 0.28), and 0.0% in the HN019 group (p=0.03). A similar trend was observed for parentally-reported infections, with 25.0% in the placebo group, compared with 14.1% in the HN001 group (p=0.12) and 9.4% in the HN019 group (p=0.02). No infants in the HN019 group were prescribed antibiotics or antivirals, compared with 3 (4.7%) in the HN001 group and 7 (10.9%) in the control group. No cases of diarrhoea were reported in any of the infants over the 12-week study period, and no differences in stool frequency or characteristics were observed. The probiotic-containing follow-on formulae were well tolerated and no adverse events were reported. Interestingly, faecal analysis conducted at the end of the study, showed that while *B. lactis* was detected significantly more often in infants that received HN019, a PCR used to detect HN001 showed widespread occurrence of HN001 or HN001-like *L. rhamnosus* species across all three groups.

Conclusion: In conclusion, this study directly compared the benefits of two different probiotics when added to follow-on infant formula. While HN001 showed trends toward reduced infections, HN019 showed superior performance in terms of significantly reduced incidence of physician-confirmed respiratory infections, parentally-reported infections, and antibiotic/antiviral use in Chinese infants aged 6 to 15 months.
Disclosure of Interest: J. Dekker Conflict with: Study funded by Fonterra, NZ, Conflict with: Dr Dekker is an employee of Fonterra NZ, Conflict with: Fonterra NZ manufactures and markets the probiotic strains used in the study, L.-M. Xu: NoneDeclared, H. Qian: NoneDeclared, X.-Y. Sheng: None Declared
OBJECTIVES AND STUDY: Thyroid function has been often described as altered in obese children, but the reason of this condition is not well understood. Aim of the study: to analyse the relationship between thyroid function, adiposity and other metabolic features obesity related.

METHODS: We evaluated anthropometric, biochemical, metabolic data and thyroid functionality in 803 obese children and adolescents (395 girls, mean age 9.43±2.5 yrs).

RESULTS: Mean BMI z-score was 2.2±0.53. Thyroid functionality data were as follow: mean TSH 2.8±1.3 µUl/ml, mean fT3 4.5±0.6 pg/ml, mean fT4 1.2±.4 ng/dl. TSH levels were above cut-off laboratory range in 10% of our population and the 0.2% (2 pts) of the whole population presented TSH≥10 µUl/ml. We found a significant positive correlation between TSH levels and BMI z-score (rho=0,121, p=0.001), even after adjustment for age and sex (r=0.117, p=0.001); a positive correlation was also observed between fT3 and BMI z-score (rho=0.161, p<0.001), but not for fT4 (p=0.787). TSH and fT3 were also positively associated with Waist to Height ratio (WtHr, rho=0.114, p=0.002 and rho=0.095, p=0.011 respectively). No correlation was found between thyroid functionality and: Homa index, z-score of blood pressure and hepatic steatosis.

CONCLUSION: Our data suggest a relationship between obesity and serum TSH and fT3 levels. In particular, WtHr, marker of visceral fat, seems to be directly related to TSH levels. It is not clear whether thyroid alteration are cause or consequence of fat excess, but metabolic active visceral fat could have a role in this relationship.

DISCLOSURE OF INTEREST: None Declared
EVALUATION OF VITAMIN D STATUS IN A PAEDIATRIC POPULATION OF SOUTHERN ITALY

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Objectives and Study: Hypovitaminosis D is frequent in children and a correlation between different pathologies has been detected. Italian data on vitamin D status and risk factors for hypovitaminosis D during pediatric age are lacking. Aim of the study: to analyze vitamin D status and the relationship between plasmatic concentrations of Vitamin D and cause of hospitalization in a pediatric population of Northern Apulia (South Italy).

Methods: Serum 25-hydroxyvitamin D (25OHD) concentration was assessed in 1055 children and adolescents (6.8±4.8 ys) living in the Northern Apulia and afferent to the University Hospital of Foggia. Vitamin D status was defined as follows: deficiency with serum 25OHD < 10 ng/ml, insufficiency among 10-29.9 ng/ml, sufficiency with serum 25OHD among 30-100 ng/ml. Collected data included age, gender and cause of hospitalization.

Results: The study population consisted of 531 male (6.4±4.8 ys) and 524 female (7.1±4.7 ys). The mean level of serum 25 OHD in our population was 21.34±10.24 ng/ml. No difference was recorded between 25 OHD levels in male and female (20.8±10 vs 21.8±10.4 ng/ml, p=0.146). The prevalence rates of vitamin D deficiency, insufficiency, sufficiency and toxicity were 11%, 73%, 15.4% and 0.6% respectively. Children affected by vitamin D deficiency and insufficiency were older than those with sufficient levels (6.59, 7.16 and 5.28 yrs, p<0.001). Children admitted for obesity had lower levels of 25 OHD (19±7.3 ng/ml) than children hospitalized for other conditions (p=0.018). In particular, in our obese population (154 pts, mean age 9.7±2.7, 76 girls) the prevalence rates of vitamin D deficit, insufficiency and sufficiency were 9%, 86.2% and 4.8 % respectively. But no statistical correlation was observed between vitamin D levels and BMI z-score (p= 0.474), vitamin D levels and HOMA index (p=0.993).

Conclusion: Vitamin D deficiency and insufficiency are very common in children living in our region. Older children seem to be at higher risk of low vitamin levels. Obese children seem to be at higher risk for Vitamin D deficiency. The reason of this condition is not clear but further investigations are needed to define guidelines on vitamin D supplementation in pediatric population, especially according to age and to understand the metabolic significance of this profile.

Disclosure of Interest: None Declared
MALNUTRITION IN CHILDREN UNDERGOING GENERAL ANESTHESIA: PREVALENCE AND RISK FACTORS
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Objectives and Study: Malnutrition is present in 10 to 15% of hospitalized children, and is known to can influence morbidity and mortality after surgery. The aim of this work was to study the prevalence and factors associated with malnutrition in children undergoing general anesthesia.

Methods: During the 10 month-period, 985 children admitted to the pre-anesthesia visit were included during a 10 month-period. Weight and term at birth, anthropometric data, clinical nutritional assessment, underlying disease, surgical procedure, pediatric nutritional risk score (PNRS), and American Society of Anesthesiologists score (ASA) were recorded.

Results: Body Mass Index (BMI)<3rd percentile, Waterlow indice< 2 SD, and clinical examination diagnosed malnutrition in respectively 11%, 6,1% et 8,1% of children. PNRS found 8% of children at risk of malnutrition. In multivariate analysis, prematurity, small for gestational age, and PNRS>2 were independently associated with malnutrition.

Conclusion: This study shows that malnutrition is present in about 10% of children undergoing a procedure under general anesthesia. Systematic assessment of nutritional status with BMI and nutritional risk with Pediatric Nutritional Risk Score are useful at the pre-anesthesia visit.

Disclosure of Interest: None Declared
**Nutrition**

**Clinical Nutrition**

PO-N-0418

**DIETARY INTAKE IN INFANTS WITH COMPLEX CONGENITAL HEART DISEASE: A CASE-CONTROL STUDY ON MACRO- AND MICRONUTRIENT INTAKE, MEAL FREQUENCY AND GROWTH**

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**Objectives and Study:** Congenital heart disease (CHD) is one of the most common congenital anomalies in children, often presented at birth or in early infancy. Infants with complex CHD have an increased energy expenditure due to an elevated metabolic rate often associated with congestive heart failure including tachypnea and tachycardia. This combined with difficulties in feeding and an inadequate intake, put these children at risk of malnutrition and growth failure. The actual intake of macro- and micronutrients in outpatient CHD infants over a 6 month period in infancy are not described in the literature. The aim of this study was to prospectively investigate the distribution between macro- and micro nutrient intake, meal frequency and growth in children with CHD.

**Methods:** At 6, 9 and 12 month of age, a 3 day food diary and anthropometric data were collected in 11 infants with severe CHD and 22 healthy age- and feeding matched controls. Macro- and micronutrient intake, meal frequency and growth were calculated.

**Results:** Compared to the healthy controls, CHD infants had statistically significantly higher intake of fat at 9 months of age (4.8 vs. 3.6 g/kg/d), a higher E% from fat, (40.6 vs 34.5) and a lower E% from carbohydrates (46.1 vs 39.6) at 12 months of age, and a lower intake of iron (7.22 vs 9.28 mg/d) at 6 months of age. Meal frequency was significantly higher at 6 and 9 months of age (p< 0.01). Mean z-score weight for height, weight for age and BMI for age were significant lower (p<0.01) at all time-points.

**Conclusion:** Despite higher intake of energy from fat and a higher meal frequency, the intake does not meet the needs for growth, and the results may indicate low intake of micronutrients in CHD infants.

**References:**


Disclosure of Interest: None Declared
USE OF A HYPERCALORIC FORMULA CONTAINING SYMBIOTIC AND DHA IN MALNOURISHED CHILDREN: FAILURE TO THRIVE AND INFLAMMATION

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Objectives and Study: The objective was to analyse the usefulness of a hypercaloric formula containing symbiotic and docosahexaenoic acid (DHA) in children with non-organic failure to thrive, regarding digestive tolerance, nutritional variables and inflammatory response. Hospital Ethics Committee approval and parental consent in all participants were obtained.

Methods: Multicentric, prospective, randomized controlled intervention study. Children ≥1 year with body mass index (BMI) ≤-1SD and with no documented organic disease were allocated, by double-blind method, in the intervention (hypercaloric formula with symbiotic and DHA) or in the control group (without symbiotic and DHA). Energy requirements were estimated using basal metabolic rate, physical activity factor and recovery needs. The formula was prescribed to help meeting these requirements; all patients consumed at least the minimum daily amount of formula prescribed. Nutritional variables and fecal calprotectin (FCp, N<30 μg/g faeces), as a marker of inflammatory response, were registered on inclusion (M0) and after 6 months of treatment (M6).

Results: 100 patients included (60% male). Mean age 5.88±4.56 y. No age differences between intervention and control group. No formula-related adverse events reported. FCp showed significant negative relation with BMI (p<0.001) and age (p<0.05) at M0. Patients ≤3 y showed significantly worse values of weight and BMI z-scores, fat body mass (FBM, as %normal value for age) and bioimpedance phase angle. Evolutive results: table 1. Patients with FCp>100 showed significantly worse values of weight, BMI, FBM and body cell mass.

<table>
<thead>
<tr>
<th></th>
<th>Intervention M0</th>
<th>Intervention M6</th>
<th>Control M0</th>
<th>Control M6</th>
</tr>
</thead>
<tbody>
<tr>
<td>BMI z-score</td>
<td>-2.1±0.12</td>
<td>-1.78±0.9</td>
<td>-2.25±0.11</td>
<td>-1.98±0.7</td>
</tr>
<tr>
<td>FBM (% normal value)</td>
<td>63±17</td>
<td>73±23.9</td>
<td>66±23</td>
<td>76.4±40</td>
</tr>
<tr>
<td>Phase angle (bioimpedance)</td>
<td>4.43±0.77</td>
<td>4.84±1.40</td>
<td>4.41±0.75</td>
<td>4.78±0.89</td>
</tr>
<tr>
<td>Body cell mass (%lean body mass in bioimpedance)</td>
<td>42.6±8.45</td>
<td>45.4±5.57</td>
<td>45±7.5</td>
<td>45.43±5.77</td>
</tr>
<tr>
<td>FCp (μg/g faeces)</td>
<td>66.6±96</td>
<td>50±41</td>
<td>41±31.8</td>
<td>58±83</td>
</tr>
</tbody>
</table>
Conclusion: Hypercaloric formula was safe and contributed to enhance nutritional status in both groups. In patients with non-organic failure to thrive, FCp showed high values and was a marker of poor nutritional condition. In the group treated with symbiotic and DHA, mean FCp decreased after 6 months. Further follow-up is needed to confirm these findings.

COMPARISON OF RATIO BETWEEN THE WAIST CIRCUMFERENCE BY THE HEIGHT AND BMI AS PREDICTORS OF HYPERTENSION

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Objectives and Study: To evaluate the correlation of blood pressure (BP) with body mass index (BMI), lean and fat mass of students in an urban area.

Methods: Cross-sectional study of blood pressure (BP) of a random sample of 1082 school children (from 6 to 7 and from 9 to 10 years old) from public schools in Florianópolis, SC, Brazil. BP was measured using the same technique recommendation and blood pressure levels were classified into percentiles of reference NHBPEP. BP was considered abnormal when blood pressure levels were higher than 90 percentile (p) of reference, without discriminating the risk hypertension (p90 to 95) and hypertension (p > 95). We analyzed the Pearson correlation (r) of BP with z score (z) of BMI (WHO 2007), the z Lean Muscle Area of the Arm (zLMAA), the z Fat Muscle Area of the Arm (zFMAA) and the percentage (%) of LMAA.

Results: The analysis of the relationship between Systolic (S) BP with z LMAA showed no correlation, r 0.17 (95% CI, 0.11 to 0.23) p < 0.0001. Disatolic (D) BP also showed correlation with LMAA z, r 0.23 (95% CI, 0.18 to 0.29) p < 0.000. For the z score FMAA correlation with SBP was 0.31 (95% CI, 0.26 to 0.37) and p < 0.0001, and for BPD was 0.22 (95% CI, 0.16 to 0.27) p < 0.0001. Correlations of % of LMAA with SBP (r - 0.27, 95% CI -0.33 to -0.22, p< 0.0001) and DBP (r - 0.11, 95% CI - 0.17 to -0.05, p 0.0005) were reversed.

Conclusion: the BP levels tend to be more severe when the LMAA corresponds to a smaller proportion of the total area of the arm. The FMAA seems to be the marker of body composition that, in isolation, best indicates the risk of hypertension.

Disclosure of Interest: None Declared
Objectives and Study: Hospital malnutrition plays a role in the progress of the disease. The purpose of the study is to investigate the occurrence of hospital malnutrition of under five-year-old children at Moewardi Hospital and to describe the current risks groups.

Methods: A cohort prospective study was conducted in patients under five-year-old children who hospitalized at Moewardi Hospital from May 2014 to September 2014. Patients who had organomegaly, oedema, malignancy and critical illnesses were excluded. Patients were followed up at the start of hospitalized up to discharged from the hospital. Walker and Hendricks criteria were used to define hospital malnutrition (HM). Data were processed based on WHO Anthro 2006 and SPSS 16. The processed data were analysed with logistic regression.

Results: A total of 268 patients were included in this study. Of 268 subjects, 53.35% were male, 86.19% suffered from infectious diseases, and 11.19% had 7 days or more length of stay. Subjects who suffered from HM were 120 patients (44.78%) with 66 patients (55.00%) were male, 107 patients (89.17%) had infectious diseases, and 23 patients (19.17%) had 7 days or more length of stay. Length of stay of 7 days or more was as a risk group for HM (OR: 4.78; 95% CI: 1.97 – 11.57).

Conclusion: Hospital malnutrition among under five-year-old children at Moewardi hospital is about 44.78%. Length of stay of 7 days or more is as a risk group for HM. The longer the patients stay at the hospital, the more HM the patients get. Thus, in order to prevent HM, paediatric nutrition care should be implemented properly for all patients.

Disclosure of Interest: None Declared
SEASONALITY OF VITAMIN D STATUS IN A PAEDIATRIC POPULATION: NOT ENOUGH EVEN IN SUMMER?

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Objectives and Study: Vitamin D is a prohormon involved in calcium homeostasis and bone health. Seasonal variation of vitamin D levels are well described in literature: rising in summer, but falling in winter. Aim of the study: to analyse the relationship between vitamin D levels and seasonality in a large pediatric population of Southern Italy.

Methods: The study population consisted of 1055 children and adolescents (mean age 6.8±4.8, range 0.02-17.74 yrs) living in the Northern Apulia and afferent to the Pediatric Department of the Hospital of Foggia. Serum 25-hydroxyvitamin D (25OHD) concentration was assessed and Vitamin D status was defined as follows: deficiency with serum 25OHD < 10 ng/ml, insufficiency among 10-29.9 ng/ml, sufficiency with serum 25OHD among 30-100 ng/ml. Collected data included age, gender and season of hospitalization.

Results: Mean level of serum 25 OHD in our population was 21.34±10.24 ng/ml. Significant vitamin D variations were recorded according to the season in which blood samples were drawn, mean levels were: 18.6±10 ng/ml during winter, 18.9±7.8 ng/ml during spring, 27.8±11.2 ng/ml during summer, 21.3±10.2 during autumn (p<0.001). The prevalence rates of vitamin D deficiency, insufficiency and sufficiency were in summer were: 1.8%, 66.3% and 31.9% respectively.

Conclusion: Vitamin D levels are strongly influenced by seasonality, but according to our results only 31.9% of children presented sufficient pattern during summer. It's important to establish screening, supplementation guidelines and pediatric cut-off levels to optimize vitamin D status in children.

Disclosure of Interest: None Declared
NUTRITIONAL OUTCOMES POST AUTOLOGOUS INTESTINAL RECONSTRUCTION SURGERY FOR SHORT BOWEL SYNDROME

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Objectives and Study: Patients undergoing bowel reconstructive surgery for short bowel syndrome have poor enteral tolerance immediately post surgery. The nutritional status is often maintained solely by parenteral nutrition (PN). Enteral feeds and diet are started as early as possible to stimulate intestinal adaptation, which is a vital phase in achieving enteral autonomy and weaning off PN. To assess the nutritional outcomes of infants with intestinal failure following autologous reconstruction surgery and identify dietary factors associated with the difficulties of weaning PN.

Methods: This was a retrospective study of 23 patients (47% males, gestational age range 27 – 40 weeks) undergoing autologous reconstructive surgery at an intestinal rehabilitation unit from 2006 to 2013 (identified by those with ongoing dietetic management within the unit). Aetiologies of SBS were gastroschisis, small intestinal atresia, mid gut volvulus, malrotation and necrotizing enterocolitis. Forty four percent had more than one congenital gastrointestinal condition.

Results: The patients underwent longitudinal intestinal lengthening and tailoring (n=8), serial transverse enteroplasty (n=5), combination of techniques (n=4) and the remainder tapering enteroplasty. Post-operative survival rate was 100%. The patients were divided into 2 groups, those off PN (n=10) and those continuing to require PN (n=13). Of the off PN patient group (PN mean 516 days) 40% continue to require enteral nutrition via a gastrostomy while those remaining on PN (PN mean 842 days) 31% are also fed via a gastrostomy. Compliance of hydrolysed feed was 87% of the on PN group days compared to 129% hydrolysed and 160% modular feed of the off PN group days (continuing with the advised feed choice post PN). The advised dietary restrictions (milk, egg, wheat and soya) were adhered to by 42 - 60% of the PN days in the off PN group whereas 26 – 37% of the PN days in the on PN group. All patients who achieved enteral autonomy gained weight to higher percentiles post surgery.

Conclusion: PN is required post reconstruction surgery for extended periods. Oral intake is increased as tolerated and gastrostomy feeding is used where required. Potential dietary factors associated with successful weaning of parenteral nutrition include early eating experience, short duration on PN prior to surgery, hydrolysed formula as the feed of choice and adhering to the dietary restrictions. Parental compliance is a major factor in this cohort of patients.

Disclosure of Interest: None Declared
YOGURT FOR GASTROINTESTINAL HEALTH OUTCOMES: SYSTEMATIC REVIEW AND META-ANALYSIS

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Objectives and Study: It has been postulated that yogurt may act on gut health. This may explain its use in some common gastrointestinal conditions. Here, we aim to systematically evaluate the efficacy of yogurt consumption for the management of acute gastroenteritis (AGE) in children, and also for preventing antibiotic-associated diarrhea (AAD) in both children and adults.

Methods: A scoping review of the evidence of the health benefits conferred by the consumption of yogurt, followed by two separate systematic reviews, has been performed. A number of databases, including MEDLINE, EMBASE, and the Cochrane Library, with no language restrictions, were searched up to September 2014 for randomized controlled trials (RCTs) evaluating the effect of yogurt consumption in the treatment of AGE and in the prevention of AAD. The risk of bias was assessed using the Cochrane risk of bias tool.

Results: For AGE outcomes, four RCTs (n = 448), all performed in hospital setting, were included. Compared with placebo/no intervention, yogurt consumption had no significant effect on stool volume and inconsistent effect on the duration of diarrhea or stool frequency. Treatment success (or failure) rates were similar in both groups. Compared with placebo, the duration of hospitalization was shorter in children who received yogurt, but the difference was of a borderline significance. Total weight gain increased for those treated with yogurt.

For prevention of AAD, two included RCTs assessed the effect of yogurt. Compared with no intervention, yogurt consumption reduced the risk of diarrhea in the fixed effect model (2 RCTs, n=314, relative risk, RR 0.56, 95% confidence interval, CI 0.31 to 1.00). Significant heterogeneity between the trials was detected (I²=67%). The significant reduction in the risk of diarrhea was lost in the random effect model (RR 0.45, 95% CI 0.11 to 1.75).

Conclusion: The effect of yogurt consumption on the majority of AGE outcomes and for preventing AAD was inconsistent. However, the data are limited and all included trials had important methodological limitations.
Disclosure of Interest: B. Patro-Gołąb Conflict with: This review was partially supported by the Danone International Institute., R. Shamir Conflict with: This review was partially supported by the Danone International Institute., H. Szajewska Conflict with: This review was partially supported by the Danone International Institute.
BIO - ELECTRIC IMPEDANCE ANALYSIS (BIA) OF THE BODY COMPOSITION OF CHILDREN AND ADOLESCENTS WITH SICKLE CELL ANAEMIA IN ENUGU, NIGERIA

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Objectives and Study: Background: Body composition indices are widely used to evaluate growth and nutrition in children particularly those with sickle cell anaemia (SCA) known to have impaired growth and poor nutrition as well as impaired skeletal maturation and delayed puberty.

Objectives: The study is aimed at determining the body composition of children and adolescents with SCA.

Methods: Consecutive selection of SCA children aged 6 – 18 years who served as subjects and their age and gender matched school children with HbSS (controls) selected using multi-stage systematic sampling was undertaken. It was a cross sectional descriptive study conducted at the paediatric haematology-oncology clinic of University of Nigeria teaching Hospital Enugu. BIA was used to determine the body composition parameters including weight, percentage body fat, visceral fat percentage, body mass index (BMI), skeletal muscle percentage (SMP) and resting metabolic rate. Data was analyzed using SPSS 16.0 at P = < 0.05.

Results: One hundred and thirty two subjects and controls respectively were studied. Subjects had lower body composition parameters compared to controls with the older males subjects aged 10 – 18 years having lower body composition indices (weight, height, BMI, visceral fat %, SMP and RMR) compared to the controls. Visceral fat percentage was low in both subjects and controls.

Conclusion: Children with SCA particularly the older males have impaired body composition indices. There is need to conduct further studies to determine the longitudinal aspects of growth as well as quantitative and qualitative assessment of nutritional intake in children with SCA.

Disclosure of Interest: None Declared
USE OF BODY COMPOSITION MEASUREMENTS IN PAEDIATRIC PATIENTS: IDENTIFYING MALNUTRITION AND PREDICTING CLINICAL OUTCOMES

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Objectives and Study: To determine baseline body composition (BC) in children admitted to a tertiary paediatric hospital, and examine associations with length of stay (LOS) and weight loss during admission.

Methods: Children aged 5-18yrs admitted to a tertiary referral hospital with expected stay >3 days had measurements of weight (WT), height (HT) and BC (lean mass by Dual Energy X-ray Absorptiometry (LMDXA) and bioelectric impedance analysis (LMBIA); fat mass (FM) by DXA and 4-site skinfold thicknesses (SFT)) within 48 hours of admission. Standard deviation scores (SDS) were calculated from UK BC reference data 1. Diagnosis, nutritional management, predicted LOS and mobility were recorded, with WT and actual LOS at discharge.

Results: 128 children (mean age 10.7yr; 49.2% male) were studied; 54.7% from medical and 45.3% from surgical wards, most with multiple and chronic diagnoses. Median LOS was 7 (range 1-65) days. On admission, children had significantly low HT and LM, with high BMI and SFTs. 19% had LMDXA < -2SDS, compared to 12% LMBIA and WT, and 2% BMI. Lower WT and LMDXA were predicted by immobility (wheelchair use), and artificial/liquid parenteral or enteral nutrition (EN/PN). Lower BMI, FM, and LMBIA were also predicted by EN/PN; with a greater effect for full versus partial EN/PN. Baseline WT, BMI and BC did not correlate significantly with actual or predicted LOS. Children with higher baseline WT, BMI and FM lost more WT by discharge.
Table 1: Measurements of children admitted to hospital

<table>
<thead>
<tr>
<th></th>
<th>Triceps SFT</th>
<th>FM DXA</th>
<th>LM DXA</th>
<th>LM BIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>1.7</td>
<td>3.1</td>
<td>10</td>
<td>90</td>
</tr>
<tr>
<td>3</td>
<td>1.9</td>
<td>3.2</td>
<td>10</td>
<td>4.1</td>
</tr>
<tr>
<td></td>
<td>0.17 (0.9)</td>
<td>0.19 (1.2)</td>
<td>-0.91 (1.5)*</td>
<td>-0.72 (1.3)*</td>
</tr>
<tr>
<td></td>
<td>1</td>
<td>5</td>
<td>19</td>
<td>12</td>
</tr>
<tr>
<td></td>
<td>0</td>
<td>6</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>90</td>
</tr>
</tbody>
</table>

*1-sample t-test, p<0.05; mean(SD); %; %score/100

**Conclusion:** Children admitted to this hospital are short with abnormal BC characterized by low LM and variable FM, frequently not apparent from WT/BMI, with implications for nutritional management. DXA and BIA were feasible and acceptable techniques whilst SFT were less so. Immobility and nutritional support were the most significant predictors of abnormal BC. BC measurements did not correlate with LOS and WT loss during admission, probably reflecting the limitations of generic outcomes for this heterogeneous group. Further research will target specific patient groups using disease-specific outcomes to establish the usefulness of BC measurements for nutritional management of these children.

**References:** Wells JC et al. AJCN 2012;96:1316
Disclosure of Interest: None Declared
**IMPACT OF MALNUTRITION ON THE MINIMAL RESIDUAL DISEASE PERCENTAGE AT THE END OF REMISSION INDUCTION IN CHILDREN WITH ACUTE LYMPHOBLASTIC LEUKEMIA**

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**Objectives and Study:** In Mexico, the acute lymphoblastic leukemia (ALL) represents 40% of the total cases of cancer in children. Current treatment options show 80% survival rates but this is based on individualized treatment protocols, which consider clinical, laboratory and molecular approaches. Despite changes to improve health care in Mexico the above mentioned results are seldom obtained. Actually consider minimal residual disease (MRD) as an independent indicator. The nutritional status at the time of diagnosis and its predictive prognosis is controversial and malnutrition might be a key factor for a negative response to the treatment. Our objective was to correlate the nutritional status and the percentage of MRD at the end of remission induction (RI) in children with acute lymphoblastic leukemia at the Morelia Children’s Hospital in Mexico.

**Methods:** Thirty-eight ALL de novo cases were evaluated based on their initial nutritional status. We determined the weight/height indicator based on the Waterlow classification at the time of diagnosis and at the end of RI.

**Results:** Out of the 38 patients, 13 showed signs of malnutrition with no significant correlation (p=0.362) with MRD. But the percentage of malnourished patients in our study at the time to diagnosis was 34.2% when compared the percentage of malnourished children at the end of RI which was 57.9% its significant correlation (p=0.000) It might be possible that the nutritional status does not affect LLA directly but it might exacerbate other health conditions such as a depletion in the immune system.

**Conclusion:** There are various studies that have included correlations between malnutrition and disease prognosis and the response to treatment with no conclusive results. It is necessary to establish an evaluation protocol of the nutritional status during cancer treatment for ALL in order to know what will be the outcome of the disease.

**References:** Lange, B.J., Gerbing, R.D., Feusner, J., et al, Mortality in overweight and underweight children with acute myeloid leukemia, JAMA, 2005; 293 (2), 203-211.


Disclosure of Interest: L. Garcia-Rojas Vazquez Conflict with: I declare that I have no conflict of interest, L. ARROYO CRUZ Conflict with: I declare that I have no conflict of interest, E. PEREZ RIVERA Conflict with: I declare that I have no conflict of interest
HEALTH-RELATED QUALITY OF LIFE, NUTRITION AND PHYSICAL ACTIVITY AFTER A MULTIMODAL OBESITY INTERVENTION

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1Ministry of Education, Universities and Research, Foggia, 2Paediatrics, University of Foggia, Foggia, Italy

Objectives and Study: In the context of a multi-modal obesity program, incorporating fun-type skill-based physical activities, exercise training and nutritional education, this study examined changes in body composition, actual and perceived physical abilities (PPA), health-related quality of life (HRQoL), enjoyment of physical activity (EnjPA), and food intake in children.

Methods: The Eurofit and Fitnessgram tests of standing long jump (SLJ), 1kg medicine-ball throw (MBT), 4×10m shuttle-run (SR), 10m sprint, trunk lift and sit-ups were administered before (T0) and after (T1) a 6-month program (two 2h sessions/week) in 18 obese and overweight (ow) children (9 boys and 9 girls; 11.3±0.4 yrs). EnjPA and individuals' perceptions of strength, speed and agility were measured with the Physical Activity Enjoyment Scale and the Perceived Physical Ability Scale for Children, respectively. HRQoL assessing physical, emotional (EF), social (SF), and school (SC) functioning was evaluated using the Pediatric Quality of Life Inventory (PedsQL 4.0). Nutritional data were collected with a 7-day food diary.

Results: From T0 to T1, BMI z-score (1.8±0.4 vs 1.5±0.4; p<.001) and percentage of body fat (39.5±6.3 vs 36.4±7.0; p<.001) decreased. With regard to actual and PPA, there were significant changes over time in the SLJ (99.2±20.6 vs 106.6±19.8 cm; p<.04), MBT (4.7±1.0 vs 5.5±0.9 m; p=.1), SR (19.2±1.4 vs 18.4±1.6 sec; p<.05), sit-ups (10.8±6.9 vs 18.2±4.8 n/rep; p=0.02) and perception of competence (16.9±2.4 vs 18.2±2.0; p<.02), with children showing better performances and higher PPA scores at the end of the program. For HRQoL outcomes, significant time effects were shown, with participants reporting greater EnjPA (p<.05) and higher psychosocial (EF+SF+SC) scores at T1 compared to T0. At the end of the intervention, children showed reductions in the total and commercial food caloric intake (p<.001), with higher protein (p=.003) and lower fat (p<.001) consumptions (Tab. 1).

<table>
<thead>
<tr>
<th>Variable</th>
<th>T0 (M±SD)</th>
<th>T1 (M±SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HRQoL scores</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>79.0±14.5</td>
<td>82.7±11.1</td>
</tr>
<tr>
<td>Psychosocial health</td>
<td>78.1±16.9</td>
<td>84.9±11.6</td>
</tr>
<tr>
<td>EnjPA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Positive feeling scale</td>
<td>36.2±5.4</td>
<td>37.9±6.8</td>
</tr>
<tr>
<td>Negative feeling scale</td>
<td>9.9±4.3</td>
<td>9.0±3.9</td>
</tr>
<tr>
<td>Dietary intake</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Caloric intake (kcal/die)</td>
<td>1834.0±300.6</td>
<td>1368.17±175.4</td>
</tr>
<tr>
<td>Proteins (%)</td>
<td>13.9±1.8</td>
<td>17.7±3.4</td>
</tr>
</tbody>
</table>
Fats (%)  
38.3±4.5  
32.0±3.7

Carbohydrates (%)  
47.6±4.6  
50.0±4.1

Commercial food calorie intake (kcal/die)  
751.0±255.0  
265.0±150.6

**Conclusion:** Findings highlight the importance of combined dietary-behavioral-PA interventions among ow children, and emphasize the importance of directing such interventions toward improving EnjPA that could lead to increased exercise adherence and promotion of the health benefits associated with it.

**Disclosure of Interest:** None Declared
THE EFFECT OF GLUCOMANNAN ON BODY WEIGHT IN OVERWEIGHT OR OBESE CHILDREN AND ADULTS: A SYSTEMATIC REVIEW OF RANDOMISED CONTROLLED TRIALS

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1The Medical University of Warsaw, Warsaw, Poland

Objectives and Study: Glucomannan (GM), a soluble fiber derived from the plant Amorphophallus konjac, is marketed as being helpful in reducing body weight. However, the data supporting this claim are scarce. We aimed to systematically evaluate the effects of GM on body weight (BW) and body mass index (BMI) in otherwise healthy obese or overweight children and adults.

Methods: The MEDLINE, EMBASE, CENTRAL, and Google Scholar databases were systematically searched up to June 2014 for randomized controlled trials (RCTs) assessing the effectiveness of GM compared with placebo. The primary outcome measures were BW and BMI.

Results: Six eligible RCTs, only one performed in children, were included. In adults, three RCTs reported a significant reduction in BW in the GM group compared with the control group at the following different time points during the intervention: at week 2 (mean difference [MD] 0.21 kg, 95% confidence interval [CI] [0.13 to 0.29]); at week 4 (MD 2.04, 95% CI [0.52 to 3.56]); at week 5 (MD 1.3, 95%CI [0.89 to 1.71]); and at week 8 (MD 3.17, 95% CI [1.29 to 5.05]). Only one RCT reported the beneficial effect at more than one time point. None of the RCTs reported a favorable effect of GM on BMI.

Conclusion: In otherwise healthy overweight or obese adults, there is some evidence that in the short term GM may help to reduce BW, but not BMI. Data in children are too limited to draw any conclusions.

Disclosure of Interest: None Declared
NUTRITION GROWTH AND HEPATIC FUNCTION IN CHILDREN WITH ATAXIA TELANGIECTASIA

Ashraf Soliman 1, Mohammad Ehlayel 1, Vincenzo Desanctis 2
1 Hamad Medical Centre, Doha, Qatar, 2 Quisisana Hospital, Ferrara, Italy

Objectives and Study: Ataxia telangiectasia (AT) is a primary immune deficiency disease characterized by immunodeficiency, neurological manifestations, with increased tendency to infection, malignancy, autoimmune diseases and delayed growth. We measured growth and nutritional parameters and related biochemical background in 13 children with AT.

Methods: We studied growth parameters height (Ht), weight, body mass index (BMI) and calculated the HtSDS of 13 patients (age 7.7 ± 3.5 years) with AT in relation to their mid-parental height SDS (MPHtSDS). We measured their serum calcium (Ca), phosphorus (PO4), alkaline phosphatase (ALP), alanine transferase (ALT), serum ferritin, and creatinine and albumin concentrations. Endocrine investigations included the assessment of serum free thyroxine (FT4), thyrotropin (TSH), insulin-like growth factor-I (IGF-I) and morning cortisol. Complete blood count and serum immunoglobulins (IgG, IgM and IgA antibodies) were also measured. Growth data were correlated to hormonal and immune data.

Results: 31% of patients with AT had short stature (HtSDS < -2). However, their MPHtSDS denoted that their short stature was familial because 4 out of 13 had MPHtSDS < -2. They had low BMI (38% had BMISDS < -1.5) and 2 of them had low serum albumin and IGF-I concentrations, denoting malnutrition. Elevated serum ALT (38%) and ferritin (22%) in some patients suggest immune-related inflammation in the liver. Eight out of 13 patients had vitamin D deficiency (<20ng/ml) however, their serum Ca and PO4 levels were in the normal range. BMISDS and HtSDS were correlated negatively with age (r = -0.675, and -0.56 respectively p < 0.001) denoting deterioration of the nutritional status and growth with time. None of the growth parameters were correlated with the immunoglobulin (IgG, IgM or IgA) levels.

<table>
<thead>
<tr>
<th></th>
<th>HtSDS</th>
<th>BMI</th>
<th>MPHtSDS</th>
<th>BMI SDS</th>
<th>IGF-I</th>
<th>Albumin</th>
<th>ALT</th>
<th>Ferritin</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mean</strong></td>
<td>-1.4</td>
<td>15.</td>
<td>-1.3</td>
<td>-0.76</td>
<td>149</td>
<td>39.2</td>
<td>42.</td>
<td>324.0</td>
</tr>
<tr>
<td><strong>SDS</strong></td>
<td>1.2</td>
<td>2.4</td>
<td>1.1</td>
<td>1</td>
<td>110</td>
<td>7.2</td>
<td>24.</td>
<td>606.3</td>
</tr>
<tr>
<td><strong>Number of patients investigated</strong></td>
<td>13.0</td>
<td>13.</td>
<td>13.0</td>
<td>13</td>
<td>8.0</td>
<td>13.0</td>
<td>13.</td>
<td>9.0</td>
</tr>
<tr>
<td><strong>Abnormal</strong></td>
<td>38%</td>
<td>38</td>
<td>31%</td>
<td>38%</td>
<td>38%</td>
<td>15%</td>
<td>38</td>
<td>22%</td>
</tr>
</tbody>
</table>
**Conclusion:** Patients with AT had high prevalence of growth retardation and nutritional abnormalities (decreased HtSDS, BMI, BMISDS, IGF-I, and albumin) that increase with age. Full nutritional follow up and support is necessary to avoid delayed growth.

**Disclosure of Interest:** None Declared
VALIDATION OF A FOOD FREQUENCY QUESTIONNAIRE FOR ADOLESCENTS IN CROATIA

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1 Children's hospital Zagreb, 2 UHC "Sestre Milosrdnice" Zagreb, 3 Department for Pediatric Gastroenterology, Children's Hospital Zagreb, Zagreb, Croatia

Objectives and Study: The food frequency questionnaire (FFQ) is a tool for the estimation of food and nutrient consumption and it has become important method in epidemiologic studies. Validation of new FFQ is necessary because poor nutrient intake data may lead to false associations between diet and disease. The aim of the study was to develop a FFQ and evaluate its relative validity for adolescents who are living in Croatia.

Methods: The final version of the FFQ was composed of 87 food items previously identified according to their contribution in nutrients and overall importance within the eating habits of this population group. The validation study, which was undertaken during a 1-month period was administered to a sample of 100 healthy children (68 % female and 32% male; age mean 15.4 years, range 12 to 18 years) who completed a two 3-day nonconsecutive food records (3D-FR) applied at intervals of 21 days and one FFQ at the end of the study.

Results: The mean nutrient intake values of the FFQs were higher than those of the 3-day FR. The average median difference between the 2 instruments was approximately for energy and macronutrients 18%. In table 1 we provide results for Spearman rank correlation analyses between nutrients from the FFQ and 3D-FR for the entire sample and they were positive and generally statistically significant. For the macronutrients Spearman rank correlation analyses between FFQ and FR nutrients were positive with r ranging from 0.31 for fats (P<0.05) to carbohydrates 0.57 (P<0.01). For the micronutrients Spearman rank correlation was also positive with r ranging from 0.22 for thiamin (P<0.05) to riboflavin 0.55 (P<0.01). Cross-classification analysis revealed that on average, 79% of FFQ validation study participants were classified in the same or adjacent quartile of nutrient intake when comparing data from the FFQ and 3-day FR. Bland-Altman plots were used to assess the concordance between the mean energy and nutrient values estimated from the two tools and the results showed for energy, protein and zinc the most significant validity parameters, and zinc was found to show the best concordance.

<table>
<thead>
<tr>
<th>Nutrients</th>
<th>r</th>
<th>Nutrients</th>
<th>r</th>
<th>Nutrients</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy, kcal</td>
<td>0.51**</td>
<td>Dietary fiber, g</td>
<td>0.18</td>
<td>Vitamin C, mg</td>
<td>0.15</td>
</tr>
<tr>
<td>Carbohydrates, g</td>
<td>0.57**</td>
<td>Sodium, mg</td>
<td>0.34*</td>
<td>Thiamin, mg</td>
<td>0.22*</td>
</tr>
<tr>
<td>Total fat, g</td>
<td>0.31*</td>
<td>Potassium, mg</td>
<td>0.33*</td>
<td>Riboflavin, mg</td>
<td>0.55**</td>
</tr>
<tr>
<td>Protein, g</td>
<td>0.49**</td>
<td>Iron, mg</td>
<td>0.38*</td>
<td>Niacin, mg</td>
<td>0.41*</td>
</tr>
<tr>
<td>Saturated fatty acids, g</td>
<td>0.55**</td>
<td>Zinc, mg</td>
<td>0.49**</td>
<td>Vitamin B6, mg</td>
<td>0.33*</td>
</tr>
<tr>
<td>Polyunsaturated fatty acids, g</td>
<td>0.25*</td>
<td>Magnesium, mg</td>
<td>0.42*</td>
<td>Vitamin B12, mg</td>
<td>0.47*</td>
</tr>
</tbody>
</table>

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<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Value</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Monounsaturated fatty acids, g</td>
<td>0.43*</td>
<td></td>
</tr>
<tr>
<td>Copper, mg</td>
<td>0.28*</td>
<td></td>
</tr>
<tr>
<td>Cholesterol, mg</td>
<td>0.45*</td>
<td></td>
</tr>
<tr>
<td>Vitamin A, µg</td>
<td>0.25*</td>
<td></td>
</tr>
</tbody>
</table>

*P<0.05; **P<0.01

**Conclusion:** Results of this study indicate that a simple self-administrated questionnaire completed by adolescents is a valid tool for measuring nutrient intake in studied group.

**Disclosure of Interest:** None Declared
GROWTH AND LIVER FUNCTION IN CHILDREN ON LONG-TERM PARENTERAL NUTRITION

Maria Immacolata Spagnuolo 1,* Serena Orlando 1 Ilaria Liguoro 1 Fabrizia Chiatto 1 Carmela Langella 1 Sara Viscovo 1 Andrea Lo Vecchio 1 Alfredo Guarino 1

1 University Federico II, Napoli, Italy

Objectives and Study: Few data are available about growth in children with intestinal failure (IF) on long-term Parenteral Nutrition (PN). Short stature and delayed puberty onset have been reported. Liver failure also represents a major complication in children on PN. The aim of this study was to evaluate the growth and the liver function in a paediatric population on PN (2000-2014).

Methods: Children receiving long-term PN (>6 months) were retrospectively enrolled. Anthropometrics and liver parameters were collected. Weight-for-age (WFA) and height-for-age (HFA) were expressed as SD-scores, considering values <-2SD as markers of malnutrition. Serum liver enzymes were expressed as mean ± SD. The Student t-test and the chi-squared method were performed to compare the variables.

Results: Among the 30 children seen for long-term PN, 20 met the inclusion criteria (11 males; 80.4±58.5months). After 12 months of PN, the number of children with WFA<-2SD decreased from 16/20 (80%) at diagnosis to 6/20 (30%) (p=0.0036). Similarly, 14/20 (70%) patients resulted <-2SD for HFA at admission compared with 4/20 after 12 months of PN (20%)(p=0.0036). Furthermore, only 1/5 children receiving PN > 10 years had a HFA <-2SD. All patients treated with ursodeoxycholic acid had stable and normal mean levels of liver parameters over time.

Conclusion: Over the past 14 years, management of PN has been improved, leading to better results regarding growth and liver complication. Twelve months of PN can significantly improve the growth of children with IF, with 70% and 80% of patients reaching the normal range for weight and height respectively. These data are confirmed in the children receiving PN>10 years. No patient was affected by intestinal failure associated liver disease.

Disclosure of Interest: None Declared
BODY COMPOSITION, PHYSICAL ACTIVITY AND QUALITY OF LIFE IN PAEDIATRIC PATIENTS WITH CROHN’S DISEASE

Inês Asseiceira 1, Tânia Furtado 2, Sara Azevedo 3, Teresa Rodrigues 3, Moreira Ana Catarina 2, Ana Isabel Lopes 3

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Objectives and Study: Crohn’s disease (CD) in paediatric patients has been associated with poor nutritional status and delayed growth and maturation. Body composition alterations as well as levels of physical activity and quality of life have so far been poorly characterized. We aim to assess nutritional status, by anthropometric measures and electric bioimpedance, physical activity (PA) levels and Quality of Life (QoL) in CD patients and compare to a healthy control group.

Methods: In a convenient sample with 31 paediatric CD patients, 21 in remission and 10 with mild active disease were compared with 79 healthy controls. Mean age were 12.3±2.8Y and 15.0±2.7Y, respectively. Mean Activity disease according to Paediatric Crohn’s Disease Activity Index (PCDAI) was 6.3±5.8. Body Mass Index (BMI), weight, height, tricep skinfold, Fat Mass (FM) and Fat Free Mass (FFM) were evaluated. The upper arm muscle area (UMA) was calculated. PA was assessed by a Portuguese version of Baecke et al questionnaire and QoL by IMPACT III and KIDSCREEN 27 in case group and control group, respectively. Statistical analysis was conducted with IBM® SPSS® v.22.

Results: Weight, height and BMI z-scores were lower in CD patients as compared to control subjects (p=0.001; p=0.011 and p=0.002, respectively). Concerning to BMI 74.2% in CD group and 59.5% in control group were eutrophic. The remaining anthropometric parameters were similar in patients with active or remissive disease. In CD group, PCDAI was inversely related to PA in patients with active disease (r=-0.747;p=0.02). PA levels were significantly higher in control group, 8.6±1.5 vs 7.5±1.4 (p=0.001; difference 95%CI [-1.8;-0.5]). Also PA levels were inversely related to FM (r=-0.484;p<0.001) and directly related to FFM (r=0.607;p<0.001). QoL in CD group was 138.1±21.4 and this parameter was directly related to PA (r=0.399;p<0.001).

Conclusion: In this sample most of the CD patients were eutrophic despite the differences observed in the two groups related to body composition. Globally CD patients had a high QoL, and in this group, the patients with higher QoL tend to have more PA. Our data further emphasized the relevance of integrate nutritional status, QoL optimization and encouraging PA practice in CD patients.

Disclosure of Interest: None Declared
IronCHEQ Questionnaire as a First Step Screening Tool for Detecting Iron Deficiency in Toddler

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1Dept Pediatrics - Faculty of Medicine Universitas Indonesia, 2Faculty of Medicine Universitas Indonesia, Jakarta, Indonesia

Objectives and Study: Universal iron supplementation is posing children to morbidity and mortality in malaria endemic area. Screening test is become important before application of iron supplementation. Unfortunately universal screening test is quite expensive for developing countries like Indonesia. For that reasons non invasive screening by scoring system for detection toddler at risk of iron deficiency is needed. An ironcheQ questionnaire was designed as the first step screening tools for detecting high risk iron deficient toddlers before undergone blood examination. The aim of the study to validate and searching for the cut-off of the questionnaire’s total score that gives highest sensitivity, specificity, positive predictive value and negative predictive value

Methods: The questionnaire was validated and applied to 300 healthy toddlers choosen randomly from 5 primary health care in Jakarta to correlate the total score with dietary iron intake and serum’s ferritin. Dietary iron intake was assessed by 3 days food record.

Results: The IroncheQ has sufficient validity (r>0,4) and reliability (kappa 0,4-1). The questionnaire of 3 items with cut-off total score of 4 had sensitivity 80,4%, specificity 67%, PPV 53,8% and NPV 87,7% in correlation with dietary iron intake, whereas had sensitivity 71,6%, specificity 61%, PPV 43,6% and NPV 83,6% in correlation with serum’s ferritin

Conclusion: IroncheQ questionnaire can be used as the first step screening tool for detecting iron deficient toddler

Disclosure of Interest: D. Sjarif Conflict with: Danone Nutricia Indonesia, S. Tjia Conflict with: Danone Nutricia Indonesia, K. Yuliarti Conflict with: Danone Nutricia Indonesia, A. Kekalih Conflict with: Danone Nutricia Indonesia
**Nutrition**

**Clinical Nutrition**

PO-N-0435

**DIETARY INTAKE IN CHILDREN AND ADOLESCENTS WITH CHRONIC LIVER DISEASE**

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1Hospital de Clínicas de Porto Alegre, Porto Alegre, Brazil

**Objectives and Study:** To assess the dietary intake of children and adolescents with chronic liver disease.

**Methods:** Cross-sectional study comprised of 43 children and adolescents with clinical diagnosis of chronic liver disease, regularly attended at the Paediatric Hepatology Unit, Hospital de Clínicas de Porto Alegre, Brazil. The assessment of dietary intake was assessed through a three-day food record completed by parents and/or caregivers.

**Results:** The average caloric intake (± SD) presented was 1331 (± 455.2) kcal/day and its median (P25-P75) daily adequacy compared to Dietary Reference Intakes (DRI) found was 108.6% (89-128)(IOM, 2002/2005). The average macronutrient distribution from total caloric intake was equal to 58.2% in the group of carbohydrates, 13.1% of protein and 28.7% of lipids. Consumption of zinc and calcium was below the estimated average requirement by the age of 4, both girls and boys. Five children were breastfed and 67% reported consumption of cow's milk. The use of extensively hydrolyzed protein formula, exclusively or in combination with breast milk reached 16.3%. Enteral nutrition occurred in 4.7% of all patients. The consumption of any type of caloric supplement, such as carbohydrate module or medium chain triglyceride was present in 32.6%.

**Conclusion:** Median daily caloric adequacy presented was below specific recommendation for children and adolescents with chronic liver disease. Low intake of micronutrients such as zinc and calcium in this population deserves attention.


**Disclosure of Interest:** None Declared
NUTRITIONAL INTERVENTION IN PAEDIATRIC PATIENTS WITH OSTEOGENESIS IMPERFECTA

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Objectives and Study: Study the consumption of milk and soda beverages in paediatric patients with Osteogenesis Imperfecta (OI) before and after nutritional intervention.

Methods: A cohort study of subjects of both genders, aged between 2 and 18 years old, diagnosed with OI at the Reference Center for Osteogenesis Imperfecta of Rio Grande do Sul, Southern Brazil. Intake of milk was analyzed through number of glass (200ml) per day (0 - does not consume, 1- consumes less than 1 glass /day, 2- consume 1 to 2 glasses/day, 3- consume 3 or more glasses/day). Soda beverages was analysed through the frequency of glass (200 ml) consumption during a week (1- daily consumption, 2- consume on weekends, 3- less than 1 glass/week, 4- do not consume). The data on consumption was assess by food frequency questionnaire before and after a nutritional intervention for a rich calcium diet recommendation. The Ethics Committee of the Hospital de Clínicas de Porto Alegre approved this study (number 11-0585).

Results: 52 patients were evaluate, 29 were female and a mean age of 50.83 ± 129.48 months. Milk consumption at baseline showed that 0= 4(7.7 %), 1= 9(17.3%), 2= 28(53.8 %) and 3= 11(21.2%). After nutritional intervention none of the subjects did not consume milk, 1= 4(7.7%), 2= 29 (55.8 %) and 3= 19 (36.5%). For soda beverages at baseline showed 1= 19 (36.5%), 2= 27 (51.9%), 3= 2(3.8%) and 4= 4 (7.7%). After the intervention was observe that 1= 11 (21.2%), 2= 30 (57.7 %); 3= 7 (13.5 %) and 4 = 4 (7.7%). A significant difference before and after nutrional intervention was observed (p = 0.002 for milk and p=0.012 for soda beverages consumption).

Conclusion: In this study, was observe an increase in milk consumption, consequently calcium intake, and a decrease in the frequency consumption of soda beverage after nutrional intervention. This shows the importance of nutritional intervention in the multidisciplinary treatment of OI.


Disclosure of Interest: None Declared
CHARACTERISTICS OF PAEDIATRIC OBESITY IN A REFERRAL CENTRE OF BRAZIL.
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Objectives and Study: To describe demographic, clinical and laboratory characteristics of obese pediatric patients and compare them between the different degrees of obesity.

Methods: Cross-sectional study. The data was collected from medical records of all pediatric patients at the admission in an ambulatory referral center of a university located in the southeastern region of Brazil, from 2006 to 2012. The nutritional indicator used was Weight/Height (W/E) to the patients, calculated by the formula [W/H= Weight/Height corrected for p50 of Height]. To their mothers, we calculated the Body Mass Index (BMI) by the formula BMI = Weight/Height2. The variables studied were sex, birth weight (Low birth weight < 2,500g and High birth weight > 4,000g), weight (g) and length (m) at first attendance, weight (g) and length (m) of the mother, blood glucose (g/dL), cholesterol Total (RV<150 mg/dL), HDL (RV>45 mg/dL), LDL (<100 mg/dL) and triglycerides (<100 mg/dL). For assessing obesity, were stipulated as cutoffs of P/E (grade I and II obesity > 120% at 139%; grade III obesity > 140%) and of adult BMI (≥ 25 to <30 overweight and obese ≥ 30). The Kruskal-Wallis test was used to compare the clinical and laboratory characteristics between the two groups of patients (P/E> 140% and P/E <140%). The significance level was p< 0.05. The program used was Epi info 7.

Results: There were 89 patients, 50.6% male, mean age 68.9 months. The mean of P/E was 157.1 (± 25.4). Birth weight was obtained of 93.2% (83/89) patients, mean of 3,282 g (± 613.5). Maternal BMI mean, observed in 77.1% (64/83) of records, was 29.1 (± 5.6). Blood glucose was requested to 82% (73/89) of patients, with a mean of 81.7 mg/dL (± 8.1). Regarding the lipid profile, total cholesterol mean (76/89 patients) was 162.2 mg/dL (± 29.3); triglyceride mean (70/89), was 87.0 mg/dL (± 39.8); LDL mean (73/85) was 103.0 mg/dL (± 26.7) and HDL mean (73/89) was 39.4mg/dL (± 9.8). There was none statistical difference between the two groups of patients (p<0.05).

Conclusion: Although living in a developing country, patients showed mean % P/E featuring grade III obesity. The birth weight mean was not characteristic of low birth weight or of high birth weight. Mean maternal BMI showed that the weight of mothers was already next levels of obesity. The means of laboratory tests found themselves elevated to the levels of total and LDL cholesterol. Therefore, this patients had marked obesity, but without some determinants of obesity present in a country undergoing nutrition transition, such as low birth or high weight.

Disclosure of Interest: None Declared
Nutrition
Clinical Nutrition
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DRAMATIC REDUCTION IN CRBSI RATES IN A REGIONAL HOME PARENTERAL NUTRITION SERVICE: TAUROLOCK OR CYCLED ENTERAL ANTIBIOTICS (CEA)?

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Objectives and Study: Achieving reduction in catheter-related blood stream infection (CRBSI) rates in Home Parenteral Nutrition (HPN) patients is important for long-term morbidity and mortality. We have previously described the effect of cycled enteral antibiotics (CEA) prophylaxis on CRBSI rates in our population1 and wished to examine the effects of our changes in clinical practice, namely the use of Taurolock prophylaxis and CEA on CRBSI rates.

Methods: Retrospective analysis of CRBSI rates among long-term HPN patients in a tertiary paediatric service 2008-2013. Basic demographics were gathered, patients were selected for prophylaxis on basis of early or inpatient CRBSI, or clinician perception of ‘high risk’ for CRBSI. CRBSI rates (expressed as per 1000 central venous catheter (CVC) days) were analysed for each patient and also stratified as cohorts of ‘Taurolock’, ‘CEA’ or ‘neither’. Data was compared to the historical cohort1. CVC occlusions, CVC removal rates and locus of CRBSI origin (community vs. hospital acquired) were also observed.

Results: Twelve patients (5 received Taurolock and/or CEA) received PN over 9,738 CVC days at a median age of 620 days when commencing PN. There were 14 CRBSIs compared to 132 CRBSIs in 9,512 CVC days1 (1.4 vs. 13.9 CRBSI/1000CVC days, p<0.05). Although Taurolock and CEA treated patients both had lower rates of CRBSI whilst on treatment (1.9 vs. 2.7/1000 CVC days and 1.9 vs 2.5/1000 CVC days respectively), these were not significant. The lowest CRBSI rates were observed in patients in the ‘neither’ group (0.79/1000-CVC days). CRBSIs were almost equally likely to occur in hospital as at home. There was no trend to CVC removal rates in either prophylaxis group.

Conclusion: A dramatic reduction in CRBSI rates has occurred in our service over the last decade. However the effect of single interventions are difficult to interpret when comparing to historical cohorts and the reduction in CRBSI cannot be attributed to Taurolock or CEA alone. Other markers of care such as improved nursing skills and dissemination of skills are difficult to study. Patient selection of those at ‘high risk’ of CRBSI may be appropriate when considering those for prophylaxis. The prior admission to hospital as a risk factor for CRBSI warrants further study.


Disclosure of Interest: None Declared
THE ROLE OF OVERWEIGHT IN ALCOHOL AND TOBACCO CONSUMPTION IN ADOLESCENCE

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Objectives and Study: The aim was to examine the prevalence of alcohol/tobacco consumption among overweight adolescents in treatment for weight control, overweight adolescents without treatment and a control group with normal weight, and to examine the roles of weight, age, gender, treatment condition, and psychosocial variables in the presence of those risk behaviors.

Methods: A total of 370 participants who were aged between ≥ 14 and ≤ 19 years old, were divided in three groups: 83 overweight adolescents in treatment (recruited at Gastroenterology and Pediatric Nutrition outpatient of Braga’s Hospital), 82 overweight adolescents who were not receiving treatment for weight control and 205 Normal BMI adolescents. It’s a cross-sectional study. The study followed ethical procedures as outlined in the Declaration of Helsinki. An anthropometric evaluation was made and socio-demographics and psychosocial features were evaluated using self-report questionnaires. Substance consumption behaviors were compared across the three groups using a binary logistic regression analysis. The two risk-taking behaviors were also analyzed using hierarchical logistic regression. Age, gender, weight status, treatment status and psychological dimensions were treated as predictive variables.

Results: Almost twenty-five percent of the healthy weight group, 25.6% of the overweight group without treatment and 10.8% of the overweight group being treated, assumed themselves as smokers. Therefore, 68.8% of the healthy weight group, 69.5% of the overweight community group and 32.5% of the overweight clinical group, revealed to consume alcohol. Overweight adolescents presented risk ratios very similar or even lower (in case of the clinical group) than the ones got by their healthy weight peers. The increase of age, not being integrated in a treatment for weight control and higher satisfaction with intimate relationships predicted alcohol consumption. Weight status was not a predictor of alcohol and cigarette use.

Conclusion: Overweight adolescents are not necessarily at increased risk of consuming alcohol and tobacco. Other variables related to outpatient treatment for weight control, perceived body image and social support are more closely linked to substance consumption, than is weight status.

Disclosure of Interest: None Declared
**Objectives and Study:** Growth retardation and malnutrition are quite common findings in children with coeliac disease (CD) and inflammatory bowel disease (IBD). In addition to body weight, length and body mass index body fat and muscle mass can be followed-up by body composition measurement. The aim of the study was to investigate body composition and dietary intake in children with CD and IBD.

**Methods:** 9 patients with CD (median age 13 y, range 10-16 y) and 18 patients with IBD (16 y, 11-17 y; 10 Crohn and 8 UC patients) visiting a gastrointestinal outpatient clinic. The diagnosis of CD and IBD had been done 70 (3-154) months and 46 (8-180) months ago respectively. All the CD patients were in remission. None of the IBD patients had flare at the time of the study although 13/18 (72%) had been on prednisolone earlier; the latest regimen 31 (4-78) months ago. Control group (n = 30) included healthy bodyweight matched children (13 y, 13-14 y) who had participated in an allergy prevention study. Bioelectrical impedance measurement of body composition was conducted by InBody 720 and nutrient intake data was calculated by the Nutrica software based on a four day food diary.

**Results:** Weight, height, muscle mass and fat percent (median, range) were comparable among the study groups (Table).

<table>
<thead>
<tr>
<th></th>
<th>Controls (n=30)</th>
<th>CD patients (n=9)</th>
<th>IBD patients (n=18)</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Weight (kg)</td>
<td>55 (36-81)</td>
<td>55 (33-75)</td>
<td>56 (26-89)</td>
<td>0.99</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>164 (151-180)</td>
<td>164 (148-170)</td>
<td>166 (140-186)</td>
<td>0.43</td>
</tr>
<tr>
<td>Muscle mass (kg)</td>
<td>23 (17-38)</td>
<td>22 (15-29)</td>
<td>24 (13-40)</td>
<td>0.39</td>
</tr>
<tr>
<td>Body fat %</td>
<td>16 (8-36)</td>
<td>22 (11-35)</td>
<td>19 (6-33)</td>
<td>0.52</td>
</tr>
</tbody>
</table>

*Kruskal-Wallis H test

After the standardization of nutrient intake in relation to energy intake, differences between the groups were found in sucrose (g/MJ, p=0.03) and magnesium (g/MJ, p=0.02) intakes, both being lower in the CD group than in the control group. Intakes of iron, folate, magnesium and potassium were lower than recommended (Nordic Nutrition Recommendations) in all the groups. The relative energy intake was also below the estimated need of energy in all the groups (67% in controls, 61% in CD and 93% in IBD) being significantly greater in the IBD group than in the control group (p=0.038). The groups were pooled (n=55) to study the correlation between nutrient intake and body composition. Surprisingly, a
negative correlation between energy intake in relation to estimated need of energy (%) and bodyweight (rho=-0.43, p=0.001), body mass index (rho=-0.28, p=0.04), fat mass (rho=-0.55, p<0.0001) and fat percent (rho=-0.50, p<0.0001) were found.

**Conclusion:** Body composition among children with inactive CD, quiet IBD and healthy children was similar. Nutrient intakes among the groups were mostly comparable too. The intakes of some nutrients were at a lower level than recommended. Thus it would be important to have a focus on adequate nutrient and energy intake in all children with CD and IBD.

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

*Clinical Nutrition*

PO-N-0441

**EFFECT OF BREAST FEEDING VERSUS ARTIFICIAL FORMULA ON IRON STATUS OF INFANT WITH BETA THALASSEmia MAJOR**

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**Objectives and Study:** Thalassemia Major or Cooley's anemia. This is the most severe form of beta thalassemia in which the complete lack of beta protein in the hemoglobin causes a life-threatening anemia that requires regular blood transfusions and extensive ongoing medical care. These extensive, lifelong blood transfusions lead to iron-overload that must be treated with chelation therapy to prevent early death from organ failure. **Our objective is** Comparing serum iron and serum ferritin among infants with beta thalassemia major up to one year on exclusive breast-feeding versus exclusive artificial formula

**Methods:** Sixty infants with previously diagnosed as beta thalassemia major beta were selected from out-patient clinic of thalassemia at Zagazig university hospital in Egypt, during the period from 2007 to 2013 Patients were classified according to type of feeding into three groups, **group 1:** exclusive breast feeding **group 2:** Exclusive artificial formulae feeding suitable for age and **group 3** on breast feeding and artificial formulae. **Inclusion criteria:** infants below one year on regular blood transfusion. **Exclusion criteria** included other syndromes of thalassemia and infant started the addition of solid foods.

All patients were subjected for full history and examination especially weight, blood transfusion and full feeding history. The following investigations, blood picture, serum iron and serum ferritin were done regularly every month.

**Results:** Our results shows that there was good gain weight in breast-fed group than others. Serum iron and ferritin were higher in artificial fed group with no significant difference,

**Conclusion:** We should encourage breast feeding among infant with beta thalassemia major to avoid further elevation of sera iron and ferritin

**Disclosure of Interest:** None Declared
NUTRITIONAL ASSESSMENT OF HOSPITALISED CHILDREN WITH LIVER DISEASE AND ITS RELATION TO PROGNOSIS

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Objectives and Study: Objective: To evaluate the nutritional status of pediatric liver disease patients on admission to the hospital and its effect on outcome

Methods: Method: We prospectively analyzed the nutritional status of 59 consecutive patients during their first 24 hours of admission, at the Hepatology Unit at Cairo University Pediatric Hospital, using the following indices: weight/age, height/age, weight/height, body mass index/age, arm circumference/age and triceps skinfold/age, subscapular skinfold /age, and mid upper arm circumference /age

Results: Results: The study included 59 cases, 30 were females (50.8%). The median age of the patients was 8.5 months (IQR : 44.5) ; 41 patients (69.5%) suffered from cholestatic disorders of infancy. According to measurements: 35.6% were underweight, 49.2% were stunted, 10.2% were wasted by weight for length/height percentile and 5% were wasted by body mass index (BMI); 49% had percentage of ideal body weight below 89% ; 27.2% had head circumference below 3rd percentile; 59.4% had triceps skin fold (TSF) below 5th percentile; 66.1% had subscapular skin fold (SSF) below 5th percentile; 56% had arm circumference below 5th percentile. There was no correlation between these growth parameters and mortality. However, we found a positive correlation between triceps skinfold and hospital stay. Patients with unfavourable outcomes had higher bilirubin, lower albumin levels, and lower lymphocytic counts

Conclusion: Only triceps skinfold was found as a useful predictor for a prolonged hospital stay. Serial measurements may be more effective.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Evidence on the association of vitamin D with cardiometabolic risk factors in youth is very limited. We examined whether low serum vitamin D levels (25-hydroxyvitamin D [25(OH)D]) are associated with cardiovascular risk factors in a pediatric population from Asuncion, Paraguay.

METHODS: We conducted a cross-sectional analysis of 209 fasting children without diagnosed diabetes or hypertension. Cardiometabolic risk factors were measured using standard methods and defined according to age-modified Adult Treatment Panel III definitions. Participant characteristics were described using means and proportions and their 95% confidence intervals (CIs). Mean 25(OH)D concentrations according to subgroups were compared by independent-sample t tests. Statistical significance was defined at the P < .05 level using 2-sided tests.

RESULTS: Mean 25(OH)D was 34.9 ng/mL. The mean serum 25(OH)D was lower in the subgroup of patients with cardiovascular risk factors: abdominal obesity (p = .57), hypertension (p = .44), high fasting glucose (p = .95), low HDL-cholesterolemia (p = .82), high triglycerides (p = .34) and metabolic syndrome (p = .42), however this difference was not statistically significant.

CONCLUSION: In this pediatric population from Asuncion, Paraguay, serum vitamin D is lower in those patients with cardiovascular risks factors, but this difference is not statistically significant. More studies are needed to determine whether low levels of vitamin D in childhood and adolescence may impact on the subsequent development of cardiovascular disease in adulthood.


DISCLOSURE OF INTEREST: None Declared
IRON AND VITAMIN D DEFICIENCY IN HEALTHY YOUNG CHILDREN IN WESTERN-EUROPE: CURRENT EATING HABITS DO NOT MEET THEIR NEEDS

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Objectives and Study: Iron deficiency (ID) and vitamin D deficiency (VDD) are the two most common micronutrient deficiencies worldwide that may lead to impaired neurodevelopment and rickets. Supplementation policy exists for vitamin D, although compliance is low and guidelines differ across countries. Iron supplementation policy only exists for iron deficient anemia, not for ID. To prevent deficiencies, the concept of milk fortification for young European children has been suggested. We conducted a study to investigate the effect of a micronutrient-fortified formula given for 20 weeks on the iron and vitamin D status of healthy 12-36 months old children in Western-Europe. Here we address the baseline prevalence of ID and VDD and report its risk factors.

Methods: In order to determine the prevalence of ID and VDD, we took a venous blood sample of children living in Germany, the Netherlands and the United Kingdom from 2012 to 2014. Parents were asked to fill out a questionnaire regarding their child’s demographic- and socio-economic characteristics, food intake, sun exposure, day care attendance and medical history. ID was defined as a serum ferritin <12 µg/l in the absence of infection (CRP <10 mg/l). VDD was defined as a serum 25(OH)D <50 nmol/l.

Results: In our homogenous population of 325 children (95% from Caucasian race; 56% male; mean age 21 months; 51% on formula) the overall prevalence of ID and VDD was 11.8% and 22.8%, respectively. ID was associated with the use of primarily cow’s milk (OR 3.31, 95% CI 1.56-7.02) and formula use had a protective effect on ID (OR 0.23, 95% CI 0.10-0.53). VDD was also associated with the use of cow’s milk (OR 8.18, 95% CI 4.36-15.34) and age (OR 1.11, 95% CI 1.07-1.15). Vitamin D supplement use had a protective effect on VDD (OR 0.16, 95% CI 0.07-0.38). Multivariate analysis also showed that the present use of any kind of formula was associated with a lower prevalence of ID and VDD.

Conclusion: Despite current nutritional recommendations and health care system, ID and VDD are common even in healthy young Caucasian children. Health programs focusing on adequate iron and vitamin D intake at an early age should be implemented to prevent deficiencies.

Disclosure of Interest: M. Akkermans Conflict with: The study was funded by Danone Nutricia Research, J. van der Horst-Graat Conflict with: Employee of Danone Nutricia Research, S. Eussen Conflict with: Employee of Danone Nutricia Research, H. van Goudoever Conflict with: The study was funded by Danone Nutricia Research.
funded by Danone Nutricia Research, F. Brus Conflict with: The study was funded by Danone Nutricia Research
**Nutrition**

**Neonatal Nutrition**

PO-N-0445

**BIFIDOGENIC EFFECT OF A PRE AND PROBIOTICS SUPPLEMENTED INFANT FORMULA IN INFANTS BORN FROM HIV+ MOTHERS AFTER NORMAL OR CAESAREAN DELIVERY**

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**Objectives and Study:** Strategies to promote a gut microbiota similar to the one found in breastfed infants, in formula-fed infants includes the addition of prebiotics and/or probiotics to infant formula (IF). Here we intended to evaluate whether an IF supplemented with bovine milk-derived oligosaccharides (BMOS) and *B. lactis* promotes higher level and *Bifidobacteria* diversity than a formula without pre- or probiotics, in caesarian or vaginal delivered infants

**Methods:** 430 healthy full term infants, whose HIV+ mothers had elected to exclusively formula feed her infant, were randomized at birth into this controlled, double-blind, multicenter trial of 4 parallel groups. The first 2 groups consisted of caesarean-delivered infants assigned to the test IF (n= 92) (a starter IF with BMOS (total OS: 8g/L) + *B. lactis* CNCM I-3446 or a control IF (n=101), the second 2 groups consisted of vaginally-delivered infants randomized to the same test (n=115) or control (n=113) IF. The primary outcome was to evaluate *Bifidobacteria* fecal counts at 10 d and up to 3 mo test vs control, and caesarean vs normal-delivered babies. GI tract colonization with other bacteria and fecal pH were assessed.

**Results:** Among infants born by caesarean section, fecal *Bifidobacteria* counts were significantly higher at 10 d in the test vs control: 8.99 +/-1.44 vs 7.71 +/-1.68 log cfu/g of feces, p=0.002. This difference was maintained at 28 d (p<0.001) and 3 mo (p=0.001). In contrast, for infants born by normal delivery, there was no significant difference in *Bifidobacteria* count at 10 d between the test and control IF groups (p= 0.126), while differences were observed at 28d (p<0.001) and 3 mo (p<0.001). At 10 and 28 d, fecal pH of infants fed the test IF was significantly lower than in those fed the control IF, irrespective of delivery mode; vaginal delivery: 4.93 vs 5.59 p<0.001(10 d) and 5.01 vs 5.71 p< 0.001 (28 d), caesarian delivery: 5.14 vs 5.65 p=0.009 (10 d), 5.06 vs 5.75 p<0.001 (28). The acidification effect only persisted among caesarean-born babies.

**Conclusion:** Infant formula supplemented with BMOS + *B. lactis* induced a strong bifidogenic effect, correcting from birth the low Bifidobacterium level found in cesarean born babies. The supplemented IF lowered fecal pH and improved the fecal microbiota in both normal and caesarean-delivered infants.
Disclosure of Interest: P. Cooper Conflict with: research grant received for which abstract is submitted, K. Bolton Conflict with: research grant received for which abstract is submitted, S. Velaphi Conflict with: research grant received for which abstract is submitted, N. de Groot Conflict with: Nestec SA employee, S. Pecquet Conflict with: Nestec SA employee, P. Steenhout Conflict with: Nestec SA employee
FREQUENCY OF CHOLESTASIS AND PLASMA CONCENTRATION OF AMINO ACIDS IN THE NEONATE WITH TOTAL PARENTERAL NUTRITION

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Objectives and Study: To compare the incidence of parenteral nutrition-associated cholestasis (PNAC) and plasma levels of methionine, cysteine and taurine in the neonate with total parenteral nutrition receiving an intravenous paediatric amino acids solution based on the breast milk aminogram (TrophAmine 10%) and an intravenous solution of paediatric amino acids based on the umbilical cord aminogram (Primene 10%).

Study: A double-bind randomized controlled trial

Methods: A total of 88 neonates admitted to the neonatal intensive care unit, with birth weight ≥ 1000 g, gestational age ≥ 30 weeks, and treated with parenteral nutrition (PN) were randomly assigned to receive two different intravenous amino acid solutions (43 Primene [PG]; 45 TrophAmine [TA]). Cholestasis was defined as a serum direct bilirubin >2 mg/dL for two consecutive weeks of PN. Blood samples were obtained before starting with the parenteral nutrition and again at 7 and 14 days of PN. Plasma amino acid concentrations were determined by Ultra High Resolution liquid chromatography. Continuous variables were compared using the Wilcoxon rank-sum test or t Student, whereas categorical variables were compared using the Fisher exact test.

Results: Twenty nine participants assigned to the P group and Twenty four to the TA group were lost during follow-up. TPN was suspended for several reasons (good tolerance to enteral feeding, removal of central catheter by colonization, dysfunctional central catheter, and deaths). Therefore, it was only possible the inclusion to this analysis of 35 neonates, 14 in the P group and 21 in the TA group. There were no differences at the beginning of PN among neonates who received P and those who received TA. Cholestasis incidence in both groups was similar (P 21.4%, TA 28.6%; P = 0.47). On Day 14, methionine plasma concentrations was significantly lower in P group than TA group (27 μmol/L Vs 32.9 μmol/L, P = 0.044); as opposed, taurine concentration was significantly higher for same group (72.4 μmol/L Vs 45.3 μmol/L, P < 0.0001), whilst cysteine concentration was not different. (44.8 Vs 62.8; P = 0.359).

Conclusion: Although there were no differences in the cholestasis incidence, taurine concentration was lower in patients receiving the TA solution, which is a risk factor that may be a parenteral nutrition-associated cholestasis development. Further studies are required to determine whether the administration of amino acids intravenous solution based on the breast milk aminogram may increase PNAC risk.

Disclosure of Interest: None Declared
MILK OLIGOSACCHARIDES MODULATE COLONIC MICROBIOTA OF NEONATAL PIGLETS
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Objectives and Study: Human milk oligosaccharides (HMOs) are the third largest solute in human milk after lactose and fat and serve as nutrients for the resident infant gut microbiota. Sialyllactose (SL) is an acidic HMO that has important biological functions, but its effect on modulating colonic microbiota is not well characterized. We previously reported that supplementation of formula with 3’- or 6’-SL can enrich ganglioside SA in the brain of suckling piglets. The current study aimed to determine if different isomers of SL modulate the microbiome of developing neonatal piglets.

Methods: Day-old pigs were randomized among 6 diets (control, 3’-SL at 2 or 4g/L, 6’-SL at 2 or 4g/L, or 2g/L polydextrose + 2g/L galacto-oligosaccharide; n=9 per group) and fed 3 times per day for 21 days. Pigs were euthanized and intestinal digesta were analyzed from the proximal (PC) and distal colon (DC). The microbiome analysis was performed via 16S rDNA Illumina sequencing.

Results: Dietary SL did not affect feed intake, growth or fecal consistency. Sampling location and treatment caused significant changes in the microbial taxa of the PC and DC (P<0.05, Adonis test). There was a significant microbiome difference between control and 4 g/L 6’-SL diets (P<0.01, Adonis test). Specifically, an increase in bacterial taxa belonging to the phyla Actinobacteria and Bacteroidetes was observed (P<0.01).

Conclusion: In conclusion, supplementation of formula with a diet containing SL modulates gut associated microbiota of suckling piglets. Supported by Mead Johnson Nutrition.

EFFECTS OF HUMAN MILK OLIGOSACCHARIDES ON INTESTINAL FUNCTION AND NECROTISING ENTEROCOLITIS IN PRETERM PIGS

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Objectives and Study: Human milk oligosaccharides (HMOs) may mediate prebiotic and anti-inflammatory effects of milk in the infant intestine. This is of particular importance for preterm infants born with an immature gut and therefore being highly susceptible to dysfunction and necrotizing enterocolitis (NEC). We hypothesized that an HMO-supplemented infant formula (IF) improves intestinal function and NEC resistance after birth, and tested this in a pig model of preterm infants.

Methods: Preterm pigs (n=112) were fed IF (Lacprodan, Arla Fi; Pepdite and Liquigen-MCT, SHS International) supplemented with a blend of either 5 HMOs including free sialic acid (5-HMO) or >25 different HMOs including free sialic acid, fucose and lactose (25-HMO), respectively (Glycom). In short-term experiments, 5-HMO (5 g/L) or 25-HMO (6 g/L) IF were compared to controls for 5 days after birth. In a longer-term experiment, the 5-HMO (10 g/L day 1-4; 5 g/L day 5-11) in IF (Alprem, Nestlé Nutrition) was compared to control for 11 days after preterm birth. The 5-HMO effects on intestinal cell proliferation and IL-8 secretion was investigated in IPEC-J2 cells.

Results: All added HMOs were found in urine and faeces of HMO pigs, and the formation of short chain fatty acids in the colon was higher in the HMO pigs, relative to controls (P<0.05). Development of NEC during the first 5 days was similar between control pigs and the 5-HMO (38 vs. 39%) and 25-HMO groups (63 vs. 74%), respectively, and only colon weights increased in the 25-HMO vs. control pigs (15%, P<0.01). In the 11-day experiment, NEC incidence tended to be lower in the 5-HMO vs. control group (56 vs. 79%), whereas dehydration and diarrhoea was more pronounced at day 7 and onwards, dehydration being higher for HMO pigs (P<0.05). Expression of MUC1, MUC2, IAP, TNFa, IFNy, IL10, TLR4, TGFβ, IL12, and IL17 was higher in the 5-HMO pigs after 11 days relative to controls. The 5-HMO blend decreased enterocyte proliferation (-30%) and LPS-induced IL-8 secretion (-10%) in IPEC-J2 cells (P<0.05).

Conclusion: Supplementation of IF with HMOs had limited effects after 5 days, but tended to improve NEC resistance within 11 days after preterm birth, yet diarrhoea and dehydration were more pronounced. Together, we conclude that 5-10 g/L HMOs induce limited acute effects on the immature new-born intestine. Longer exposure to HMOs (e.g. several weeks) may be required to induce beneficial effects to support immune and microbial defence and homeostasis in the immature intestine.
Disclosure of Interest: None Declared
**Nutrition**

**Neonatal Nutrition**

PO-N-0449

**PROTEIN AND CALORIC DEFICIT DURING THE NEONATAL PERIOD IN INFANTS WITH BIRTH WEIGHT LESS THAN 1500 G AND ITS ASSOCIATION WITH BLOOD PRESSURE IN THE ADOLESCENCE**

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**Objectives and Study:** VLBW frequently present postnatal malnutrition at hospital discharge. This phenomenon is associated with short- and long-term adverse outcome. Its association with high arterial tension levels in the adolescence has not been reported.

To evaluate the association between higher than 75% percentile systolic (SBP) and diastolic blood pressure (DBP) in adolescents with VLBW at birth and their nutritional deficits during the first 28 days of life.

**Methods:** Prospective cohort. VLBW patients enrolled in a follow-up program that in the neonatal period received an intensive early nutritional support and in whom the nutritional deficits were prospectively recorded.

**Results:** 137 patients were followed-up. Pc 75th was 113 mmHg for SBP and 63 mmHg for DBP.

Table show the characteristics of subjects with or without SBP and DBP above 75th percentile respectively. In a multivariate analysis protein deficit and BMI persisted significant for high SBP. Neonatal caloric deficit was associated with higher DBP. For each gram of neonatal protein deficit the probability that SBP were above the 75th percentile at the adolescence increased 5% (95%CI 0.5-8).

For each point of BMI increase, the probability of SBP above the 75th percentile increased 37% (95%CI 15-64).

<table>
<thead>
<tr>
<th></th>
<th>SBP &gt;75th Pc n=36</th>
<th>SBP &lt;75th Pc n=101</th>
<th>p</th>
<th>DBP &gt;75th Pc n=39</th>
<th>DBP &lt; 75th Pc n=98</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>BW in g (r)</td>
<td>1310 (780-1700)</td>
<td>1240 (620-1790)</td>
<td>ns</td>
<td>1260 (620-1500)</td>
<td>1260 (750-1490)</td>
<td>ns</td>
</tr>
<tr>
<td>GA in weeks (r)</td>
<td>30 (27-34)</td>
<td>30 (24-36)</td>
<td>ns</td>
<td>30 (26-35)</td>
<td>30 (24-36)</td>
<td>ns</td>
</tr>
<tr>
<td>Male Gender n (%)</td>
<td>20 (55)</td>
<td>46 (46)</td>
<td>ns</td>
<td>21 (53)</td>
<td>45 (46)</td>
<td>ns</td>
</tr>
<tr>
<td>BW Z-score Median (r)</td>
<td>0.00</td>
<td>-0.25 (-2.2/1.6)</td>
<td>ns</td>
<td>-0.68 (-3.5/2.2)</td>
<td>-1 (-3.48/2)</td>
<td>-0.6 (-3.6/2.2)</td>
</tr>
<tr>
<td>Caloric Deficit in Kcal Median (r)</td>
<td>- 530 (-1248/6.6)</td>
<td>- 344 (-1200/1039)</td>
<td>ns</td>
<td>-613 (-1248/-102)</td>
<td>-338 (-1200/1039)</td>
<td>0.00</td>
</tr>
<tr>
<td>Protein Deficit in g Median (r)</td>
<td>- 21 (-43/3.66)</td>
<td>-13 (-52/46)</td>
<td>0.044</td>
<td>-20.7 (-44/3.7)</td>
<td>-13.7 (-52/43)</td>
<td>ns</td>
</tr>
<tr>
<td>Age at Evaluation in years</td>
<td>12 (10-14)</td>
<td>11 (9-14)</td>
<td>0.01</td>
<td>12 (10-14)</td>
<td>11 (9-14)</td>
<td>ns</td>
</tr>
<tr>
<td>Z-score at Evaluation Median (r)</td>
<td>1.4 (-2.17/5.1)</td>
<td>0.42 (-2.5/3.9)</td>
<td>0.001</td>
<td>0.95 (-2.5/4.6)</td>
<td>0.5 (-2.2/5.1)</td>
<td>ns</td>
</tr>
<tr>
<td>BMI Median (r)</td>
<td>22 (15-34)</td>
<td>18 (13-26)</td>
<td>0.001</td>
<td>21 (12-34)</td>
<td>18.7 (14.29)</td>
<td>0.02</td>
</tr>
</tbody>
</table>

**Conclusion:** Higher SBP is associated with neonatal protein deficit and BMI at the adolescence, while caloric deficit is associated with higher DBP.

**Disclosure of Interest:** F. General Conflict with: Supported by Nutricia Bagó Argentina
THE DIVERSE HUMAN MILK OLIGOSACCHARIDE CONTENT OF BREAST MILK
Nicholas Andreas 1,* Matthew Hyde 1 Suzan Jeffries 1 Isabel Garcia-Perez 1 Neena Modi 1 Elaine Holmes 1
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Objectives and Study: Previous research has identified Human Milk Oligosaccharides (HMO) as a highly variable component of breast milk. HMO are complex carbohydrates serving multiple functions, including acting as an anti-infective agent for the infant. HMO biosynthesis is in large part determined by Lewis blood group and secretor status, which are genetically determined [1]. We hypothesised that the diverse profiles of HMO could be assessed using 1H NMR spectroscopy, and that individual HMOs contributing to differences between profiles would be identifiable.

Methods: Milk samples were obtained from 108 mothers, at 7 days and 3 months post-partum. Samples were solvent extracted and 1H NMR spectra acquired for the aqueous fraction. Data were analysed using multivariate data analysis to define the component describing the largest proportion of variation, and to compare different groups of mothers, defined by their spectral profiles.

Results: There was a substantial decrease in the abundance of HMO at 3 months compared to seven days post-partum. Furthermore, large differences in the specific types of HMO were identified. In the PCA scores plot, two broad groups of mothers were identified, each identified by distinct HMO profiles, known to be determined by maternal genotype. Based on the types of oligosaccharides produced one group, thought to be secretors (Se+), produced a preponderance of HMO known to be products of the gene fucosyltransferase 2, such as 2′-fucosyllactose. The other group, thought to be non-secretors (Se−), did not produce these HMO, but had an increased quantity of other HMO, including 3′-fucosylactose, present in their breast milk. Overlaying the NMR spectra, identified the types of HMO produced. The interaction between the Lewis blood group (Le+/Le−) and secretor gene status produce four types of breast milk. All four types were present in our cohort, (Se+/Le+), (Se+/Le−), (Se−/Le+) and (Se−/Le−).

Conclusion: HMO are believed to have important prebiotic properties. Additionally, data show an association between maternal non-secretor status, and increased infant infection risk [2]. We have shown that human milk HMO profile may be characterised rapidly using 1H NMR spectroscopy. This provides opportunity for a stratified medicine approach in future interventional studies involving manipulation of the infant microbiome to reduce infection risk.


Disclosure of Interest: N. Andreas Conflict with: NJA has received funding from Danone and Medela to attend an educational conference, M. Hyde Conflict with: MJH has received funding from Danone to attend an educational conference, S. Jeffries: None Declared, I. Garcia-Perez: None Declared, N.
Modi Conflict with: NM was speaker honorarium for an educational meeting funded by Nestle International in which they had no organisational involvement, E. Holmes: None Declared
ROLE OF NUTRITIONAL SUPPORT TEAM IN IMPROVING OUTCOMES IN NEONATAL INTESTINAL FAILURE.

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Objectives and Study: The provision of parenteral nutrition (PN) forms part of standard practice in neonatal intensive care units to support nutrition and growth. Providing adequate nutrition during this vulnerable stage of development is of paramount importance and dictates the long term outcomes. The neonatal population is the largest single patient group receiving PN and to date, there are no standardised guidelines or funding arrangements in the UK to support its use. The aim of this retrospective cohort study was to look at the impact of provision of support via a multidisciplinary team on growth, mortality, length of hospital stay and time taken to achieve enteral autonomy.

Methods: In our unit a multidisciplinary neonatal nutrition support team (NST) was established in 2011. This comprised of a neonatologist, pharmacist, dietician pediatric surgeon and gastroenterologist. Neonates receiving PN for greater than 28 days were identified from Badgernet. Outcome data was compared between those born between January 2009 to December 2011 to those between January 2011 to December 2013. This included anthropometry, outcome, duration of PN and length of stay in hospital.

Results: A total of 128 cases were identified where neonates had received PN for greater than 28 days. The demographics are as in the following table.

<table>
<thead>
<tr>
<th></th>
<th>Pre NST</th>
<th>Post NST</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>49</td>
<td>80</td>
<td></td>
</tr>
<tr>
<td>Birth Weight (gms)</td>
<td>866.5</td>
<td>822.5</td>
<td>NS</td>
</tr>
<tr>
<td>Gestation Age (weeks)</td>
<td>26</td>
<td>26</td>
<td>NS</td>
</tr>
<tr>
<td>PN duration (days)</td>
<td>39</td>
<td>40</td>
<td>NS</td>
</tr>
<tr>
<td>SDS Weight at birth</td>
<td>-0.307</td>
<td>-0.239</td>
<td>NS</td>
</tr>
<tr>
<td>SDS Weight at discharge</td>
<td>-2.16</td>
<td>-1.37</td>
<td>0.03</td>
</tr>
<tr>
<td>Change in SDS weight from birth to discharge</td>
<td>-1.37</td>
<td>-1.83</td>
<td>0.04</td>
</tr>
<tr>
<td>Length of stay (days)</td>
<td>86.9</td>
<td>58.89</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Conclusion: Since the inception of a Neonatal NST in 2011, there has been a significant improvement in discharge weights and length of stay, demonstrating the efficacy of such an MDT. For further improvements to be achieved additional resources may be necessary to monitor growth within this risk group.

Disclosure of Interest: None Declared
FACTORS ASSOCIATED WITH THE CHOICE OF BOTTLE FEEDING FOLLOWING BIRTH OF A TERM/NEAR-TERMSingleton Infant

Terence Lao 1,*
1Department of Obstetrics & Gynaecology, Shatin, Hong Kong

Objectives and Study: Objectives and Study:
Breast feeding is generally preferred to bottle feeding due to the associated advantages for the infant. Nevertheless, despite active promotion, a significant proportion of our parturients still adopted bottle feeding after delivery. A retrospective cohort study was therefore performed to examine the significant factors associated with the choice of bottle feeding after delivery of a singleton live-born infant at ³34 weeks gestation in our hospital.

Methods: Methods:
The singleton live births at ³34 weeks gestation managed from 1998 to 2013 in our hospital were reviewed to audit the incidence of breast feeding, with the data extracted from a master database used to provide statistics to the local hospital authority. The mode of feeding was coded as breast feeding if the mother adopts breast feeding before hospital discharge. The mode of delivery, common complications, and infant outcome were compared between mothers who chose bottle feeding versus those adopting breast feeding, using chi square test with calculation of the odds ratio (OR) and 95th % confidence interval (CI).

Results: Results:
Of the 73278 cases that satisfied the inclusion criteria, breast feeding was adopted by only 51.1%. More primiparas, compared with multiparas, adopted breast feeding (55.2% versus 46.1%, p<0.001), but there was no difference in the incidence of mothers aged ³35 years among the breast feeding versus bottle feeding groups (19.9% versus 19.4%). The significantly different factors associated with increased bottle feeding are shown in the table.

<table>
<thead>
<tr>
<th>Factor</th>
<th>Bottle Feeding</th>
<th>Breast Feeding</th>
<th>P</th>
<th>OR (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Caesarean delivery</td>
<td>19.7</td>
<td>15.2</td>
<td>&lt;0.001</td>
<td>1.37 (1.32-1.42)</td>
</tr>
<tr>
<td>Pre-eclampsia</td>
<td>1.3</td>
<td>0.8</td>
<td>&lt;0.001</td>
<td>1.54 (1.34-1.78)</td>
</tr>
<tr>
<td>Preterm birth</td>
<td>5.3</td>
<td>4.3</td>
<td>&lt;0.001</td>
<td>1.24 (1.15-1.34)</td>
</tr>
<tr>
<td>Postpartum haemorrhage</td>
<td>3.5</td>
<td>2.7</td>
<td>&lt;0.001</td>
<td>1.30 (1.18-1.42)</td>
</tr>
<tr>
<td>HBsAg positive</td>
<td>11.3</td>
<td>8.0</td>
<td>&lt;0.001</td>
<td>1.47 (1.40-1.54)</td>
</tr>
<tr>
<td>Macrosomia (³4kg)</td>
<td>4.0</td>
<td>2.9</td>
<td>&lt;0.001</td>
<td>1.39 (1.28-1.50)</td>
</tr>
<tr>
<td>Low birthweight (&lt;2.5kg)</td>
<td>4.9</td>
<td>3.8</td>
<td>&lt;0.001</td>
<td>1.31 (1.21-1.42)</td>
</tr>
<tr>
<td>5th minute Apgar score &lt;7</td>
<td>0.6</td>
<td>0.2</td>
<td>&lt;0.001</td>
<td>3.72 (2.83-4.89)</td>
</tr>
<tr>
<td>NICU admission</td>
<td>28.0</td>
<td>24.2</td>
<td>&lt;0.001</td>
<td>1.22 (1.17-1.26)</td>
</tr>
</tbody>
</table>
Results expressed in %.

**Conclusion:**
While the association between mode of delivery, obstetric complications, and infant condition at birth with the choice of bottle feeding may not be surprising, the association with maternal HBsAg carriage was unexpected because of the active-passive immunisation given at birth to infants born to HBsAg positive mothers. Further studies are warranted to enhance uptake of breast feeding in HBsAg positive mothers.

**Disclosure of Interest:** None Declared
A RANDOMISED CONTROL TRIAL COMPARING INITIATION OF TOTAL ENTERAL FEEDS ON 1ST DAY OF LIFE WITH STANDARD FEEDING REGIMEN IN STABLE VERY LOW BIRTH WEIGHT INFANTS BORN BETWEEN 30-34 WEEKS AND 1000 TO 1500 GRAMS

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Objectives and Study:
1. To assess the feasibility of total enteral feeds on first day of life without increase in feed intolerance or NEC
2. Does reduced need of IV access result in decreased incidence of sepsis?

Methods:
Stable VLBW admitted between ≥ 30-34 weeks of gestation and between 1000-1500 grams admitted within 24 hours of life to NICU without any risk factors and fulfilling inclusion criteria were randomized to total enteral feeds or standard feeding regimen group after consent. Infants in total enteral feeds (Gp I) were started on feeds at the rate of 80ml/kg on day 1 and subsequently increased at the rate of 20ml/kg/day subject to tolerance and infants in standard feeding regimen (Gp II) were started on feeds at the rate of 20ml/kg/day on day 1 and the rest amount was supplemented through parenteral nutrition and feeds were increased at the rate of 20ml/kg/day. Parenteral nutrition (PN) was given along with enteral feed to meet the full nutritional requirement and PN support was gradually withdrawn with increasing enteral acceptance.

Results:
There were 31(47.6%) and 33(52.4%) infants in group I & II respectively. The mean gestational age (SD) and mean birth weight (SD) were 31.45(3.62) & 31.09(1.26) weeks and 1359 (135.97) gms & 1305 (153.08) gms in group I & II respectively. On intention to treat analysis infants on total enteral feeds (Gp I) reached significantly earlier on 180 ml/kg/d (6.94+2.86 vs. 10.33+3.53 days, p=0.000). None of the infants in either groups developed NEC and number of incidence of feed intolerance in both groups were comparable. The incidence of culture positive sepsis was higher in Gp II with higher number of days in IV fluids though it was not of statistical significance (22.5% vs 10.7%, p=0.18).

Conclusion:
Hemodynamically stable VLBW infants between ≥30-34 weeks and 1000-1500 grams on 1st day of life can be initiated on full enteral feeds, while monitoring for possible side effects.

References:
4. Salhotra A, Ramji,S. Slow versus fast enteral feed advancements in very low birth weight infants; a randomized controlled trial.Indian Pediatr 2004; 41:435-441.
Disclosure of Interest: None Declared
LONG TERM PARENTERAL SUPPLEMENTATION OF VITAMIN A IN PRETERM NEONATES: TIME FOR A CHANGE OF PRACTICE?

Amit Saha 1, LV Marino 1, R.M. Beattie 1, Colin Harper 1, Tracy Coelho 1, Freya Pearson 1, Akshay Batra 1
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Objectives and Study: Premature infants have lower levels of Vitamin A at birth compared to term infants and are therefore at greater risk of deficiency, particularly if on long term parenteral nutrition. The recommended intake of Vitamin A in preterm infants remains controversial and is based on expert opinion. The only intravenous preparation currently available in the UK, Vitlipid N (Fresenius Kabi, Runcorn, UK) provides 920 IU/kg/day at the recommended dose of 4ml/kg/day. This study aims to assess the adequacy of this dose of Vitamin A in infants on parenteral nutrition (PN) for >28 days.

Methods: We identified neonates who received PN for > 28 days between January 2009 and December 2013. Those who were on >50% of total calories via parenteral route and had their serum vitamin A, D and E concentrations measured at 4-6 weeks of age were included in the study. Additional data collected from case notes included; demographics, gestational age, diagnosis, duration of PN and anthropometry. Vitamin A deficiency was defined as serum concentration below 200µg/L (0.7µmol/L) and severe deficiency, with depleted liver stores, as below 100µg/L (0.35µmol/L).

Results: 43 cases fulfilled the inclusion criteria and were included. 39 of them were premature. The most common indication for PN was gut immaturity associated with preterm delivery in 24 cases followed by presence of congenital or acquired gut disorders in 19. At 4-6 weeks of age, 31/43 (72%) had vitamin A deficiency; with 15/43 (35%) having severe deficiency. There was a higher proportion of preterm infants who were deficient 30/39 (77%), of whom 4/5 (80%) remained deficient at 90 days, despite ongoing supplementation. None of the infants included were deficient in vitamin D or E.

Table 1: Demographic and anthropometric profile of babies on long-term PN

<table>
<thead>
<tr>
<th></th>
<th>Vitamin A deficiency Median (25th – 75th percentile)</th>
<th>No vitamin A deficiency Median (25th - 75th percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number (Total 43)</td>
<td>31</td>
<td>12</td>
</tr>
<tr>
<td>M:F</td>
<td>18:13</td>
<td>7:5</td>
</tr>
<tr>
<td>Gestation Age (weeks)</td>
<td>26 (25-28)</td>
<td>30.5 (25.25 - 35.5)</td>
</tr>
<tr>
<td>Birth weight (gms)</td>
<td>815 (695-1090)</td>
<td>1760 (803-2742)</td>
</tr>
</tbody>
</table>

Conclusion: This study shows that preterm infants who receive PN > 28 days have Vitamin A levels that are below the currently accepted range. As Vitlipid N is a fixed preparation, there is no scope of increasing Vitamin A dosage without altering the levels of vitamins D and E, without exposing infants...
to toxic amounts. The authors recommend that additional studies are required to determine appropriate recommended nutrient intakes for this vulnerable population thereby preventing vitamin A deficiency.

**Disclosure of Interest:** None Declared
IMPACT OF LIPID QUALITY IN PERINATAL PERIOD ON INFLAMMATION AND NEUROGENESIS

Anne-Laure Dinel 1,∗ Corinne Joffre 1 Pascale Le Ruyet 2 Sophie Layé 1
1INRA, Bordeaux, 2Lactalis, Retiers, France

Objectives and Study: The innate immune system of the brain is principally composed of microglial cells, which, once activated, protect neurons against insults (infectious agents, lesions etc.). Activated microglial cells produce inflammatory cytokines that act specifically through receptors expressed by the brain. The functional consequences of chronic brain cytokine action are the alteration in cognition, affect and behaviour, a hallmark of altered well-being. Limiting synthesis of inflammatory cytokines in brain could be crucial during perinatal period to prevent cognitive alteration in adulthood.

Polyunsaturated fatty acids of the n-3 family (n-3 PUFA), in particular docosahexaenoic acid (DHA), are very potent anti inflammatory agents. DHA are highly incorporated in the brain during the developmental period. Evaluating optimal level of DHA in developing brain is a real challenge in perinatal nutrition.

The present project aimed at evaluating the impact of different dietary fat matrix (vegetable or dairy lipids) with or without DHA/arachidonic acid (ARA) on neurophysiological alterations (neuroinflammation, neurogenesis) induced by a post-natal inflammation. In particularly, lipids could modulate phenotypes of microglial cells and improve hippocampal neurogenesis.

Methods: Pregnant CD1 mice and their offspring were fed since day 1 of gestation with different diets: 1) equilibrated with dairy lipids (dairy lipids, sunflower, rapeseed oil) with or without DHA (0.2%) and ARA (0.5%), 2) equilibrated with vegetable lipids (palm, sunflower, rapeseed oil) with or without DHA (0.2%) and ARA (0.5%), 3) diet with vegetable lipids deficient in PUFA n-3.

At postnatal day (PND) 14, pups were injected intraperitoneally with lipopolysaccharide (LPS, 100µg/kg) from E.coli. 3h after injection, half animals were sacrificed to evaluate phenotype of microglial cells and neurogenesis in dentate gyrus of the hippocampus.

Results: Our results showed that microglial phenotype depends of dietary fat matrix. The number of CD86+ cells (pro-inflammatory phenotype) is significatively decreased in animals fed with dairy lipids. Moreover those animals fed with dairy lipids presented an increase of hippocampal neurogenesis at postnatal day 14. Analysis of neurotrophic factors showed a decrease of BDNF activity associated with an increase of TrkB receptor activity. Finally, phosphorylation of glucocorticoid receptors was decreased in those animals.

Conclusion: To conclude, our results showed that consumption of dairy lipids diet protect from neuroinflammation and its consequences after a postnatal inflammation.

Disclosure of Interest: None Declared
LATE PRETERM BIRTH IS A RISK FACTOR FOR DEVELOPING FEEDING DIFFICULTIES DURING HOSPITAL STAY

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1 Fondazione IRCCS Ca’ Granda Ospedale Maggiore Policlinico, Neonatal Intensive Care Unit, Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy

Objectives and Study: The proportion of late preterm births has markedly increased during the past two decades accounting for 70% of preterm birth. Late preterm infants have been recognized to be at higher risk for medical problems than term infants. The aim of this study was to investigate the prevalence of feeding difficulties during hospital stay in a cohort of infants born late preterm and to identify the factors that most contribute to the occurrence of feeding difficulties shown by these infants.

Methods: We performed a single-centred retrospective observational study. Inclusion criteria was gestational age 34 0/7 to 36 6/7. Basic characteristics (birth weight, gestational age, being born appropriate or small for gestational age, being a twin, gender), feeding problems (need for parenteral nutrition and/or intravenous fluids and/or tube feeding) were collected from the infants’ computerized medical charts. Data were expressed as mean±SD or percentage (%). Logistic regression analysis was performed to identify which variables were independently associated with the occurrence of feeding difficulties.

Results: A total of 1768 (n=359 with gestational age equal to 34 weeks, n=571 with gestational age equal to 35 weeks and n=838 with gestational age equal to 36 weeks) late preterm infants admitted to our Institution in 2011-2012-2013 were included in the study. Mean birth weight was 2404±419 g. Of the enrolled infants 468 were twins, 869 were males, 451 were small for gestational age. Feeding difficulties were present in 592 infants: 78 infants needed parenteral nutrition, 598 infants needed intravenous fluids and 46 infants needed tube feeding. At logistic regression analysis birth weights≤2000g, gestational age equal to 34 weeks, being male and being SGA were associated with a higher risk of feeding difficulties occurrence (OR=8.3, 95% 5.4-12.9, p<0.0001; OR=4.7, 95% 3.5-6.3, p<0.0001; OR=1.3, 95% 1.03-1.66, p=0.02; OR=1.4, 95% 1.0-2.1, p=0.04).

Conclusion: The findings of this study confirm that late preterm infants are at high risk of having feeding difficulties during hospital stay, especially if males, born small for gestational age at the lowest birth weight and gestational age.

Disclosure of Interest: None Declared
Objectives and Study: The gold standard for infant nutrition during the first 6 months of life is breastfeeding, however only in those cases that is not possible, it will be recommended the use of infant formulas (IFs). Human milk (HM) differs from the IF in regard to composition and functionality. The gangliosides (GG) are bioactive compounds present in HM and IF that play an essential role in the cognitive development, prevention of intestinal infections in infants, inhibition of certain pathogens and immune-intestinal development during the first month of life. In order to improve IFs composition to be closer to HM, it is of interest to characterized these compounds in IFs. The aim of this work is to determine the total gangliosides content in commercial infant formulas from three different European countries and the intake estimation.

Methods: Twelve IFs from three different countries in Europe (Spain: 5, Czech Republic: 4, and Sweden: 3) were analysed. A spectrophotometric method was applied. Briefly, first neutral lipids were removed by washing with cold acetone of sample; then, the fat fraction was extracted using chloroform-methanol (4°C) in different proportions. The fat extract was subjected to Folch partition system with KCl for polar lipids. Finally, it was purified by dialysis (48h) and was lyophilized. Total GG were quantified as lipid-bound sialic acid (LBSA) using the resorcinol reagent and Neu5Ac standards (2, 5, 10 and 15 µg) (λ= 580nm). For estimation of total GG intake, average reported milk intake volumes (mL/day) from several clinical studies, including 1113 infants from 1 to 6 months of life were used.

Results: The content of total gangliosides ranged from 0.3 and 1.5 mg LBSA/l (Spain: 0.8±0.4 Czech Republic: 0.5±0.3 and Sweden: 0.8±0.4). The minimum and maximum mean intake of total gangliosides in infants could be estimated at about 0.23 and 1.51 mg LBSA/day (1 month: 0.23-1.15, 2 months: 0.27-1.33, 3 months: 0.27-1.36, 4 months: 0.28-1.42, 5 months: 0.3-1.51 and 6 months: 0.26-1.33)

Conclusion: The content of gangliosides in infant formulas were similar to published values using similar methodology but lower than in mature HM. The variation in the content of gangliosides could be related with the different ingredients sources used in the formulation of the IFs. The highest content of total gangliosides was 1.5 mg/l. The partially substitution of vegetal fat by bovine milk fat or/and the addition of Milk fat Globule Membrane (MFGM) ingredients could be an interesting approach to be closer to human milk from the composition point of view. The highest gangliosides intakes were shown at 4 and 5 months of life.
**EXCLUSIVE BREASTFEEDING AT 4-6 WEEKS OF AGE IS ASSOCIATED WITH LONGER TELOMERE LENGTH IN LATINO PRESCHOOL CHILDREN**

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**Objectives and Study:** Telomere length (TL), as a marker of cellular aging, is associated with rapid attrition during the first 5 years of life. In adulthood, shorter TL is associated with chronic disease processes and exposure to oxidative stress but little is known about risk factors for TL shortening in childhood, although early life experiences and exposures including dietary and weight factors are known to impact chronic disease risk in adulthood. We assessed dietary, feeding and weight-associated risk factors from birth for shorter TL at age 4 and 5 in a cohort of urban, low-income Latino children in San Francisco.

**Methods:** Latina mothers were recruited prenatally in San Francisco during the 2nd at 3rd trimesters of pregnancy at two local hospitals (n=201). From 4-6 weeks of age, dietary recall information was collected including initiation of breastfeeding, breastfeeding duration, exclusive breastfeeding and age of introduction of solids using 24-hour dietary recalls and food frequency questionnaires. Blood spot measurements of TL were examined through finger prick from Latino mothers and children. We examined TL by qPCR using genomic DNA from dried blood spots in a sample of 108 4-year old, Latino children and their mothers and 92 5-year old children during years 4 and 5 of follow-up of our original cohort.

**Results:** Longer TL (in base pairs) was associated with exclusive breastfeeding at 4-6 weeks of age (Coeff=316.31 95%CI (10.06-622.02) p=0.04), longer maternal TL (Coeff=623.49 95%CI (263.67-983.31); p<0.01) and increasing paternal age (Coeff=30.33 95%CI (2.87- 57.80) p=0.03). Introducing other foods or drinks in addition to breastmilk or replacement milk substitutes before 4-6 weeks of age was associated with shorter TL at 4 and 5 years (Coeff=-422.57 95%CI (-735.68—109.45).

**Conclusion:** Early dietary factors, in particular exclusive breastfeeding at 4-6 weeks of age, may have long term impacts on child health, as evidenced by longer TL at 4 and 5 years of age.

**Disclosure of Interest:** None Declared
COMPARISON OF A POWDERED, ACIDIFIED LIQUID, AND NON-ACIDIFIED LIQUID HUMAN MILK FORTIFIER ON CLINICAL OUTCOMES IN PREMATURE INFANTS

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Objectives and Study: The use of human milk fortifiers (HMF) is crucial to meet the high nutritional requirements of human milk (HM)-fed premature infants. There is a trend to transition from powdered to new liquid fortifiers to optimize nutrition and decrease the risk of contamination. We recently compared growth and outcomes among infants receiving a powdered HMF (P-HMF) supplemented with powdered protein modular, or acidified liquid HMF (AL-HMF). The acidified product contributed to metabolic acidosis and poor growth. A non-acidified liquid HMF (NAL-HMF) and a liquid protein modular are now commercially available. Our objective was to compare growth and clinical outcomes of HM-fed preterm infants fortified with P-HMF, AL-HMF, or NAL-HMF.

Methods: An IRB approved, retrospective chart review compared outcomes for infants born <2000 grams who received one of three human milk fortifiers. Infant growth, enteral nutrition and tolerance, laboratory values, and demographic information were compared between groups. No infants were excluded based on acuity.

Results: 120 infants were included (P-HMF= 46 AL-HMF= 23 NAL-HMF= 51). Growth in the AL-HMF group was slower (median 23.66 gms/day compared to P-HMF 31.27 gms/day and NAL-HMF 31.74 gms/day (p<0.05)). Also significant was growth in gms/kg/day, median 10.59, 15.37, and 14.03 respectively (p<0.0001). Infants in the AL-HMF group were smaller at 36 weeks corrected gestational age compared to NAL-HMF infants (2073 vs. 2381 gms, p<0.05). Despite decreased growth, the AL-HMF group received more calories (p=0.21) and protein (p<0.0001), mean intake of 129 cal/kg/day and 4.2 gms protein/kg/day compared to P-HMF 117 cal/kg, 3.7 gms protein/kg and NAL-HMF 120 cal/kg, 4.0 gms protein/kg/day. The AL-HMF group also exhibited lower carbon dioxide levels after day of life 14 and 30 compared to the other groups (p<0.0001 and p=0.0038). Three infants (13%) in the AL-HMF group developed NEC vs. no infants in the other two groups (p=0.0056).

Conclusion: Liquid products are preferred in the NICU, the AL-HMF contributed to metabolic acidosis and did not achieve appropriate growth despite higher nutrient intake. The NAL-HMF, achieved similar adequate growth compared to the P-HMF. The non-acidified liquid product with liquid protein supplement may be a more optimal choice in a group of high acuity, low birth weight infants.

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NUTRITIONAL SUPPLEMENTATION AMONGST PRETERM AND TERM NEONATES
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Objectives and Study: Nutritional requirements amongst preterm and term neonates differ from older infants and change rapidly. Compositions of vitamin supplements vary. Doses of supplements should be adjusted according to the type of milk the infant is receiving. There are currently no national guidelines on nutritional supplementation, but local protocols exist based on growth and nutrition studies and guidance provided by expert groups. The aim of this study was to establish current practices in neonatal supplementation in neonatal units across England and to compare these dosing regimens to guidance provided by ESPGHAN.5

Methods: A national cross sectional questionnaire study of Neonatal units across England was conducted between January and March 2014. Firstly, the existence of a local policy was established. Then, details of the supplements used, their brands, dosing, criteria for initiation and the impact of gestational age, weight and feeding type were recorded. The first ten telephone interviews were completed with two researchers present to ensure consistency of approach and then further interviews were conducted by either researcher. If no response was received or no details were available, one further attempt was made to contact the unit. The results were recorded in a proforma and then collated and entered into a spreadsheet for analysis. Comparison to ESPGHAN guidance was completed.

Results: The survey collected data from 91 neonatal units (53% response rate). It was found that 10% of neonatal units had no fixed policy on supplements. The protocols regarding supplementation involved predominantly folic acid, Vitamin A, Vitamin D and iron. In regards to folic acid, when supplementing Expressed Breast Milk (EBM), 36% of hospitals prescribed 50mcg of folic acid daily, whilst 37% of units prescribed no folic acid. For remaining units, the dose varied from 50mcg daily to 1mg weekly. Similar results were obtained when looking at the Vitamins A and D. When considering Iron supplementation, over 65% of units prescribed iron supplementation with various feeds types whereas 27% did not supplement with iron at all. 46% of units recognised that no additional iron supplementation is needed for babies receiving preterm formula.

Conclusion: Dosing of all nutritional additives varied greatly across the country. Only a small proportion of units actually achieved dosing within ESPGHAN recommended limits in all supplements. More than 80% of units are in-fact overdosing Iron, potentially causing toxicity. The huge variation in practical prescribing that have been highlighted by this study support the need for a standardised supplementation regime based on available evidence.
Disclosure of Interest: None Declared
INTEGRATIVE ANALYSIS OF THE EFFECT OF AN INFANT FORMULA ENRICHED IN POLYAMINES ON THE MICROBIOME AND HOST CHANGES DURING LACTATION IN BALB-C MICE MODEL

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Objectives and Study: Milk polyamines are essential for post-natal maturation of the gut and immune system. Infant formulas have lower polyamine content than breast milk, and when used for infant feeding could be partially responsible for the differences in health status found between breast fed infants and formula fed infants. As immune system development and microbial colonization patterns are closely related in newborns, the objective of this work was to integrate different data-sets statistically using different methodologies to obtain an understanding of global microbe-host interaction and the effects of polyamine supplementation during lactation.

Methods: The study design includes four different treatment groups: 1) mice fed via normal lactation; 2) early weaned mice fed commercial infant formula; 3) and 4) early weaned mice fed infant formula enriched with polyamines. Data about the microbial composition determined using fluorescent in situ hybridization and qPCR, the immune cell populations analyzed by fluorescence activated cell sorting and the host response determined by transcriptomics focused on immune system pathways were integrated. Heat map–based clustering analysis was performed using the heatmap.2 function from the gplots R package. R package ade4 was used to assess differences between the feeding groups by performing a between-class analysis (BCA). The statistical significance of the BCA was evaluated with a Monte Carlo test, based on 999 replicates.

Results: The BCA showed that normal lactation was completely separated from infant formula–fed groups and polyamine-enriched formula (high concentration) from commercial infant formula and infant formula enriched with low concentration of polyamines on the basis of the first axis of the BCA. The Monte Carlo test showed that the differences between groups were statistically significant (p=0.001). Clustering analysis groups the different individuals with results similar to those of the BCA. Differences in gene expression might explain why polyamine-enriched formula modulates the immune system and microbial colonization patterns during lactation in a similar way to that seen in normal lactation.

Conclusion: The results suggest that polyamines can modulate immune system development and intestinal microbial colonization patterns in a manner similar to that polyamines present in breast milk. This study needs to be replicated in infants but potentially represents a relatively simple solution that could have substantial benefits, including promoting better growth and development.
OBJECTIVES AND STUDY: After birth, the gastro-intestinal tract (GIT) is rapidly colonised by a diversity of microorganisms. Neonatal gut colonisation is influenced by environmental exposure to microorganisms, age, diet and host-specific factors such as gestational age at birth (term vs. preterm), but the exact mechanisms are still poorly understood. Using piglets as models for both preterm and term infants, we investigated how different feeding regimes just after birth influenced GIT microbial colonisation short term (5 d) and more long-term (26 d).

METHODS: Preterm (90% of full gestational age) and term piglets were delivered by caesarean section and reared in the same environment. They were given either parenteral nutrition (PN-PRETERM, n=25; PN-TERM, n=14) or parenteral nutrition supplemented with enteral bovine colostrum (16-64 mL/kg/d, ENT-PRETERM, n=34; ENT-TERM, n=22) for 5 d, followed by full enteral feeding (150-180 mL/kg/day, bovine milk) until d 26. Gut microbiota (GM) composition was determined in colon contents at d 5 and 26 using MiSeq-based tag-encoded 16S rRNA gene targeted high throughput amplicon sequencing.

RESULTS: Analysis of similarities (ANOSIM) of uniFrac distance metrics showed that at d 5 GM was significantly affected by gestational age (PRETERM vs. TERM) and feeding regime (PN vs. ENT, both P<0.05). By d 26, the GM remained different between preterm and term piglets while the effect on GM of the early diet (PN or ENT) had disappeared. At d 5 Enterobacteriaceae generally dominated the GM of all piglets, but with more Lachnospiraceae and Verrucomicrobiaceae in the GM of the TERM piglets. In the PRETERM piglets the abundance of 2 different Enterobacteriaceae phylotypes, were the major difference between the two feeding regimes (PN vs. ENT). At day 26 Enterobacteriaceae still dominated the GM of both TERM and PRETERM piglets, but the PRETERM harboured more Lactobacillus while the TERM piglets harboured more of a phylotype assigned to the Verrucomicrobiaceae.

CONCLUSION: Shortened gestational age at birth, leading to immature GIT structure and function, influences the GM composition in piglets at least until d 26 of life. The initial feeding regime (TPN vs. MEN) affects the GM short-term but has no lasting effects.

Disclosure of Interest: None Declared
OBJECTIVES AND STUDY: Pre- and probiotics beneficially affect the host by improving the survival and establishment of live microbes from dietary sources in the gastrointestinal tract. We have previously demonstrated adequate growth in healthy term infants receiving a routine cow’s milk-based formula with a prebiotic blend of polydextrose (PDX) and galactooligosaccharides (GOS), or the probiotic Lactobacillus rhamnosus GG (LGG) added to partially or extensively hydrolyzed formulas. The objective of the current study was to establish that a formula with pre- and probiotics provides adequate growth.

METHODS: In this multi-center, double blind, controlled, parallel-group, prospective study, infants received one of two formulas from 14-120 days of age: marketed, routine infant formula with PDX/GOS (Control, n=171), or a similar investigational formula with PDX/GOS and LGG (1x10^6 CFU/g powder) (LGG, n=177). The primary outcome for this study was growth rate from 14 to 120 days. Growth rates from 14 to 30, 60, 90, and 120 days of age were analyzed by gender using ANOVA. Tolerance was assessed at each time point by 24-hour parental recall of stool characteristics, fussiness, and gas. Medically-confirmed adverse events were recorded.

RESULTS: There were no differences between groups in infant characteristics at birth and there was no difference in study completion rate. There were no statistical differences detected in the rate of weight gain (g/day) from 14 to 120 days of age for males (Control, 31.3 ± 0.7; LGG, 31.6 ± 0.6) or females (Control, 27.3 ± 0.7; LGG, 25.7 ± 0.7). Relative to normal, there was less parent-reported fussiness in the LGG group at 60 (p=0.02) and 90 (p=0.01) days of age. No significant differences were detected in between study groups in gas or stool frequency/consistency. No differences in medically-confirmed adverse events were detected.

CONCLUSION: Results of this study demonstrated that the investigational formula with PDX/GOS and LGG was safe and well-tolerated and associated with normal growth when fed to healthy term infants from 14 to 120 days of age.

**Objectives and Study:** Human milk is the gold standard of infant nutrition during the first months of life. Its composition is currently not possible to mimic completely. It contains minor components such as bioactive peptides with activities such as antioxidant, antihypertensive, antibacterial and/or immunomodulator. These compounds seem to perform their functions when they are hydrolysed during the infant digestion and they have specific functions according with their amino acids sequence. The aim of this study was to identify bioactive peptides after an *in vitro* digestion in a new extensively hydrolysed formula, which may have a relevant role in the nutritional treatment of cow’s milk allergy in infants.

**Methods:** The hydrolysis procedure consisted on the simulation of gastric and intestinal digestion of the samples by *in vitro* enzymatic treatment. Based on the modifications introduced by different authors, reduced concentrations of digestive enzymes and specific time of digestion were performed to simulate infant gastrointestinal conditions. Soluble fraction was filtered and the water-soluble extract was subjected to ultrafiltration through a hydrophilic 3000 Da membrane. The hydrolysates were injected into an HPLC system which was connected on-line to an Esquire-LC quadrupole ion trap instrument for RP-HPLC-MS/MS analysis, according to the method of Hernández-Ledesma et al 2004. The m/z spectral data were processed using Data Analysis 3.0 (Bruker Daltonik) and transformed to spectra representing mass values. MS(n) spectra were processed in BioTools 2.1 (Bruker Daltonik) to perform peptide sequencing.

**Results:** The ultrafiltration permeates contained a high number of fragments; 75 fragments, with a molecular weight lower than 1000 Da, were selected from the chromatogram: 73% of them derived from whey and 27% from casein. 14 fragments were identified which could have ACE inhibitory activity (SLSQSK, EMPFPK, VVPFLQ, VRGPFPI, LHLPLP, LHLPLPL, IIAEK, LDIQK, ALPMH, ALPMHI, VLDTDYG, GLDIQK, LDAQSAPL, VAGTWY). Among others, there was also identified VLNENL, which could have immunomodulatory and antibacterial effects; SLAM and SAMA, derived from β-lactoglobulin and found in WYSAMA bioactive peptides, which is known by its antioxidant effects, and the fragments IPAVF and ISQPE which could develop antibacterial effects.
**Conclusion:** Some of the bioactive peptides found in this therapeutic formula could be isolated, produced and clinically tested with the aim to produce supplements for special medical purposes such as prevention or treatment of allergy.


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Objectives and Study: Infants, even more so than children or adults, rely to a significant extent on dietary triglycerides (“fat”) for their energy requirements. The infant’s digestive tract is well equipped to absorb fat from maternal milk, with approximately 90% efficiency. With infant formula, however, efficiency is lower, due to fatty acid – calcium soap formation (especially palmitic acid) and excretion via feces. This is also associated with a loss of calcium. During the digestive process, free fatty acids (“FFA”) released from triglycerides through lipases must be solubilized in micellar or vesicular phases in order to be taken up by absorptive enterocytes. Improved solubilization of fatty acids in such structures could help improve fat absorption from infant formula in vivo. Phospholipids are of major importance for the formation of vesicular and micellar structures during digestion. We aimed to test, in vitro, if addition of milk fat globule membranes (MFGM) as a natural source of phospholipids to infant formula could increase solubilization of palmitic- and other fatty acids, thereby possibly increasing fat absorption in vivo.

Methods: MFGM from cow’s milk was rehydrated and homogenized and either used as such (“MFGM”) or after subsequent ultra-sonication to yield homogenous, structured MFGM (“sMFGM”). We first tested the capacity of MFGM or sMFGM to solubilize FFA from a dried lipid film in the presence of calcium. Next, we tested whether addition of (s)MFGM to infant formula enhanced FFA solubilization from a lipid film. Lastly, we tested whether formula enriched with (s)MFGM and subsequently digested in a two-step process (mimicking gastric- and small-intestinal digestion) enhanced solubilization of endogenously formed palmitic- and other fatty acids in the aqueous (i.e. non-pellet non-cream) phase.

Results: Both MFGM and sMFGM significantly increased solubilization of FFA, even in the presence of calcium. Addition of MFGM and sMFGM to infant formula significantly increased solubilization of FFA, with sMFGM being slightly superior to MFGM. Addition of MFGM and sMFGM to infant formula slightly accelerated triglyceride hydrolysis in vitro, but had no significant effect on the final extent of lipolysis. Enrichment of formula with MFGM (and especially sMFGM) led to a small but statistically significant increase in solubilization of FFA (including palmitic acid) in the aqueous phase, suggesting potentially increased bioavailability.

Conclusion: The addition of MFGM to infant formula may enhance solubilization of poorly soluble fatty acids, such as palmitic acid, in the aqueous phase of gastrointestinal digestive juices, even in the presence of calcium. The in vivo relevance of this phenomenon remains to be tested.

Disclosure of Interest: None Declared
**Objectives and Study:** The fatty acid composition of human milk is known to vary between mothers and populations. The concentration of docohexanoic acid (DHA) is particularly variable in human milk (HM). To examine the role of maternal diet and genetics in HM DHA levels, we collected HM, plasma and DNA samples from Cincinnati mothers of term and preterm infants.

**Methods:** Plasma and HM samples were analyzed for determination of DHA status; samples were collected at 1 week of life from preterm mothers and at 4 weeks of life from term mothers. Maternal fatty acid desaturase (FADS) single nucleotide polymorphisms (SNPs) were analyzed by pyrosequencing (preterm infants) and by Immunochip on Illumina platform (term infants). HM DHA was extracted using Bligh-Dyer technique and analyzed by gas chromatography. Dietary analysis included three 24 hour dietary recalls for both preterm and term mothers.

**Results:** HM DHA concentrations (mol-wt% ± SD) were 0.595 ±0.30 in preterm infants compared to 0.176 ±0.085 in term infants. Maternal dietary intakes of DHA from both studies were less than the current RDA (200 mg/d) with intakes of 32.95 ± 0.04 mg/d for preterm mothers, compared to 76.23 ± 0.13 mg/d for term mothers. In the preterm and term mothers, the minor allele SNP rs174575 was significantly associated with lower levels of HM DHA, p<0.05 and p<0.03 respectively. There were no significant relationships between dietary intake and milk DHA levels.

**Conclusion:** The differences in HM DHA values between preterm and term infants could be attributed to differences in stage of lactogenesis, but data from our preterm and term infants do not indicate a rapid decline in DHA in the first month of life. We suggest that genetics and low dietary DHA intake are contributing factors to low levels of DHA in HM and do not meet the adequate needs of the infant.

Objectives and Study: Fetal brain maturation is disrupted by preterm birth. Inflammation as reflected by changed serum cytokine concentrations during the neonatal period can further harm neurodevelopmental outcomes. Neutral (scGOS/lcFOS) and acidic (pAOS) oligosaccharides are known to lower cytokine concentrations during the neonatal period and may therefore improve neurodevelopmental outcomes in preterm infants at 24 months of age.

Methods: 113 infants (GA<32 weeks or BW<1500 g) received scGOS/lcFOS/pAOS or placebo supplementation between day 3-30 of life. Serum samples were collected at days 1, 7, and 14. Serum cytokine concentrations of IL-1, IL-2, IL-4, IL-6, IL-8, IL-10, IL-17, TNF-α and IFN-γ were determined by Luminex Immuno assay. Influence of cytokine concentrations during the neonatal period were tested by ANCOVA. At 24 months, 101 infants were eligible for follow-up by Bayley Scales of Infant Development (BSID) II or III. Furthermore, influencing factors (gestational age, birth weight, sex, and ≥ 1 serious neonatal infection) were determined.

Results: In total, 77/101 (76%) infants participated in the follow-up study, 38 in the supplemented and 39 in the placebo group. Baseline characteristics at birth were not different in both groups; neither were distributions of BSID II and III and neurodevelopmental outcomes at 24 months. Therefore groups were combined for other influences. Of the infants, 12 % had a mental developmental index (MDI) <85 and 7% a psychomotor developmental index (PDI) <85. Lower concentrations of IL-8 (p =0.01) and higher concentrations of IL-4 (p=0.01) at day 7 were positively associated with the MDI. Lower concentrations of IL-4 (p= 0.05), IFN-γ (p= 0.03) and TNF-α (p=0.01) at day 14 were positively associated with the PDI; reduced IL-1β concentrations were only weakly associated (trend, p=0.08). Neither cytokine concentrations at birth nor neonatal infections were associated with neurodevelopmental outcomes (p> 0.05).

Conclusion: Oligosaccharide supplementation did not improve the neurodevelopmental outcomes at 24 months in very preterm infants. Our findings suggest that serum cytokine concentrations during the neonatal period are associated with neurodevelopmental outcomes at 24 months of age. Our study population showed low percentages of MDI and PDI <85. Either group sizes may need to be larger or mean gestational should be shorter to allow detection of differences in neurodevelopmental outcomes between the supplemented and placebo group.
Disclosure of Interest: J. Van Den Berg: None Declared, E. Westerbeek: None Declared, T. Bröring-Starre: None Declared, J. Garssen Conflict with: Nutricia research; supplier oligosaccharides, R. van Elburg Conflict with: Nutricia research; supplier oligosaccharides
ASSESSMENT AND COMPARISON OF IMPACT OF FORTIFICATION OF THE OSMOLARITY OF HUMAN MILK

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Objectives and Study: To compare the osmolarity of EBM (expressed human milk), EBM fortified with HMF Lactodex, HIJAM and FM-85 fortifiers.

To compare the incidence of feed intolerance and NEC in the groups receiving EBM fortified with Lactodex and FM-85.

Methods: Methods: Sixty samples of expressed human milk stored at 4 °C, from mothers of very low birth weight babies (<1500 g) after 7 days of delivery were analyzed. Osmolarity of unfortified human milk (n=15) and milk fortified with Lactodex HMF (n=15), HIJAM (n=15) and FM-85 (n=15) was assessed. Osmolarity was measured by the Genotec Osmomat 030 (Wheecon Instruments) using one ml of left over EBM. Data on NEC and feeding intolerance was recorded in the groups receiving EBM fortified with Lactodex and FM-85.

Results: A total of 60 samples were analyzed. The mean gestation (SD) and birth weight (SD) of the babies were 30.43±2.3 weeks and 1241± 243 g respectively. The mean osmolarity (SD) of unfortified human milk and milk fortified with HMF Lactodex, HIJAM and FM-85 were 293.53 (12.39), 378.40 (34.4), 419.73 (30.65) and 451.20 (39.18) respectively which differed significantly (p <0.001). On post-hoc Bonferroni analysis, there was significant difference in the osmolarity in between the groups except FM -85 and HIJAM. No increase in incidence of feeding intolerance and NEC was seen in the groups receiving EBM fortified with Lactodex and FM-85.

Conclusion: Conclusion: Fortification of human milk with fortifier containing increasing protein content increases osmolarity without increasing the risk of feed intolerance and NEC.

Disclosure of Interest: None Declared
ADMINISTRATION OF BIFIDOBACTERIUM BREVE TO HUMAN MILK-FED PRETERM INFANTS

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Objectives and Study: Background: Human milk and probiotic microbes decrease the risk of necrotizing enterocolitis (NEC) in premature infants, however understanding of mechanisms of protection and comparisons of different species of probiotic organisms are limited. Blooms of Enterobacteriaceae have been described just prior to the onset of NEC.

Objective: Determine changes in the fecal microbiota of premature infants receiving Bifidobacterium breve (B. breve).

Methods: Method: Twenty-nine premature infants (median gestational age 28 weeks, range 23-32 weeks) cared for in the neonatal intensive care unit (NICU) of the King Edward and Princess Margaret Hospital in Perth, Australia were treated with B. breve at a dose of 3 x 10^9 cfu/day. Samples of feces, urine, and stool were obtained just prior to initiation of the probiotic (pre) and again two weeks later (post). 16S ribosomal RNA from the feces was analyzed by next generation sequencing. Bifidobacterium subspecies analysis and quantitation of human milk oligosaccharide content of the milk, urine, and feces is in process.

Results: Results: A significant increase in relative abundance of fecal bifidobacteria was noted with initiation of B. breve (2.5% pre and 5% post, p<0.01). Administration of B. breve was also associated with increases in fecal Enterobacteriaceae (3.5% pre and 10% post, p<0.01), Enterococcaceae (1.5% pre and 4% post), and Clostridiaceae (<0.1% pre and 1.5% post, p<0.01) and significant decreases in fecal Moraxellaceae, Streptococcaceae, and Pseudomonadaceae (p<0.01).

Conclusion: Conclusions: Administration of B. breve was associated with increased colonization with commensal bifidobacteria and with increased levels of fecal Enterobacteriaceae. An increase in fecal Enterobacteriaceae in premature infants has previously been demonstrated with administration of B. lactis, whereas administration of B. infantis was associated with a decrease in fecal Enterobacteriaceae. We hypothesize that B. lactis and B. breve share common mechanisms of colonization that differ from those of B. infantis. Analyses of the fecal bifidobacteria at the subspecies level and analyses of the oligosaccharide content of the milk, urine, and fecal samples will likely shed further light on differences between these common probiotic strains.

Disclosure of Interest: None Declared
THE IMPACT OF CHANGES IN DIETARY LIPID STRUCTURE ON GROWTH AND BODY COMPOSITION DEVELOPMENT IN INFANTS: RATIONALE AND DESIGN OF THE VENUS STUDY

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Objectives and Study: Human milk (HM) has been shown to have a protective effect against obesity later in life. Besides compositional differences HM contains large fat globules (4-10 μm) that are complex structures with multi-layer membranes, embedded functional proteins surrounding a triglyceride core. Infant milk formula (IMF) contains small lipid droplets (<0.5 μm) with proteins at the lipid-water interface. We developed a concept IMF with large, phospholipid coated, lipid droplets (Nuturis®), which showed protective effects against adipose tissue accumulation in animal studies [1,2]. The VENUS study is a randomized controlled clinical study to examine the effect of supplementation with the Nuturis® concept formula on growth and body composition development in infants.

Methods: Primary outcomes are growth and formula tolerance during the first year of life using regular weight and height measures as well as skinfold thickness and diary recordings. At two years, ultrasound measures to obtain a proxy of abdominal adipose tissue distribution will be taken [3].

Results: A total of 539 infants were recruited between June 2012 and July 2014 and randomly assigned to either receive Nuturis® or one of two different control formulas. Infants were randomised at the point when their mothers chose to start using formula milk during the first year of life, either completely or partially. This new design, encouraging breastfeeding after study enrolment, could be described as a 'best after breast design' and allows for differences in individual duration and intensity of the used products during the intervention period. A subgroup of the total recruited infants will serve as an exclusive breast feeding reference group.

Conclusion: The VENUS study will explore the potential contribution of the modified dietary fat structure to limit early adipose tissue growth. This approach may contribute to the development of new strategies relevant to reduce the risk of excessive weight gain during infancy.


Disclosure of Interest: Y. S. Chong Conflict with: part of an academic consortium receiving funding from Abbott, Nestec and Danone, E. van der Beek Conflict with: employee of Danone, L. Shek: None Declared, A. Winokan Conflict with: employee of Danone, K. Kwek: None Declared
SIALIC ACID CONTENT IN INFANT FORMULAS AND THE INTAKE ESTIMATION IN THREE EUROPEAN COUNTRIES

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Objectives and Study: Human milk (HM) is the optimal feeding for the first months of life of the newborn but when breastfeeding is not possible, many infants are fed with infant formulas (IFs). Sialic acids (N-acetyleneuraminic acid-Neu5Ac and N-glycolyneuraminic-Neu5Gc) are bioactive compounds present in HM and in less concentration in IFs. Sialic acids play an important role in infants' brain development, immunity against infections and the development of the digestive system. In order to improve IFs composition to be closer to HM, it is of interest to characterised these compounds in IF. The aim of this work was to determine the different sialic acids (Neu5Ac and Neu5Gc) content in infant formulas from three European countries, and to estimate sialic acid intakes.

Methods: Twelve IFs from three different countries in Europe (Spain: 5, Czech Republic: 4 and Sweden: 3) were analysed. A chromatographic method (HPLC-fluorescence) was applied. Briefly, 0.75 g of IF were hydrolyzed with H2SO4 0.05 M, centrifuged (1000xg/4°C/10min), purified by ion exchange (2mL of Dowex 1x8), ultrafiltered (Microcon Ultracel YM-10, 13000xg/4°C/10min) and derivatized (DMB 50°C/2.5h). The Neu5Ac and Neu5Gc contents were determined by used calibration curve: Neu5Gc (1.6 - 8 ng/ assay) and Neu5Ac (12.5 - 250.8 ng/assay). For estimation of sialic acid intake, average reported milk intake volumes (ml/day) from several clinical studies, including 1113 infants from 1 to 6 months of life were used.

Results: Sialic reproducibility of twelve calibration curves injected on different days (n=12) was evaluated and no significant differences (p<0.05) were found. Average: y=17025.27x-8201.33 (R²=0.9927) for Neu5Ac and y=12892.99x-3912.56 (R²=0.9987) for Neu5Gc. The retention time of Neu5Ac and Neu5Gc were 8.1±0.2 min and 10.2±0.3 min, respectively. The minimum and maximum mean contents of the corresponding IFs were: Neu5Ac (126-251.4 mg/l: Spain: 179±33 Czech Republic: 217±29 and Sweden: 169±25) and Neu5Gc (1.4-9.7 mg/l: Spain: 6.7±1.8 Czech Rep: 5.7±1.6 and Sweden: 3.8±1.4). The minimum and maximum mean contents of the corresponding IFs intakes were Neu5Ac (95.13-248.89 mg/day) and Neu5Gc (1.07-9.61 mg/day).

Conclusion: The contents of sialic acids in IFs were similar to published values using similar methodology but lower than in mature HM. More research is need to both increase the levels of Neu5Ac to reach human milk levels, and to evaluate the potential health benefits. The highest sialic acid intakes was at 4 and 5 months.

Objectives and Study: Adequate nutrition during infancy is essential to ensure healthy growth and development of children and may have an effect on the incidence of atopy and obesity. The aim of this cohort study was to identify the breastfeeding and formula feeding patterns in Italian infants under 24 weeks of age and their determinants.

Methods: We analysed a cohort of 314 Italian infants at risk of atopy. Infants who did not receive breast milk were randomized to receive a prebiotic or standard formula. Mothers recorded type of infant feeding (breast milk, study formula, mixed feeding) and amount of milk consumed. Baseline characteristics including type of delivery, weight and length at birth, gestational age, number of siblings, mother's age, smoke in pregnancy and mother's and father's education were collected and compared with inferential statistics.

Results: 118 out of 314 infants (37.6%) were exclusively breastfed (EBF) until 24 weeks of life. The rate of EBF in the first month of life was 92.6%. 196 infants (62.4%) received formula feeding (FF) and of these 30 (15.3%) were exclusively formula fed (EFF). In the group of mixed feeding (MF), the mean duration of EBF was 60±40 days. The amount of formula milk in MF infants was 54.8±45.3ml/Kg (median value 49.2, range 30-156.4 ml). In the EFF group the mean amount of formula was 99.4±40.83 ml/kg and the mean time of starting formula was 45±16 days. A greater number of mothers delivered their infants vaginally (212;67.5%) versus caesarean section (102;32.5%). An earlier age of onset of formula feeding was significantly associated with caesarean delivery and natural delivery was associated with a longer mean time of breastfeeding (p<.001). A significant difference was found in the father's education between formula and breastfed infants (lower secondary school in 17.9% vs 7.6% respectively, p=.004).

Conclusion: The breastfeeding initiation rate in Italian infants is high, however a wide pattern of formula feeding exists in this population variably related to baseline characteristics. These data serve as a baseline for intervention studies in order to evaluate the efficacy and applicability of feeding strategies aimed at reducing the risk of atopy and obesity.

Disclosure of Interest: G. Ranucci Conflict with: The study was supported by Mead & Johnson Nutrition., M. I. Spagnuolo Conflict with: The study was supported by Mead & Johnson Nutrition., V. Buccigrossi Conflict with: The study was supported by Mead & Johnson Nutrition, F. Visentin Conflict with: Mead & Johnson Nutrition, A. Gambino Conflict with: The study was supported by Mead & Johnson Nutrition, P. Baiardi Conflict with: The study was supported by Mead & Johnson Nutrition, C.
Giaquinto Conflict with: The study was supported by Mead & Johnson Nutrition, A. Guarino Conflict with: The study was supported by Mead & Johnson Nutrition
CAN GROWTH BE OPTIMISED IN ENTERALLY FED VERY LOW BIRTH WEIGHT INFANTS WHO RECEIVE STEROIDS AS COMPARED TO PEERS?

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Objectives and Study: Growth is essential for optimal outcomes in <1500 gms, but is often compromised in infants receiving steroid therapy for improved respiratory management. DART, a 10-day course of dexamethasone used to wean ventilatory support has been associated with poor weight, length and head circumference at term-corrected age. Despite anticipated poor growth, nutrition management strategies vary significantly among treated infants. Our objective is to analyze outcomes of aggressive enteral nutrition practices on growth for infants who received DART therapy compared to untreated peers.

Methods: An IRB approved retrospective review compared outcomes for infants born <1500 gms. 8 study infants received DART therapy and were compared to 16 controls. Descriptive statistics and Wilcoxon rank sum test were used to compare infant growth, enteral nutrition, laboratory data, and demographics between the groups. Associations of categorical variables were assessed with the Fisher's exact test.

Results: Study infants were significantly younger and were smaller in weight, length and head circumference at birth (p<0.05). At 36 weeks corrected age, there were no significant group differences in weight, length, or head circumference. There were no differences in infants <10th% on the Fenton growth curve at discharge (p=0.29). Growth to 36 weeks was similar (median 16 gms/kg/day control, 15.2 gms/kg/day DART group (p=0.56)). DART infants received more calories and protein, median 131 vs 121 calories/kg/day (p=0.027) and 4.4 vs. 4.2 gms protein/kg/day (p=0.025). DART infants received higher caloric densities of feedings, median 30 vs 27 cal/oz (p=0.01). Average enteral nutrition during DART therapy was 138 cal/kg and 4.5 gms protein/kg/day. There were no differences in highest glucose (p=0.09), BUN (p=0.71), or ALK PHOS (p=0.15). Control subjects weaned off O2 earlier than DART group (p=0.001). 6% of the control group discharged on oxygen compared to 62% in the DART group (p=0.0069).

Conclusion: Adequate growth in weight, length, and head circumference can be achieved for infants receiving DART therapy by optimizing enteral nutrition. Additional calories and protein during therapy may contribute to growth without significant concern for metabolic intolerance. Infants receiving DART require oxygen longer than controls. This is attributed to baseline need for DART therapy.

Disclosure of Interest: None Declared
**Objectives and Study:** The effectiveness of standard fortification of maternal milk (MM) in supporting appropriate protein intake of preterm neonates (PN) has been debated due to the high variability of nutrient content of MM. This study aimed at evaluating the effect of individualized MM fortification based on MM analysis and targeting the recommended daily protein intake on nutritional intake, nutritional status, and serum biochemistry of PN.

**Methods:** In a prospective randomized study, PN (GA<32 weeks) fed their own mothers’ milk were randomly assigned into the standard fortification group (SFG) and the individualized fortification group (IFG) in which fortification was based on MM analysis targeting to a protein intake of 3.5–4.5 g/kg/d. The intervention started when oral feeding reached the 100ml/kg/d (T1) and lasted until a body weight of 2000g (T2). Nutritional intake, nutritional status and serum biochemistry were assessed weekly during the intervention period and at 40 weeks post-conceptionally (T3).

**Results:** 30 PN (14 and 16 in the SFG and IFG, respectively) were studied. In the IFG, mean protein and carbohydrate intake were lower, fat intake higher, and energy intake comparable to the SFG. The increase of weight (g/kg/d), length (cm/week), and HC (cm/week) during the intervention period as well as the z-scores of anthropometry and serum biochemistry on T1, T2, and T3 were comparable between the two groups.

**Conclusion:** Individualized MM fortification, based on mother’s milk analysis and targeting the recommended protein intake, resulted in lower protein intake without any significant effect on energy intake, nutritional status, and serum biochemistry.

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

**Neonatal Nutrition**

PO-N-0475

**PRETERM NEONATES’ FATTY ACID PROFILE IN RELATION TO MATERNAL NUTRITION STATUS AND MEDITERRANEAN DIET PATTERN**

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**Objectives and Study:** Maternal nutrition status before and during pregnancy and dietary patterns are important factors affecting breast milk’s fatty acid profile (FAP). Aim: to investigate whether mother’s nutrition status and diet quality are related to FAP of preterm neonate’s fed maternal milk.

**Methods:** Fully breast fed preterm neonates (birth weight [BW]≤1500g, gestational age [GA]≤34weeks) where followed from birth until 40th week postconceptional age(PCA).Neonates’ plasma FAP was assessed at 2000g (T1) by GC-MS. Mothers’ BMI was estimated and MedDietScore was calculated based on validated Food Frequency Questionnaire. Neonates were reexamined at 40th week PCA (T2).

**Results:** We studied 20 mother-neonate pairs. Prepregnancy and current maternal BMI were 27.55±5.33 and 29.24±5.15kg/m², respectively, and MedDietScore: 25±3.78. Good adherence to Mediterranean Diet (75th percentile≥27) was found in 8/20 mothers. MedDietScore was negatively correlated with BMI (r=-0.497, p=0.025). Neonate’s GA: 29±2.36 and BW: 1128±207. FAP did not differ significantly between neonates born to mothers with normal BMI compared to those born to overweight/obese mothers neither at T1 (PCA 35±1.6weeks) nor at T2. Similarly, FAP did not differ significantly among the three maternal MedDietScore-related groups of neonates (maternal MedDietScore:≤21, 22-26, ≥27).

**Conclusion:** Adherence to Mediterranean Diet is poor among mothers, especially the obese ones. Our results suggest that FAP of preterm neonates fed maternal milk during the first month of life is not significantly affected by maternal nutrition status nor her adherence to mediterranean diet pattern. The possible effect of maternal nutrition on FAP of preterm infants on longer breast feeding will be clarified with long-term follow up through childhood.

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

**Nutrition and Metabolism**

PO-N-0476

**SIMPLE SUGARS INTAKE FROM INFANT CEREALS IN SPAIN. A WEB-BASED CEREALS DIETARY QUESTIONNAIRE**

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**Objectives and Study:** In Spain, most infant cereals (IC) are hydrolysed in order to enhance solubility and avoid lump formation. However, simple sugar (SS) levels depend on the degree of hydrolysis. Several studies suggest that excessive SS supply during the complementary feeding promotes child’s preference for sweet flavors, leading to dental caries, diabetes and/or obesity, in later life stages. The aim of the present study was to evaluate IC feeding habits and SS intake from IC in Spanish infants aged 4-12 months.

**Methods:** A dietary questionnaire was developed based on literature and 7 in-depth interviews with mothers of infants aged 4-12 months. The questionnaire was pre-tested with a convenience sample of 282 mothers. A web-based questionnaire was then administered to 1090 mothers of infants aged 4-6 months (44%), 7-9 months (45%) and 10-12 months (11%). We collected information on family socio-demographic characteristics, infant characteristics, IC feeding habits (cereals type, frequency and mode of preparation) and amounts of IC ingested. In order to calculate SS intakes, we conducted a nutritional study of the six main Spanish brands covering the most sold IC varieties.

**Results:** 88.7% of infants consumed IC daily (twice: 52.8%, once: 32.1%, > two times: 15%). IC were prepared with follow-on formula (52%), infant formula (26%), breast milk (11%) and other milks (11%). The preferred feeding mode were baby bottle (64.7%) followed by plate (25.5%) and 9.8% using both. Scoops were the main measurement tool used (70.9%). The number of scoops added depended on infant’s age and mode of preparation. For Infants aged 4-9 months between 2 and 4 scoops were added on the bottle and between 4 and 8 scoops were added on plate. For Infants aged 10-12 months between 3 and 6 scoops were added to bottle and between 5 and 8 scoops were added on plate. The varieties of IC most consumed in Spain were “Multicereals” (43%) and “8 Cereals with Honey” (34%). The mean SS content in the 6 main brands of IC these varieties was 27.74 ± 4.22 g/100 g of product. Three brands added sucrose. The SS ingested daily from IC was ranged from 5.6 to 11.2 g of SS daily in infant aged 4-9 months and ranged from 8.4 to 16.8 g in infant aged 10-12 months. Without considering other foods of the global diet, IC provide SS between 4.08-9.74% of total energy intake per day.

**Conclusion:** Our results indicate that SS intake from IC is high. Given that from a cultural perspective IC tend to be excessively sweet in Spain and that cereals are the usually the first solid introduced, there is an opportunity for a gradual step wise reduction of the content of SS.

**Disclosure of Interest:** M. Bernal Conflict with: Hero Spain, J. Haro Conflict with: Hero Spain, S. Roman: None Declared, S. Bodenstab Conflict with: Hero Group, L. Sanchez-Siles Conflict with: Hero Group
EFFECTS OF A FOLLOW-ON FORMULA WITH A LOW-GLYCAEMIC INDEX: DOUBLE BLIND RANDOMISED TRIAL

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Objectives and Study: Formula fed infants have been reported to show higher postprandial glucose and insulin responses than breastfed infants, which may be related to greater fat deposition and increased later risk of obesity. Therefore, effects of the glycaemic load of a meal on plasma glucose and insulin during the postprandial period may be important. We aimed to investigate the acceptance, tolerance and the effect on postprandial glycaemia and insulinaemia of a follow-on formula with a low-glycaemic index.

Methods: Healthy term infants aged 4 to 8 completed months (n=50) were randomized double blind to receive for 4 wk a low-glycaemic follow-on formula (IF, 2.1g isomaltulose (Palatinose™)/100mL) or an isocaloric control formula (CF) providing 2.2g maltodextrin/100mL and otherwise identical composition. Anthropometry, nutrition, sleep patterns and tolerance parameter were assessed. On day 29 urine and capillary blood 60min after start of feeding were obtained.

Results: Of the 25 infants randomized to IF and 25 to CF, 24 and 21, respectively, completed the study. The subjects in both formula groups were similar regarding demographic data. Both formulae were well accepted without significant differences in time of crying, flatulence, stool characteristic and the occurrence of adverse events. Energy intake from formula, complementary feeding and rating of meals were not different between both groups. Anthropometric data adjusted for the respective baseline value and age was not statistically different between groups. After adjustment for volume of meal, time for meal and age, insulinaemia 60min after start of feeding (100-120mL formula) was not statistically different while glycaemia was 122(105,140) mg/dL in IF group and 111(100,123) in CF group (Median(IQR), p=0.01). Urinary c-peptide/creatinine ratio did not differ after adjustment for age (IF 81.5(44.7,96.0) vs. CF 56.8(37.5,129), p=0.43). Urinary c-peptide/creatinine ratio is correlated with weight gain (R=0.51, p<0.01) and total intake of energy (R=0.31, p=0.045), protein (R=0.42, p<0.01) and fat (R=0.40, p=0.01).

Conclusion: Both formulae were tolerated well. The expected reduced postprandial blood glucose and insulin was not shown, possibly due to limitations of the trial conditions in this age group, in particular blood withdrawal at a single time point only. Insulin secretion is a driver of infant weight gain. Non-invasive assessment of urinary c-peptide excretion might be a suitable marker for energy and protein intake of infants aged 4 to 8 months.
Disclosure of Interest: M. Fleddermann: None Declared, A. Rauh-Pfeiffer: None Declared, H. Demmelmaier: None Declared, L. Holdt: None Declared, D. Teupser: None Declared, B. Koletzko Conflict with: No conflict of interest is declared by all authors. This study was funded by BENE0 Group, Germany, and supplied the respective formulae. BENE0 reserves the exclusive right to use the results and data for possible Health Claim requests.
SENSITIVE IMAGING TECHNIQUES DEMONSTRATE LCPUFA-INDUCED IMPROVEMENT OF CEREBROVASCULAR FUNCTION, GRAY MATTER INTEGRITY AND FUNCTIONAL CONNECTIVITY IN MILDLY OBESOGENIC APOE*3LEIDEN MICE


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Objectives and Study: Being a major global health problem, obesity is associated with impaired cognition and brain structure. Researchers demonstrated beneficial effects of dietary long-chain polyunsaturated fatty acids (LCPUFAs) on cognition and obesity. In this present study, we investigated if early intervention with LCPUFAs can prevent potential detrimental effects of a mild obesogenic diet on brain structure and function.

Methods: Four-week old male ApoE*3Leiden mice were fed regular chow with or without a mixture of arachidonic acid (ARA, 0.129 wt%) and docosahexaenoic acid (DHA, 0.088 wt%). From 14 until 26 weeks of age, mice received a mildly obesogenic high-fat/high-carbohydrate (HFHC) diet. All mice were assessed in cognitive tests such as the Morris water maze. 13 and 26 week-old animals were examined with neuroimaging (11.7 T Bruker scanner) to assess cerebral blood flow (CBF) and vasoactivity (ASL), white and gray matter integrity (DTI), and to monitor brain connectivity (rsfMRI). Mice were sacrificed, brains were harvested and immunohistochemically examined to investigate cerebrovascular integrity.

Results: Early life LCPUFA supplementation significantly improved spatial learning abilities in later life. Furthermore, ARA&DHA supplementation in early life was found to counteract the HFHC-induced changes in CBF in mice at 26 weeks of life. This finding was further supported by significant diet-effects in the number of GLUT-1 positive blood vessels. In the hippocampus, somasensory and motor cortex the mean diffusivity levels of these mice fed a HFHC-diet were increased, which indicates a loss of gray matter integrity. On the other hand, this loss could be inhibited by prior LCPUFA supplementation. rsfMRI analyses demonstrated a decreased functional connectivity between in particular the ventral hippocampus, motor and somatosensory cortex in the HFHC-fed mice, while mice with early ARA&DHA supplementation were protected against these detrimental effects.

Conclusion: Our results suggest that LCPUFA supplementation early in life is able to protect against detrimental effects of an obesogenic diet on vascular function, gray matter integrity and functional connectivity later in life. Furthermore, these findings demonstrate that sensitive imaging techniques are suitable to detect subtle diet effects on brain structure and function in specific brain regions.
Disclosure of Interest: I. Arnoldussen: None Declared, V. Zerbi: None Declared, H. Noordman: None Declared, P. Wielinga: None Declared, R. Kleemann: None Declared, T. Kooistra: None Declared, G. Gross Conflict with: Mead Johnson provided funding for this study., E. van Tol Conflict with: Mead Johnson provided funding for this study., M. Schoemaker Conflict with: Mead Johnson provided funding for this study., A. Kiliaan: None Declared
BIOACTIVE WHEY PROTEIN CONCENTRATE AND LACTOSE STIMULATE GUT FUNCTION IN PRETERM PIGS

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Objectives and Study: Formula feeding is associated with feeding intolerance, necrotizing enterocolitis (NEC) and compromised intestinal health in preterm neonates. Reduced levels of bioactive proteins in commercial whey protein concentrate (WPC) and the replacement of lactose with maltodextrin in formulas may play a role. The effect of two WPCs, with either high or low levels of bioactive proteins (WPC H or L), were investigated in preterm pigs (Exp 1). Levels of lactoferrin, IgG and IGF-I were higher in WPC H than L (5-, 3-, and 3-fold). Each WPC was included in formulas based on either lactose or maltodextrin to test the interaction between protein and carbohydrate fractions. In Exp 2 we investigated whether bioactive proteins in WPC can be preserved by reduced thermal processing and whether this bioactive WPC (Bio) improves intestinal health, relative to a conventionally produced WPC (Con).

Methods: 92 caesarean-delivered preterm pigs were administered increasing doses of formulas for 4 days (16-120 mL/kg/d). In Exp 1, pigs were fed WPC H or WPC L contained in lactose- (lactose/maltodextrin: 3/1) or maltodextrin-dominant (maltodextrin/lactose: 3/1) formulas (4 groups, n =15-16). In Exp 2, pigs were fed Bio or Con contained in lactose-dominant formulas (2 groups, n=15-16). NEC, feeding intolerance, and intestinal indices, including morphology, permeability, hexose absorptive capacity, and brush border enzymes were evaluated.

Results: A reduction in thermal processing preserved lactoferrin and TGF-β2 in Bio (3- and 10-fold vs. Con). Weight gain, NEC incidence (49% across groups) and haematology were similar among groups. In Exp 1, regardless of the carbohydrate fraction, pigs fed WPC H showed or tended to show increased mucosal mass (P<0.05) and villus height (P=0.09), relative to WPC L pigs. Only in lactose-dominant formulas did WPC H stimulate hexose absorptive capacity and lactase activity relative to WPC L (P<0.05). In Exp 2, no Bio pigs had feeding intolerance, compared with 7/16 Con pigs (P<0.01). Bio pigs also tended to show higher hexose absorptive capacity (P=0.09) and lower gut permeability (P=0.07).

Conclusion: WPC with higher levels of bioactive proteins improves gut maturation, but mainly when contained in lactose-based formulas. Reduced thermal processing preserves bioactive proteins in WPC and improves feeding tolerance and intestinal functions. Lactose-based formulas containing WPC with maximal preservation of bioactive proteins could be important to support intestinal maturation and health in sensitive newborn infants.
Disclosure of Interest: Y. Li Conflict with: Was employed at Arla Foods Ingredients when part of the study was performed, D. N. Nguyen: None Declared, T. Thymann: None Declared, D. E. W. Chatterton: None Declared, A. S. Kvistgaard Conflict with: Arla Foods Ingredients, S. B. Bering: None Declared, P. T. Sangild: None Declared
**Objectives and Study:** Metabolic Syndrome (MS) is a clinical condition frequently present in obese children and characterized by insulin resistance, dyslipidemia, abnormalities in glucose metabolism, hypertension and visceral adiposity. A link between obesity and iron deficiency has been already suggested, but poor data are available on the possible role of MS in iron metabolism. **AIM OF THE STUDY:** To assess the association between iron status and MS in a large population of Italian obese children and adolescents.

**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 Iron, Transferrin, Ferritin concentration, Hemoglobin and Mean Corpuscular Volume (MCV) of red blood cells. Total Iron Binding Capacity (TIBC) and Transferrin Saturation were calculated for each patient. We defined MS using modified Criteria of American Heart Association. Data were age-weighted.

**Results:** The prevalence rate of MS in our population was 13.07%; accordingly, patients were divided in two groups: Group A (105 pts with MS, mean age 9.9±2.4 aa), Group B (698 pts without MS, mean age 9.3±2.55 aa, p= 0.028). Obese children of Group A had significantly higher BMI z-score than children of Group B (2.4±0.5 vs 2.2±0.5, p= 0.0001). TIBC and transferrin were higher in children of Group A compared with children of Group B (Table). Differences in haemoglobin levels were not significant between groups (p=0.139), but patients of Group A had mean MCV lower than Group B, in spite of higher levels of Ferritin (Table). Spearman’s correlation between MS_AHA diagnosis and TIBC was low, but significant (rho: 0.082, p= 0.022). Statistical association was maintained after adjustment for age, sex, and BMI z-score (r: 0.072, p= 0.028). Correlation between MCV and MS, adjusted for age and sex, was also significant (r:-0.101, p= 0.005).

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**Conclusion:** Our results suggest that iron metabolism could be altered in obese children with MS. It could be related to the reported low-grade inflammation induced by proinflammatory cytokines in obese individuals. Further studies are required to understand this association.
Disclosure of Interest: None Declared
MONITORING CALCIUM AND PHOSPHATE METABOLISM IN CHILDREN WITH PARENTERAL NUTRITION AND INTESTINAL FAILURE – WHAT ARE USEFUL MARKERS?

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Objectives and Study: To achieve growth in children with intestinal failure (IF) on total parenteral nutrition (TPN) it is essential to monitor calcium/phosphate metabolism. Bone composition in IF is monitored by DXA and pQCT. However, the contribution of serum and urine parameters reflecting bone metabolism is not clear in this setting. We analysed calcium/phosphate/sodium parameters in IF-children and there correlation with bone metabolism/longitudinal growth.

Methods: Single center, retrospective study of 45 children with IF in an intestinal rehabilitation programme (2010-2013). Age range was 3 mths to 17 yrs, 4.2±4.5 yrs (median±SD), 24/45 were female. 23/45 pts. had motility/malabsorption disorders. 22 had short bowel syndrome, 6/22 with ileocelecal valve. Residual short bowel length was 19.3±20.7 cm. We analyzed alkaline phosphatase (AP), parathyroid hormone (PH), 25-OH-cholecalciferol (calcidiol) status. By 24 hour urine collection we measured urine excretion of calcium, phosphate, sodium, creatinin. Corresponding bone parameters areal bone mineral density (aBMD), trabecular bone density, bone mineral content (BMC) and strength strain index (SSI) were determined. Body calcium/phosphate retention was defined as PN intake–urine excretion.

Results: Height-SDS was -2.3, weight-SDS -1.4, aBMD-SDS -1.7±1.9 with osteopenia in 6, osteoporosis in 4 pts. SSI-SDS was -1.4±2.3 whereas trabecular bone density was normal. Calcium urine excretion (Ca/Crea) showed a hypercalciuria rate of 55.6% and was positively correlated with body phosphate retention. Body phosphate retention correlated with aBMD (r=0.71, p<0.05). Urine sodium excretion positively correlated with sodium PN intake and SSI-SDS (r=0.77, p<0.01). Body calcium retention was significantly reduced (-58 ± 83.5%, -211 to 129%) positively correlated with phosphate retention and negatively correlated with phosphate TPN intake. In addition SSI-SDS correlated with height-SDS and TPN caloric intake. Parathyroid hormone correlated negatively with calcium urine excretion, SSI-SDS, trabecular bone density, BMC and calcidiol levels. No correlations were found for either body calcium retention with bone parameters or with AP. Interestingly trabecular bone density did not correlate with serum and urine parameters of calcium/phosphate metabolism in this study.

Conclusion: We found a strong association of urine excretion for calcium/phosphate and sodium, calculation of calcium/phosphate body retention and parathyroid hormone to representative markers of bone composition (aBMD and SSI). Therefore these markers may serve as reliable parameters of bone metabolism in children with IF on TPN. A prospective study is on the way to confirm these observations.
Disclosure of Interest: None Declared
**Objectives and Study:** As obesity is associated with risk factors related to cardiovascular disease there is need for early preventive strategies. One suggested approach is gut microbiota modulation by feeding probiotics in early life. In animal models, the probiotic *Lactobacillus paracasei* ssp. *paracasei* F19 (LF19) exerts beneficial metabolic effects, including upregulation of genes involved in energy homeostasis and reduction of body fat. Studies in children are however scarce. In a randomised subsample of the study described below we observed lower levels of palmitoleic acid in infants fed LF19. Palmitoleic acid correlates strongly with visceral adiposity in children and unfavourable blood lipid profile in adults. Therefore, we hypothesised that feeding LF19 during weaning would induce long-term programming effects on the metabolic and inflammatory profile.

**Methods:** In a double-blind, placebo-controlled trial, 179 infants were randomised to cereals with or without LF19 $10^8$ CFU daily from 4 to 13 months of age. At age 8-9 years, 120 children entered a clinical follow-up. The inflammatory and metabolic profile was determined in serum after overnight fasting using multiplex immunoassay technology and ELISA.

**Results:** Contradictory to our hypothesis LF19 had no impact on the assessed biomarkers. However, independently of LF19, overweight/obese children had increased plasma C-peptide (p=0.009), plasminogen activator inhibitor-1 (p=0.024), leptin and serum high-sensitivity C-reactive protein (hsCRP) levels (both p<0.001) compared with normal weight children. Plasma leptin (p<0.001) and serum hsCRP (p=0.001) remained increased when obese children were excluded, revealing an aberrant metabolic and inflammatory state already in overweight, pre-pubertal children.

**Conclusion:** Probiotic products targeting the paediatric population are rapidly increasing on the market even though their long-term safety and efficacy have not yet been fully evaluated. This study provides further evidence that early feeding with LF19 does not impact the metabolic and inflammatory profile in a long-term perspective. The aberrant metabolic profile in overweight children observed already at a young pre-pubertal age underscores the need for early preventive strategies.

**Disclosure of Interest:** F. Karlsson Videhult: None Declared, Y. Andersson: None Declared, I. Öhlund: None Declared, H. Stenlund: None Declared, O. Hernell Conflict with: Semper and Arla Foods, Conflict with: Member of Scientific Advisory Board of Semper and Hero, C. E. West Conflict with: Funding and speaker honoraria from Arla Foods, Conflict with: Arla Foods and Nestlé Nutrition
Effect of fatty acid optimisation of complementary food on LC-PUFA status in healthy infants: Results of the randomised controlled trial PINGU

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Objectives and Study: With the introduction of complementary food the intake of long-chain n-3 fatty acids (n-3 LC-PUFA) such as docosahexaenoic acid (DHA) usually decreases. Considering potential beneficial effects of the DHA status on visual and cognitive development in infancy, the randomized controlled intervention study PINGU examined food based strategies for optimization of endogenous n-3 LC-PUFA status during in period of complementary feeding.

Methods: Two approaches of dietary n-3 PUFA supply via complementary food in the second 6 months of life were tested: a) usage of n-3 alpha-linolenic-(ALA)rich rapeseed oil to increase the endogenous DHA synthesis (intervention group rapeseed oil, IG-R) or b) intake of preformed DHA via fish twice a week (IG-F). The control group (CG) received commercial jars with n-6 linoleic acid rich corn oil. The dietary intervention covered the complementary feeding period starting -as generally recommended in Germany- at the age of 4 to 6 months of age and ending at the age of 10 months. Fatty acid status was assessed in plasma and erythrocyte (RBC) membrane phospholipids.

Results: Complete data of fatty acid profiles before and after intervention were available from 158 infants. At the end of the intervention concentrations of eicosapentaenoic acid (EPA), DHA, and total n-3 LC PUFA in RBC was higher in IG-F as compared with CG (each p<0.0001). In IG-R higher values in RBC were observed for ALA (p=0.0002), the ratio of ALA to Linoleic Acid, and EPA (both p<0.0001). The DHA status did not differ between IG-R and CG.

Conclusion: Regular fish consumption during the period of complementary feeding leads to an improved EPA- and DHA-status in the second six months of life. The usage of rapeseed oil in amounts common in commercial vegetable-potato-meat meals enhances the endogenic EPA synthesis, but is not sufficient to improve the DHA status.

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Disclosure of Interest: None Declared
RELATIONSHIP BETWEEN CHEEK CELL FATTY ACIDS COMPOSITION AND BEHAVIOUR DEVELOPMENT IN CHILDREN

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Objectives and Study: Omega-3 fats have been replaced in many modern diets by saturated and artificial fats and to some extent by omega-6 fats. The latter are also essential to health, but an appropriate balance is required, and relative deficiencies of omega-3 appear to underlie a wide range of physical and mental health conditions that pose increasing problems in developed countries. So, there seems to be a relationship between the state of fatty acid profile and behavioral problems that children exhibit.

Methods: In a total of 132 Spanish and German children participants in the NUHEAL study the Child Behavioural Check List (CBCL) Test was implemented; moreover, cheek cells were sampled at 8 years to obtain the fatty acid (FA) profile. FA in cheek cells were measured according Klingler et al. (2011). A non-parametric test (U Mann-Whitney Test) was performed using SPSS 20.0. The FA included in the analyses were γ-linolenic acid (GLA), α-linolenic acid (ALA), Linoleic acid (LA), Arachidonic acid (AA), Eicosapentaenoic acid (EPA), Docosapentaenoic acid (DPA) and Docosahexaenoic acid (DHA).

Results: There were a relationship between ALA and the presence of externalizing problems; ALA and LA concentrations in check cells were correlated to Attention problems; furthermore, DHA, EPA, and DPA showed both correlations with Plays and Sporting Competences.

Conclusion: Association between FA levels in cheek cells and behavior problems were demonstrated in children aged 8. These results reflect the importance of diet during school age on behavior development and suggest a potential bad impact during this stage of development and so long-lasting effects for later ages of life.

**This work was supported by the NUTRIMENTHE EU Project, Grant agreement nº: 212652

Disclosure of Interest: None Declared
**Nutrition**

**Nutrition and Metabolism**

PO-N-0485

**INCREASED CARDIOVASCULAR RISK FACTORS IN CHILDREN BORN THIN BUT WITH APPROPRIATE BIRTHWEIGHT: A SECONDARY ANALYSIS OF THE EU CHILDHOOD OBESITY PROJECT TRIAL**

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**Objectives and Study:** We assessed the relation between thinness at birth and subsequent cardiovascular risk factors at 6 years of life in children who were born at term with appropriate weight for gestational age.

**Methods:** This is a secondary analysis of data from the EU Childhood Obesity Project (CHOP) Trial (clinicaltrials.gov NCT00338689). Ponderal index (PI) at birth was calculated from data obtained by hospital staff at delivery. Children were classified as “thin” (PI<25th percentile) and “not thin” (PI>25th percentile). At 5.5 yrs, serum triglycerides, total, LDL and HDL cholesterol, and at 6 yrs, weight, height and systolic (SBP) and diastolic (DBP) blood pressure [mmHg] were measured, and body mass index z-score (BMI z-score) was calculated. Hypertension was defined as SBP or DBP ≥90th percentile for height (US Dept. of Health 2005).

**Results:** Anthropometry and blood pressure were measured in 544 children at age 6 yrs. Children born thinner remained significantly thinner at 6 yrs (BMI z-score, Table 1). Children born thin had significantly higher triglyceride concentrations, SBP and DBP than those born not thin (Table 1). There were no differences in serum cholesterol levels. The Odds Ratio for hypertension at 6 yrs was 1.91 (95%CI: 1.13, 3.24) among infants born thin, compared to those born not thin.

Multivariate linear regression models indicated that being thin at birth increased SBP at 6 yrs by 2.4mmHg, whereby overweight or obesity at 6 yrs increased SBP by 7.5mmHg.

Table 1. Anthropometry and blood pressure at 6 yrs by size at birth mean (SD).

<table>
<thead>
<tr>
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<th>THIN AT BIRTH</th>
<th>NOT THIN AT BIRTH</th>
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<tbody>
<tr>
<td>BMI SDS (6yrs)</td>
<td>0.16 (1.16)</td>
<td>0.39 (1.17)</td>
<td>0.030</td>
</tr>
<tr>
<td>Systolic Blood Pressure [mmHg] (6yrs)</td>
<td>100.6 (10.6)</td>
<td>97.3 (11.0)</td>
<td>0.002</td>
</tr>
<tr>
<td>Diastolic Blood Pressure [mmHg] (6yrs)</td>
<td>57.9 (7.2)</td>
<td>56.4 (7.7)</td>
<td>0.037</td>
</tr>
<tr>
<td>Triglycerides [mg/dl] (5.5yrs)</td>
<td>74.3 (51.0)</td>
<td>61.9 (34.7)</td>
<td>0.019</td>
</tr>
</tbody>
</table>
**Conclusion:** Healthy children born with appropriate weight for their gestational age but with a low ponderal index have increased cardiovascular risk factors at early school age.

**ACKNOWLEDGEMENT:** This work has been financially supported by the Commission of the European Communities (FP7-289346-EARLY NUTRITION) and the European Research Council (ERC-2012-AdG – no.322605 META-GROWTH

**Disclosure of Interest:** None Declared
PRE-DIGESTION OF MILK FORMULA WITH MICROBIAL LIPASE IMPROVES OMEGA 3 AND 6 ACCRETION TO BRAIN AND RETINA AND AFFECTS BEHAVIOUR IN YOUNG EXOCRINE PANCREATIC INSUFFICIENCY (EPI) PIG MODEL

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Objectives and Study: Pancreatic insufficiency is often associated with neurological alterations, due to malnutrition and malabsorption of fat and fat-soluble vitamins. Surgical ligation of pancreatic ducts in pigs causes impaired excretion of pancreatic enzymes including lipases, and thus mimics conditions in human neonates (Goncharova et al., 2014). Our study aimed to highlight the effect of pre-digestion of dietary fat on long chain polyunsaturated fatty acids (LCPUFA) accretion in neural tissue (hippocampus and retina) and the behaviour of pigs with EPI.

Methods: EPI pigs (operated at age of 6 weeks) were fed for 6 weeks with NAN formula (Nestle, Sweden) enriched with LCPUFA: 1% docosahexaenoic acid (DHA, omega-3) and 2% arachidonic acid (AA, omega-6) from fish oil. Three groups of EPI pigs were studied: control EPI group, fed with enriched formula - EF (EPI, n=6), treatment EPI group fed with EF, pre-hydrolyzed with microbial lipase (ML), (EPI+ML, n=7). Additional control group of non-operated, healthy pigs of the same age were fed with EF (Control, n=6). The effect of consumed pre-digested fat was monitored by changes in the accretion of AA and DHA in neural tissue expressed as changes of their levels in hippocampus and retina. Pig behaviour was monitored using a MSH-Video program and daily activity of animals was estimated.

Results: Six weeks of feeding with EF formula pre-hydrolyzed with ML, compared to the group of EPI pigs fed non-hydrolyzed formula resulted in significant improved absorption of LCPUFA in neural tissue (accretion of both AA and DHA was improved by 10%) and reduced the stereotipic activity of EPI pigs from initial 30% activity to 16% of the observation time, compared to the control pigs who were active for 20% of the time. Both biochemical and behavioural parameters of EPI+ML animals didn’t differ significantly from those in healthy control pigs.

Conclusion: We concluded that dietary fat pre-digestion with microbial lipase normalizes behaviour of experimental animals and increases neural tissue accretion of LCPUFA that are essential for normal growth and development of newborn and have important visual, cognitive, and cardiovascular health benefits throughout a person’s life.

Disclosure of Interest: None Declared
THE IMPACT OF MATERNAL IRON STATUS, OVERWEIGHT AND OBESITY ON INFANT NEURODEVELOPMENT

Staffan K. Berglund 1,* Francisco Jose Torres-Espínola 1 Luz García-Valdés 1 Maria-Teresa Segura 1 Cristina Martínez-Zaldivar 1 Jesus Florido 2 Cristina Campoy 1 3 The PREOBE Group 1 1 EURISTIKOS Excellence Centre for Paediatric Research, University of Granada, 2 Department of Obstetrics and Gynaecology, School of Medicine, University of Granada, 3 Department of Paediatrics, University of Granada, Granada, Spain

Objectives and Study: Pre-pregnancy overweight and obesity are negatively associated with neurodevelopment in the offspring. However, the mechanisms are unclear and a causality is yet not determined. The conditions are also known risk factors for maternal iron deficiency (ID) which also may contribute to impaired neurodevelopment in the child. In this study, we explored how maternal ID during pregnancy and pre-gestational overweight and obesity, affect neurodevelopment in the offspring.

Methods: The PREOBE study is a cohort study of 331 pregnant women from Granada (Spain) and their offspring. The mothers were actively included during pregnancy into four different groups based on their pre-gestational body mass index (PG-BMI) and their gestational diabetes status; normal weight controls (n=132), overweight (n=56), obese (n=64), and gestational diabetic (n=79). Ferritin, Transferrin saturation, and Mean Cell Volume were analysed at 34 weeks of gestation and at delivery and ID was defined when all of these indicators were below their cut-off. At 18 months we assessed the offspring with the Bayley III scales of neurodevelopment (n=197) and used regression analyses to explore possible associations of maternal ID and overweight or obesity (PG-BMI ≥25 kg/m²) with neurodevelopment.

Results: Maternal ID at 34 weeks negatively associated with Composite Motor Scores (p=0.040) and maternal ID at delivery with Cognitive Scores (p=0.025) and with Receptive (p=0.014), Expressive (p=0.022) and Composite Language Scores (p=0.008). Maternal overweight or obesity negatively associated with Gross Motor Scores (p=0.036). Multivariable analyses showed that the effects of ID on neurodevelopment remained after controlling for maternal overweight or obesity and for gestational diabetes. Interaction analyses showed that the effect on Language Scores from ID at delivery was stronger in the normal weight group. No other interactions between the risk factors were found. Furthermore, the risk contribution from overweight or obesity on Gross Motor Score remained after controlling for presence of ID in pregnancy.

Conclusion: ID in early third trimester is associated with impaired Motor Development and ID around delivery with poorer Cognitive and Language development. However, these risk effects do not...
positively interact with presence of overweight or obesity and neither do they contribute to the small negative effect of this risk factor observed on Gross Motor Development. The results suggest that the two risk factors both negatively associate with child neurodevelopment but that they should be considered independent of each other.

Disclosure of Interest: None Declared
ESSENTIAL FATTY ACID PATTERN CORRELATES TO INSULIN-LIKE GROWTH FACTOR-I AND GROWTH DURING INFANCY.

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Objectives and Study: IGF-I regulates fetal and infant growth and is influenced by nutrition. IGF-I levels are very low in intrauterine growth retarded and in preterm infants (1) and has in animal experiments been associated with neonatal levels of essential fatty acids (2). The aim of this study was to assess early levels of essential fatty acids and IGF-1 in term infants and relate those to growth up to 3 years of age.

A longitudinal population-based cohort from West Sweden comprising 388 healthy infants was followed from birth to three years of age. Breast milk at two days and four months and serum from cord blood and at 2 days, 4, 12 and 36 months of age were collected and analyzed for fatty acids and serum also for IGF-1. Length and weight were measured. Complete series of all measures were obtained in 132 infants.

Methods: Serum phospholipid fatty acids were analyzed by capillary gas-liquid chromatography and IGF-I using the IDS-iSYS-technique. Significance was set at p<0.01.

Results: IGF-I showed a positive correlation to linoleic acid (LA) (r=0.61, p<0.001) and a negative correlation to arachidonic acid (AA) (r=-0.57, p<0.001) in the neonates. Similarly, AA correlated negatively to birth length (r=-0.26, p<0.01) and birth weight (r=-0.33, p<0.001), whereas LA had no correlation to birth size. IGF-1 in cord blood correlated mainly to birth weight (r=0.41 r<0.001) and to some extent to birth length (r=0.17 p=0.001). Breastfed infants had at four month of age a lower omega-6/omega-3 ratio than formula fed infants (5.6 vs 8.5, p<0.01) and lower IGF-1 (43µg/L vs 62µg/L, p<0.001). Weight and height at 3 years of age (r=0.25, p<0.001 and r=0.30, p<0.001) correlated to IGF-1 at the present time. There were no significant correlations between the omega-6/omega-3 ratio or omega-3 fatty acids and weight, length or IGF-1 at birth or later.

Conclusion: At birth, IGF-I levels correlated to omega-6 fatty acid concentrations and AA was negatively associated with birth weight and length. Both at birth and during infancy, IGF-I levels were mainly positively related to weight and to less degree to length. During infancy, formula fed were found to have higher IGF-I levels and lower AA level.


Disclosure of Interest: None Declared
SEVEN NOVEL DELETERIOUS LEPR MUTATIONS FOUND IN EARLY-ONSET OBESITY: A DELON6-8 SHARED BY SUBJECTS FROM REUNION ISLAND, FRANCE SUGGESTS A FOUNDER EFFECT

Hélène Huvenne 1•Johanne Le Beyec 2•Dominique Pépin 2•Rohia Alili 3•Patricia Pigeon-Kherchiche 4•Erwan Jeannic 5•Marie-Laure Frélut 6•Jean-Marc Lacorte 8•Marc Nicolino 7•Amélie Viard 8•Martine Laville 9•Séverine Ledoux 10•Patrick Tounian 11•Christine Poitou 3•Béatrice Dubern 11•Karine Clément 3

1•Hôpital Saint Vincent, Lille, 2•Nutrigénétique, 3•ICAN Institute, Paris, France, 4•Félix-Guyon Hospital, 5•ASFA, St Denis, Réunion, 6•Bicêtre Hospital, Kremlin-Bicêtre, 7•Mother and Child Hospital, Lyon, 8•Robert Debré Hospital, Reims, 9•Lyon-Sud Hospital, Lyon, 10•Louis Mourier Hospital, Colombes, 11•Armand-Trousseau Hospital, Paris, France

Objectives and Study: Infrequent mutations have been reported in the leptin receptor gene (LEPR) in humans with morbid obesity and endocrine disorders. However LEPR mutations are rarely examined in large populations from different ethnicities in a given country. We estimated the prevalence of LEPR mutations in French patients with severe obesity and evaluated mutated patients phenotype.

Methods: We sequenced the LEPR gene in 535 French morbidly obese participants. We conducted clinical investigations to determine whether individuals with a novel shared mutation display particular characteristics relative to obesity history, body composition, hormonal functions and outcome of bariatric surgery.

Results: We identified 12 patients with a novel LEPR mutation (p.C604G, p.L786P, p.H800_N831del, p.Y422H, p.T711NfsX18, p.535-1G>A, p.P166CfsX7). Six unrelated subjects were carriers of the p.P166CfsX7 mutation leading to deletion overlapping exons 6 to 8. All subjects originated from Reunion Island (France). Their clinical features (severe early-onset obesity, food impulsivity and hypogonadotropic hypogonadism) did not differ from other new LEPR mutation carriers. Results concerning weight loss surgery were inconsistent in homozygous LEPR mutation carriers. Heterozygous LEPR mutation carriers exhibited variable severity of obesity and no endocrine abnormality.

Conclusion: Among 7 newly discovered LEPR mutations in this French obese population, we identified a LEPR frameshift mutation shared by six subjects from Reunion Island. This observation suggests a founder effect in this Indian Ocean Island with high prevalence of obesity and supports a recommendation for systematic screening for this mutation in morbidly obese subjects in this population.

Disclosure of Interest: None Declared
**Nutrition**

**Nutrition and Metabolism**

PO-N-0490

**SALT SENSITIVITY OF BLOOD PRESSURE AT AGE 7-8 YEARS IN PRETERM BORN CHILDREN**

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1Department of Paediatrics, VU University Medical Center, Amsterdam, Netherlands

**Objectives and Study:** Preterm birth is associated with hypertension in later life. The mechanisms underlying this relation remain to be clarified. In adults, salt sensitivity (SS) has been recognized as a cause of hypertension and has been related to birth weight and obesity. In children, research on these relationships is scarce.

We aimed to assess the effects of birth characteristics and anthropometric measures on SS in 7-8-year old children born <32 weeks of gestation and/or with a birth weight <1500 g. Children for the current study were recruited from a cohort (n=152) that participated in a nutritional randomized controlled trial during the first 6 months of life.

**Methods:** Of the original cohort, 79 children (40 males) aged 7.9 [7.6-8.3] years, were enrolled. They were born at a gestational age of 30.71 [29.28-31.57] weeks with a birth weight of 1314±304 g. Anthropometry and dual-energy X-ray absorptiometry (DEXA) were performed. Before and after a 7-day high-salt diet, blood pressure (BP) was measured, using an automatic device (Dynamap®). Mean arterial blood pressure (MAP) was calculated. During the high-salt diet, children used salt supplements (0.12 mg/kg/day) in addition to their regular diet. Salt sensitivity was defined as delta MAP of ≥5%.

**Results:** Sixty-three subjects completed both study days and were included in the salt sensitivity analyses. The prevalence of SS was 15.9%. Salt sensitive subjects had lower BMI, fat mass and baseline systolic BP (sBP) and diastolic BP (dBP) compared with the salt resistant subjects. Birth characteristics and height at age 0, 3, 6, 12 and 24 months and 7-8 years were similar in both groups.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Total population</th>
<th>SS n=10</th>
<th>SR n=53</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>FM term age, kg#</td>
<td>0.3 [0.15-0.44]</td>
<td>0.15 [0.09-0.27]</td>
<td>0.31 [0.15-0.45]</td>
<td>0.036</td>
</tr>
<tr>
<td>FM 6 months, kg#</td>
<td>1.81 [1.35-2.24]</td>
<td>1.10 [0.85-1.55]</td>
<td>1.96 [1.62-2.36]</td>
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**Age 7-8 years**

<table>
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<tr>
<th>Variable</th>
<th>Total population</th>
<th>SS n=10</th>
<th>SR n=53</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trunk fat, kg#</td>
<td>2.16 [1.75-2.85]</td>
<td>1.73 [1.26-2.06]</td>
<td>2.24 [1.81-2.97]</td>
<td>0.011</td>
</tr>
<tr>
<td>BMI, kg/m²</td>
<td>15.27±2.06</td>
<td>13.78±1.74</td>
<td>15.5±1.82</td>
<td>0.008</td>
</tr>
<tr>
<td>Height, cm</td>
<td>129.51±5.57</td>
<td>128.28±5.94</td>
<td>129.54±5.78</td>
<td>0.531</td>
</tr>
</tbody>
</table>
Table 1. Characteristics of salt sensitive (SS) and salt resistant (SR) subjects.
*Data were compared with independent samples t-test or Mann-Whitney U-test as appropriate.
#Parameters measured with DEXA.

Data expressed as mean±SD or median [IQR]. FM = fat mass. BMI = body mass index.

**Conclusion:** Salt sensitive subjects have lower fat mass from infancy onwards and lower baseline BP at age 7-8 years. We did not find the relation between obesity and salt sensitivity as usually found in adults. However, this may only become apparent after future fat accretion. Therefore, long term follow up studies on body composition in preterm born children are required.

**Disclosure of Interest:** None Declared
**Objectives and Study:** Probiotics have been proposed for the treatment of dyslipidemia. We aimed to evaluate efficacy, tolerability and safety of a new symbiotic formulation containing a combination of the probiotic *Lactobacillus paracasei* B21060 and prebiotics (arabinogalactan, xiloooligosaccharides) in the treatment of children affected by familial hypercholesterolemia (FH).

**Methods:** Prospective, randomized, case-control study involving otherwise healthy FH subjects (aged 6–12 yrs) consecutively observed at two Tertiary Centers for Pediatric Nutrition. Two groups of six months intervention: active group, received a low saturated fats diet plus the symbiotic (2.5×109 cfu, bid); control group, received low saturated fats diet alone. The plasmatic lipid profile was assessed by peripheral blood sampling at baseline (T0) and after six months of intervention (T1). Same subjects were re-evaluated after additional 6 months of observation (T2) from the end of the therapeutic course, to see whether the effect was sustained even after treatment.

**Results:** 40 FH children were enrolled (20 in active group receiving the symbiotic: 8 male, median age 8.4 yrs, BMI 17.6; 20 in control group receiving a placebo: 8 male, median age 7.5 yrs, BMI 17.0). All subjects completed the study. At T1 a reduction of C-LDL, total cholesterol, LDL/HDL ratio was observed in both groups, but the differences were significant only in active group (median value (IQR) C-LDL: 221(55) vs 192(33), p < 0.01; total cholesterol: 280(31) vs 260(43), p < 0.05; LDL/HDL: 4.0 (1.5) vs 3.5 (1.3), p < 0.05). At T2 patients in active group showed stable total cholesterol and C-LDL serum level. The symbiotic preparation was well accepted and tolerated by the patients. Adherence to symbiotic doses was >90%, no side effects were observed.

**Conclusion:** The symbiotic containing *Lactobacillus paracasei* B21060 is able to significantly reduce lipid biomarkers in children with FH. The treatment was well accepted and tolerated by patients. Our results further support the efficacy of this therapeutic strategy against pediatric FH. Further studies are advocated to better define the mechanism of action and the potential of a long term use of this strategy.

**Disclosure of Interest:** L. Leone Conflict with: Bracco, Milan, Italy, R. Nocerino Conflict with: Bracco, Milan, Italy, M. Malamisura Conflict with: Bracco, Milan, Italy, A. De Matteo Conflict with: Bracco, Milan, Italy, V. Bruno Conflict with: Bracco, Milan, Italy, B. Malamisura Conflict with: Bracco, Milan, Italy, R. Berni Canani Conflict with: Bracco, Milan, Italy
SENSORY ACCEPTABILITY OF INFANT CEREALS WITH WHOLEGRAIN IN SPAIN

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Objectives and Study: In the past cereals were consumed as whole grain (WG) but after the industrial revolution these were converted into a more acceptable and longer shelf life refined grains. This process implied the removal of some health promoting components (fiber, minerals and phytonutrients). In Spain, infant cereals (IC) are the first food recommended to be introduced during the complementary food period and 99 % of the IC market is refined. Evidence suggests that food preferences are developed early and may persist in later childhood and adulthood. As commercial infant foods play an important role in shaping babies’ diets, it is a responsibility of baby food companies’ R+D departments to design and develop products that improve the diets of young children from the nutritional and sensorial point of view. Our objective was to test whether an IC product with 30 % of WG is equally accepted by mothers and children as the same cereal without WG.

Methods: A total of 82 mother-infant pairs were recruited through advertisement in kindergartens. Healthy infants between 4 and 24 months old were included, all of them had started the introduction of cereals in their diets. Mothers-infants pairs participated in a 2 day experimental study. On day 1 infants were fed infant cereal with whole grain (ICW) and day 2 non-whole grain (ICNW). Mothers fed the infant at home until the infant refused the spoon three consecutive times or finished the portion. Acceptance was rated by mother and child on a hedonic scales (4-points for children, 7 points for adults). Other attributes like color, smell, and taste were evaluated by the mother. Statistical analysis was carried out using SPSS v.18.0.

Results: The timing of introduction of IC was <4 months: 3%, 4-6 months: 87.5% >7 months: 10%. Acceptability for ICW and ICNW in both infants and mothers were very similar (Infants: 3.73 ± 0.44 for ICW and 3.68 ± 0.51 for ICNW p=0.912; Mothers 6.28 ± 0.67 for ICW and 6.25 ± 0.66 for ICNW, p=0.53). No significant differences among the remaining parameters were observed. The age of introduction of cereals did not affect the infants’ acceptance of both cereals (all p> 0.3). Approximately 80% of the infants ate the full cereal portions offered.

Conclusion: IC with 30% WG were well accepted by both infants and mothers. There is an opportunity to introduce WG cereals in infants who are used to consume refine IC thereby accelerating the exposure of WG in early life. More research is needed with regard to both acceptability of higher percentages of WG in the product and possible imprinting effects.

**Objectives and Study:** To investigate the prevalence of vitamin D deficiency among obese children and adolescents, and the correlations between serum 25-hydroxyvitamin D level and body composition, metabolic risk factors, respectively, with the aim of providing evidence to improve the prevention and treatment of children and adolescents obesity.

**Methods:** We used crossed-sectional baseline data from the obese children and adolescents who accepted the follow-up intervention in our Department. On their first visit, all subjects underwent anthropometric measurements, abdominal ultrasonography detection and blood indicator examination. We obtained height, weight, body fat percentage (Fat%), BMI, visceral fat area (VFA), periumbilical abdominal Fat thickness (PAFT), fasting blood glucose (FBG) and insulin (FINS), 2 hour postprandial blood glucose (PBG) and insulin (PINS), triglyceride (TG), total cholesterol (TC), 25-OHD, and PTH. Student's t test, Pearson's correlation analysis and partial correlation analysis were performed to research the relationships between the serum 25-OHD level and body composition, and metabolic indicators.

**Results:** This study enrolled 87 children and 17 adolescents, aged 4~18 (9.69±3.66) years old. Respectively, with serum 25-OHD level of 30, 20, and 10ng/ml as the cut-off points to define vitamin D sufficient, insufficient, deficiency and severe deficiency, the incidence of which in sequence was 2.88% (3/104), 25% (26/104), 65.38% (68/104), 6.73% (7/104). 25-OHD<20ng/ml was classified as VD deficiency (VDD) group (n=75), and 25-OHD≥20ng/ml as non-deficiency (VDND) group (n=29). There was no significant difference between two groups in age and sex. Compared with VDND group, the serum PTH, FINS level and HOMA-IR of VDD group were significantly higher (p<0.05). Fat%, PBG, PINS, PAFT, VFA, TC and TG of VDD group were higher than those of VDND group, but the differences were not significant (p>0.05). Moreover, serum 25-OHD level was negatively associated with age, BMI, Fat%, waist circumference (WC), hip circumference (HC), VFA, PAFT and serum PTH (p<0.05). However, the correlation between serum 25-OHD level and FINS, PBG, and HOMA-IR was not significant (p>0.05). After adjusting for age and sex, serum 25-OHD level still had significantly negative correlations with BMI, Fat%, VFA, WC, and HC.

**Conclusion:** The incidences of vitamin D deficiency and insufficiency in obese children and adolescents were very high. Serum PTH, FINS level and HOMA-IR of vitamin D deficiency group were significantly higher than those of vitamin D non-deficiency group. Serum 25 OHD level reduced significantly with the increase of age, and was negatively associated with body composition and anthropometric parameters, such as BMI, Fat%, VFA, WC, HC. Nevertheless, the related reasons and mechanisms need further exploration.
Disclosure of Interest: None Declared
Nutrition

Nutrition and Metabolism

PO-N-0494

ASSESSMENT OF THE IMPACT OF FEEDING METHOD (BOLUS VS. CONTINUOUS INFUSION) ON CARBOHYDRATE METABOLISM IN ENTERALLY FED CHILDREN WITH NEUROLOGICAL IMPAIRMENT

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Objectives and Study: Continuous enteral nutrition (EN) is often only possible way to obtain adequate body mass and length in children with neurological impairment not tolerating EN provided in boluses. That non-physiological manner of feeding may theoretically induce carbohydrate metabolism disorders and potentially entail risk of vascular complications. Impact of feeding method (bolus vs. continuous infusion) on carbohydrate metabolism in enterally fed children with neurological impairment was studied.

Methods: Study enrolled 39 patients (25 girls, 14 boys, mean age 8.58 years ±5.38) with neurological impairment (level IV and V, Gross Motor Function Classification System) who were enterally fed for at least 6 months. 25/39 of those were nourished by boluses (group Bf), 14/39 received continuous infusion lasting 18-20 hrs. (group Cf). Blood glucose level was measured as short- and HbA1C as a long-term mean glucose level.

Results: Mean HbA1C level was 5.04±0.43%. No statistically significant differences in HbA1C depending on the feeding method were found (mean HbA1C in group Bf was 5.00±0.36 vs. 5.11±0.53 % in group Cf, p=0.45). Mean glucose level in both the groups was 83.69±8.5mg/dl (Bf:81.56±4.25mg/dl; Cf: 87.48±6.5mg/dl; p>0.05). Hypoglycemia was statistically significant more common in children in Bf group compared to Cf group (6/25 vs. 1/14; p=0.046). Mean diet energy value for children fed by boluses was lower compared to that for children fed by continuous infusion (62.3 kcal/kg in group Bf vs. 73.36 kcal/kg in group Cf).

Conclusion: 1. Continuous enteral feeding did not affect short- and long-term hyperglycemia risk in children with neurological impairment
2. Bolus feeding impacted on hypoglycemia risk the above group of patients

References:

Disclosure of Interest: None Declared
Objectives and Study: Diet and physical activity are recognized as important factors to prevent obesity. Dairy products (DPs) consumption has been shown to have beneficial effects on body weight. This study aimed to investigate the relationship of body mass index (BMI) with DPs (milk, cheese and yogurt) consumption and physical activity habits in school children.

Methods: This cross-sectional study included 7116 randomly selected 6-18 years old school children. The height and weight were determined using standard anthropometric methods and BMI was calculated for each child. Dietary intake of DPs and physical activity habits were assessed via a self-report questionnaire. Children were divided into four groups by the amount of dairy products. Also, children were divided into four groups according to their physical activity. Comparisons were performed by BMI percentile values with DPs consumption and physical activity. Multiple linear regression analysis was used to estimate the association between milk, yogurt, cheese intake and BMI.

Results: The study included a total of 7116 children; 3445 (48.4%) females and with a mean age of 11.7±2.7 years (range, 5.8-18.9 years). Most of children (84%) consumed DPs, all together. There were 64 (0.9%) children that do not consume any DPs. There were no statistically significant differences between the genders and age. Children who never consumed milk, yogurt and cheese were 9.4%, 8.7% and 4.9%, respectively. Children who consumed milk, yogurt and cheese everyday were 40.1%, 40.3% and 55%, respectively. The children with high amount of milk intake had low BMI percentile than others. The highest milk consumption was found in underweight and lowest milk consumption was found in obese children (P> 0.05).

There was not a significant relationship between the BMI and yogurt or cheese consumption. After adjusting for confounders milk intake was more likely to have lower BMI, compared with yogurt and cheese intake ($\beta = 0.325$, $P = 0.000$; $\beta = 0.164$, $P = 0.006$ and $\beta = 0.074$, $P = 0.2$, respectively).

Interestingly, children with more physical activity had more BMI values than others (55.18±31.02% vs. 52.60±32.03%, $P = 0.001$). Boys were more active than girls (57.9% vs. 41 %, $P < 0.001$).

Conclusion: High amount of milk consumption seems to have a protective effect on overweigh/obesity in schoolchildren. There is no any relationship between BMI and cheese, yogurt consumption, and physical activity.

Disclosure of Interest: None Declared
ADIPONECTIN, INSULIN AND INSULIN-LIKE GROWTH FACTOR II (IGF-II) IN HUMAN MILK

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Objectives and Study: Human milk is considered the optimal nutrition for infants. The composition of human milk and its variation may be of importance for health outcomes in recipient infants. We studied macronutrient and hormone contents in European human milk samples.

Methods: We analysed the composition of 597 human milk samples collected at 1 to 4 months postpartum by women in 5 European countries (the Netherlands, Italy, Spain, Hungary, and Germany) who participated in the PreventCD study (www.preventcd.com).

Results: Milk contents of protein (1.04±0.27g/dl, M±SD), fat (2.3±1.4g/dl) and carbohydrate (6.6±0.4g/dl) were similar to previously reported data. Adiponectin concentration was 18.5±6.4ng/ml with a wide range from 3.1 to 55.7 ng/ml. Concentrations decreased from month 1 (19.8±7.1ng/ml) to month 4 (17.3±5.6ng/ml, p<0.001). The peptide hormone was positively correlated to protein content (r=0.33, p<0.01). Milk insulin content (13.3±10.1mU/l) was stable over the lactation period studied but showed diurnal variation, with higher milk insulin levels in evening feedings (17.1±17.5mU/l) than in morning feedings (10.0±6.5mU/l, p<0.001). Milk insulin concentration and variation were higher in obese women (39.0±32.2mU/l) than in normal weighted women (12.7±10.2mU/l, p<0.001). IGF-II, the predominant insulin-like growth factor in human milk, was found at 15.5±5.6 ng/ml and decreased over the course of lactation (month 1: 17.8±5.5ng/ml, month 4: 12.9±4.2ng/ml, p<0.001). A positive correlation between IGF-II levels and protein content was observed (r=0.54, p<0.01). Maternal pre-pregnancy weight showed a negative correlation with breast milk IGF-II levels (r=-0.32, p<0.001).

Conclusion: Milk composition changes during the lactation period and within the day but also within individual women. Protein, adiponectin and IGF-II, but not insulin, decrease with longer lactation, which suggests different mechanisms of secretion into milk. Milk insulin shows a similar diurnal variation as plasma insulin, thus we assume insulin transfer from blood into milk. We consider adiponectin and IGF-II synthesis in the mammary gland likely. Pre-pregnancy weight influences milk insulin and IGF-II levels. The potential impact on child growth and development deserves further investigation.
PLASMA AMINO ACIDS AS BIOMARKERS OF INTESTINAL ABSORPTIVE FUNCTION IN CHILDREN WITH SHORT BOWEL SYNDROME.

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Objectives and Study: In patients with short bowel syndrome (SBS) the main indicator of weaning off parenteral nutrition (PN) is the residual small bowel. Citrulline is a nonprotein amino acid produced mainly by enterocytes of the small bowel and is a precursor to arginine and ornithine. Plasma citrulline and other amino acids concentration may thus reflect the remnant small bowel mass and its function. The objective of this study was to analyze the value of plasma amino acids assays for improving assessment of the small bowel adaptation in children with SBS.

Methods: 47 patients (23 females and 24 males) with SBS aged 0,5 - 18,1 years (median: 7,4 years) were selected for the study. The median duration of PN was 6 years 7 months. 8 patients were already weaned off PN. 23 patients had extended small intestine resection (remnant small intestine <40 cm). Plasma amino acids were determined by ion-exchange chromatography followed by post-column ninhydrin derivatization. The student’s t-test and Pearson’s correlation test was used to analyze the results.

Results: Mean citrulline concentration in the research sample was 16,68 µmol/l (2,6-42,2), mean arginine concentration was 44,48 µmol/l (14-78,4), and mean ornithine concentration was 41,39 µmol/l (21,1-65,3). The length of remnant intestine (cm) had influence on arginine and ornithine concentration in plasma (p=0,004, r=0,36; p=0,016, r=0,42). In group of 23 patients with remnant small intestine <40 cm, citrulline and arginine concentration were lower than in group of 24 patients with remnant small intestine ≥ 40 cm (p=0,09; p=0,02). The mean concentration of citrulline and arginine in patients with extended small intestine resection was respectively 13,36 µmol/l; 38,4 µmol/l and in patients with remnant small intestine ≥ 40 cm 19,85 µmol/l; 50,05 µmol/l respectively. Citrulline, arginine, ornithine concentration was also negatively correlated with number of days of PN (p=0,000; p=0,040; p=0,001). In 8 patients weaned off PN, citrulline and ornithine concentration was significantly higher than in patients dependent on PN (p=0,001; p=0,002). The mean concentration of citrulline and ornithine in patients dependent on PN was respectively 14,89 µmol/l; 38,73 µmol/l.

Conclusion: Citrulline, arginine and ornithine may have predictive value in prognosis for patients with SBS particularly with unknown intestine status. Concentration of citrulline ≥15 µmol/l and ornithine ≥39 µmol/l may determine good prognostics for weaning off PN. Amino acids concentration may be biomarkers of intestine absorptive function, helpful in decisions about weaning off PN but it should not be the only considered parameter.
Disclosure of Interest: None Declared
**Nutrition**

**Nutrition and Metabolism**

PO-N-0498

**SLEEP AND ULTRA-PROCESSED INTAKE IN EARLY CHILDHOOD: A LONGITUDINAL ANALYSES**

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**Objectives and Study:** To assess whether shorter sleep at preschool age predicted the higher intake of energy and ultra-processed food for children of preschool and school age.

**Methods:** Cohort study conducted with 345 Brazilian children of low socioeconomic status aged 3-4 years and 7-8 years. Dietary data were collected through two 24-hour recalls and children’s ultra-processed foods intake was assessed. Mothers reported the number of hours that the children had slept the past 24h before the interview.

**Results:** Total energy intake at preschool and school-age was significantly higher in shorter-sleeping children, with children who slept <10h/d consuming an average of 117 kcal/d (95% CI: 50–184) more than those sleeping for >10 h/d at 3-4 years; and an average difference of 62 kcal/d (95% CI: 7–117) at 7-8 year. Regarding changes in diet from pre-school to school-age, the total energy increased by 54 kcal/d (95% CI: 19–91) and 19 kcal/d (95% CI: -66–104) in children who slept ≥10 and <10 h/d at preschool age, respectively. However, the intake of energy from ultra-processed foods increased only in those children who slept <10 h/d (mean difference, 95% CI: 17.0, 14.6–19.4). The percentage of daily energy provided by ultra-processed foods remained constant in children who slept ≥10 h/d (Table 1)

**Table 1**

<table>
<thead>
<tr>
<th>Dietary variables</th>
<th>&gt;10h</th>
<th>10h</th>
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<tbody>
<tr>
<td><strong>3-4y</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy</td>
<td>1492±253</td>
<td>1610±327*</td>
</tr>
<tr>
<td>%E Ultra-processed foods a</td>
<td>45.1±6.1</td>
<td>31.4±4.9*</td>
</tr>
<tr>
<td><strong>7-8 y</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Energy</td>
<td>1548±195</td>
<td>1611±513*</td>
</tr>
<tr>
<td>%E Ultra-processed foods a</td>
<td>47.7±9.2</td>
<td>48.5±8.8</td>
</tr>
</tbody>
</table>
**Conclusion:** In a sample of preschool and school children, early shorter sleep duration was associated with higher energy intake and increased consumption of ultra-processed foods, regardless the energy. These findings add new evidence to the limited literature available with children on the role that shorter sleep duration may play in relation to intake.

**Disclosure of Interest:** None Declared
Objectives and Study: Severe acute malnutrition (SAM) is one of the leading nutrition-related causes of death in children under five years. The clinical features of SAM are well documented but a comprehensive understanding of the physiology of SAM is lacking. Current treatments and therapeutic foods are therefore designed mainly based on empirical observations. Animal models of SAM may help to clarify metabolic defects and targets for intervention and therapy. We hypothesized that SAM induces marked plasma metabolite changes in malnourished piglets, used as a model for children with SAM.

Methods: Four week-old weaned female pigs were fed a nutrient-deficient maize diet (MAIZE, n=12) and or nutritionally optimized reference diet (REF, n = 12) for seven weeks. Blood plasma was collected weekly from all pigs and applied to ultra-performance liquid chromatography-time-of flight mass spectrometry (UPLC-MS) for a non-targeted profiling of metabolites with abundance differentiation. Metabolites with differentiated abundance between REF and MAIZE pigs over the time of feeding were identified with mass spectral information and verified with commercial chemical standards.

Results: The MAIZE pigs showed markedly reduced body weight gain and lean mass as well as decreased albumin and haemoglobin level relative to REF pigs. Six essential and six non-essential amino acids were differentially regulated. All were lowered in the MAIZE pigs, except histidine, although the differences between MAIZE and REF pigs were time-dependent. Histidine, proline, arginine and tryptophan showed differences from week 2, methionine, glutamic acid and phenylalanine from week 4, and asparagine, ornithine and glutamine from week 5. Betaine, N,N-dimethylglycine and sarcosine, intermediates of choline metabolism, showed higher abundance in the MAIZE pigs. Metabolites related to the gut microbiome, including hippurate, methylhippurate, a conjugated bile acid and p-cresol glucuronide, also differed between groups, possibly indicating a perturbed intestinal microbiome in the MAIZE pigs.

Conclusion: Our findings suggest that young undernourished pigs, and maybe also children, show an altered metabolism as reflected in altered plasma amino acid and choline metabolite levels. This, together with a changed microbial nutrient metabolism in the gut, may require special attention in designing therapeutic foods for refeeding the SAM children.

Disclosure of Interest: None Declared
**Objectives and Study:** Insulin resistance is high among South Asian populations starting from a young age. Poor intrauterine growth combined with rapid post natal growth, predisposes to develop insulin resistance later in life. The aim of this study is to identify insulin resistance among 8-16 year old overweight/obese school children from Gampaha district of Sri Lanka.

**Methods:** From a preliminary survey, obese (BMI for age above +2SD WHO 2007) and overweight (BMI between +1 to +2) children were recruited. After a 12 hour overnight fast, blood was drawn for fasting blood glucose (FBS) and lipid profile. OGTT was done with anhydrous glucose (1.75g/kg, max 75g) and random blood sugar (RBS) levels measured 2 hours later. Height, weight, waist circumference (WC) and blood pressure was measured. Fat mass (FM) was measured using BIA (InBody 230, South Korea). Diabetes Mellitus (DM) diagnosed by either FBS > 125mg/dl and/or 2h RBS > 200mg/dl. Impaired fasting glucose (IFG) 100-125mg/dl and impaired glucose tolerance (IGT) 140-200mg/dl.

**Results:** Two hundred and sixty four children were studied (boys 137). 46 were overweight and 218 were obese. There were 6 (2%) children with DM (Diagnosis by; FBS-1, 2h OGTT-4 and FBS+ OGTT-1). 17 had IFG, 27 had IGT and 8 had both IFG and IGT (16.3% prediabetic state).

The mean (SD) fasting insulin was 14.0(12.6) mU/L and 14.4(16.8) mU/L (p>0.05) in girls and boys respectively. 2 hour post glucose insulin (2hPGI) in girls and boys were 87.8(62.1) mU/L and 75.6(66.7) mU/L (p>0.05) respectively.

The mean HOMA-IR was 3.03(2.85) and 3.23(4.13) (p>0.05) for girls and boys respectively and 3.14(3.3) and 3.10(3.6) (p>0.05) in overweight and obese children respectively. 2hPGI was 59.7(41.3) mU/L and 86.1(67.7) mU/L (p<0.05) for overweight and obese children.

2hPGI and HOMA-IR increased with the increase in the number of abnormal metabolic parameters. HOMA-IR showed statistically significant correlation with BMI, WC, FM and WC to Height ratio (WHtR). 2hPGI levels showed stronger correlation with BMI, WC, WHtR, FM, %FM.

**Conclusion:** Significant number of children in this group had abnormal glucose homeostasis. 2hPGI level appears to be a better marker in identifying metabolic derangements early than fasting insulin/HOMA-IR. This could be due to the objective response that occurs to a measured glucose load.
and could be the first step in developing IR. It would be useful to develop a screening tool using 2hPGI levels.

**Disclosure of Interest:** None Declared
A PREBIOTIC BLEND OF POLYDEXTROSE AND GALACTOOLIGOSACCHARIDES WITH BIOACTIVE WHEY PROTEIN FRACTIONS AMELIORATES STRESS-EVOKED DISRUPTIONS IN SLEEP STATES IN RATS.

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Objectives and Study: Stress exposure can produce disruptions in the sleep cycle that may contribute to altered behavioral phenotypes. Prebiotics can selectively promote the expansion of microbial species i.e., Bifidobacterium spp. and Lactobacillus spp. in the mammalian gut that may promote stress robustness. Our previous studies showed that a prebiotic blend of polydextrose (PDX) and galactooligosaccharides (GOS) increase Bifidobacterium spp. and Lactobacillus spp. in feces. The aim of this study was to determine whether an experimental diet would modulate the sleep cycle and protect sleep architecture following stress.

Methods: Male F344 rats, postnatal day 24 (P24), were placed on either an experimental diet containing a prebiotic blend of PDX and GOS with bioactive whey protein fractions (TEST) or a control diet. Fecal samples were collected and telemetry devices were implanted to examine differences in the sleep cycle across development. Rats were exposed to an acute stressor on P87 to examine the effects of the TEST diet on stress-induced disruptions of the sleep cycle.

Results: Compared to control fed rats, TEST fed rats had equal body weight gain and greater non-rapid eye movement (NREM) sleep consolidation in early adulthood (P71, P72). In addition, rats fed the TEST diet also displayed enhanced REM rebound following acute stress exposure (P87) compared to rats fed the control diet.

Conclusion: These results demonstrate that the TEST diet can increase NREM sleep consolidation and protect against REM sleep disruptions. Future research will examine if other functional outcomes, such as cognitive processes, may be associated with these changes in sleep parameters. Supported by Mead Johnson Nutrition.

A DUAL FUNCTIONING EXTENSIVELY HYDROLYSED CASEIN MODULATES CYTOKINE SECRETION BY IMMUNE CELLS AND INSULIN RESPONSES FROM BETA CELLS IN VITRO

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Objectives and Study: Type 1 Diabetes is characterized by progressive autoimmune destruction of pancreatic β-cells. Similarly to other inflammatory diseases, immune cells contribute to tissue infiltration and cell death by secreting inflammatory mediators. Although development of the disease is linked to a predisposing genetic background, early nutrition is also known to play an important role. The aim of this study assessed whether extensively hydrolyzed casein might interfere with the release of pro-inflammatory cytokines by immune cells that are involved in β-cell damage and whether it might preserve β-cell function in vitro.

Methods: Murine and human immune cells were pre-incubated with specific extensively hydrolyzed casein and fractions thereof for one hour followed by activation of the cells with LPS or CD40L, respectively. Cytokine secretion was measured after 24 hours. Initially, the murine macrophage J774.1 cell line was used, followed by verification in human primary macrophages and dendritic cells differentiated from isolated CD14+ monocytes from blood from healthy donors. Cytokine secretions were measured using multiplex cytokine assays. Furthermore, effects of the hydrolysate on insulin secretion by BRIN-BD11 β-cells were assessed in the presence/absence of inflammatory cytokines and compared with an alanine/glucose positive control.

Results: Pro-inflammatory cytokine secretion (IL-12p40, IL-1β, IL-6) from murine macrophages were decreased by the casein hydrolysate and fractions thereof. Similarly, dose-dependent inhibition of pro-inflammatory cytokine responses (IL-1β, IL-12p70, IFN-γ, TNF-α, IL-6) was confirmed using human primary dendritic cells and macrophages. Finally, specific hydrolysate fractions that exerted anti-inflammatory effects also significantly promoted insulin secretion from β-cells following exposure to IL-1β, IFN-γ or IL-23. Not all hydrolysate fractions showed these activities, highlighting the fact that functional activity can vary greatly between different hydrolysate preparations.

Conclusion: Extensively hydrolyzed casein and some specific fractions display dual functionality; they can exert anti-inflammatory effects on different cell types of the immune system and rescue insulin secretion from β-cells impaired by inflammatory activity. These mechanisms may contribute to potential preventive effects in the development of inflammatory diseases.
**Objectives and Study:** Childhood obesity has increased dramatically in the last decades both in children and adolescents as it significantly increases the risk of adult obesity and its complications. Biomarkers would be applicable as diagnostic tools in a personalized healthcare setting and may also open door to biomarker discovery, disease diagnosis and novel therapeutic avenues for pediatric obesity.

**Methods:** We used urine sample from cohort of obese children in Korea Centers For Disease Control and Prevention in 2012 (total n. 903). And we selected all the cases with obesity and a matched control group which was sampled randomly by propensity scoring. Before a proteome analysis, high-abundance protein depletion was performed. Samples were analyzed by SDS-PAGE and protein identification was performed. Their Mass to charge values were analyzed by using high-accuracy mass spectrometry proteome profiling. The relative ratio between obesity and control samples were analyzed.

**Results:** Identified 480 proteins in urine excretion that showed significant differences between obese group and control group. Among the identified proteins, 48 proteins were up-regulated more than 2 folds.

<table>
<thead>
<tr>
<th>Prot. name</th>
<th>Molecular mass(kDa)/Superfamily</th>
<th>Fold change</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumin</td>
<td>60-70 /Globular prot.</td>
<td>45.72</td>
</tr>
<tr>
<td>Ig gamma 2</td>
<td>52/Immunoglobulin</td>
<td>32.48</td>
</tr>
<tr>
<td>Complement C3</td>
<td>185/Complement</td>
<td>24.38</td>
</tr>
<tr>
<td>Antithrombin III</td>
<td>58/Serpin</td>
<td>18.92</td>
</tr>
<tr>
<td>Lactotransferrin</td>
<td>80/Transferrin</td>
<td>10.76</td>
</tr>
</tbody>
</table>

**Table . Differential expression of urinary proteins in the case group (>10 folds)**

Also we found 118 unique proteins excreted only in case group.
Conclusion: We identified significant differences in some candidate proteins in urine that may be related to pediatric obesity. Increased urine albumin, immunoglobulin, complement and serpin superfamily were observed in obese children. This is preliminary results for development of biomarkers for pediatric obesity screening. Further studies should be performed to elucidate the meaning of these molecules for the rapid and reliable screening pediatric obesity.

Disclosure of Interest: None Declared
INFLUENCE OF PRENATAL AND MATERNAL FACTORS ON NEONATAL BODY COMPOSITION

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Objectives and Study: There is increasing evidence that body composition early in life has both immediate and long-term influence on health. It is, therefore, of importance to determine factors of influence on neonatal body composition. The aim of the present study was to investigate which parental factors were of influence on fat mass percentage (FM%) in newborns, independent of birth weight and to examine the effect of growth in fetal life on the FM%. In addition, we aimed to assess whether measurement of skinfolds could be a proxy for the FM% of the newborn.

Methods: The study population comprised 194 healthy newborns, with a gestational age between 36 and 42 weeks. Within 24 hours after birth, weight, crown-to-heel length, head circumference and whole-body composition were assessed using air-displacement plethysmography (PEA POD, Infant Body Composition System, COSMED). Standard fetal biometry data were obtained from medical records. Besides these data, maternal data, i.e. preconceptional weight and weight just before delivery, height and parity were obtained from medical records.

Results: Birth weight was related to newborn FM% (p<0.001), but there was a large variation in FM% with the same weight, even after correction for gender and gestational age. Estimated fetal weight in the second and last trimester, but not in the first trimester, were associated with FM% of the newborn (p<0.01, p<0.01, p=0.86 resp.), as well as with preconceptional BMI of the mother (p<0.01). Maternal weight gain did not correlate with FM% of the newborn. The sum of the 4 skinfolds correlated with FM% (r=0.56 p<0.001).

Conclusion: Our study demonstrates that newborns show a large variation in body composition. Estimated fetal weight, gain in third trimester, and preconceptional BMI influence FM%, but gender and maternal weight gain not. Skinfolds measured do not reliably indicate FM% in the individual newborn.

Disclosure of Interest: None Declared
THE IMPACT OF DELIVERY MODE ON GUT MICROBIOTA OF EXCLUSIVELY BREAST-FED INFANTS

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Objectives and Study: The gut microbiota is essential to human health throughout life. This work aimed to assess the impact of mode of delivery and bacterial composition of human milk on the fecal microbiota of exclusively breast-fed infants.

Methods: Thirty-one mother-infant pairs were prospectively included in this study, and they were divided into vaginal delivery (VD, n=14) or cesarean section (CS, n=17) groups according to the delivery mode. All the babies were healthy term infants and exclusively breast-fed. Clinical data were recorded, including prenatal BMI, maternal age, gestational age, mode of delivery, antibiotic administration, weight gain during pregnancy, infant anthropometric measurements. Fecal samples of infants and human milk of their mothers were collected at 6 weeks of age, and we characterized the microbiota composition using high-throughput DNA sequencing.

Results: No differences were detected in maternal age, prenatal BMI, gestational age, gestational weight gain of the mothers between the two groups. Infants in both groups showed similar birth weight, body weight at 6-week of age and weight gain. The bacterial diversity and richness in both human milk and infant feces were quite similar between the groups. The profiles of human milk microbiota were generally dominated by Firmicutes (44.9±18.8%), Proteobacteria (43.7±21.0%) and Actinobacteria (9.2±5.5%) at phylum levels, while no differences were found in the bacteria composition of human milk at both phylum and family levels. The gut microbiota of infants were dominated by Firmicutes, Bacteroidetes, Proteobacteria and Actinobacteria. Compared with vaginal delivered babies, infants born by cesarean delivery had decreased richness of bactoidetes (28.0% vs. 0.3%, p=0.001).

Conclusion: These findings advance our understanding of the gut microbiota in healthy infants and the microbiota of human milk. They also provide new evidence that delivery mode had a continual impact on the microbial community in early life.

Disclosure of Interest: None Declared
PREVENTIVE EFFECTS OF A NUTRITIONAL COMPOSITION ON DIABETIC RISK FACTORS AND COMPLICATIONS IN LDLR-/-.LEIDEN MICE

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Objectives and Study: Obesity is the hallmark of the metabolic syndrome and represents a major global health problem that frequently associates with the development of chronic inflammatory diseases, including type 2 diabetes. In this study, we have investigated a combination of a protein hydrolysate, long-chain polyunsaturated fatty acids and a probiotic strain on the development of diabetic risk factors and complications in LDLr-/-.Leiden mice during a high fat diet challenge.

Methods: Sixty-seven LDLr-/-.Leiden male mice at 12 weeks of age received a high fat diet (HFD, 45 Kcal% from lard) daily for 21 weeks with or without a combination of an extensive casein hydrolysate, docosahexaenoic acid (DHA), arachidonic acid (ARA), and Lactobacillus Rhamnosus GG (LGG). Both the high fat diet and the intervention diet were isocaloric and the casein from the obesogenic HFD was replaced with casein hydrolysate in the test diets. The addition of DHA/ARA in the test diets was controlled for in the HFD control diet. Moreover, a PBS gavage control group was included to control for potential effects of the oral gavage procedure.

Results: There were clearly beneficial effects of the hydrolysate/ARA/DHA/probiotic composition as compared to the HFD control group as revealed by reduced body weight gain, lower plasma levels of insulin, cholesterol and triglycerides, lower systemic inflammation and vascular activation markers, improved white adipose tissue quality and reduced mass, improved liver function and lower microalbuminuria as marker of kidney function. In a follow up study, evaluating the individual components of the test formulation, some of the major beneficial outcomes appeared to be driven by the hydrolysate or LGG.

Conclusion: A combination of an extensive casein hydrolysate, ARA, DHA and LGG could reduce the detrimental effects of HFD on the development of obesity and its metabolic complications. In addition, the main risk factors for the metabolic syndrome such as adipose tissue inflammation and chronic inflammation were markedly reduced. The underlying mechanisms are subject of further research.

LEPTIN GENE POLYMORPHISMS AND THEIR ASSOCIATION WITH SERUM LEPTIN LEVELS IN INFANCY

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Objectives and Study: Leptin is a hormone that regulates food intake and energy metabolism. Leptin (LEP) gene is one of the most promising candidate genes for obesity. Previous studies have tested the association of different Single Nucleotide Polymorphisms (SNPs) in LEP gene with serum leptin levels and obesity, with controversial results. The aim of this study was to investigate two SNPs of LEP gene and their association with serum leptin concentrations in infants in the first six months of life. We focused the attention on LEP G2548A and LEP A19G (NG_007450), which were predicted to modify transcription-factor binding sites and leptin production.

Methods: We enrolled 30 Caucasian infants younger than 6 months, exclusively breast-fed, hospitalized in “Pediatria 1 Lattanti”-Regina Margherita Children’s Hospital, Turin. We took anthropometric measurements (weight, length, BMI) and quantified serum leptin levels by Radioimmunoassay test. Genotyping of LEP G2548A and LEP A19G was performed using PCR-RFLP. Statistical analysis was performed using χ² test and ANOVA, setting the statistical significance at p<0.05.

Results: The allele frequencies at LEP G2548A were 0.67 (allele G) and 0.33 (allele A) and at LEP A19G 0.62 (G) and 0.38 (A), they were in Hardy-Weinberg equilibrium (χ²=0.1, p=0.75; χ²=0.25, p=0.75). Analyzing leptin serum concentration according to the genotype of each SNP, we found no significant difference. As the two SNPs were closely linked, the haplotypes were also considered. After dividing the sample according to the number of haplotypes GG, we found a significantly higher leptin level in infants with two GG haplotypes (p=0.03) (Table). No significant differences were observed for the anthropometric parameters.

<table>
<thead>
<tr>
<th>Groups</th>
<th>n. subjects</th>
<th>Media (DS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>no GG haplotype ¹</td>
<td>16</td>
<td>3.63 (1.86)</td>
</tr>
<tr>
<td>one GG haplotype ²</td>
<td>10</td>
<td>3.60 (3.34)</td>
</tr>
<tr>
<td>two GG haplotypes ³</td>
<td>4</td>
<td>8.00 (5.23)</td>
</tr>
</tbody>
</table>

¹GA/GA or AG/AG or GA/AG haplotypes. ²GG/GA or GG/AG haplotypes. ³GG/GG haplotype.

Conclusion: Our study suggests that LEP G2548A and LEP A19G are associated with plasma leptin level as a quantitative trait. The infants homozygous for the GG haplotype represented 13% of our sample and showed significantly higher levels of leptin. Based on these results, although referred to a
limited sample, genetic predisposition seems to play an important role in modulating serum levels of leptin, with possible influences on the predisposition to obesity later in life.


**Disclosure of Interest:** None Declared
Milk oligosaccharides prevent stressor-induced alterations in the colonic mucosa-associated microbiota and animal behavior.
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1 Ohio State University, Columbus, OH, 2 Mead Johnson Pediatric Nutrition Institute, Evansville, IN, United States

Objectives and Study: There are extensive bidirectional interactions between the gut microbiota and the central nervous system (CNS), and studies demonstrate that stressor exposure significantly alters gut microbiota community structure. In this study, we tested whether milk oligosaccharides would prevent stressor-induced alterations in gut microbial community composition and reduce stressor-induced anxiety-like behavior.

Methods: Mice were fed standard laboratory diet, or laboratory diet containing milk oligosaccharides 3’Sialyllactose (3SL) or 6’Sialyllactose (6SL) for two weeks prior to being exposed to either a social disruption stressor to activate the CNS or a non-stressed control condition.

Results: Stressor exposure significantly changed the structure of the colonic mucosa-associated microbiota, as indicated by changes in beta diversity. The stressor also resulted in anxiety-like behavior in both the light:dark preference and open field tests. This effect was associated with a reduction in neuronal proliferation in the dentate gyrus as indicated by doublecortin immunostaining. These effects were not evident in mice fed milk oligosaccharides; stressor exposure did not significantly change microbial community structure in mice fed 3SL or 6SL. In addition, 3SL and 6SL attenuated the effects of the stressor on anxiety-like behavior and prevented the reduction in doublecortin staining.

Conclusion: These studies indicate that milk oligosaccharides can prevent the effects of stress on the microbiota and on anxiety-like behavior, as well as modify the gut microbiota-brain axis. Supported by Mead Johnson Nutrition.

Objectives and Study: Dietary protein intake may predict growth rates in infancy. Our objective was to determine the influence of insulin-like growth factor I (IGF-I) concentrations on gains in weight and length as related to complementary feeding protein intake.

Methods: In a prospective cohort study we included healthy infants at their check-up visit at 6 months. Dietary survey was assessed using 3 days recalls and primary caregivers completed a questionnaire regarding type of early nutrition and amount of protein sources used in complementary feeding. Weight, length and skin-fold were measured during the follow up procedure as primary outcomes. IGF-I in ng/ml was measured in capillary blood samples at the age of 12 months in all infants enrolled.

Results: The study analyzed data of 102 infants, out of which 74% were initially breastfed but only 37% were still breastfed at 6 months. According to protein intake during complementary feeding, 71 of them received over 2g/kg/day of protein and 32 subjects less than 2g/kg/day. IGF-I level were lower among infants receiving less protein than in infants with a higher intake (98±17 ng/ml vs.117±24ng/ml, p<0.05). Weight gain and length gain from 9 to 12 months of age were positively associated with IGF-I levels [OR = 1.54 (95%CI 1.02-2.14) p= 0.044].

Conclusion: Protein intake during complementary feeding may play a role in IGF-I modulation but further studies need to be performed.

Disclosure of Interest: None Declared
TARGETS HYDROLYSED CASEIN AND NUTRITIONAL COMPOSITIONS BASED THEREON CAN IMPACT INFANT GUT MICROBIOTA COMPOSITION AND METABOLISM IN VITRO

Paulo de Boer 1Ivana Bobeldijk-Pastorova 1Anita M.T. Ouwens 1Jasper Kieboom 1Gabriele Gross 2Eric A.F. van Tol 2Bart J.F. Keijser 1,*
1TNO, Microbiology & Systems Biology, Zeist, 2Mead Johnson Pediatric Nutrition Institute, Nijmegen, Netherlands

Objectives and Study: The human gut microbiota plays an important role in health and disease development. For example, autoimmune diseases like Type 1 diabetes (T1D) result from a complex interplay between genetic background, diet, gut microbiota composition and metabolism, and immune system deregulation. It has been suggested that hydrolyzed casein diets may be associated with reduced risk for T1D development. In this study, we used an *in vitro* colon model to investigate the effects of specific extensively hydrolyzed casein and hydrolysate-containing infant formulas on both infant gut microbial composition and metabolism.

Methods: Specific extensively hydrolyzed casein and infant formula containing this hydrolysate were subjected to pre-digestion using the TIM-1 model simulating upper gastrointestinal conditions. Subsequently, this predigested material was introduced in different concentrations in TNO’s *in vitro* 1-screen colonic fermentation model inoculated with a faecal pool from healthy infants. Effects on microbiota community structure (16S Illumina sequencing), short chain fatty acid (SCFA) production and proteolytic digestion of the casein hydrolysate (LC-MS analysis) were assessed at different time points.

Results: Sequencing results revealed the faecal microbiota composition to be influenced by incubation with predigested infant formula containing specific extensively hydrolyzed casein, and to a lesser extent with the hydrolysate only. In particular, a general concentration-dependent decline of *Bacteroides* was observed after 18 and 43 hours of incubation, with specific effects on genera that have been associated with the development of T1D. Furthermore, butyrate production was found to be increased with the predigested formula as well as with the specific hydrolysate as compared to control conditions after 6 hours of incubation. Overall peptide profiles of the finished formula and the hydrolysate remained largely unaffected after predigestion under upper gastrointestinal conditions. However, peptide and amino acid metabolism were shown to be changed by incubation with the extensively hydrolyzed casein as reflected by the amino acid concentrations after 6 hours of fermentation.

Conclusion: This study shows that specific extensively hydrolyzed casein and corresponding infant formula can influence the microbiota composition and SCFA production in an *in vitro* model of colonic fermentation. Based on these findings, it can be speculated that corresponding effects under physiological conditions might contribute to related beneficial health effects.
**Nutrition**

**Nutrition and Metabolism**

PO-N-0511

**VITAMIN-MINERAL AND NUTRITIONAL SUPPLEMENTATION IN CHILDREN AGED 6-18 YEARS**

Mustafa Akcam 1 Tugba Koca 1 Ozgur Pirgon 1 Selim Dereci 1

1Suleyman Demirel University, Medical School, Isparta, Turkey

**Objectives and Study:** To investigate the status of vitamin-mineral and nutritional supplementation and the relationship with body mass index in school-children 6-18 years old.

**Methods:** This cross-sectional study included 7116 randomly selected schoolchildren, 6-18 years old in Isparta province, Turkey. The height and weight of the children were measured in the standard way. Then the children were questioned face-to-face about the use of vitamins, minerals and food supplements. The body mass index (BMI) was calculated for each child and comparisons were made of the BMI values of those taking supplements and those who did not.

**Results:** Of the total 7116 children in the study, there were 3445 (48.4%) females and 3671 (51.6%) males with a mean age of 11.7±2.7 years (range, 5.8-18.9 years). At least 1 supplementary substance was taken by 1428 (20%) children, of whom 48% were female and the mean age was 10.4±2.5 years. There was no statistically significant difference between the genders in respect of supplement users and non-users. The mean age of those not taking a supplement was 12.1±2.7 years. The mean age of those taking a supplement was found to be statistically significantly lower compared to those who did not take supplements (p<0.05). Supplements that were taken were quail eggs by 8.7% of children, fish oil by 7.6%, multivitamins by 3.9%, pollen by 2.4%, a nutritional product by 0.5% and zinc by 0.3%. The mean BMI values of the users of supplements were found to be statistically significantly low compared to those of non-users (p<0.005). The rates of those taking any supplement according to BMI percentiles of underweight, normal, overweight and obese were 29.7%, 20.3%, 17.9% and 13.9%, respectively.

**Conclusion:** In developed countries, one third of children take some form of supplementation. As most of the children taking supplements were healthy and of good socio-economic status, it was determined that they were used for other than medical indications. However, in undeveloped countries where there are indications because of nutritional deficiencies, the rate of use is low. In this study, the total rate of use was 1/5 and in the underweight reached 1/3. The rates of use in the overweight and obese children are noteworthy. These result shows that the rate of use in Turkey can be considered to be without indications. Unnecessary use can lead to unwanted health problems and unnecessary financial outlay.

**Disclosure of Interest:** None Declared
MODULATION OF INTESTINAL MUCOSA GENE EXPRESSION OF OBESE ZUCKER-LEPRFA/FA RATS BY BIFIDOBACTERIUM BREVE CNCM I-4035, LACTOBACILLUS PARACASEI CNBCM I-4034 AND LACTOBACILLUS RHAMNOSUS CNCM I-4036

Julio Plaza 1Luis Fontana 1Francisca Abadía 2Jose Saez Lara 3Sergio Muñoz-Quezada 3Laura Campaña 3Esther Matencio 4Fernando Romero 4Ángel Gil 5Carolina Gómez Llorente 3
1Dept. Biochemistry & Molecular Biology II, School of Pharmacy, and Institute of Nutrition and Food Technology "José Mataix", Biomedical Research Center, University of Granada, 2Dept. Cell Biology, School of Sciences, University of Granada, 3Dept. Biochemistry & Molecular Biology I, School of Sciences, University of Granada, Granada, 4R&D Hero Spain S.A, Murcia, Spain

Aim of the study: Obesity is a chronic, complex and multifactorial disease that has reached pandemic levels and is becoming a serious health problem. Intestinal microbiota is considered a main factor that affects body weight and fat mass, which points toward a critical role in the development of obesity. In this sense, probiotic bacteria might modulate the intestinal microbiota and the mucosal-associated lymphoid tissue. The aim of this study was to investigate the effects of L. paracasei, L. rhamnosus and B. breve feeding on the intestinal mucosa gene expression in a genetic animal model of obesity.

Methods: Forty-eight Zucker-Leprfa/fa and 16 Zucker-lean+/fa male rats weighing 168-180 g were used. After 5 days of adaptation, 8 Zucker-lean+/fa and 8 Zucker-Leprfa/fa rats were euthanized as a reference. The remaining 40 Zucker-Leprfa/fa rats were then randomly assigned to receive 1010 CFUs of one of the three probiotic strains, or a placebo by oral administration each day for 30 days. An additional group of 8 Zucker-lean+/fa rats received placebo. Samples of intestinal mucosa were taken and RNA isolated to carry out a differential gene expression study with an Affymetrix microarray. Results were validated by Custom array RT2 profiler PCR from Qiagen.

Results: Expression of 45 genes changed with L. paracasei feeding. We selected 4 genes based on a fold change ≥1.5 and p≤0.05 for validation by RT-qPCR. The expression of genes ALOX5AP (involved in leukotriene synthesis), EDNRB (G protein-coupled receptor that nonspecifically binds to endothelin-1, -2 and -3, with a potential role in vasoconstriction/vasodilation and cell proliferation), ADAMDEC1 (a metalloprotease whose expression increases in dendritic cell maturation), PTGS1 (enzyme involved in prostaglandin synthesis) decreased in obese rats that received this strain. Expression of 12 genes was modified by B. breve administration. Five genes were selected and validated. ADAMDEC1, COX1, EDNRB, ALOX5AP and NAIP (the latter involved in apoptosis) expression was inhibited in this group of obese rats. L. rhamnosus feeding changed the expression of 10 genes. ADAMDEC1 gene expression decreased in this group. ADAMDEC1 and EDNRB mRNAs were overexpressed in the intestinal mucosa of obese rats that received the placebo.

Conclusion: Results obtained suggest that feeding Zucker-Leprfa/fa rats with these probiotic strains modified the intestinal mucosa expression of various genes involved in different cellular processes.
Objectives and Study: To determine the prevalence of undernutrition in 6-18 aged Turkish children living in Isparta, the southern region of Turkey.

Methods: A cross-sectional study was conducted at 7 primary schools and 3 high schools in Isparta. The height and weight were measured using standard way. Weight and height Z-scores were calculated using the ANTHRO software (CDC, US). Z-scores of height between -1 and -2 were diagnosed as short stature and Z-scores < -2 were considered as stunted. Z-scores of weight between -1 and -2 were diagnosed as underweight and Z-scores < -2 were considered as wasting.

Results: 7116 children, aged 6-18 years (mean 11.7±2.7 years), were included into the study. The prevalence of underweight, wasting, short stature, and stunting among children and adolescents were 11.4%, 2.5%, 12.3%, and 1.5%, respectively. The findings showed that there was no significant difference between genders. The overall prevalence of underweight and wasting was 13.9%. The overall prevalence of short stature and stunting was 13.8%. The short stature (15.3% vs. 7.7%) and stunting prevalences (2.2% vs. 0.3%) were found higher in adolescents than younger children. The prevalence of both stunting and wasting in whole group was 0.7%.

Conclusion: Although the data are not representative of the entire country, it has been demonstrated that undernutrition prevalence is higher in school children of Turkey.
Disclosure of Interest: None Declared
FOUR COMPONENT (4C) BODY COMPOSITION IN HEPATOPULMONARY SYNDROME (HPS).
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Objectives and Study: Weight loss, loss of muscle and hypermetabolism are predictors of worse outcomes for children awaiting liver transplant. This is the first time that body composition measured by the 4C model is reported on children with HPS. The 4C model is the gold standard for in vivo differentiation of fat and fat free mass.

Methods: A 10 year old girl and a 5 year old boy awaiting liver transplant had their body composition measured. The girl had neonatal sclerosing cholangitis and the boy had biliary atresia. Both had HPS. The 4C model uses the following equations:
\[ FM = (2.747 \times BV) - (0.710 \times TBW) + (1.460 \times BMC) - (2.050 \times WT) \]
\[ FFM = WT - FM \]
FM is fat mass, BV is body volume measured by BOD POD, TBW is total body water measured by deuterium stable isotope, BMC is body mineral content measured by DXA scan, WT is weight and FFM is fat free mass.

The children had their resting energy expenditure (REE) measured by indirect calorimetry and compared to the predicted REE estimated by the FAO/WHO/UNU 1985 equations. Hypermetabolism was defined as measured REE ≥ 120% predicted REE.

Results: Both children had portal hypertension with splenomegaly and hypersplenism and no ascites on ultrasound. Both had synthetic failure (F: albumin 35 g/L, INR of 1.38, M: albumin of 29 g/L, INR of 1.43) and mild jaundice (F: total bilirubin 71 umol/L, M: 29umol/L). The girl’s shunt with a macroaggregated albumin scan was 45% total (18% without kidneys) whilst the boy’s was 11% (5%).

The girl had been diagnosed with HPS 14 months prior to the assessment, whilst the boy had only just been diagnosed.

<table>
<thead>
<tr>
<th>Measured REE (Kcal)/ predicted REE (Kcal)</th>
<th>REE/ Wt (Kcal/Kg)</th>
<th>REE /FFM (Kcal/kg)</th>
<th>RQ</th>
</tr>
</thead>
<tbody>
<tr>
<td>Female 1625 (1215)</td>
<td>51.1</td>
<td>60</td>
<td>0.72</td>
</tr>
<tr>
<td>Male 1179 (988)</td>
<td>54.3</td>
<td>75.1</td>
<td>0.76</td>
</tr>
</tbody>
</table>

Table 1 Resting energy expenditure (REE) and respiratory quotient (RQ).
**Conclusion:** Liver disease is frequently accompanied by organomegaly and fluid retention making basic anthropometric measurements meaningless. The girl has a very low BMI and the 4C model confirms she has a very low FM with a relatively preserved FFM. She is hypermetabolic with an RQ indicating lipid oxidation. The boy has a misleadingly reassuring BMI. REE/FFM shows a significant increase to his Kcal/Kg expenditure that would otherwise not be realised and may indicate he is at risk for future accelerated weight loss. Whereas more detailed body composition studies are required in these patients, these 2 cases indicate the need for early nutritional intervention.

**Disclosure of Interest:** None Declared
THE NUTRITIONAL FACTORS ASSOCIATED WITH BMI OF ADOLESCENTS IN LESS DEVELOPED RURAL AREA, SOUTHWESTERN CHINA.

Yanna Zhu 1,* Jing Ma 1, Yang Kang 1

1 Sun Yat-Sen University, Guangzhou, China

Objectives and Study: Although a growing number of studies addressing the “double burden” of malnutrition with the persistence of undernutrition and a rapid rise of overnutrition in Chinese children and adolescents, most of these studies were conducted in large cities or other urban areas. Therefore, the aim of the study was to observe whether the double burden of over and under nutrition status exists in children and adolescents living in the rural and deprived areas, such as Yunnan Province, in China.

Methods: A school based cross-sectional study was conducted from September to November 2011 in mountainous rural areas of Yunnan province, Southwestern China. School adolescents aged 11–18 years were selected randomly from five middle and high schools in this area. Weight and height were measured and recorded for each student by school doctors. A questionnaire including physical activity, sedentary behavior, dietary behaviors and parental factors was completed by students. Nutritional status was defined by the age- and sex-specific height z-scores and BMI z-scores according to the WHO 2007 reference.

Results: A total of 2347 participants, including 983 boys and 1364 girls, completed the anthropometric measurements and the questionnaire in this study. Prevalences of stunting, thinness, overweight and obesity were 5.3%, 5.3%, 10.6% and 2.4% among boys, and 3.3%, 3.5%, 5.9% and 0.7% among girls. In a multilevel model, BMI z-score was significantly associated with maternal BMI (B=0.065, 95% CI: 0.051, 0.080), paternal BMI (B=0.043, 95% CI: 0.028, 0.058), meal frequency per day (B=-0.101, 95% CI: -0.197, -0.005) and screen time on television or computers (B=0.046, 95% CI: 0.010, 0.082).

Conclusion: This study indicated that parental weight status, adolescents’ TV or computer viewing duration and fewer meals per day are associated with increasing BMI z-score.

Disclosure of Interest: Y. Zhu Conflict with: there is no conflicts of interest, J. Ma Conflict with: there is no conflicts of interest, Y. Kang Conflict with: there is no conflicts of interest
EXTERNAL SOURCES OF INFORMATION USED BY SPANISH PARENTS IN DETERMINING THE AMOUNT OF FORMULA MILK AND CEREALS NEEDED TO PREPARE THEM: AN EXPLORATORY STUDY

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Objectives and Study: Infant feeding covers a wide range of practices as breastfeeding (the gold standard), formula feeding (when breastfeeding is not possible), the introduction of solid food and the preparation of infant food amongst others. Some research shows that parental practices such as forcing children to finish their plate/bottle can disturb the ability of children to self-regulate The quantity of formula milk (FM) and infant cereals (IC) that are prepared by parents could be relevant in case the parents adopt pressuring feeding styles. Accordingly, the objectives of this study were: to identify the information sources used by parents in determining the amount of FM and IC needed to prepare them and to determine which ones are more important.

Methods: The study was completed in two-phases. In phase-one, the relevant literature was reviewed and eight in-depth interviews and one focus group with nine mothers were conducted in two Spanish cities. Interviews were recorded and transcribed. Phase-two consisted of a face-to-face survey with 141 parents recruited in four Spanish cities. Subjects were asked about the feeding habits of their child aged 0-18 months regarding FM (n=76) and IC (n=65). Participants rated information sources on a five-point Likert scale ranging from 1 (not relevant at all) to 5 (extremely relevant). Statistical analysis SPSS-18.0.

Results: The literature review and the qualitative study yielded six information sources (pediatricians, nurses/midwives, pharmacists, relatives, friends/acquaintances and product label) relevant to parents for determining the amount of FM and IC. Pediatricians’ recommendations (4.55±0.88) along with product label (4.38±0.91) were considered the most important information sources used by parents in determining the amount needed to prepare FM. Pediatricians’ recommendations significantly ranked as the most important information source for preparing IC (4.04±1.33), followed by product label (3.46±1.36). Independent t-test was used to test if the importance given to each information source in preparing the mix was different between FM and IC.

Conclusion: This research represents an initial step into the analysis of the external sources used by parents for determining the amount needed to prepare FM and IC. Our exploratory findings show that pediatricians’ recommendations are a valuable source of information for parents. Future research with larger samples is needed to confirm these preliminary findings. This study belongs to a larger research currently being conducted which is focused on the analysis of feeding practices of infants aged 0-18 months in Spain.

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DAIRY AND NON-DAIRY BEVERAGE CONSUMPTION FOR CHILDHOOD ECZEMA: WHAT HEALTH ADVICE TO GIVE?

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Objectives and Study: Many parents practice empirical dietary avoidance and supplementation and seek healthcare advice if consumption of dairy and non-dairy beverages may be beneficial or detrimental in childhood atopic eczema (AE). We investigated if frequency of consumption of beverages were associated with disease severity and quality of life.

Methods: Parent-reported frequency and amounts of drinks and beverages were recorded in consecutive AE patients, and disease severity (Nottingham eczema severity score NESS), Children Dermatology Life Quality Index (CDLQI), skin hydration (SH), transepidermal water loss (TEWL), blood pressures, resting heart rate, and body mass index evaluated.

Results: AE was associated with worse quality of life than miscellaneous noneczema skin diseases (p<0.001). Fewer AE patients drank fresh milk (trend, p=0.062) but more drank miscellaneous beverages (such as Chinese herbal tea and soymilk p=0.030) when compared with non-eczema patients. In AE, NESS correlated with CDLQI (rho=0.66, p<0.001) and reduced SH (rho= -0.32, p<0.001), whereas CDLQI correlated with a higher resting pulse rate (rho=0.25, p=0.003). Multiple logistic regression showed male (odds ratio: 0.44, 95% CI:0.20-0.97; p=0.042) and fresh milk drinking (odds ratio: 0.42, 95% CI:0.20-0.93; p=0.031) were independent factors associated with less severe disease. Moderate-to-severe impairment of CDLQI was associated with NESS (odds ratio:1.48, 95% CI:1.28- 1.71; p<0.001) and pulse rates (odds ratio:1.05, 95% CI:1.02-1.08; p=0.002) but not with reported habits of beverage consumption. Concerning cardiovascular health in AE, frequency of formula milk consumption was associated with pulse rate (rho=0.17, p=0.044), and soft drink consumption was associated with higher systolic pressure (rho=0.18, p=0.044).

Conclusion: This study is important in providing evidence for parental/patient guidance. Eczema patients who reported more fresh milk consumption have less severe disease. There is no correlation between consumption of non-dairy beverages with disease severity or quality of life, but frequency of soft drink consumption correlates with systolic pressure. It seems reasonable to advice children to drink fresh milk instead of other beverages. Soft drinks should be consumption in moderation for optimal cardiovascular and metabolic health.


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